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Opening Keynote Lecture

PL1

Optimising management of adrenal insufficiency

Eystein Husebye
University of Bergen, Bergen, Norway. Haukeland University Hospital, Bergen, Norway

Primary adrenal insufficiency (PAI) is relatively straightforward to diagnose. However, the challenge lies in considering it as a differential diagnosis due to its rarity, the gradual onset of symptoms, and the nonspecific and common nature of these symptoms. Even with optimal corticosteroid replacement therapy, patients with adrenal insufficiency often report a diminished quality of life (QoL), and studies indicate increased mortality and morbidity. Identifying the underlying cause of adrenal insufficiency is crucial, as it can have significant prognostic and therapeutic implications. For instance, patients with an autoimmune etiology are at a heightened risk for developing additional autoimmune diseases. Conventional hydrocortisone formulations have short half-lives of approximately 90 minutes, necessitating multiple doses throughout the day. Newer treatment modalities, such as extended-release hydrocortisone formulations and subcutaneous pump therapy, have shown promise in selected patients. A key challenge in managing PAI is the need to individualize replacement therapy to closely mimic physiological conditions, thereby optimizing therapeutic effects while preventing complications related to over- or underreplacement. Currently, the absence of sensitive biomarkers for assessing glucocorticoid effects in the clinical settings hinders treatment optimization. Effective management also requires the physician to take into account the patient's age, occupation, and living conditions. Additionally, patient education on self-management and emergency preparedness is a critical component of care.

DOI: 10.1530/endoabs.104.PL1

Plenary Lecture

PL2

Acromegaly is a metabolic disease

AJ van der Lely
Erasmus University MC, Rotterdam, Netherlands

GH is not just a hormone that increases IGF-I concentrations. GH, IGF-I and insulin sometimes antagonize or amplify each other's direct actions. In this interplay, for translating GH actions into IGF-I production, the production of endogenous insulin that reaches the liver via the portal vein is an essential factor. In fact, insulin decides whether GH is allowed to generate IGF-I production and release by the liver. By not considering GH, IGF-1 and insulin altogether, clinicians will not be able to assess and understand the complex changes in metabolism in which GH, IGF-I and insulin play a major role. Therefore, in case of diabetes (both type 1 and 2), in acromegaly and in liver failure, a thorough understanding of normal- and pathophysiology will certainly help the treating physician to make the right decisions on how to intervene and improve metabolism for the benefit of the patient. One of the pitfalls that endocrinologists and other clinicians frequently encounter is that they focus on the known signs and symptoms of diseases when asking about the complaints of their patients. Acromegaly patients e.g. are asked about their headaches, perspiration, oedema, and fatigue. Other complaints are easily ignored as they are considered not to be part of the classical list of signs and symptoms of acromegaly. Equally so, we also trust too much on the laboratory results and in fact, we too often tell our acromegaly patients that they should be fine when we have normalized their serum IGF-I levels. When we carefully start to listen to our patients, we must conclude that they should tell us whether they feel great or not and not the other way around.

DOI: 10.1530/endoabs.104.PL2

IES Hadden Lecture

PL3

Abstract unavailable

DOI: 10.1530/endoabs.104.PL3

Diabetes & Metabolism Plenary Lecture

PL4

Invited speaker: leveraging insights into type 1 diabetes pathogenesis from rare human pancreas biobanks

Sarah Richardson
University of Exeter, Exeter, United Kingdom

This presentation will focus on how my team and I are using state-of-the-art imaging platforms to interrogate multiple rare pancreas biobanks from around the world to develop a clearer understanding of the processes by which beta cells are targeted and destroyed in Type 1 diabetes. I will explore how the Exeter Archival Diabetes Biobank, one of the rarest collections of recent-onset T1D pancreata, has provided unique insights into potential triggers of autoimmunity, details on key immune cell types involved in beta cell destruction, and how beta cells may be fighting back. Our current work focuses on characterising the islet niche in health and disease to help define the 'root causes' of Type 1 diabetes and to identify novel beta cell protective strategies.

DOI: 10.1530/endoabs.104.PL4

IES McKenna Lecture

PL5

Abstract unavailable

DOI: 10.1530/endoabs.104.PL5

Endocrinology Plenary

PL6

State of the art in osteoporosis

Bente L. Langdahl
Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark

Osteoporosis is a common condition characterised by reduced bone mass and deteriorated bone architecture. Osteoporosis is by WHO defined as bone mineral density (BMD) T-score $<$ -2.5 at the spine or hip. Osteoporosis is a very heterogeneous condition, ranging from asymptomatic to severe in patients with fractures, especially vertebral and hip fractures, but also other central fractures are associated with morbidity and increased mortality. Management of osteoporosis is challenging as seen by the very large diagnosis and treatment gap seen in most countries across the world. Identification of patients with osteoporosis is driven by attention to clinical risk factors, most importantly fragility fractures, family history, early menopause, smoking and other diseases or treatments that increases the risk of osteoporosis. This should be easy, however, it has proven to be difficult as many other conditions demand attention from the health care systems. Treatment of osteoporosis includes a bone healthy lifestyle (sufficient intake of calcium and vitamin D, physical activity, no smoking and limited alcohol intake) and medical treatment. Implementation of bone healthy lifestyle requires patient education. Medical treatment of osteoporosis includes antiresorptive, bone forming and dual action treatments. The antiresorptives include bisphosphonates and denosumab, the bone forming treatments includes teriparatide and abaloparatide, and the dual action treatment includes romosozumab. All of the approved treatments improve BMD and reduce fracture risk, but it has been shown in head-to-head studies that bone forming and dual action treatments improve BMD and reduce fracture risk more than antiresorptive treatments in patients with severe osteoporosis. These treatments should therefore be considered in patients at high risk of fracture. All treatments with the exception of bisphosphonates are reversible and with osteoporosis being a chronic condition most patients will need sequential treatment with these medications. Recently, the FNIH-SABRE project has demonstrated that increase in total hip BMD during

treatment is a very strong predictor of the anti-fracture efficacy of any treatment. That has led to a discussion with the FDA and other regulatory authorities about possible changing the conditions for getting new treatments for osteoporosis approved, focussing more on BMD changes – this process is still ongoing. The same data, but also the clinical head-to-head trials clearly demonstrating that not all treatments are the same and bone forming and dual action treatments reduce fracture risk more rapidly and more prominently have challenged the step-wise treatment approach: all patients start with an oral bisphosphonate and are only shifted to a more potent treatment if there are indications of treatment failure. A more aggressive approach, the treat-to-target or goal-directed approach has been proposed. This approach takes the severity of osteoporosis and the actual fracture risk into consideration and suggests that patients with severe osteoporosis at high and/or imminent risk of osteoporosis should be initiated on bone forming og dual-action treatment (1).

1. Cosman F, Lewiecki EM, Eastell R, Ebeling PR, De Beur SJ, Langdahl B, Rhee Y, Fuleihan GE, Kiel DP, Schousboe JT, Borges JL, Cheung AM, Diez-Perez A, Hadji P, Tanaka S, Thomasius F, Xia W, Cummings SR. Goal-Directed Osteoporosis Treatment: ASBMR/BHOF Task Force Position Statement 2024. J Bone Miner Res. 2024 Epub.

DOI: 10.1530/endoabs.104.PL6

Closing Keynote Lecture

PL7

Island hopping: adventures in hormones, metabolism and behaviour

Stephen O'Rahilly
Institute of Metabolic Science, Cambridge, United Kingdom

For over 30 years my laboratory has studied how hormones regulate metabolism and how this regulation is disrupted in metabolic disease. Some of these actions are mediated by the central nervous system and affect appetite, food intake and other behaviours. In this talk I will present data on three hormones: insulin, leptin and GDF15. I will briefly discuss recent advances in the understanding of human insulin resistance, the role of leptin melanocortin signalling in obesity and related human phenotypes, and the actions of GDF15 as an allostatic hormone alerting the organism to a range of threats via its brainstem-restricted receptors. As someone who was born, grew up and undertook his undergraduate medical education in Ireland and moved to the UK for post graduate training, I will make some references to the close and long-standing relationships between the two islands in the field of endocrinology.

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Symposia

Reining in the Hyperactive Adrenal

S1.1

Mild autonomous cortisol secretion

Miguel Debono
Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

Mild autonomous cortisol secretion (MACS) is a state of biochemical hypercortisolaemia with ACTH independence arising in the context of adrenal incidentalomas. There are no external discriminatory features of overt Cushing's syndrome. 20 to 50% of adrenal incidentalomas are associated with MACS depending on the cut-offs used. The condition is associated with several cardiometabolic comorbidities including diabetes, hypertension, osteoporosis and metabolic syndrome. It is also associated with cardiovascular events and increased mortality. Differentiating between a hyperactive HPA axis and ACTH independence is crucial to make the right diagnosis as a significant number of overnight dexamethasone suppression tests could be false positive and may lead to patient mismanagement. Clinical evaluation and management are ideally undertaken in a multidisciplinary team as management pathways are not always straightforward. Treatment options for MACS include adrenalectomy or medical (conservative) treatment. Surgical studies have shown improvements in metabolic complications especially hypertension and Type 2 diabetes as well as amelioration of low bone mineral density and vertebral fracture risk. Questions persist. Are we referring the right patients for surgery? Is there a role for medical treatment of hypercortisolism in this patient group? How should patients managed conservatively be monitored in the long term? Identifying the best treatment pathway for each patient with MACS is fundamental to reduce morbidity and maybe mortality.

DOI: 10.1530/endoabs.104.S1.1

S1.2

Adrenal androgen excess: classic pathways and beyond

Michael O'Reilly
Royal College of Surgeons in Ireland, Dublin, Ireland

Adrenal androgen synthesis involves contributions from the classic, 11-oxygenated and alternative pathways. The zona reticularis of the adrenal cortex secretes androgen precursors such as dehydroepiandrosterone (DHEA) and androstenedione (A4) which undergo conversion in peripheral tissues to active androgens such as testosterone (T) and dihydrotestosterone (DHT). The adrenals may also produce smaller concentrations of T directly. A4 can be converted by the activity of adrenal CYP11B1 into the 11-oxygenated androgen 11-hydroxyandrostenedione (11OHA4), which then undergoes peripheral conversion into potent active 11-oxygenated androgens through the activities of the enzymes HSD11B2 and AKR1C3. Classic and 11-oxygenated androgens are elevated in a number of disorders of androgen excess in women, including polycystic ovary syndrome, congenital adrenal hyperplasia and Cushing's disease. Severe adrenal androgen excess may also be observed in adrenal tumours and in acquired or monogenic severe insulin resistance. This talk will cover the physiology and pathophysiology of adrenal androgen synthesis, as well as the diagnostic approach to patients with adrenal androgen excess.

DOI: 10.1530/endoabs.104.S1.2

S1.3

The diagnostic approach to challenging adrenal lesions

Marie Freel
Queen Elizabeth University Hospital, Glasgow, United Kingdom

Adrenal incidentalomas are an increasingly common source of referral to our endocrine services. In most cases, simple radiological and biochemical assessment and patient reassurance are all that is required. The cases that do not require further evaluation will be summarised briefly. However, an increasing number of adrenal adenomata do require careful consideration and complex discussion, usually through an adrenal MDT. I will use a series of real life cases that have resulted in challenging debate through our national adrenal MDT. In particular, I will focus on the approach to adrenal metastases, role of adrenal biopsy, minor autonomous cortisol excess and bilateral adrenal nodules. Hopefully, a combination of real life experience as well as recent updated European guidelines in this area will help inform our approach to these difficult but common clinical questions.

DOI: 10.1530/endoabs.104.S1.3

An MDT approach to NETS

S2.1

PRRT in treatment algorithims for gastrenteropancreatic NETs

Jonathan Wadsley
Weston Park Cancer Centre, Sheffield, United Kingdom

Peptide Receptor Radiotherapy (PRRT) is playing an increasingly important role in the management of gastroenteropancreatic (GEP) NETs. In this session we will consider the principles behind this treatment modality, and review the existing data demonstrating the benefit of PRRT to patients with GEP NETs. We will discuss the current position of PRRT in international guidelines regarding the management of GEP NETS. We will further consider on-going research to derive greater benefits from this treatment, including opportunities to personalise therapy via individual patient dosimetry, the use of novel ligands and novel radionuclides, and the possiblity of combination therapies, for example with radiosensitisers and with immunotherapy.

DOI: 10.1530/endoabs.104.S2.1

S2.2

Abstract unavailable

DOI: 10.1530/endoabs.104.S2.2

S2.3

Abstract unavailable

DOI: 10.1530/endoabs.104.S2.3

Bone Update

S3.1

Effects of exercise on bone health

Katherine Brooke-Wavell
Loughborough University, Loughborough, United Kingdom

Osteoporosis is a condition characterised by bone loss, architectural deterioration and increased susceptibility to fractures, which cause substantial pain and limitations in function. One in two women, and one in five men, aged over 50 will experience a fracture in their remaining lifetime. Exercise may reduce risk of osteoporotic fracture by increasing bone strength and reducing risk of falls, which precipitate many osteoporotic fractures. The types of exercise effective on bone differ from those recommended for prevention of other chronic conditions. The most effective exercise modes for increasing bone strength are those that exert high forces on bone, for instance resistance exercise or moderate to high impact exercise. The intensity of loading seems more important than the volume. As effects are local, exercise needs to load the skeletal sites at risk of fracture, such as proximal femur, spine and forearm. The most effective exercise for reducing fall risk includes individualised and challenging lower limb strengthening and balance training. Exercise may also have benefits in maintaining spinal alignment and reducing pain and physical function in those with vertebral fractures. There is substantial evidence for the benefits of exercise on bone health, but many people diagnosed with osteoporosis may limit exercise for fear of breaking a bone, hence further increasing bone loss. It is important that prompt guidance is available

about the movements where modification may be appropriate as well as the exercise that may benefit bone strength.

DOI: 10.1530/endoabs.104.S3.1

S3.2

Gut-derived peptides and bone disorders in obesity and diabetes

Nigel Irwin
Ulster University, Coleraine, United Kingdom

Bone remodelling is regulated by many endogenous factors, with recent attention on the pivotal role of gut-derived peptide hormones in this regard. Indeed, a gut-bone axis has now been described, that is coordinated largely by the secretion and action of intestinal-derived peptide hormones. In addition to this, obesity and diabetes are highly prevalent metabolic disorders that negatively affect health, and there is now a clear link between these diseases and impaired bone health. To add to this, both obesity and diabetes are associated with impaired secretion and action intestinal-derived hormones, alongside an elevated risk of bone fracture that is not fully dependent on bone mineral density (BMD) measurements. It follows that gut-derived hormones and their related long-acting analogues, with some already clinically approved for diabetes and/or obesity as well as short bowel syndrome, possess positive effects on bone to reduce fracture risk within these specific diseases. In particular, the incretin peptides, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), as well as glucagon-like peptide-2 (GLP-2), exert key direct and/or indirect benefits on bone metabolism. Furthermore, novel unimolecular gut peptide drugs that can simultaneously target multiple receptors also show particular promise for treating bone disorders. In this presentation we will provide an initial appraisal of the relationship between obesity, diabetes and bone remodelling, with a focus on the positive impact of these gut-derived peptide hormones for bone health in obesity/diabetes. Overall, drugs engineered to promote GIP, GLP-1 and GLP-2 receptor signalling, either alone or in combination, offer therapeutic promise for improving bone health and merit further preclinical and clinical investigation.

DOI: 10.1530/endoabs.104.S3.2

S3.3

Identification of the genetic determinants and clinical implications of bone marrow adiposity using deep learning in the uk biobank

Wei Xu[1], Ines Mesa-Eguiagaray[1], David Morris[2,3], Chengjia Wang[4,3], Calum Gray[3], Samuel Sjöström[2], Giorgos Papanastasiou[5], Sammy Badr[6], Julien Paccou[6], Xue Li[7], Paul Timmers[8], Maria Timofeeva[8], Scott Semple[2,3], Tom MacGillivray[9], Evropi Theodoratou[1,10] & William Cawthorn[2]
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Bone marrow adipose tissue (BMAT) is a distinct, major adipose tissue subtype that is a normal feature of mammalian anatomy. However, BMAT's pathophysiological functions and genetic determinants remain unknown. In humans, bone marrow adiposity is typically measured as the bone marrow fat fraction (BMFF) using magnetic resonance imaging (MRI). Herein, we used deep learning to measure the BMFF of the spine, femoral head, total hip, and femoral diaphysis from MRI of >45,000 participants (>42,000 white, >6,400 non-white) in the UK Biobank imaging study. We then, for the first time, established their heritability and identified the genome- and phenome-wide significant associations for BMFF at each site. Our meta-genome-wide association study (GWAS) in the white population found 67 independent single nucleotide polymorphisms (SNPs) and 54 mapped genes for the femoral head, 147 independent SNPs and 90 mapped genes for the total hip, 134 independent SNPs and 43 mapped genes for the diaphysis, and 174 independent SNPs and 100 mapped genes for the spine. Our multi-ancestry meta-GWAS, including all ethnicities, found 121 independent SNPs and 65 mapped genes for the femoral head, 314 independent SNPs and 98 mapped genes for the total hip, 234 independent SNPs and 63 mapped genes for the diaphysis, and 310 independent SNPs and 121 mapped genes for the spine. These include genes implicated with adipose biology, bone density and/or mesenchymal cell fate, as well as less-expected pathophysiological phenomena. Our phenome-wide association studies (PheWAS) identified 29 diseases associated with BMFF in the femoral head, 36 in the hip, 17 in the diaphysis, and 139 in the spine, collectively spanning over 17 disease categories. As the first GWAS and PheWAS for bone marrow adiposity, these findings provide unprecedented insight into BMAT formation and function, opening new avenues to comprehensively determine the impact of BMAT on human health and disease.

DOI: 10.1530/endoabs.104.S3.3

Type 1 Diabetes

S4.1

Abstract unavailable

DOI: 10.1530/endoabs.104.S4.1

S4.2

Abstract unavailable

DOI: 10.1530/endoabs.104.S4.2

S4.3

Hypoglycaemia - in the age of CGM

Patrick Divilly
St Vincents University Hospital, Dublin, Ireland

The use of continuous glucose monitoring (CGM) by individuals with type 1 diabetes (T1D) has revolutionized the management of hypoglycemia. Previously, hypoglycemia was defined solely by a glucose threshold. However, CGM has introduced the additional dimension of time. International consensus guidelines now define CGM-detected hypoglycemia as glucose levels below the hypoglycemic threshold for at least 15 minutes. Using this definition, a high proportion (>60%) of hypoglycemic episodes are asymptomatic, and over a third of symptomatic episodes occur at glucose levels above 3.9 mmol/l. The significance of these asymptomatic episodes remains unclear. The Hypo-METRICS study, a multinational, multicenter study conducted as part of the HypoRESOLVE consortium, explored the biopsychosocial impact of both symptomatic and asymptomatic hypoglycemia. Participants wore a blinded CGM for 10 weeks and recorded their hypoglycemia experiences in real time using a smartphone app. Data from Hypo-METRICS revealed that while asymptomatic hypoglycemia had no impact on daily functioning, any episode identified as hypoglycemia by individuals with T1D, regardless of glucose level, negatively impacted daily functioning. Additionally, the study showed that time below range as a metric correlates poorly with the lived experience of hypoglycemia. These findings have significant implications for clinical and research practices. They highlight the importance of reporting the lived experience of hypoglycemia, even in the age of CGM and its hypoglycemia metrics.

DOI: 10.1530/endoabs.104.S4.3

Genetics in Endocrinology

S5.1

Abstract unavailable

DOI: 10.1530/endoabs.104.S5.1

S5.2

Abstract unavailable

DOI: 10.1530/endoabs.104.S5.2

S5.3

Abstract unavailable

DOI: 10.1530/endoabs.104.S5.3

Obesity

S6.1

Abstract unavailable

DOI: 10.1530/endoabs.104.S6.1

S6.2

New developments in obesity and their clinical application

Alex Miras
Ulster University, Derry, United Kingdom

I will be presenting the latest developments in pharmacotherapy for obesity, the direction of travel in obesity care and offer solutions to the challenges of implementing these therapeutic advances to clinical care.

DOI: 10.1530/endoabs.104.S6.2

Tricky Pituitary Cases

S7.1

Abstract unavailable

DOI: 10.1530/endoabs.104.S7.1

S7.2

Cyclical cushing's syndrome

Kristina Isand
University of Tartu, Tartu, Estonia. Oxford University Hospitals, Oxford, United Kingdom

Cyclical Cushing's Syndrome (CS) is a rare and complex disorder, accounting for approximately 14-18% of all CS cases. It is characterized by repeated episodes of cortisol excess in blood, saliva, and/or urine, interspersed with periods of normal or even low cortisol levels, observed on at least 2-3 separate occasions. The duration of each hypercortisolemic episode can vary widely, lasting from days to years, and may occur at regular or irregular intervals. This condition is also referred to by other terms, including variable, periodic, episodic, and intermittent Cushing's syndrome. A recent systematic review by Nowak et al. revealed that the most common cause of cyclical CS is a pituitary adenoma (67%), followed by ectopic tumors (17%) and adrenal tumors (11%). Diagnosing cyclical CS is particularly challenging, as patients may present with normal laboratory results if tests are conducted during a quiescent period. This can lead to misdiagnosis or unnecessary pituitary surgeries in patients with ectopic tumors. Careful planning of inferior petrosal sinus sampling (IPSS) during hypercortisolemic states is crucial. Postoperative remission rates are generally lower in patients with cyclical CS, and the time to remission is significantly longer compared to those with non-cyclical Cushing's syndrome. Cyclical CS remains a challenging condition, even in highly specialized centers. It should be strongly suspected in patients exhibiting signs and symptoms of hypercortisolism, particularly when diagnostic results are inconclusive. Long-term observation is essential for accurate diagnosis and management.

DOI: 10.1530/endoabs.104.S7.2

Emerging Best Practice in Thyroid Disease

S8.1

Current management of low risk thyroid cancer

Kristien Boelaert
University of Birmingham, Birmingham, United Kingdom

Thyroid cancer is the most common endocrine malignancy and over the past 40 years there has been a dramatic rise in incidence globally, largely due to the detection of small low-risk papillary cancers as a consequence of increased use of thyroid ultrasonography. The vast majority of these differentiated thyroid cancers are small, often incidental, slow growing and carry an excellent prognosis. The management of these tumours has undergone a dramatic change in the last 5-10 years and a "less is more" approach has been adopted in most national and international guidelines. Whilst differentiated thyroid cancer was almost universally treated with total thyroidectomy, radioiodine remnant ablation and long term TSH suppression, the majority of the tumours are now treated with limited surgery and subsequent surveillance. There is also mounting evidence that active surveillance without any thyroid surgery and minimally invasive ablative procedures are safe and adequate treatment alternatives. This symposium will outline the current national and international guidelines relating to managing low risk thyroid cancer and highlight the most up to date evidence on novel management pathways.

DOI: 10.1530/endoabs.104.S8.1

S8.2

Safe treatment of thyroid disease in pregnancy

Carla Moran
Beacon Hospital, Dublin, Ireland. St Vincent's University Hospital, Dublin, Ireland. University College Dublin, Dublin, Ireland

Management of thyroid disease in pregnancy can be challenging. My talk will focus on the appropriate interpretation of thyroid function tests during pregnancy, the avoidance of over treatment of marginal TSH/FT4 values, appropriate and prompt management of hypothyroidism and management of thyrotoxicosis due to various aetiologies. I will also touch on fetal surveillance and neonatal TFT testing.

DOI: 10.1530/endoabs.104.S8.2

S8.3

Natural history and management of thyroid hormone resistance-beta: what can real-world data tell us?

Aled Rees
Cardiff University, Cardiff, United Kingdom

Resistance to Thyroid Hormone-β (RTHβ) is a rare disorder characterised by hormone resistance in the pituitary-thyroid axis which results in elevated, circulating thyroid hormones. Although some patients display features of hyperthyroidism, the natural history of RTHβ with respect to cardiovascular disease or death is unknown. In this presentation, I will review our recent data which used a linked health record approach in Wales to demonstrate reduced survival and increased cardiovascular risk in patients with RTHβ. Compared to unaffected controls, RTHβ patients exhibited a three-fold increase in all-cause mortality or major cardiovascular events, particularly excess risks of atrial fibrillation and heart failure. The median age of first occurrence of any adverse event was 11 years earlier in patients compared to controls. Positive associations were observed between thyroid hormone levels at baseline and cardiovascular morbidity or death, suggesting that lifelong exposure to elevated thyroid hormones mediates the increased morbidity and mortality. Conventional treatments for hyperthyroidism (antithyroid drugs, radioiodine ablation or thyroidectomy) did not control thyroid hormone levels effectively. Our findings suggest that careful management of cardiovascular risk in RTHb patients is warranted and that clinical trials of therapies that target hormone resistant pathways are needed.

DOI: 10.1530/endoabs.104.S8.3

Type 2 Diabetes

S9.1

Exercise in individuals with type 2 diabetes: can we predict changes in glycaemic control and weight during training?

James Dorling
University of Glasgow, Glasgow, United Kingdom

In individuals living with type 2 diabetes, exercise is a method of improving body composition and glycaemic control. Studies have shown that aerobic and resistance training interventions decrease total and regional adiposity, including visceral fat, and reduce glycated haemoglobin (HbA1c). There is, however, stark inter-individual variability in responses to training: some individuals display substantial improvements in body composition and glycaemic control, whilst others do not improve or even worsen. Efforts have consequently been made to highlight factors that predict changes in body composition and markers of glycaemic control during exercise training. Recent work indicates that non-exercise activity and eating-related behaviours are associated with total fat and visceral fat reductions during exercise, and there is evidence demonstrating that early variations in weight during training regimens predict long-term improvements in body composition. With regards to glycaemic control, less has been established, but there is evidence indicating that central adiposity, fitness, and certain medications are related to HbA1C changes during exercise training. Further work is needed to firmly elucidate factors associated with exercise-induced changes in body composition and glycaemic control. This will help refine interventions so individuals with type 2 diabetes can optimise improvements in health during exercise training.

DOI: 10.1530/endoabs.104.S9.1

S9.2

Community Diabetes - setting up a service, value based health care

Glynis Magee
Regional Centre for Endocrinology and Diabetes, Royal Victoria Hospital, Belfast, United Kingdom

With the increasing prevalence of diabetes and the complexity and landscape of diabetes therapies updating regularly, there is a need for care processes to adapt to meet the needs of all groups - so that expertise can be offered and delivered to the entire diabetes population in the right place, at the right time. This session focuses on the structuring and setting up of diabetes care at a local level and suggested steps in how to establish and evolve the community service to meet current demands.

DOI: 10.1530/endoabs.104.S9.2

S9.3

Using healthcare data to improve diabetes health care policy and practice

Helen Colhoun
University of Edinburgh, Edinburgh, United Kingdom

In Scotland, a standardised electronic health record (Scottish Care Information-Diabetes (SCI-diabetes)) has been in use for patient care in diabetes since the late 1990s, gaining nationwide coverage by mid-2000s. The record uses a unique healthcare identifier, the Community Health Index (CHI) number, which is also used on all other administrative health datasets in Scotland. SCI-Diabetes dashboards provide summary information enabling clinical teams to evaluate achievement in processes of care. These have been important for improving quality of care that is reported annually through a national audit. In addition to these aspects, we established a National Diabetes Research Data Platform to enable linkage of useful datasets with the data in the SCI-Diabetes record in a secure environment. This yields a pseudoanonymised database, updated annually with those newly diagnosed, and rich in a wide range of data. This has many uses, for example, understanding healthcare burden and socioeconomic trends in disease incidence and prevalence, observational pharmacoepidemiology studies and building prediction tools to support clinical decision making. In this talk Professor Colhoun will outline the architecture of the system, some of the critical challenges in establishing such a system and will give examples of its use for informing policy and practice.

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PCOS across lifespan

S10.1

Abstract unavailable

DOI: 10.1530/endoabs.104.S10.1

S10.2

Expanding diagnostic and biochemical aspects of polycystic ovary syndrome: steroid metabolomics in PCOS

Eka Melson[1,2] & Wiebke Arlt[1,2]
[1]MRC Laboratory of Medical Sciences, London, United Kingdom; [2]Institute of Clinical Sciences, Imperial College London, London, United Kingdom

Polycystic ovary syndrome (PCOS) is a common condition that affects about 10% of women of all ages. PCOS increases the risk of metabolic dysfunction, including type 2 diabetes and cardiovascular diseases. Androgen excess is a cardinal feature of PCOS, driving metabolic dysfunction. The guidelines on PCOS suggest using elevated testosterone as a diagnostic criterion for PCOS. Recent evidence has implicated other androgens, including the 11-oxygenated androgens, in the diagnosis of PCOS. Furthermore, elevated androgens have been shown to correlate with the risk of metabolic dysfunction in women with PCOS. This lecture reviews the implication of androgen excess in driving metabolic dysfunction in PCOS. The lecture also discusses the use of steroid metabolomics in PCOS, which could help with risks and therapeutic stratification in women with PCOS.

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S10.3

Fertility treatment and pre-conception optimisation

Lucy Ann Behan
Tallaght University Hospital, Dublin, Ireland. Coombe Fertility Hub, Dublin, Ireland. Trinity College Dublin, Dublin, Ireland

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy affecting women of reproductive age women and has effects from adolescence to menopause with a prevalence between 10% to 13% (1). In this talk with reference to evidence based international guidelines (1) and clinical expertise I will discuss rationale, methods and evidence of pre-conception health optimisation for women with PCOS and potential obstetric outcomes, including challenges around obesity management. I will also discuss a fertility investigation pathway and management algorithm, including clinical scenarios to illustrate the recent updated International PCOS guidelines. Ref (1) 2023 International Evidence-based Guideline for Assessment and Management of Polycystic ovary Syndrome, Journal of Clinical Endocrinology and Metabolism 2023

DOI: 10.1530/endoabs.104.S10.3

Diabetes in Pregnancy

S11.1

Type 2 diabetes in pregnancy – a growing challenge

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The prevalence of type 2 diabetes (T2DM) in pregnancy is increasing rapidly worldwide. Most guidelines for diabetes during pregnancy are based on studies in women with type 1 diabetes (T1DM) and as a result, there is an urgent need to improve the knowledge of pregnant women with T2DM. As pregnancy induces insulin resistance in maternal tissues the insulin resistance might be worse in pregnant women with T2DM in the light of the pathophysiology of T2DM, where insulin resistance in itself plays an important role. In addition, pregnant women with T2DM are often older, more obese and show a greater ethnic variation, why pregnant women with T2DM may encounter different challenges during pregnancy, compared to women with T1DM, potentially contributing to a risk of treatment failure, hyperglycemia, and adverse outcomes. The talk will give an overview of cardiometabolic risk factors, co-morbidities, trajectories of glycemic control and insulin resistance in pregnant women with type 2 diabetes both with pre-existing T2DM (P-T2DM) and women with new T2DM (N-T2DM), diagnosed in pregnancy. How these exposures and risk factors affect adverse outcomes for mother and child and how treatment challenges faced by pregnant women with T2DM both before and during pregnancy can be handled will also be addressed.

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S11.2

Using technology to improve diabetes pregnancy outcomes

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Hybrid closed-loop systems providing automated glucose responsive insulin delivery are set to revolutionise the management of type 1 diabetes. However, pregnancy poses formidable challenges, including more stringent glucose targets, gestational changes in insulin sensitivity and day to day variations in insulin pharmacokinetics. Therefore, hybrid closed-loop systems that are effective outside pregnancy, cannot guarantee clinically relevant glycaemic benefits throughout pregnancy. In this session, I summarise the evidence from two pivotal randomised trials, suggesting that the benefits of hybrid closed-loop therapy during type 1 diabetes pregnancy are system-specific, with only one system offering clinical benefits to a generalisable patient population, regardless of previous technology use and across all maternal HbA1c categories. There are stark inequalities in diabetes technology access, and an urgent unmet need for high quality data in women of reproductive years living with type 2 diabetes, who now outnumber those with type 1 diabetes.

DOI: 10.1530/endoabs.104.S11.2

S11.3

Abstract unavailable

DOI: 10.1530/endoabs.104.S11.3

Managing Hypothalamic Syndromes

S12.1

Abstract unavailable

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S12.2

Abstract unavailable

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S12.3

Unravelling hypothalamic obesity: navigating the challenges and exploring future solutions

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The hypothalamus plays a central role in the neuroendocrine regulation of energy homeostasis and appetite. Congenital or acquired disruption of hypothalamic nuclei disrupts the balance between energy intake and expenditure is leading to rapid and excessive weight gain. Hypothalamic obesity (HO) is further complicated by disturbances in the hypothalamic-pituitary axis, sleep disruption, visual impairment, and neurological and vascular sequelae. Among suprasellar tumours, craniopharyngioma is the most common cause of acquired hypothalamic obesity, either directly or secondary to surgical or radiotherapeutic interventions. Current strategies for managing HO include optimising pituitary hormone replacement, restricting calorie intake, increasing physical activity, behavioural interventions, pharmacotherapy, and bariatric surgery. Pharmacotherapeutic approaches involve stimulants that increase energy consumption, agents that reduce sympathomimetic activity, anti-diabetic agents and direct modification of cerebral satiety signalling through stimulation of cocaine-amphetamine regulated transcript. Pharmacological studies of HO report weight loss or stabilisation but reported intervention periods are short, and others report no effect. More recently, GLP1 receptor agonists (GLP1RA) have shown improved outcomes in the treatment of HO, potentially related to GLP1RA action on extra-hypothalamic brain centres. Other therapies currently being trailed include Methionine Aminopeptidase Inhibitors therapy decreasing lipogenesis, increasing fat oxidation, and increasing lipolysis, and Tesomet (tesofensine and metoprolol). New agents targeting pro-opiomelanocortin (POMC), MC4 receptors and AgRP/NPY neurons, in the hypothalamus may offer better outcomes. The challenge in achieving weight loss, modification in eating behaviour and improvement in energy expenditure in acquired HO reflects the complexity of hypothalamic control of energy homeostasis and feeding. Defining the location of hypothalamic damage may support the development of targeted therapies. There is a need for novel or combined approaches to achieve significant and sustained weight loss in HO. Placebo-controlled trials using current single or combination therapies are thus necessary to determine the efficacy of these treatments.

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How Do I...? Sessions

How do I…? 1 (Diabetes)

HDI1.1

How do i manage NG feeding-related hyperglycaemia?

Eoin Noctor
UL Hospitals Group, Limerick, Ireland. University of Limerick, Limerick, Ireland

Enteral feeding is a common indication for inpatient consultation among inpatients with diabetes. Multiple different insulin regimens to treat hyperglycaemia resulting from this are in clinical use. In this practical session, we, review recent consensus guidelines from the Joint British Diabetes Societies (2024) and the Endocrine Society (2022), the evidence behind these recommendations, the differences between them, and describe a practical approach to managing glycaemic control in the hospitalised patient with diabetes.

DOI: 10.1530/endoabs.104.HDI1.1

HDI1.2

How do i manage diabetes across time zones

Aine Cunningham
Galway University Hospitals, Galway, Ireland

Living with diabetes should not be seen as a constraint to travelling especially across time zones. This session will aim to increase health care professional's confidence and knowledge in enabling people living with diabetes to travel confidently and safely. It will examine up to date guidelines in this area and highlight practical aspects of long haul flying when it comes to diabetes medication. This session will discuss the self-management techniques that people with diabetes need to manage their insulin whether on Hybrid close loop pump or daily insulin injections. This session will also look at aspects such as enabling individuals to prepare a checklist for their journey and important advice on the managing diabetes whilst travelling across the world.

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HDI1.3

Abstract unavailable

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HDI1.4

How do i manage severe hypertriglyceridaemia?

Gary Roulston
Belfast Health and Social Care Trust, Belfast, United Kingdom

Hypertriglyceridaemia is a commonly encountered scenario in clinical practice. Rare monogenic disorders can cause severe hypertriglyceridaemia, but more commonly, elevated triglycerides are secondary to a combination of genetic susceptibility and environmental factors. Common secondary causes include obesity, uncontrolled diabetes mellitus, alcohol misuse, nephrotic syndrome and various medications. An important first step to management is addressing these factors, before considering commencing medication. The aim of management of hypertriglyceridaemia is to reduce the risk of pancreatitis in those with severely raised triglycerides, and to also reduce the modest risk of cardiovascular disease associated with moderately raised triglycerides. Severely raised triglycerides may also interfere with various laboratory measurements, such as sodium, causing either false or unreportable results in some cases. This talk will review the current treatment strategies for hypertriglyceridaemia. As well as risk factor modification, it will review drug therapies, including statins, fibrates, and omega-3 fatty acids. Severe hypertriglyceridaemia associated with pancreatitis will respond to standard protocols in most cases, though therapies such as plasmapheresis may very occasionally be used. There are also newer specialised medications that are reserved for monogenic disorders.

DOI: 10.1530/endoabs.104.HDI1.4

HDI1.5

Managing frailty in older people with diabetes

Alan Sinclair
fDROP and King's College, London, United Kingdom

Talk summary - Frailty is a frequent non-vascular complication of diabetes and usually has more importance than other diabetes complications in terms of functional loss and survival. Only until fairly recently has frailty been measured in UK healthcare systems. This short lecture will discuss common frailty measures, primary care and hospital pathways for management, goals of therapy glycaemic targets, and specific issues in glucose lowering.

DOI: 10.1530/endoabs.104.HDI1.5

HDI1.6

How do i approach diabetes distress?

Mark Davies
Belfast Health and Social Care Trust, Belfast, United Kingdom

Diabetes distress is the emotional distress that results from living with diabetes and the burden of relentless daily self-management. Severe diabetes distress affects around one of four people with type 1 diabetes, one in five people with insulin-treated type 2 diabetes, and one in ten people with non-insulin treated type 2 diabetes. Greater diabetes distress is associated with suboptimal diabetes self-management and impaired general emotional well-being. This talk will highlight evidence-based interventions clinicians can employ in everyday practice.

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How do I…? 2 (Endocrinology)

HDI2.1

How do i use copeptin and hypertonic saline in AVP disorders

Julie Refardt
Erasmus MC, Rotterdam, Netherlands

Polyuria polydipsia syndrome is a disorder characterized by excretion of large amounts of hypotonic urine. Three entities have to be differentiated: AVP-deficiency (central diabetes insipidus) resulting from a deficiency of the hormone arginine vasopressin (AVP) in the pituitary gland or the hypothalamus, AVP-resistance (nephrogenic diabetes insipidus) resulting from resistance to AVP in the kidneys and finally primary polydipsia, which involves excessive intake of large amounts of water despite normal AVP secretion and action. Distinguishing between the different types can be challenging. In addition to a detailed medical history, physical examination and imaging studies, copeptin based tests have recently been introduced showing a high diagnostic accuracy. This talk will focus on how to use copeptin in the differential diagnosis of AVP-deficiency and how to perform the required tests.

DOI: 10.1530/endoabs.104.HDI2.1

HDI2.2

How do i treat psychiatric complications of cushing's syndrome?

Niki Karavitaki
Department of Metabolism and Systems Science, School of Medical Sciences, University of Birmingham, Birmingham, United Kingdom. Department of Endocrinology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Psychiatric manifestations are amongst the most distressing complications in Cushing's syndrome (CS) and are associated with the severity of the cortisol excess. Depression and anxiety disorders are the most common, whereas mania and psychotic disorders are less frequently reported. Although depression and anxiety disorders improve after successful treatment of the CS, longitudinal studies have shown that they do not fully resolve. Further psychiatric symptoms described in patients in remission include, amongst others, maladaptive personality traits, emotional lability and apathy. Assessment of the mental health

status of the patient is of major importance both at diagnosis and during follow-up. The initial approach when managing psychiatric complications in CS is to treat the hypercortisolism. This is further supported by the view that response to antidepressant or antipsychotic medications may not be optimal until the control of cortisol excess. When successful management of the hypercortisolism takes a long interval, psychoeducation and/or psychotherapy may be considered until this is achieved. Selective serotonin re-uptake inhibitors are considered the first choice if antidepressant treatment is required, and low dose clonazepam has been suggested to manage severe anxiety. Treatment of severe psychotic symptoms or psychotic depression is challenging, and atypical antipsychotics may be offered, keeping in mind the possibility of lack of response when CS is active. Psychiatric care in patients with CS in remission is similar to that offered in cases without this condition, and treatment options include psychological, psychosocial and/or pharmacological interventions. Finally, education of patients and their families and direction to support groups are additional important approaches to improve psychiatric comorbidities in CS.

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HDI2.3

Abstract unavailable

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HDI2.4

Abstract unavailable

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HDI2.5

Abstract unavailable

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HDI2.6

How do i select and prepare a patient for parathyroid surgery?

Marcia Bell
Galway University Hospital, Galway, Ireland. University of Galway, Galway, Ireland

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia. It is frequently identified in women, usually in their postmenopausal years, with a female/male ratio of, on average, 3:1. The prevalence of PHPT is known to vary by country and race. It is currently recognised that PHPT includes three clinical phenotypes: hypercalcaemia with overt target organ involvement, mild asymptomatic hypercalcemia with or without target organ involvement, and normocalcaemic hyperparathyroidism (NPHPT) with or without target organ involvement. It is important that a robust clinical and biochemical diagnosis of PHPT is established before consideration of appropriate management. The gold standard for PHPT and NPHPT management is surgery and should be recommended to those who meet any one of the criteria for surgery[1]: Age <50 years; hypercalcaemia $>$ 0.25 mmol/l (1 mg/dl) above the upper limit of normal; skeletal involvement including a fracture or bone mineral density (BMD) by *T*-score ≤ -2.5 at any site; renal involvement including reduced renal function, nephrocalcinosis, nephrolithiasis or significant hypercalciuria. Surgery for PHPT should be carried out by surgeons who frequently perform parathyroidectomy. Surgical success is further enhanced by preoperative localisation of the abnormal parathyroid tissue carried out at centres experienced in current best localisation modalities. During this session the recently updated guidelines on the evaluation and management of primary hyperparathyroidism will be discussed and recent research which allows for improved selection and preparation of appropriate patients for parathyroidectomy will be considered.

Reference

1. Bilezikian *et al* J Bone Miner Res 2022 Nov;37(11):2293-2314.

DOI: 10.1530/endoabs.104.HDI2.6

Skills Sessions

Approaching Artificial Intelligence with…Intelligence

SK1.1

How to use AI for academic writing

Ian Turner
University of Derby, Derby, United Kingdom

Generative Artificial Intelligence (GenAI) has emerged a powerful tool and potential ally in academic writing. This talk aims to explore how |GenAI tools can enhance various stages of the writing process, from initial research to final manuscript. Specific applications explored in the talk will include. automated literature review, citation generation and formatting, content generation and paraphrasing, and grammar and style and enhancement. The use of GenAI in academic writing has raised a number of interesting ethical dilemmas and questions around attribution, plagiarism and academic integrity and the limitations of (free) GenAI tools. These issues and more will be explored in the context of different stages of academic writing process.

DOI: 10.1530/endoabs.104.SK1.1

SK1.2

Using AI to predict bone fractures

Muhammad Javaid
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Given that osteoporosis is asymptomatic until a fragility fracture occurs, identifying patients at high fracture risk is a critical component of osteoporosis management. Traditional methods have used enhanced case finding to identify patients with risk factors such as specific medications (glucocorticoids, aromatase inhibitors), specific comorbidities (rheumatoid arthritis), or presenting with a fragility fracture. Screening of the general older female population has also been tested, which reduces hip fracture risk. AI offers the opportunity to enhance patient identification through two broad strategies: clinical data and imaging. AI algorithms have been trained on electronic health record data to predict short-term fracture risk successfully. AI algorithms have been trained to identify vertebral fractures and estimate bone mineral density using multiple imaging modalities, including plain X-ray, CT, and DXA VFA. A key element in vertebral fracture identification is the definition used to train models, including semi-quantitative, fully quantitative approaches, and algorithm-based qualitative methods. In addition, algorithms are being trained to estimate bone density from images taken without synchronous calibration phantoms and algorithms that combine skeletal and non-skeletal features. However, identifying patients at high fracture risk is insufficient to provide clinical benefit. Clinical services introducing these tools into clinical practice need to address local data regulatory and IT infrastructure requirements and develop the clinical pathway capability and capacity needed to translate these AI innovations into real patient and societal benefits.

DOI: 10.1530/endoabs.104.SK1.2

Genetics in Endocrinology

SK2.1

Abstract unavailable

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SK2.2

Abstract unavailable

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SK2.3

Hereditary pituitary diseases

Marta Korbonits
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As with disorders of many other systems, the genetic aspect of pituitary diseases has exponentially changed over the last 2 decades. Some result in loss of function of the gland while others cause tumours and excess of hormones; some present as an isolated problem while others as part of a syndrome. Among the pituitary hormone deficiency syndromes, apart form the classical GH, TPIT, hypogonadotrophic hypogonadism and AVP deficiencies, newer diseases have also been described such as IGSF1-related disease or complex syndromes affecting hypothalamus/pituitary development-related transcription factors. Regarding pituitary tumours, in addition to isolated pituitary disease (*AIP*-related and X-linked acrogigantism) and the classical multiple endocrine neoplasia syndromes (Carney complex, MEN1 and McCune-Albright syndromes), pituitary tumours have now, although rarely, been described in traditionally non-endocrine tumour syndromes such as Lynch syndrome and most recently related to the breast cancer gene *CHECK2*. Most of these diseases are rare, so the clinician's role is to recognise and record the signs and symptoms and to consider the possibility of genetic disease. With a high quality phenotype and with the help of the currently available genetic test panels, usually the correct diagnosis can be set up. However, genetic testing might also bring unexpected results or variants where pathogenicity is uncertain. Therefore, careful discussion between the clinician, the clinical geneticist and sometimes with specialist of a particular genetic disease is needed to decide on appropriate diagnosis and management.

DOI: 10.1530/endoabs.104.SK2.3

A beginner s guide to translational research

SK3.1

Abstract unavailable

DOI: 10.1530/endoabs.104.SK3.1

SK3.2

Investigator-initiated clinical trials: dreams or reality?

Andrew Smyth
University of Galway, Galway, Ireland

This session will address the elements of investigator-initiated clinical trials from the perspective of an investigator-initiated trial to be done with an academic (non-industry) environment. The session will describe the requirements for clinical trials (regulated vs. non-regulated) focusing on investigational medicinal products (drugs), but the wider messages will apply to other study formats informed by actual experience of investigator-initiated clinical trials in the clinical research ecosystem in Ireland.

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Navigating UK/Irish Training for International Graduates

T1.1

The future NHS workforce- do we still need to rely on international medical graduates?

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The UK has historically relied on Internationally qualified clinicians making a significant contribution to the NHS workforce. According to the GMC workforce report (2023), the number of International Medical graduates (IMG) has increased year on year. Over 50% of new doctors joining in 2022 had qualification outside the UK. There is a persistent Global demand of skilled healthcare staff and a predicated NHS workforce gap of 260,000–360,000 staff by 2036. The proportion of doctors leaving the workforce has only returned to the pre-pandemic level of just under 4%. UK graduates under the age of 35 have a lower leaving rate than the corresponding age groups of non-UK graduates and have a relatively high rate of return (43%) compared with IMG who are under 35 (15%) or UK graduates aged 35 to 50 (18%). However, a growing proportion of doctor's plan to leave the profession because of high levels of dissatisfaction and high risk of burnout. The number of Locally Employed (LE) doctors is growing much faster than the number of SAS doctors. In 2021, there were more than twice as many LE doctors (22,576) as there were SAS doctors (10,349). Of the IMG, LE doctors who joined in 2014, 26% were in postgraduate training four years after joining, increasing to 39% for the 2018 cohort. Hypothetically, even accounting for planned increase in medical schools and increases proposed in long term workforce plan almost a third (32%) of all doctors would be IMGs in 2036. Despite increases to domestic supply, IMGs will remain a crucial component of the future workforce. It is therefore vital that the UK has an inclusive and supportive cultures that successfully induct and integrate doctors from a wide range of backgrounds.

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T1.2

Abstract unavailable

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T1.3

Abstract unavailable

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Plenary Orals

PLO1

Damaging mutations in LXRα uncouple lipogenesis from hepatotoxicity and implicate hepatic cholesterol sensing in human liver health

Sam Lockhart[1], Milan Muso[1], Ilona Zvetkova[1], Brian Lam[1], Allessandra Ferrari[2], Erik Schoenmakkers[1], Katie Duckett[1], Jack Leslie[3], Beatriz Romartínez-Alonso[4], John Tadross[1], Raina Jia[1], Eugene Gardner[1], Katherine Kentistou[1], Yajie Zhao[1], Felix Day[1], Alexander Mörseburg[1], Kara Rainbow[1], Deb Rimmington[1], Matteo Mastantuoni[1], James Harrison[1], Meritxell Nus[1], Khalid Guma'a[1], Sam Sherratt-Mayhew[1], Xiao Jiang[5], Katherine Smith[5], Dirk Paul[5], Ben Jenkins[1], Albert Koulman[1], Maik Pietzner[1], Claudia Langenberg[1], Nick Wareham[1], John Schwabbe[4], Krish Chatterjee[1], Fiona Oakley[3], Derek Mann[3], Peter Tontonoz[2], Anthony Coll[1], Ken Ong[1], John Perry[1] & Stephen O'Rahilly[1]
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The nuclear receptor LXRa activates lipogenic gene expression in hepatocytes. Its inhibition has been proposed as a strategy to treat MASLD. To understand the impact of reducing LXRa activity on human health we examined the association between the carriage of rare loss of function mutations in *NR1H3* (encoding LXRa) and metabolic and hepatic phenotypes. We identified 63 rare predicted damaging variants in the ligand binding domain of LXRa in 454,787 participants in UK Biobank. On functional characterisation, 42 of these were found to be severely impaired. Consistent with loss of the lipogenic actions of LXRa, carriers of damaging mutations in LXRa had reduced serum triglycerides (ß=-0.13 s.d. $\pm$0.03, $P = 2.7\text{x}10^{-5}$, N(carriers)=971). Surprisingly, these carriers also had elevated serum liver enzymes (e.g. ALT: ß=0.17s.d. $\pm$0.03, $P = 1.1\text{x}10^{-8}$, N(carriers)=972) with a 35% increased risk of clinically significant elevations in ALT (OR=1.32, 95%CI:1.15-1.53, $P = 1.2\text{x}10^{-4}$, N(carriers)=972), suggestive of hepatotoxicity. We generated a knock-in mouse carrying one of the most severely damaging mutations (*Nr1h3* p.W441R) which we demonstrated to have dominant negative properties. Thse mice developed severe hepatitis and fibrotic liver injury when fed a western diet, despite markedly reduced steatosis, liver triglycerides and lipogenic gene expression. This phenotype was rescued by viral over-expression of wildtype LXRa specifically in hepatocytes, indicating a cell-autonomous effect of the mutant on hepatocyte health. While homozygous LXRa-KO mice showed some evidence of hepatocyte injury, the phenotype of the $\text{LXRa}^{\text{W441R/W441R}}$ mouse was much more severe, suggesting mutations that co-repress target genes can result in pathological impacts more severe than those seen with simple absence of the receptor. Taken together, our findings implicate LXRa in the maintenance of human liver health, identify a new murine model of rapidly progressive fibrotic liver disease and caution against LXR antagonism as a therapeutic strategy for MASLD.

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PLO2

Crinecerfont, a corticotropin-releasing factor type 1 receptor (CRF1) antagonist, reduced excess adrenal androgens and enabled glucocorticoid dose reductions in adults with classic congenital adrenal hyperplasia: results from cahtalyst™

Richard J. Auchus[1], Oksana Hamidi[2], Rosario Pivonello[3], Irina Bancos[4], Gianni Russo[5], Selma Witchel[6], Andrea M. Isidori[7], Patrice Rodien[8], Umasuthan Srirangalingam[9], Florian W. Kiefer[10], Henrik Falhammar[11], Debroah P. Merke[12], Nicole Reisch[13], Kyriakie Sarafoglou[14], Gordon B. Cutler[15], Julia Sturgeon[16], Eiry Roberts[16], Vivian H. Lin[16], Jean L. Chan[16] & Robert Farber[16]
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Introduction
Classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency (CAH), a genetic condition characterized by cortisol deficiency and excess adrenal androgens, typically requires management with supraphysiological glucocorticoid (GC) doses. This multinational Phase 3 study (CAHtalyst™) evaluated whether crinecerfont, an oral CRF_1 antagonist, can reduce GC dose while maintaining androgen control in adults with CAH.
Methods
Adults ($\geq$18yrs) with CAH on GC doses $>$13 mg/m^2/d in hydrocortisone equivalents (HCe) and normal or elevated androstenedione were randomized (2:1) to crinecerfont 100 mg BID or placebo for 24wks. GC doses were maintained stable for 4wks, then reduced over 8wks to target of 8-10 mg/m^2/d, followed by adjustment over 12wks to maintain androstenedione control ($\leq$120% of baseline or $\leq$upper limit of normal).
Results
In 182 randomized participants (122 crinecerfont, 60 placebo), $>$95% completed 24-wk treatment. Mean$\pm$SD baseline GC dose was 17.6$\pm$4.9 mg/m^2/d HCe (32$\pm$9 mg/d), with elevated pre-GC androstenedione (22$\pm$25 nmol/l) and 17-hydroxyprogesterone (287$\pm$268 nmol/l). At Wk4, crinecerfont-treated participants had significant least squares (LS) mean reductions in androstenedione (10.4 nmol/l) and 17 hydroxyprogesterone (-181.6 nmol/l) vs placebo (+1.6 nmol/l; LS mean difference [LSMD: -12.0 nmol/l; $P < 0.0001$] and 4.7 nmol/l [LSMD: -176.9 nmol/l; nominal $P < 0.0001$], respectively). At Wk24, there was greater GC dose reduction while maintaining androstenedione control with crinecerfont (-27% [-4.8 mg/m^2/d]) vs placebo (-10% [2.5 mg/m^2/d]; LSMD: -17%; $P < 0.0001$), with 63% vs 18% achieving physiologic dose $\leq$11 mg/m^2/d with androstenedione control ($P < 0.0001$). Crinecerfont led to greater decreases vs placebo in body weight (-1.5% vs -0.1%, LSMD: -1.4%) and HOMA-IR (0.6 vs 0.4, LSMD: -0.3) at Wk24, and greater increases in bone turnover markers osteocalcin and CTx. Fatigue and headache were the most common adverse events.
Conclusions
Crinecerfont represents a novel treatment option to improve androgen control for patients with CAH. Participants on crinecerfont experienced reductions in androstenedione while GC dose was stable, enabling significant percent reductions in GC dose while maintaining androstenedione control.

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Oral Communications

Oral Communications

OC1

Differential tissue, and dose-specific adverse effects of exogenous glucocorticoids: implications for clinical practice

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Background
Prednisolone is the most prescribed exogenous glucocorticoid (GC). Despite extensive research on GC-induced side effects, key unanswered clinical questions remain about the dose threshold and tissue-specific sensitivity to adverse effects.
Aim
To compare the effects of 10, 15, and 20 mg of oral prednisolone for 7-days on the liver, skeletal muscle, adipose tissue, and bone.
Methods
We conducted a retrospective study on healthy male volunteers who participated in the FIND-IT (10 mg/day, $n = 6$), PUSH-UP (15 mg/day, $n = 10$), or TICSI (20 mg/day, $n = 15$) studies. Liver and skeletal muscle insulin sensitivity was assessed during a low-dose hyperinsulinaemic-euglycaemic clamp (LHEC) using stable isotope tracers to measure M/I value, endogenous glucose production (EGP), and glucose disposal (Gd) rates. Adipose tissue insulin sensitivity was evaluated through microdialysis across the LHEC and RNA-sequencing analysis of adipose tissue biopsies. Osteocalcin served as a marker for bone-related adverse effects.
Results
One week of 10 mg prednisolone did not affect liver, skeletal muscle, or adipose insulin sensitivity. However, 15 mg and 20 mg doses impaired liver and muscle glucose handling by reducing M/I value (15 mg $P = 0.01$; 20 mg $P < 0.001$) and Gd (15 mg and 20 mg $P < 0.001$) while increasing EGP (15 mg $P = 0.005$; 20 mg $P = 0.04$). Adipose tissue insulin sensitivity decreased in the 15 mg and 20 mg groups, as shown by increasing NEFA (15 mg $P < 0.001$; 20 mg $P = 0.002$) and glycerol levels (15 mg $P < 0.001$; 20 mg $P = 0.002$). RNA-sequencing analysis of adipose tissue biopsies demonstrated similar dysregulated gene profiles after both 10 mg and 20 mg doses. Osteocalcin levels showed similar reductions with higher prednisolone doses (15 mg $P = 0.002$; 20 mg $P < 0.001$), with published data indicating that 10 mg for 7-days reduces osteocalcin levels in healthy subjects.
Conclusions
GC-induced side effects are dose- and tissue-dependent. Compared to bone and adipose, liver and skeletal muscle appear relatively resistant to low-dose (10 mg) prednisolone. Prospective studies are needed to confirm these findings and understand their clinical implications.

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OC2

The orphan G protein-coupled receptor 35 (GPR35) has an anti-resorptive role in primary human osteoclasts

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The physiological role of the orphan G-protein coupled receptor 35 (GPR35) is currently unknown. Expression of the GPR35 gene and protein are downregulated in osteoporosis patients and in mouse models of the disease. *Gpr35*-knockout mice have reduced bone mass, while a synthetic GPR35 ligand, rescues bone loss in rodent osteoporosis models indicating that GPR35 has an important role in bone. Our previous studies demonstrated *GPR35* is highly expressed in human osteoclasts, and we sought to determine the receptor's function in these cells. We differentiated human PBMCs to mature osteoclasts and assessed effects of GPR35 synthetic agonists, Zaprinast and TCG1001, on osteoclast activity and differentiation. Both agonists stimulated significant reductions in osteoclast bone resorption, TRAP activity, and downregulated expression of *MMP9,* a gene that regulates osteoclast bone resorption. These effects were prevented by pre-incubation of cells with a GPR35-specific antagonist. In contrast, GPR35 activation had no effect on the number of osteoclasts or nuclear translocation of NFAT, a transcription factor that drives osteoclast differentiation, suggesting GPR35 may not regulate osteoclast development. To understand the signalling pathways activated by GPR35 in osteoclasts, we measured the phosphorylation of secondary messengers known to have important roles in osteoclast activity using AlphaLISA assays. Upon GPR35 stimulation, we observed reduced phosphorylation of cSrc, which stimulates actin ring formation necessary for bone resorption, and decreased phosphorylation of Akt and NFκB that drive transcription of genes required for bone resorption. Finally, we used chemical inhibitors and siRNA knockdown to show that GPR35 couples to $G_{i/o}$ and $G_{12/13}$, but not to $G_{q/11}$ to stimulate these signalling pathways. Our findings demonstrate that GPR35 has an important inhibitory role in human osteoclast activity and have defined the signalling pathways that drive these processes. GPR35 represents a promising novel target to reduce osteoclast activity that could be exploited for osteoporosis treatments.

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OC3

The relation of microvascular complications to a new interpretation of glycaemic variability from continuous glucose monitoring in people with type 1 diabetes (T1D)

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Introduction
Microvascular and macrovascular complications in type 1 diabetes T1D) may be linked to endothelial stress due to glycaemic variability. This work aimed to examine whether determination of glycaemic parameters including glucose variability (GV) over an 18month period is associated with microvascular clinical sequelae.
Methods
Freestyle Libre 15-minute glucose values were downloaded for 89 T1DM individuals for up to 18 months from 2021 to 2023 and were analysed via three novel glucose management indices: glucose management indicator (GMI), average glucose fluctuation (AGF), time spent above a high blood glucose threshold. Our measured clinical outcomes included glomerular filtration rate (eGFR), average annual change in eGFR following a previous reading at least 4 years previously, and current retinal screening status.
Results
Results for 89 individuals (44 men/45 women) were analysed over 18 months. Mean age was 43years and the mean duration of diabetes was 18years. A total of 3.22 million readings were analysed, giving an average of 10.3 mmol/l blood glucose. Those with the largest change in glucose from reading, to reading summated over time (18months) showed the greatest change in eGFR of 3.12ml/min/1.73m^2 ($P = 0.007$). People with a higher proportion of glucose readings >18mmol/l showed a fall in eGFR of 2.8 ml/min/1.73 m^2 ($P = 0.009$) and experienced higher rates of sight threatening retinopathy (44% of these individuals) ($P = 0.01$) as did 39% of individuals in the highest tertile of glucose levels. ($P = 0.008$).
Conclusion
Those T1D individuals in the highest tertile of reading-to-reading glucose change, showed greatest change in eGFR. Those with a higher proportion of glucose readings >18mmol/l also showed a fall in eGFR and experienced higher rates of retinopathy as did people with higher mean glucose. Discussions with T1D individuals could reflect on how % recorded glucose above a critical level and degree of change in glucose are important in avoiding tissue complications.

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OC4

Selective sweep mapping identifies obesity candidate mutations in labrador retrievers

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Obesity is a public health crisis for both man and man's best friend: both human and canine obesity have increased significantly in the last thirty years, driving research to understand obesity genetics. Dogs are an ideal model organism to study mammalian obesity, given their shared physiology with humans. Pure-bred dogs have reduced genetic diversity due to population bottlenecks and artificial selection. Consequently, genomic regions under positive selection may carry "footprints" detectable as selective sweeps. As Labrador Retrievers are predisposed to obesity compared to other breeds, we hypothesized that obesogenic alleles may be fixed or nearly-fixed in Labradors but at low frequency or absent in low-risk breeds. We searched for signs of positive selection using selective sweep detection statistics, Tajima's D and Integrated Haplotype Score, in 316 dogs' SNP genotype data. We found 1829 genes in 83 possible regions of positive selection, which contained 16 obesity candidate genes, identified by comparison with literature. We prioritised genetic variants within those genes as candidates for obesity if they were significantly more common in Labradors than in breeds with low obesity risk ($P < 0.05$). We then tested their association with body condition score (BCS), food motivation, and weight, in 592 Labradors. Top candidate variants included a 3'UTR variant in MC4R. The wild-type allele was relatively-fixed in Labradors and significantly associated with food motivation. Secondly, a missense variant was found in NUDT16L1, an RNA-binding protein suppressing ciliogenesis. Labradors were relatively-fixed for the wild-type allele, which associated significantly with BCS. Finally, a 3'UTR variant in the adiponectin receptor *ADIPOR1* correlated significantly with weight. We demonstrated the domestic dog's unique population structure can facilitate identifying novel variants. We suggest methods of further investigation of candidate variants for canine obesity, in genes previously associated with human obesity, but in which variants have yet been found in humans or dogs.

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OC5

Multiplex immunofluorescence identifies novel role for STING upregulation in pituitary neuroendocrine tumours

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Background
Pituitary neuroendocrine tumours (PitNETs) have almost invariably benign histopathological characteristics but result in comorbidity and mortality. There has been interest in the composition of the PitNET immune microenvironment, particularly with the advent of immunotherapy-associated hypophysitis linked to PD-L1 and CTLA-4 checkpoint inhibitors. The innate immune cGAS-STING pathway is activated by DNA damage and DNA damage is a known feature of somatotrophinomas. Enhanced understanding of the PitNET immune microenvironment may yield novel biomarkers and therapeutic targets.
Aim
To explore the immune microenvironment composition of functioning PitNETs fulfilling the clinical diagnoses of acromegaly, prolactinoma and thyrotrophinoma using multiplex immunofluorescence and digital image analysis.
Methods
PitNET tissues (growth hormone-secreting $n = 63$, thyrotrophinoma $n = 5$, prolactinoma $n = 11$) resected between 01/01/2000-09/07/2019 were retrieved *via* the Northern Ireland Biobank. Normal pituitary adjacent to Rathke cleft cyst was used as control ($n = 4$). Samples were stained with two multiplex immunofluorescence panels each containing six biomarkers and scanned using PhenoImager HT. Panel 1: CD3, CD4, CD8, CD20, Ki-67, synaptophysin. Panel 2: CD3, CD68, STING, PD-L1, CTLA-4, synaptophysin. Biomarker quantification was undertaken using QuPath. GraphPad Prism was used for statistical analysis.
Results
PitNETs did not have significantly higher tumour infiltrating CD4+ ($p = 0.990$), CD8+ ($p = 0.567$) T lymphocytes or CD20+ B lymphocytes ($p = 0.186$) compared to normal pituitary. There were significantly higher levels of total CD68+ macrophages ($p < 0.001$) and CD68+STING+ macrophages ($p < 0.001$) in PitNETs compared to normal pituitary. There was significantly higher STING expression in tumour cells compared to normal pituitary ($p < 0.001$).
Conclusions
This is the first time that multiplex immunofluorescence and digital image analysis have successfully been used for simultaneous biomarker quantification in PitNETs. The data indicate that T and B lymphocytes do not play a significant role in PitNETs. However, macrophages and the innate cGAS-STING pathway are upregulated in this cohort of functioning PitNETs and represent novel areas for further investigation.

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OC6

Once-daily oral administration of gpr55 agonist ml-184 has direct and indirect benefits on β-cell and gastrointestinal health in obese-diabetic mice

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Background
G-Protein-Coupled Receptor GPR55, a member of the endocannabinoid system, has gained significant interest as a treatment for diabetes. This study aimed to investigate GPR55 as a drug target using a novel GPR55-agonist, ML-184 (high selectivity EC50=0.26μM), and the downstream induction of signalling pathways.
Methods
High-fat-fed (HFF) C57BL/6 mice were treated with a daily oral dose of ML-184 (0.1μmol/kg) alone or in combination with Sitagliptin (50 mg/kg) for 21-days. After long-term treatment of obese-diabetic mice, food intake, metabolic effects (insulin sensitivity, glucose tolerance, insulinotropic response), islet morphology, tissue gene (qPCR) and protein (immunohistochemistry) expression, biochemical analytes and intracellular signalling were investigated.
Results
ML-184 alone and in combination with Sitagliptin, improved glucose tolerance (26-30%, $P < 0.001$) and enhanced insulin sensitivity (29-37%, $P < 0.05$-0.01) and insulinotropic response (63-110%, $P < 0.001$) in HFF mice. Islet Ki-67 staining found that ML-184 increased β-cell proliferation in HFF mice (7%, $P < 0.001$), and upregulated pancreatic gene expression of GPR55 (78%, $P < 0.01$), ERK1 (56%, $P < 0.01$) and ERK2 (43%, $P < 0.05$). ML-184 increased β-cell area (45%, $P < 0.01$) and β-cell mass (45%, $P < 0.05$), and decreased α-cell area (59%, $P < 0.001$) and mass (43%, $P < 0.01$). There was a marked increase in circulating GIP following monotherapy (47%, $P < 0.05$) and dual agonism (ML-184/sitagliptin) (203%, $P < 0.001$). qPCR showed that dual agonism also significantly upregulated GIP gene expression in jejunum (90%, $P < 0.05$). Food intake was reduced by 26-36% ($P < 0.001$) by ML-184 and dual agonism (ML-184/Sitagliptin). HFF jejunal gene expression of GPR55 and JNK1 were upregulated by 336% and 472% ($P < 0.001$), respectively, while dual agonism decreased their expression by 58% ($P < 0.05$) and 72% ($P < 0.01$).
Conclusions
ML-184 is a viable option for T2DM drug development, as GPR55 agonism has beneficial effects on β-cells partially mediated by GIP from gastrointestinal K-cells, as well as gastrointestinal benefits mediated by direct GPR55 activation in the intestine evoking potent antimotility effects leading to reduced food intake.

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OC7

Thyroid hormone analogue (Triac) therapy in resistance to thyroid hormone beta reduces hyperthyroid symptoms, lowers circulating thyroid hormones and metabolic rate effectively, without adverse effects

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Background
The treatment of Resistance to Thyroid Hormone beta (RTHbeta) is challenging because no therapy restores the euthyroid state in all tissues. Triac (triiodothyroacetic acid), a centrally-acting thyroid hormone analogue that preferentially activates thyroid hormone receptor beta, is reported to be beneficial in case reports or small case series.
Methods
We have treated a cohort of adult RTHbeta patients, all with heterozygous mutations in *THRB* and hyperthyroid symptoms, with Triac for up to a decade. Here, we describe the clinical, biochemical, metabolic and cardiac responses to therapy. Patients in whom the HPT axis was altered (due to ATDs, thyroid surgery or radioiodine) were excluded.
Results
A total of eight adult patients (aged 18-54 years, 4 female) were treated with Triac. Median Triac dose used was 2.4 mg per day (range 1.4-3.5 mg) and duration of therapy varied from <1 yr to 12 years. Response to therapy was analysed (Biochemistry, HSS: Hyperthyroid Symptoms Score, SHR: sleeping heart rate, REE: resting energy expenditure). 7 of 8 patients achieved normal circulating FT4 (measured by immunoassay; mean FT4 fell from 31.2 pmol/l to 18.3 pmol/l, RR 10.5-21) and 5 of 6 achieved normal total T3 concentrations (measured by LC-TMS; mean TT3 fell from 2.89 to 1.52 nmol/l, RR 1.09-2.24). Mean reductions in other parameters included; HSS reduction from 17/40 to 9/40, SHR reduction from 60 to 56bpm, REE (measured as Z score) fell from $+1.375$ to $+0.66$. Triac was well tolerated and there were no reported side effects. No patients discontinued therapy.
Conclusions
Triac therapy in RTHbeta reduces hyperthyroid symptoms, lowers circulating FT4 and TT3 concentrations and reduces basal metabolic and heart rate effectively, without adverse effects. Whether longer-term Triac treatment alters adverse cardiovascular outcomes recently associated with RTHbeta remains to be determined.

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OC8

Investigation of the differential impact of oral classic and 11-oxygenated androgen precursor administration on downstream androgen metabolism and insulin sensitivity in women with polycystic ovary syndrome (PCOS)

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Androgen excess is a cardinal biochemical feature of PCOS and correlates closely with markers of insulin resistance. 11-oxygenated androgens are elevated in women with PCOS, however, their relationship with metabolic dysfunction is unclear. The aims of this study were (i) to evaluate the downstream impact on androgen metabolism of oral classic and 11-oxygenated precursor administration and (ii) to delineate the differential impact of androgen excess on insulin sensitivity in women with PCOS. An interventional, open-label study was conducted in 20 women with PCOS. Metabolic phenotyping including hyperinsulinaemic-euglycaemic (HI-EG) clamp testing was carried out at baseline and after 7days of androgen precursor administration. Participants were randomized 1:1 to receive 150 mg of either 11-ketoandrostenedione (11KA4) or dehydroepiandrosterone (DHEA) once daily for 7 days. Serum and urinary multi-steroid profiling was performed by liquid chromatography-tandem mass spectrometry. Enrichment of C^{13}-labelled glucose in exhaled breath samples was determined by gas chromatography-mass spectrometry. Twenty women with PCOS were enrolled ($n = 10$ in each arm); Median age was 30.9 years (IQR 26-33), median BMI 34.9 kg/m^2 (IQR 28.4 – 36.2). Following 7days of 11KA4 150 mg daily, we observed significant increases in serum 11KA4, 11β-hydroxyandrostenedione, 11-ketotestosterone and 11β-hydroxytestosterone(all $P < 0.05$). Urinary 11-oxygenated androgen metabolites also increased significantly ($P < 0.01$). Oral DHEA daily resulted in upregulation of classic androgens in both serum and urine, without any significant change in the 11-oxygenated androgen profile. On HI-EG clamp testing, glucose infusion rates, unadjusted for insulin, did not change significantly after either DHEA or 11KA4 administration. Oral administration of the androgen precursors are a powerful *in vivo* tool to study downstream classic and 11-oxygenated androgen metabolism. Our results demonstrate that orally administered DHEA is converted to androstenedione and further to testosterone, but that conversion of androstenedione to enter the 11-oxygenated pathway is only possible in the adrenal and not following oral ingestion and hepatic first pass.

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OC9

Pregnancy induced pancreatic islet expansion is compromised by consumption of cafeteria diet

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Background
Pregnancy induces pancreatic islet β-cell mass expansion, but the exact mechanisms responsible remain unclear. It is nevertheless believed that disturbances in the process contribute to the development of gestational diabetes. The current study investigates the impact of pregnancy and cafeteria diet on islet morphology, cellular proliferation/apoptosis as well as endocrine cell lineage plasticity.
Methods
Non-pregnant and pregnant Ins$1^{Cre/+}$;*Rosa26-eYFP* transgenic mice with fluorescently tagged beta cells were maintained on either normal rodent breeding diet or cafeteria diet comprising brie cheese, peanuts, peanut butter, Nutella and chocolate with 30% sucrose water. Pancreatic tissue was obtained at 18 days gestation and immunohistochemical changes in islet morphology were assessed.
Results
Normal diet Ins$1^{Cre/+}$;*Rosa26-eYFP* pregnant mice displayed increased ($P < 0.01$) body-weight and slightly elevated ($P < 0.05$) blood glucose. Cafeteria feeding attenuated this weight gain, whilst causing further increases ($P < 0.01$) in glucose. Pregnant Ins$1^{Cre/+}$;*Rosa26-eYFP* mice exhibited typical 1.5-2.0-fold expansion in islet area and β-cell area. These changes were related to increased β-cell proliferation and survival (0.2-3.0-fold, $P < 0.001$) as well as enhanced α and ductal β-cell transdifferentiation (1.3-3.0-fold, $P < 0.01$-0.001), alongside a 6.0-fold increase ($P < 0.001$) in β-cell neogenesis. In contrast, pregnancy-induced islet adaptations were severely compromised by consumption of a cafeteria diet, with no significant expansion of islet or β-cell area. Moreover, high levels of β-cell apoptosis (0.2-3.0-fold, $P < 0.001$) and reduced proliferation (0.8-1.2-fold, $P < 0.05$), together with increased β-cell dedifferentiation (1.5-3.0-fold, $P < 0.001$) and a lack of β-cell neogenesis adaptations, were observed in pregnant mice maintained on a cafeteria diet.
Conclusion
Augmentation of β-cell mass during gestation arises through various mechanisms that include proliferation and survival of existing β-cells, transdifferentiation of α and ductal cells as well as β-cell neogenesis. Remarkably, cafeteria feeding almost entirely annuls these pregnancy-induced islet adaptations, which may contribute to the development of gestational diabetes in the setting of dietary-induced metabolic stress.

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OC10

Gonadotropin rise following intranasal kisspeptin administration is increased in women with hypothalamic amenorrhoea compared to healthy women

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Background
Kisspeptin administration by intravenous/subcutaneous routes activates hypothalamic GnRH neurons to stimulate reproductive hormone release and is under rapid development for treating common reproductive disorders, including hypothalamic amenorrhoea (HA). However, these invasive routes limit patient acceptability. Intranasal offers a novel non-invasive delivery route, which would be clinically preferable. Herein, we compare the reproductive endocrine responses after intranasal kisspeptin administration in healthy women to women with HA.
Methods
Randomised, double-blinded, placebo-controlled, crossover study in 11 healthy women during the follicular phase (mean age 21.6±0.9yrs, BMI 21.8±0.9kg/m^2) and 10 women with HA (age 25.8±2.7yrs, BMI 20.6±1.3kg/m^2). After intranasal delivery of kisspeptin-54 (12.8nmol/kg) or 0.9%-saline (placebo), reproductive hormones were measured every 15minutes for 4hours. Mean±SEM presented.
Results
Intranasal kisspeptin-54 administration rapidly and robustly stimulated gonadotropin release in both cohorts. However, LH and FSH release were significantly augmented in women with HA, compared to healthy women: mean area under the curve (AUC) for the change in LH across 4hours 117.7±44.5h•IU/litre (healthy women) vs 600.6±146.7h•IU/litre (women with HA) ($P = 0.003$). Consistently, mean AUC for the change in FSH was -24.7±22.4h•IU/litre (healthy women) vs 474.9±237.3h•IU/litre (women with HA) ($P = 0.04$). The mean maximal change in LH following kisspeptin-54 was three-fold greater in women with HA at 4.4±0.7IU/l vs 1.5±0.3IU/l in healthy women ($P = 0.0009$). Similarly, the mean maximal change in FSH was over six-fold greater in women with HA at 3.1±1.3IU/l vs 0.5±0.2IU/l in healthy women ($P = 0.05$).
Summary
Intranasal kisspeptin robustly stimulates reproductive hormone release in healthy women, with an even greater stimulation in women with HA. Therefore, intranasal kisspeptin offers not only a novel, effective, safe, and non-invasive route of administration for the management of reproductive disorders but also a potential simple diagnostic test to identify women with HA.

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Case Report Oral Communications

CR1

Refractory hypercalcaemia in advanced metastatic pancreatic neuroendocrine tumour controlled on weekly denosumab

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Background
Hypercalcaemia of malignancy (HCM) is the commonest metabolic complication of malignancies. However, this is relatively rare among patients with neuroendocrine tumors (NET). Management of HCM remains a challenge for clinicians, especially in cases of refractory hypercalcaemia.
Case Report
A 37-year-old lady was referred to the NET service in June 2021 following the finding on imaging of a huge inoperable pancreatic mass with peritumoural varices and liver metastases. Biopsy revealed a well differentiated Grade 2 pancreatic NET (pNET) and somatostatin analogue therapy was commenced. On tumour progression, she completed 4 cycles of peptide receptor radionuclide therapy (PRRT) in May 2022. Her condition was complicated by development of Type 3c Diabetes Mellitus, episodes of variceal bleed and symptomatic hypercalcaemia [corrected calcium 3.09mmol/l (N 2.14-2.56); phosphate 0.43mmol/l (N 0.8-1.5); parathyroid hormone 0.5 pmol/l (N 1.6-6.9)], where confusion and lethargy were predominant features. She responded well to saline diuresis and intravenous Zolendronic Acid (ZA), maintaining a stable calcium level for a year. Her condition deteriorated thereafter when she was hospitalised for severe hypercalcaemia on two occasions (corrected calcium of 3.34mmol/l and 3.7mmol/l respectively) despite receiving monthly ZA and was switched over to monthly subcutaneous Denosumab 120 mg. Despite this, calcium level drifted above 3.0mmol/l before the next dose and the dose interval was shortened to two-weekly and then weekly. Over the last two months, weekly Denosumab 120 mg and daily home fluid administration have minimised her hospital admissions for symptomatic hypercalcaemia. Due to bleeding risk and performance status, other active treatments were not possible, but control of the hypercalcaemia has allowed quality time with her family.
Conclusion
HCM in pNET is associated with a poor prognosis and is highly refractory to treatment. To our knowledge, this is the longest period of weekly high dose Denosumab usage and illustrates an alternative approach in such difficult cases.

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CR2

Use of radiofrequency ablation (RFA) in the management of thyroid nodules – a single centre experience

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Radiofrequency ablation (RFA) is a minimally invasive technique using thermogenesis to induce tissue necrosis. Initially used to treat hepatocellular carcinoma, RFA is now used to treat numerous conditions including thyroid nodules. We present the use of RFA in 3 individuals with thyroid disease attending our centre. A 31-year-old female presented with symptoms of hyperthyroidism. Her TSH <0.02mIU/l (0.27-4.2), Free T4 (FT4) 20.2 pmol/l (11.9-21.6) and Free T3 (FT3) 8.5 pmol/l (3.1-6.8). Ultrasound demonstrated 1.5 cm cystic nodule in the left lobe of thyroid (TIRADS 1). Pertechnetate scan confirmed increased uptake in the nodule. Fine needle aspiration (FNA) was Thy 1. She was contemplating pregnancy and following discussion underwent RFA of the toxic nodule. Restoration of her thyroid function occurred post RFA; TSH 1.18mIU/l (0.4-4.2), FT4 14.8 pmol/l (9-22) and FT3 5.0 pmol/l (3.1-6.8). A 40-year-old female presented with a large nodule in the right lobe of thyroid. She was clinically and biochemically euthyroid; TSH 0.82mIU/l (0.4-4.2), FT4 12.8 pmol/l (9-22). Ultrasound demonstrated enlarged right lobe of thyroid. A solid cystic nodule replaced much of the lobe measuring 6.7x5.4x3.8cm (TIRADS 2). FNA was benign (Thy 2). RFA of the nodule resulted in reduction in the cystic component of the nodule. A 75-year-old gentleman presented with subclinical thyrotoxicosis; TSH <0.05mIU/l (0.4-4.2), FT4 15.6 pmol/l (9-22) in the setting of a large multinodular goitre extending to sternal notch. Pertechnetate scan confirmed increased uptake throughout the gland, more marked on the right side corresponding to a right sided nodule on ultrasound measuring 3.8cm. FNA was benign (Thy 2). RFA resulted in reduction in size of nodule to 1.9cm. These 3 cases show that RFA is a safe and effective way to manage both toxic and symptomatic thyroid nodules. It is an excellent alternative to surgery. To our knowledge, these are the first cases using RFA in thyroid disease in Ireland.

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CR3

Adrenocorticotropin (ACTH) independent cushing's syndrome in pregnancy secondary to overproduction of adrenal luteinizing hormone/human chorionic gonadotropins receptors

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We describe a case of a women with Cushing's syndrome and bilateral adrenal nodules who presented with symptoms and signs of Cushing's syndrome that manifested during pregnancy which unfortunately ended in a miscarriage in first trimester. Investigations showed raised urinary cortisols, failure of suppression of cortisol with dexamethasone and suppressed ACTH. CT adrenals showed bilateral macronodular adrenal hyperplasia. Patients's history suggested she had similar symptoms with her earlier pregnancies which all ended up in miscarriages and resolution of symptoms following miscarriages. History also revealed that since last 2 years she was on ovulation induction treatment (IVF-C human chorionic gonadotropins) and Menotrophin (it contains FSH and LH). Considering that she had a strong history of recurrent symptoms during pregnancy it was highly likely that Cushing syndrome was due to overproduction of adrenal luteinizing hormone/chorionic gonadotropins receptors with pregnancy plus prolong stimulation due to exogenous FSH/lH and human chorionic gonadotropins rather than primary adrenal adenomas. She was commenced on monthly long acting GnRH (Leuprolide) injections. After receiving three dosages there was marked improvement of Cushing's symptoms and and her urinary cortisol normalised to lower end of normal. By 3rd month she had lost 10 kg of weight, had normal blood pressure and was euglycemic.

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CR4

Pregnancy induction with pulsatile gonadotropin releasing hormone pump (GNRH) therapy in a patient with a KISS1 receptor mutation associated normosmic congenital hypogonadotropic hypogonadism and a very low anti-mullerian hormone: a case study

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We present a case of a thirty year old female with a history of primary amenorrhoea due to hypogonadotropic hypogonadism (HH) who was further investigated as family history revealed a brother and sister with normosmic hypogonadotropic hypogonadism due to a homozygous pathogenic variant c.1195T > A in the KISS1 receptor gene. Our patient carried the same homozygous mutation, and both parents (unrelated) were heterozygous carriers. KISS1-receptor mutations are a rare cause of congenital hypogonadotropic hypogonadism, present in 2-4% of cases. Kisspeptin is now known to be a key factor in stimulation of puberty and overall fertility. As part of fertility planning aged 25, an anti-mullerian hormone (AMH) level was found to be very low at 0.3 pmol/l (NR > 20 pmol/l for this age) and transvaginal ultrasound showed no antral follicles. Following a lack of response to gonadotropin stimulation in an attempt to preserve oocytes by vitrification, she was referred to a reproductive endocrinology centre. It was hypothesised that the very low AMH level was potentially due to lack of exposure to endogenous GNRH and trial of gonadotropin releasing hormone (GNRH) pump was commenced. This led to regular menstrual cycles and ovulation was confirmed by ultrasound and elevated luteal progesterone. After six months of GnRH pump therapy, AMH increased to 3.98 pmol/l. Subsequently, when the patient was ready to actively try to conceive, and following confirmation of normal fallopian tubes and normal semen analysis, she was restarted on GnRH pump therapy. She conceived without other intervention, on the seventh menstrual cycle. Data surrounding fertility in congenital hypogonadotropic hypogonadism secondary to KISS1R mutations is limited and this case highlights that anti-mullerian hormone may be unreliable in this cohort, and that gonadotropin therapy may not always be successful in HH, likely in this case due to the low AMH and finally that conception is possible with GnRH pump therapy.

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CR5

Gastrointestinal morbidity related to delayed diagnosis of pheochromocytoma

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Background
Although pheochromocytoma is feared for its acute life-threatening complications, in some patients the symptoms can be subtle. This leads to delayed diagnosis and chronic morbidity. We report 2 cases who presented with long history of major gastrointestinal manifestations related to a pheochromocytoma Case 1: A 51-year-old female had severe constipation for 12 years. No bowel pathology was identified on ultrasonography, colonoscopy, colonic transit studies and isotope defecography. She had hypertension and poorly controlled diabetes. During a period of acute worsening, partial colectomy was planned but deferred as a preoperative CT scan identified left 4x3cm adrenal lesion and recent onset hypokalemia. Further investigations confirmed ACTH secreting- pheochromocytoma with a positive 68-Ga-DOTA scan. She had an uneventful left adrenalectomy, (histology confirming pheochromocytoma) with complete resolution of bowel symptoms and biochemical abnormalities. Case 2: A 50-year-old male presented with 12 years of severe constipation, anorexia, distention and weight loss. He had type-2 diabetes and resistant hypertension. Extensive bowel investigations were unremarkable, but an abdominal CT revealed 11x10cm heterogeneous right adrenal mass alongside features of bowel obstruction. Elevated urinary metanephrines confirmed pheochromocytoma and MIBG scan showed increased uptake. A few days prior to surgery, he presented with rapidly progressive congestive heart failure to which he unfortunately succumbed.
Discussion
Gastrointestinal pseudo-obstruction is rare and seen in 5-15% of patients of pheochromocytoma. The adrenergic effects of catecholamines can lead to severe gastrointestinal dysmotility, resistant to medical management. Bowel perforation is seen in 15% of these patients. Identifying the condition is important as surgeries performed with undiagnosed pheochromocytoma are associated with mortality close to 80%. Excision of pheochromocytoma is the most effective way of achieving resolution of bowel symptoms.
Conclusion
These cases underscore the need to consider pheochromocytoma in patients presenting with unexplained chronic severe gastrointestinal symptoms and an adrenal lesion.

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CR6

GLP1 receptor agonist and sulphonylurea treatment in KCNJ11 permanent neonatal diabetes

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Heterozygous activating mutations of the *KCNJ11* gene are the most common cause of permanent neonatal diabetes. High dose sulphonylurea (SU) therapy usually results in long-term glycaemic control. A 32-year-old woman presented at four weeks old with hyperglycaemia, ketonuria and acidosis. She was treated with insulin throughout childhood and adolescence. She was later diagnosed with a *KCNJ11* mutation (R201H, c.601C > A). She successfully transitioned to SU on a second attempt at age 24; transferring from 50units of insulin to glibenclamide 0.44 mg/kg/day with improved glycaemic control and HbA_{1c} of 44mmol/mol. After seven years of SU therapy, HbA_{1c} was 71mmol/mol despite incremental glibenclamide dose increase to 40 mg twice daily (1.3 mg/kg/day). This was in the context of a busy job, stable weight and BMI 26.7kg/m^2. HbA_{1c} worsened despite a trial of bolus insulin aspart 4units with breakfast. Liraglutide 0.3 mg daily was commenced at age 32 and increased to 0.6 mg. She switched to semaglutide 0.25 mg which was then up titrated to 0.5 mg for convenience. Bolus insulin was stopped and glibenclamide was reduced to 35 mg/day (0.6 mg/kg/day) to offset nocturnal hypoglycaemia post-exertion. HbA_{1c} reduced to 44mmol/mol at six months and 47mmol/mol at twelve month follow up. Weight reduced from 64.2kg to 58kg and BMI was normal at 24.2kg/m^2. SUs act downstream of the SU receptor and activate the K_{ATP} < channel through a route independent of ATP to stimulate insulin release. Glucagon-like peptide 1 agonists (GLP1a) bypass the SUR receptor to secrete insulin but are dependent on cAMP. Sufficient levels of cAMP are only achieved in KCNJ11 diabetes with SUs. Concomitant GLP1a treatment augments the glucose lowering effect of SU in the *KCNJ11* R201H mutation.

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Oral Poster Presentations

Oral Posters 1 – Endocrinology 1

OP1

Gene methylation status in delayed puberty

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Self-limited delayed puberty is a condition that is frequently familial with strong genetic determinants. It has been linked to coding region sequence variation by next generation sequencing of affected individuals, identifying genetic regulation of gonadotropin-releasing hormone (*GnRH)* pathways underlying this condition. However, the role of epigenetic modifiers of human pubertal timing is underexplored. The hypothalamic-pituitary-gonadal axis is unique as it is active in three phases of life: foetal, infancy and then from puberty onwards. In-between these phases of life it is dormant. This is a process highly likely to be regulated by changes in DNA methylation. We analysed DNA methylation using the illumina EPIC array, for patients ($n = 92$) with delayed puberty who had no identified genetic cause for the condition, and related unaffected controls ($n = 20$). Quality control, annotation of CpG sites and differential methylation analysis was undertaken in R Studio. This revealed differentially methylated CpG sites between cases and controls linked to important genes known to play a role in the control of puberty and growth. Specifically, differentially methylated CpG sites were identified in both enhancer and promoter regions of these genes. Within the top 5 enhancer-associated CpG sites, two were linked to *CADPS2* with q values $3.21x10^{-19}$ and $7.31x10^{-17}$ respectively. Key genes involved in upstream regulation of *GnRH* include *TAC3, KMT2A* and *SIRT1* which showed increased methylation in CpG sites, within enhancer or promoter regions, in individuals with delayed puberty compared to controls. Genes associated with differentially methylated cytosines were then analysed to identify cellular pathways that were dysregulated. Over representation analysis identified multiple KEGG pathways previously associated with growth dysfunction as significantly altered. These included the cAMP pathway($p = 8.85x10^{-08}$), the neuroactive ligand-receptor interaction pathway ($p = 1.63x10^{-05}$) and focal adhesion pathway ($p = 1.63x10^{-05}$). Our results suggest that changes in methylation of key regulatory genes contribute to the phenotype of self-limited delayed puberty.

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OP2

Audit on the Management of Cystic Prolactinomas

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Introduction
Cystic prolactinomas were historically considered resistant to dopamine agonists. However, recent case series including one by Faje et al. have highlighted their potential efficacy. We conducted an audit of cystic prolactinomas in Beaumont Hospital to assess this further.
Methods
Cystic prolactinomas were defined as a macroadenoma with a cystic component exceeding 50% of the adenoma volume and a prolactin of at least 2,000mIU/l. Data was extracted from patient's medical records fulfilling this criterion.
Results
Fourteen patients with predominantly cystic prolactinomas were identified. Median age at presentation was 26 years (IQR 18.5-48.75), with an equal sex distribution. At diagnosis, 86% ($n = 12$) of patients had gonadotropin deficiency, while visual field (VF) defects were observed in 29% ($n = 4$). All patients were initially medically treated; the median cabergoline dose was 1 mg (IQR 0.5-3.75) per week. Gonadotropin deficiency and VF defects resolved in 71% ($n = 10$) and 75% ($n = 3$) of patients, respectively, with medical therapy. Prolactin normalised in 71% of patients ($n = 10$) after 4 months (IQR 4-12.5) on medical therapy. Prolactin declined from 9,831mIU/l initially (IQR 3,910-36,056) to 207mIU/l (IQR 93-743) after 35 months of follow up (IQR 25-69). Tumour shrinkage occurred in 79% ($n = 12$) of patients; the maximal adenoma diameter reduced from 17.5 (IQR 15-24.25) mm to 8mm (IQR 15-24.25), while the cystic component reduced from 13.5 (IQR 9.5-19.25) to 6mm (IQR 15-24.25) at last follow up. Four cystic prolactinomas involuted completely. Despite these responses, two patients underwent transsphenoidal surgery, one for a persistent VF defect while another had no biochemical or anti-tumour response to cabergoline.
Conclusion
Cabergoline therapy led to a rapid normalisation of prolactin levels and significant tumour shrinkage in over 70% of patients with cystic prolactinomas, including those with larger tumours and visual field defects. These findings strongly support the use of cabergoline as the first-line treatment for predominantly cystic prolactinomas.

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OP3

Immunomodulation of severe graves' disease: graves'-plasma cell depletion (PCD) trial

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Introduction
Hyperthyroid Graves' Disease affects 3% of women and 0.5% of men over a lifetime, with only 50% of patients experiencing remission following antithyroid drug therapy. The humoral immune response involves the production of Thyroid Stimulating Hormone Receptor antibodies (TRAbs) from plasma cells. This study aims to provide proof of principle that Daratumumab, a monoclonal antibody targeting cell-surface CD-38 on plasma cells, could modulate the immune response in Graves' disease compared to conventional anti-thyroid drug therapy alone.
Method
30 patients with severe Graves' disease were recruited across this 2-stage clinical trial. All patients had newly diagnosed or relapsed Graves' disease within the previous 12 months, with FT4 $\geq$ 50 pmol/l and TRAb levels $>$10IU/l. Patients were randomised to placebo or different doses of daratumumab. Follow up visits were scheduled at 4,6,12 and 24 weeks with changes in serum TRAb as the primary outcome.
Results
The cohort had a male to female ratio of 8:22 of a mean age of 41yrs and mean TRAb level at screening of 56.5U/l. 13 patients randomised to the highest doses of Daratumumab (9 mg/kg and 16 mg/kg), showed a median TRAb reduction of 72% at week 12, compared to 51% in the placebo group. All patients receiving Daratumumab, experienced reductions in immunoglobulins IgA (79%) $>$IgM (54%)$>$IgG (37%) by 6 weeks. Compared to total IgG, a more potent reduction in TRAb antibodies was observed, suggesting that thyroid plasma cells actively involved in the autoimmune response were preferentially targeted by daratumumab.
Conclusion
This study demonstrates proof of principle that Daratumumab can modify the immune response in Graves' disease. Continued patient follow-up is necessary to determine whether this will translate to improve the chances of remission in severe Graves' Disease.

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OP4

GIP receptor agonist and antagonist alter testicular morphology and sperm parameters in high-fat diet fed obese mice

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Background
Glucose-dependent insulinotropic polypeptide (GIP) secreted by K-cells in the intestine is an incretin that stimulates insulin secretion from pancreatic beta-cells. The aim of this study is to explore the extra-pancreatic effects of GIP on male fertility using diet-induced obese mice.
Methods
Male *Swiss* TO-mice ($n = 8$) on high-fat diet (HFD) or normal diet (ND) for 8-weeks received twice-daily intraperitoneal injections of ($DAla^2$)GIP, mGIP(3-30) (25 nmol/kg bw) or saline vehicle (0.9% (w/v) NaCl) for 7 days. Metabolic parameters were regularly monitored. Terminal plasma and tissues were collected for hormone measurement. Male GIPR-Cre×Rosa26-GCaMP3 mice were used to provide evidence for GIP receptor in the testes.
Results
GIP receptor expression was found in the testis of GIPR-Cre×Rosa26-GCaMP3 mice. HFD mice exhibited significantly ($P < 0.05$-$P < 0.001$) higher body weight, blood glucose and energy intake compared to ND mice. mGIP(3-30) significantly ($P < 0.05$) decreased terminal blood glucose. Plasma GIP significantly increased after ($DAla^2$)GIP while both ($DAla^2$)GIP and mGIP(3-30) increased ($P < 0.05$-$P < 0.01$) corticosterone levels. ($DAla^2$)GIP was able to increase ($P < .0.05$) testosterone levels compared to HFD. Sperm analysis showed a significant ($P < 0.001$) decrease in sperm count after HFD and remained unaltered by GIP. ($DAla^2$)GIP and mGIP(3-30) decreased ($P < 0.05$-$P < 0.01$) motility compared to ND mice, displaying increased number of static sperm cells. However, progressive motility increased significantly ($P < 0.05$-$P < 0.01$) with ($DAla^2$)GIP and mGIP(3-30) compared to ND and HFD mice. While HFD and GIP treatments did not alter testis weight, ($DAla^2$)GIP and mGIP(3-30) significantly ($P < 0.05$-$P < 0.01$) increased tubule diameter in the testes. mGIP(3-30) significantly ($P < 0.01$-$P < 0.001$) decreased spermatogenic epithelium thickness compared to ND and HFD groups
Conclusion
These data suggest an active role for GIP in regulating fertility and reproductive physiology in males. Hence, targeting GIP receptors could be a unique therapeutic target for obese and diabetic male individuals.

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Oral Posters 2 – Diabetes/Obesity/Metabolism 1

OP5

The role of soluble epoxide hydrolase in metabolic-associated fatty liver disease

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Metabolic-associated fatty liver disease (MAFLD) is a metabolic disorder characterized by excessive lipid accumulation and is associated with irreversible liver cirrhosis and liver cancer. Epoxyeicosatrienoic acids (EETs), which are synthesized from fatty acid metabolism, function primarily as a regulator of vascular tone, anti-inflammation, and angiogenesis. Soluble epoxide hydrolase (sEH) is a key enzyme that converts EET to the less biologically active dihydroxyeicosatrienoic acid (DHET). Thus, the inhibition of sEH is a potential approach to prolong beneficial effects of EETs, and even attenuates high-fat diet (HFD)-induced obesity. However, the regulatory mechanism controlling its effect on hepatic lipid metabolism remains unclear. In present study, sEH knockout (KO) mice and wild type (WT) mice fed with either HFD or chow diet for 16 weeks were used to test our hypothesis. Our results showed that sEH KO mice exhibited lower body weight and liver weight compared with WT mice. Deficiency of sEH significantly reduced HFD-induced hypertriglyceridemia and increased hepatic lipid accumulation compared with the WT group. Meanwhile, results of western blotting showed that deficiency of sEH can activate AMPK signaling, which is a key regulator of cellular energy homeostasis. This activation results in reduced lipid accumulation in hepatocytes. To explore the underlying mechanisms, model of AML12 hepatocytes co-incubated with oleic acid to induce intracellular lipid accumulation were used. Treatment of TPPU, an inhibitor of sEH, caused a dose-dependent reduction in intracellular lipid droplets through AMPK signaling pathway in AML12 hepatocytes. TPPU also down-regulated expressions of genes and proteins associated with de novo lipogenesis in AML12 hepatocytes. In conclusion, our study demonstrated that deficiency of sEH activated AMPK-mediated suppression on de novo lipogenesis in liver and ameliorated fatty liver.

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OP6

11β-HSD1 inhibitor efficacy in type 2 diabetes is cortisol-dependent

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Cortisol excess drives multiple adverse effects including hypertension, dyslipidemia, and delayed wound healing. Activation of cortisol by the enzyme 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) has shown promise as a therapeutic target for these comorbidities but clinical progress has been hampered by variable 11β-HSD1 inhibitor efficacy. Transcriptomic profiling by RNA-seq found 611 11β-HSD1 target genes in primary skin fibroblasts ($n = 3$), and 814 target genes in skin biopsies from people with type 2 diabetes treated for 35 days with the selective 11β-HSD1 inhibitor AZD4017 (400 mg bi-daily, $n = 11$) or placebo ($n = 6$). Targets included genes involved in wound healing (e.g., MMP1, VEGFA, CD163, SOX4, KRT5), epidermal integrity (e.g., CLDN3, DSC2, DSG2, SPHK2) extracellular matrix remodelling (e.g., TNC, LOXL1, TIMP3, HAS3, P3H3, PLOD1), coagulation (e.g., F3, PROS1, SERPINE1, ADAMTS13, ST3GAL4), lipid metabolism (e.g., IRS2, LEP, HMGCS2, APOB, DEGS2), and inflammation (e.g., IL1B, IL6, PTGS2, CX3CL1). Serum steroid profiles were measured by liquid chromatography-mass spectrometry. Changes in expression of 45 11β-HSD1 skin target genes, blood pressure, lipids, and wound healing correlated ($r > 0.3$ or < -0.3, $P < 0.05$, $n = 17$) with changes in 1) cortisol levels (serum cortisol/dehydroepiandrosterone sulfate) and 2) peripheral 11β-HSD1 activity (serum cortisol/cortisone). People with low baseline cortisol levels treated with AZD4017 ($n = 3$) were more comparable to those treated with placebo, whereas placebo-treated people with a reduction in cortisol levels ($n = 2$) were more comparable to those treated with AZD4017. These findings pave the way for more effective targeting of 11β-HSD1 inhibitor treatment, improving the accuracy of future clinical studies, alongside new mechanistic insights for 11β-HSD1 in delayed wound healing and cardiovascular comorbidities. Larger trials are now warranted to fully explore the therapeutic potential of 11β-HSD1 inhibitors.

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OP7

Hybrid acylated and non-acylated GLP-1 and apelin receptor co-agonist peptides, show promising acute *in vivo* anti-hyperglycaemic actions in normal healthy and insulin resistant diet-induced obese mice

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Incretin mimetics, alongside associated hybrid co-agonist peptides, which activate GLP-1 and other receptors are leading the way to more effective therapeutic options for management of obesity and type 2 diabetes. The adipokine apelin, which activates the APJ receptor, has shown anti-diabetic and obesity related therapeutic utility following pre-clinical testing. The present study investigated several novel hybrid co-agonist peptides, derived from exendin-linker-apelin (ELA) and apelin-linker-exendin (ALE). Co-agonists were first assessed for their efficacy in lowering plasma glucose following an intraperitoneal glucose tolerance test (ipGTT). The ipGTT (18 mmol/kg) was performed following simultaneous ($t = 0$) or delayed (2, 4, 8, 24 and 36 h prior) i.p. injection with non-acylated ELA or ALE peptides (25 nmol/kg) either in normal healthy male NIH mice ($n = 8$), or in insulin resistant diet-induced obese (DIO) mice ($n = 6$) previously fed on a high-fat diet (45% fat) for 12-14 weeks. Additional, ipGTT studies in healthy mice ($n = 6$-8) were performed with acylated peptide analogues, modified at Lys^{12}, Lys^{27} or Lys^{38} side-chains within the co-agonist ELA sequence. The hybrid analogue ELA showed promising acute *in vivo* insulinotropic actions when administered to healthy or DIO mice. ELA reduced plasma glucose concentrations in DIO mice immediately after an ipGGT (43% reduction $AUC_{0\text{-}120\ min}$ glucose, $P < 0.001$) and retained efficacy (30% reduction $AUC_{0\text{-}120\ min}$, $P < 0.001$) up to 24 h post peptide injection. The reverse analogue ALE, lacked anti-hyperglycaemic efficacy. Acylated ELA(Lys^{12}) and ELA(Lys^{38}) analogues retained highly effective glucose-lowering actions with $AUC_{0\text{-}105\ min}$ values reduced by 40-48% ($P < 0.01$) vs glucose alone, when administered 4 h in advance of an i.p. glucose load in healthy mice. The ELA(Lys^{12}) analogue retained anti-hyperglycaemic activity (27% $AUC_{0\text{-}105\ min}$ reduction; $P < 0.05$) up to 24 h after acute administration to mice. In conclusion, hybrid co-agonist acylated and non-acylated ELA peptide analogues, demonstrated sustained improvements in glucose tolerance in normal and DIO mice.

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OP8

Abstract unavailable

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Oral Posters 4 – Diabetes/Obesity/Metabolism 2

OP9

The impact of social deprivation on development and progression of diabetic kidney disease- a retrospective cohort study

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Introduction
Social deprivation is increasingly recognised as a risk factor for complications of diabetes, including diabetic kidney disease. The effect of deprivation on rate of decline in renal function has not been explored in the Irish Health System to date.
Aim
The aim of this study is to explore the association between social deprivation and the development and progression of diabetic kidney disease in a cohort of adults living with diabetes in Ireland.
Methods
This is a retrospective cohort study using an existing dataset of 4464 people living with diabetes who attended the diabetes centre at University Hospital Galway from 2012 to 2016. The database contains clinical, demographic and laboratory data and was updated to include longitudinal laboratory measurements up to January 2023. Individual's addresses were used to calculate deprivation indices using the Pobal Haase Pratschke (HP) deprivation index. Rate of renal function decline (absolute and percent) was calculated using linear mixed-effect models.
Results
In participants with type 1 diabetes, there was a statistically significant difference in baseline creatinine (higher in more deprived group). In participants with type 2 diabetes, there was a statistically significant difference in baseline smoking rates, body mass index and systolic blood pressure (all higher in more deprived groups) despite a higher rate of antihypertensive use in more deprived groups. Unadjusted linear regression models showed a statistically significant relationship between absolute ($P = 0.016$) and percent ($P = 0.022$) decline in renal function and deprivation indices (faster decline in more deprived participants).
Conclusions
Our study demonstrates differences in baseline clinically relevant variables across deprivation categories. Furthermore, we have demonstrated a faster rate of decline in renal function in more deprived people living with diabetes. This highlights a need for targeted interventions for deprived populations, in order to mitigate the additional risk imposed by social deprivation.

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OP10

Access to psychological medicine services improves outcomes in vulnerable patients with diabetes

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People with diabetes mellitus experience increased rates of psychiatric disorders which may have a negative impact on glycaemic control[1]. Psychological supports and interventions may ameliorate this. We aimed to examine the impact of psychiatric and psychological interventions on patient engagement and glycaemic metrics in adults attending a single tertiary level diabetes centre. People with diabetes who had been referred for psychiatric evaluation in our centre between 2015-2022 were included in this study. Clinical information, glycated haemoglobin (HbA1c), rate of inpatient admission and missed outpatient appointments were gathered retrospectively from medical records. Thirty-eight people were included, the median age was 32 (range = 19-60). The majority were female (52.6%), and had type 1 diabetes mellitus (86.1%). At baseline mean HBA1c was 86.5mmol/mol ($\pm$ 23.5mmol/mol), mean missed outpatient appointments 3.8 appointments/year ($\pm$4.0) and mean hospitalisations from diabetes 0.6 admissions/year ($\pm$1.1). Following psychiatric and/or psychology intervention, HBa1c improved (86.5mmol/mol vs 79.4mmol/mol, decrease of 7.1mmol/mol, $P < 0.002$) and patients has less hospital admissions due to diabetes at one year (0.6 $\pm$1.1 vs 0.2 $\pm$0.5, $P = 0.04$). 46% of patients showed greater engagement in their care by having fewer unattended appointments. Our data highlights that adults with diabetes and comorbid psychiatric disorders have poor glycaemic control and service engagement at baseline. There was however, a statistically significant improvement in these parameters with psychiatric and psychological interventions stressing the importance of such services as part of the multidisciplinary management of people with diabetes mellitus.

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OP11

Associations between fear of hypoglycaemia and step-count among adults with type 1 diabetes and insulin-treated type 2 diabetes: findings from the hypo-metrics study

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Introduction
Hypoglycaemia is a key barrier to physical activity in people with diabetes. We explored the association between hypoglycaemia fear and daily step-count in adults with type 1 diabetes (T1D) and insulin treated type 2 diabetes (T2D).
Methods
Participants from the Hypo-METRICS study wore a Fitbit Charge 4 activity monitor, blinded continuous glucose monitor and reported episodes of hypoglycaemia on a smartphone app for 10-weeks. Participants also completed the Hypoglycaemia Fear Survey-II (HFS-II) score, which measures fear of hypoglycaemia and comprises of behaviour (behaviours to avoid hypoglycaemia and their negative consequences) and worry (specific concerns about hypoglycaemic episodes) subscales. Associations between HFS-II scores and median daily step-count were modelled using a generalised regression model, controlling for age, gender, time below range 3.9mmol/l, rate of reported hypoglycaemia, and hypoglycaemia awareness (as measured by GOLD score).
Results
A total of 266 people with T1D and 306 people with T2D (88% vs 91% white, 46% vs 63% male, median age 46 vs 63 years, HbA1c 7.3% vs 7.5%, HFS-II total score 27 vs 22, average step-count 8790 vs 5880 steps/day) were included. In people with T2D increased HFS-II behaviour sub-score and worry sub-score were independently correlated with reduced-step count (incidence rate ratio [IRR] 0.95, confidence interval [CI] 0.93-0.97, $P < 0.001$ and IRR 0.95, CI 0.92-0.98, $P = 0.005$ respectively). In people with T1D, increased HFS-II behaviour sub-score was associated with a reduction in step-count (IRR 0.98, CI 0.96-1.00, $P = 0.048$), however the worry sub-score was not significantly associated with step count ($P = 0.2$).
Conclusion
In people with T2D, both fear of hypoglycaemia worry and behaviour are associated with reduced daily step-count. In people with T1D only hypoglycaemia avoidance behaviour is associated with reduced daily step-count. Addressing fear of hypoglycaemia and providing education and clinical support for managing glucose and exercise may support physical activity in people with diabetes.

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OP12

Real-world outcomes of smart insulin pens in adults with diabetes mellitus attending an irish tertiary hospital

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Smart insulin pen technology offers insights into insulin dosing frequency and adherence patterns to assist patients and healthcare professions in treatment planning and diabetes control. We aimed to audit insulin smart pen use and glycaemic outcomes in a cohort of adults with diabetes attending a tertiary level diabetes centre. People with diabetes who were given insulin smart pens (NovoPen 6 or Novopen Echo Plus) in our centre were included in this audit. Clinical information, glycated haemoglobin (HbA1c), smart pen data, glucose metrics including continuous glucose monitor (CGM) data and self-monitoring of blood glucose (SMBG) data were gathered retrospectively from medical records as well the Glooko and DEXCOM CLARITY online platforms. Data collection was carried out in November and December 2023. Nineteen people were using insulin smart pens in our centre and the majority ($n = 18$ [94.7%]) using a smart pen for bolus administration of insulin aspart. The median age was 39 years (range 18-67), 12 (63.2%) were female, 17 (89.5%) had type I diabetes mellitus, mean duration of diabetes was 17.6 ($\pm$11.4) years and mean HbA1c was 81.4mmol/mol ($\pm$25.4). Improvements in time in range (23.5% $\pm$16.5 vs 34.8% $\pm$19.4, $P = 0.02$); level 2 time above range (47.8% $\pm$21.0 vs 37.4% $\pm$9.5, $P = 0.049$) and mean glucose (13.8mmol/l $\pm$2.5 vs 12.7 mmol/l $\pm$2.8, $P = 0.036$) were seen in smart pen users. A trend to improvement in HbA1c was demonstrated with smart pen use (81.4mmol/mol $\pm$25.4 vs 77.7 mmol/mol $\pm$15.6, $P = 0.17$). Though this is a small cohort, our data is consistent with other studies suggesting improvements in glycaemic metrics with smart insulin pen use. As the use of these connected devices grows, improved awareness, education and resource availability among healthcare providers and patients is required to harness the benefits of this technology.

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Oral Posters 3 – Endocrinology 2

OP13

A tiered, evidence-based approach to exome sequencing analysis in early-onset primary ovarian insufficiency

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Background

Sequencing of Primary Ovarian Insufficiency cohorts have identified variants in > 100 "POI genes" in up to 50% of women but establishing pathogenicity is challenging. Early-onset POI (EO-POI; adolescents) may have a distinct genetic profile.

Methods

We performed exome sequencing (Nonacus) in an EO-POI cohort. Filtering (QCI) retained variants which were 1) rare/novel (MAF < 0.01%), 2) predicted pathogenic *in silico*, 3) enriched in the cohort compared to gnomAD v4.0 controls; and 4) pathogenic/likely pathogenic (ACMG). Further filtering used three categories: 1) variants in genes on the Genomics England Primary Ovarian Insufficiency PanelApp; 2) variants in other genes previously associated with POI; and 3) homozygous variants.

Results

A total of 149 women with EO-POI were recruited (31 familial POI, 17 kindreds, 8 consanguineous; 118 sporadic POI; 81.2% ($n = 121$) primary amenorrhea). Of 17 familial POI kindred, 11 (64.7%) had a Category 1 or 2 variant ($n = 6$ Category 1: *STAG3, MCM9, PSCM3IP, YTHDC2, ZSWIM7* (homozygous) and *POLR2C* (heterozygous); $n = 5$ Category 2: *NLRP11* and *PRKD1* (heterozygous), *PLEC, IGSF10, KMT2A* (homozygous), *PDE3A, POLR2H, MSH6, CLPP* (polygenic)). A total of 65.3% ($n = 77$) women with sporadic POI had a Category 1 or 2 variant (20.3% ($n = 24$) Category 1 and 42.4% ($n = 50$) Category 2; 30.9% heterozygous, 9.4% homozygous, 21.8% polygenic). Most heterozygous variants were present in gnomAD controls. The cohort was then screened for Category 3 variants, revealing 10 novel POI candidate genes in 8 women. These included genes with animal gonadal insufficiency models (*PCIF1, DND1, MEF2A, TGFBR1*), DNA repair genes (*XRCC1, MMS22L*, *RXFP3*), mitochondrial genes (*PPAN, CLUH, COQ10B, MRPS14*), and others (*C4orf33, ARRB1*).

Discussion

Using a tiered, evidence-based approach, we characterise the genetic landscape of EO-POI as complex and frequently multigenic. The pathogenicity of single heterozygote variants in EO-POI is often uncertain. Autosomal recessively inherited, monogenic POI accounts for a distinct EO-POI subset. We propose novel POI candidate genes.

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OP14

Bone fragility and beyond: prevalence and impact of clinical signs, symptoms, and events in children with osteogenesis imperfecta

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Objectives

The IMPACT Survey explored self- and proxy-reported experiences of the clinical, humanistic, and economic impact of osteogenesis imperfecta (OI), a rare hereditary connective tissue disorder associated with low bone mass, bone fragility and variable secondary features. While the risk of fractures in children with OI has been well documented in previous studies, this analysis explores the prevalence and impact of OI-related clinical signs, symptoms and events (SSEs) beyond bone fragility.

Methods

An international survey in eight languages (fielded online July–September 2021) was developed with the Osteogenesis Imperfecta Federation Europe and the Osteogenesis Imperfecta Foundation (USA). The survey was open to adults (aged $\geq$18 years) or adolescents (aged $\geq$12–17 years) with OI, caregivers (CGs) with or without OI, of individuals with OI, and other close relatives; overall 2,208 individuals participated. Data were cleaned, coded, and analysed using Microsoft Excel.

Results

CGs without OI responded on behalf of 325 children with OI (aged 0–11, mean age 5.6 years, 42% female). The children's OI was described as mild (23%), moderate (51%) or severe (24%); type 1 (24%), 3 (27%) and 4 (14%) were most common. Over a 12-month period, the most frequently reported clinical SSEs were pain ($n = 231$, 71%), ranked as moderately or severely impactful by 51% of children, fractures ($n = 220$, 68%) which moderately or severely impacted 57%, and fatigue ($n = 153$, 47%), which moderately or severely impacted 27%. Certain SSEs were less prevalent, but commonly moderately or severely impactful for those who experienced them, for example, sleep disturbance ($n = 63$, 75%) and mental health problems ($n = 72$, 74%). The impact of clinical SSEs varied depending on the demographics and clinical characteristics of children, such as OI severity, OI type and sex.

Conclusion

Children with OI often experience debilitating fractures and other OI-related SSEs which have a substantial impact on their lives.

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OP15

A UK single-centre experience of the use of osilodrostat in pituitary MRI negative cushing's disease

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Introduction

In up to 50 percent of Cushing's disease patients, corticotroph adenomas are not clearly identified on MRI and long-term medical treatment to lower cortisol may be needed. Osilodrostat, which inhibits 11 beta hydroxylase, is effective in normalising urinary free cortisol (UFC). We are the UK's first centre to use osilodrostat for Cushing's disease in MRI negative patients.

Method

Five patients (one male) with Cushing's disease (excluded ectopic ACTH secretion by IPSS) started osilodrostat when there was no demonstrable adenoma on pituitary MRI.

Results

An initial daily dose of osilodrostat at 2-4 mg was started, followed by dose increments every 2-4 weeks aimed at normalising UFC levels. By week 2, the median daily dose was 4 mg, increasing to 8 mg by week 12. There were significant reductions in UFC concentrations, with a median decrease of 57.29% (range: -67.4% to +12.9%) after 2 weeks and 86.2% (range: -98.9% to -50.6%) after 12 weeks. Four out of five patients achieved normal UFC concentrations by week 12. Median ACTH concentration rose from 51.8 ng/l to 116 ng/l at week 12 (normal

range: 10-30 ng/l). Mild to moderate increases in testosterone levels in female patients were noted without causing clinically apparent hyperandrogenism (median 1.5 nmol/l at baseline to 7.3 nmol/l at week 12). Blood pressure improved, leading to reduced antihypertensive medications in three of four patients. One patient with type 2 diabetes mellitus experienced a significant reduction in HbA1c from 80mmol/mol to 50 mmol/mol by week 20. No side effects were reported.
Conclusion
Osilodrostat rapidly normalises UFC levels and is well-tolerated. ACTH levels increased during treatment, possibly due to reduced negative feedback after achieving eucortisolaemia. Further studies are needed to assess long-term efficacy.
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OP16

Investigating metastatic potential in papillary thyroid microcarcinoma (PTMC)

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Background
PTMCs are papillary thyroid carcinoma nodules measuring $\leq$1cm. While the American Thyroid Association (ATA) do not recommend biopsy or follow-up for PTMC nodules, classifying it as a benign condition, some individuals develop cervical lymph node metastases (LNM), challenging its benign classification.
Methods
We identified 52 cases of PTMC among 2,000 thyroid patients from 156 MDT meetings at Cork University Hospital (CUH) between January 2013 and December 2018, and January 2022 to May 2022. Conducting retrospective database review, we stratified patients by presence or absence of LNM, analysing factors associated with metastases using crude tests of association and logistic regression.
Results
Of the 52 patients, 16 (31%) exhibited metastases; 1 (2%) patient exhibited sclerosing metastasis to adipose and skeletal muscle tissue. Another patient exhibited infiltrative growth patterns, while a third demonstrated extra-nodal lymphovascular invasion. 9 (17%) patients with LNM were identified pre-operatively. 7 (13%) patients had incidental PTMC discovery with LNM during surgery for benign conditions. The sizes of metastases ranged from 4mm to 28mm, and the number of positive nodes ranged from 1 to 15. Preliminary crude tests of correlation demonstrated that, nodules $\geq$5mm, extrathyroidal extension, and patient age $\leq$45 years correlated significantly with metastases ($P = 0.004$, $P = 0.007$, $P = 0.01$ respectively). When adjusting for confounding variables through regression analysis, these associations persisted. Furthermore, following this adjustment, a significant association between male gender and metastases was unveiled (OR 7.355, 95% CI 1.354-39.960, $P = 0.021$).
Conclusion
PTMC is a condition possessing malignant potential. Nodules $\geq$5mm, with extrathyroidal extension in male patients $\leq$45 years, are more likely to metastasise. Follow-up should be considered for such cases.
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Poster Presentations

Adrenal & Cardiovascular

P1

Hypoparathyroidism in aicardi-goutières syndrome (AGS)— a descriptive case report

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Aicardi-Goutières syndrome (AGS) is a genetically inherited autosomal recessive disorder characterized by progressive encephalopathy, predominant basal ganglia calcifications, and elevated cerebrospinal fluid interferon-alpha (IFN-α) levels. The clinical manifestations often include seizures, cognitive impairment, and generalized dystonia. While the prevalence of AGS remains uncertain, pathogenic variants linked with AGS have been detected in affected individuals from various ethnic backgrounds. AGS, recognized as a monogenic hereditary disorder, is divided into nine distinct types based on specific pathogenic genes, with SAMHD1 commonly associated with milder phenotypes. The disease presentation can be challenging due to its variability across stages, making it easily mistaken for other conditions such as congenital TORCH infection or metabolic disorders. Endocrinopathies in AGS are acknowledged but not extensively described. This report discusses a unique case of a SAMHD1 variant causing AGS in an 18-year-oldfemale college student, presenting with recurrent hypocalcemia secondary to hypoparathyroidism. The patient experienced various neurological and non-neurological symptoms over time, highlighting the complexity of AGS diagnosis. Imaging findings, especially through Computed Tomography, play a crucial role in identifying characteristic brain calcifications specific to AGS. This case underscores the importance of ongoing research to better understand the correlation between AGS and hypoparathyroidism, and the necessity for more defined management guidelines in this context.

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P2

Association of the CT genotype of the polymorphic marker rs12979860 of the IL28B gene with autoimmune adrenal insufficiency

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Aim
To identify associations of polymorphisms in *TLR9, IL28B, TLR2* with autoimmune adrenal insufficiency (AAI).
Methods
In $n = 54$ patients with AAI (isolated and as part of type 2 autoimmune polyglandular syndrome (APS-2; group 1a)), $n = 9$ patients with APS-1 (group 1b), $n = 32$ healthy individuals (group 2) we analyzed polymorphisms in *IL28B* (rs12979860, rs8099917), *TLR9* (rs5743836, rs352140), *TLR2* (rs5743708) by real-time polymerase chain reaction.
Results
In group 1, compared with group 2, a significant predominance of CT genotype of the polymorphism rs12979860 of *IL28B* ($P = 0.010$), and T allele of the rs5743836 polymorphism of *TLR9* ($P = 0.032$) was revealed. The CC genotype of the rs12979860 polymorphism of *IL28B* ($P = 0.025$) and allele C of the rs5743836 polymorphism of *TLR9* ($P = 0.032$) were more common in group 2 than in group 1. A comparative analysis of the distribution of haplotype frequencies of loci of *IL28B* (rs8099917-rs12979860) revealed that CCTT occurs significantly more frequently in group 2 compared to group 1 ($P = 0.024$). When comparing groups 1a and 2, significance remained only in relation to the frequencies of CT genotype of the rs12979860 polymorphism of *IL28B* ($P = 0.024$) and alleles T and C of the rs5743836 polymorphism of *TLR9* ($P = 0.044$). In group 1b, compared with group 2, there was a predominance of CT genotype of the polymorphism rs12979860 of *IL28B* ($P = 0.032$) and the CTTT haplotype of two loci of *IL28B*: rs8099917 and rs12979860 ($P = 0.020$).
Conclusions
Patients with AAI differ from healthy individuals by a more frequent carriage of CT genotype of the polymorphic marker rs12979860 of *IL28B*. The T allele of the rs5743836 polymorphism of *TLR9* is a prognostic marker that increases the likelihood of developing AAI, while CC genotype at the rs12979860 polymorphism of *IL28B*, CCTT haplotype of two loci of the *IL28B* (rs8099917-rs12979860) and allele C of the rs5743836 polymorphism of *TLR9*, perform a protective role in this disease.

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P3

A rare case of co-existing anti-HMGCR immune-mediated necrotising myopathy and pheochromocytoma

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Case History
A 60 year-old male presented to ED with an elevated Creatinine Kinase (CK) of 16,685IU/l (40-320), ALT 788 IU/l (9-59), AST 785 IU/l (11-34) and lower limb fatigue and weakness. There was no upper limb or skin involvement. He had a ST-Elevation Myocardial Infarction in 2022, Coeliac Disease, and Trigger Finger. Statin therapy was stopped, and IV fluids commenced. CK down trended to 11,000IU/l in 24 hours. He was discharged with urgent rheumatology follow-up. 10days later, he presented with progressive weakness and difficulty swallowing food. He was admitted for further work-up.
Investigations
MRI thigh showed extensive symmetrical pelvic and thigh myositis bilaterally. Muscle biopsy revealed myonecrosis of the thigh. EMG studies exhibited fibrillations, percussion myotonia and polyphasic compound motor units. Ultrasound liver and standard autoimmune panel were normal. OGD showed no evidence of oesophageal pathology. CT-TAP for paraneoplastic work up showed a left 26 Hounsfield units, 3.1cm enhancing adrenal mass. Adrenal functional work-up revealed plasma normetanephrines of 3990 pmol/l (<1050) and plasma metanephrine of 1160 pmol/l (<360). Pituitary profile and 24 hr urinary free cortisol collection were normal. Extended Myositis panel was positive for Anti-HMGCoA Reductase antibody 363CU (<20).
Results and Treatment
Methylprednisolone, mycophenolate and IVIG were commenced followed by maintenance prednisolone for treatment of immune mediated necrotising myopathy. He was alpha blocked with doxazosin and then phenoxybenzamine prior to adrenalectomy. Steroid regimen was successfully weaned.
Conclusion and Points for Discussion
This case highlights the (i) importance of cross-speciality input and (ii) two rare potential causes of myopathy. (i) Multi-speciality input allowed us to arrive at two rare diagnoses and for adequate surgical preparation pre-op. (ii) Immune-mediated necrotising myopathy and pheochromocytoma are rare potential causes of myopathy. Given the lack of other symptoms usually present with pheochromocytoma, it's more likely that this was an incidental finding.

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P4

Antihypertensive and comorbid medication patterns in patients referred to a specialist hypertension service: implications for work up and subsequent management

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Introduction
The antihypertensive (AHT) medication choice, and the use of other drugs that affect the blood pressure (BP) have implications on the work up and management strategy of hypertension referrals.
Methods
We collected data from 300 referrals to a specialist hypertension service (sampled from referrals received between March 2023-24).
Results
a) 96.7% of the referrals were from primary care, the rest were from emergency care or another secondary care clinic. b) AHT usage: angiotensin converting enzyme inhibitors - 47.6%, angiotensin receptor blockers - 24%, calcium channel blockers - 53.9%, Thiazide/thiazide like diuretics - 17.7%, Spironolactone - 6.3%, Beta-blockers - 17.3%, alpha-blockers - 17.7%, Loop diuretics - 2.8%, and one patient each on Hydralazine, methyldopa, and moxonidine. c) 54.4% of patients were on antidepressants. This may cause worsening of hypertension, and orthostatic hypotension in this population.[1] Selective Serotonin Reuptake Inhibitors were the most commonly used and they may interfere with primary hyperaldosteronism testing by leading to high renin and aldosterone levels.[2] d) Other drug classes identified that may also cause a worsening of hypertension were - NSAIDs (9.4%), anti-migraine agents (6.7%), anti-psychotics (4.7%) and glucocorticoids (2.7%). e) The mean number of AHT agents in this population was 1.6. This is lower than 2.6, the average number needed to achieve goal BP in clinical trials.[3] The mean SBP was 150.01 mmHg (SD 12.02), which also supports room for up-titration at the point of referral. 45.3% were on a single agent.

Conclusions
This information will be useful for other hypertension services to clarify their local work up strategy for hyperaldosteronism, and will also help in streamlining AHT up-titration.
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P5

Adrenal crisis precipitated by omission of regular intramuscular depo-medrone injections: the importance of counselling for adrenal insufficiency in rheumatology patients on long term exogenous steroids
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Background
Prolonged use of exogenous steroids is common for the treatment of many rheumatological conditions, this can result in suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Adrenal insufficiency can lead to life threatening adrenal crisis if undertreated or not recognised.
Clinical Case
A 55-year-old woman with a history of sero-negative arthritis had been receiving monthly intramuscular (buttock/hip) injections of 120 mg Depo-medrone for the previous ten years prescribed by her rheumatologist. She was unable to avail of biologic therapies due to a previous history of breast carcinoma. She was awaiting a discectomy for back pain/lumbar disc prolapse and as a result had missed her regular monthly Depo-medrone IM injections. One week later and prior to the planned back surgery she present three times to her local emergency department with vomiting, hypotension and abdominal pain and was subsequently admitted to hospital on the third attendance when the possibility of an adrenal crisis was recognised. A short synacthen test, revealed a low baseline cortisol of 12, with a 30-minute cortisol of 68 nmol/l (RR $>$ 450). Adrenal/sellar imaging was normal with negative adrenal antibodies. Subsequently, the patient was promptly initiated on intravenous hydrocortisone therapy and fluids, then stepped down to oral hydrocortisone with clinical improvement, a medi alert bracelet was recommended for enhanced patient safety and the patient was counselled on steroid sick day rules.
Discussion
The potential for long term systemic glucocorticoids to cause adrenal suppression appears to be under recognized. Chronic inflammatory rheumatological conditions can in themselves contribute to alterations in HPA axis function. Given the widespread use of exogenous steroids, clinicians who prescribe these medications need to be aware of the potential risks of HPA axis suppression in addition to adequately counselling their patients on the practicalities of not omitting regular steroid medication and education on the risk of adrenal crisis.
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P6

Benefits of medical therapy with alpha-adrenergic inhibition pre-operatively for secretory paragangliomas – more than just blood pressure control
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Many symptoms of phaeochromocytomas and paragangliomas (PPGL) are due to the effects of excess catecholamines. Catecholamines exert their effect on alpha- and beta-adrenergic receptors. Before patients undergo curative surgery, guidelines recommend medical management is commenced to provide cardiovascular stability. This blockade allows restoration of normotension and normal circulating volume (reducing the risks of an intraoperative hypertensive crisis and postoperative hypotension respectively). The value of preoperative medical therapy with alpha-blockade has recently been disputed, with suggestions that an experienced team can prevent much of the intra-operative haemodynamic instability. This is undoubtedly the case and remains of the utmost importance. However this suggestion assumes rapid access to operating lists, and precludes any benefits that patients may derive from blocking the effects of ongoing catecholamine secretion while awaiting surgery. Bioimpedance is a non-invasive measure of body composition parameters. Bioimpedance analysis and measurements of serum inflammatory and immune markers were studied to explore potential additional physiological benefits of alpha-blockade therapy to PPGL patients pre-operatively, compared to matched hypertensive control patients. At baseline measurements for the PPGL cohort were suggestive of a more catabolic state compared to the primary hypertensive control patients. PPGL patients had a lower weight, lower BMI, and reduced body fat, muscle mass and BMR compared to hypertensive controls. Treatment with alpha-blockade led to a significant improvement in all of the body composition parameters. Patients with a secretory PPGL had higher levels of white blood cells, platelets, ferritin, ALT, HbA1c, Troponin T, platelet-to-lymphocyte score and systemic index score at diagnosis. These all significantly decreased pre-operatively in the presence of alpha-blockade. There were no significant changes in any of the inflammatory or immune markers in the hypertensive controls despite a similar improvement in BP. These data demonstrate the potential to reverse the catabolic and inflammatory effects of catecholamine excess with pre-operative alpha-blockade therapy.
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P7

Abstract withdrawn

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P8

Multivessel spontaneous coronary artery dissection in a young woman using cabergoline
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Introduction
Spontaneous coronary artery dissection (SCAD) is a unique clinical entity gaining rapid recognition as an important cause of acute coronary syndrome (ACS). Cabergoline induced SCAD is exceedingly rare. We present a unique case of a young woman with multivessel SCAD on a background of Cabergoline use. To date, limited literature is available on cabergoline induced SCAD and we describe the first ever reported case in our country.
Case report
A 45-year-old woman presented to the Emergency Department with acute, heavy and severe chest pain of 30-minutes duration which radiated to her arms and back while driving. Her admission vital signs were within normal limits. Her physical exam was normal and she denied both systemic illness and recent stress. She has a background of hypercholesterolemia and a prolactinoma diagnosed 20 years prior. She was lost to follow up with her endocrinologist for several years but continued to take Cabergoline 500 mg weekly since her diagnosis. Her ECG was non ischemic. Initial troponin was 671 ngl/l (0-14ng/l). The remaining bloods including full blood count, liver, renal, bone, lipid profile and HBA1c were normal. She was started on Non-ST Segment Elevation myocardial infarction (NSTEMI) management. Her echocardiogram confirmed posterior-lateral and apical hypokinesis with impaired left ventricular ejection fraction 45%. Coronary angiogram confirmed a mid to distal left anterior descending (LAD) artery SCAD. Left circumflex artery also showed SCAD extending to the distal end of obtuse marginal branch. Based on angiographic review and her hemodynamic stability she was managed conservatively based on latest SCAD guidelines. Following endocrinology input her Cabergoline was ceased.
Conclusion
Clinicians should have a high index of clinical suspicion of SCAD in young women with ACS presentations. Cabergoline induced SCAD is an uncommon but important clinical entity which must be considered in those presenting with ACS while taking this medication.
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P9

Difference in the relation between circulating free thyroxine (FT4) and thyroid stimulating hormone (TSH) levels for people taking levothyroxine compared with those who are on no thyroid hormone replacement

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Introduction
There continues to be much discussion around optimization of thyroid hormone status in hypothyroid individuals. We looked the way that FT4/TSH relate to each other in people who underwent a check of thyroid function (TFT) split between those on levothyroxine replacement (monitoring-test) and those who underwent TFT check as a screening test for thyroid hormone imbalance not-on-levothyroxine.
Methods
TFT test (FT4/TSH) results were taken from the Salford Hospital (UK) laboratory system for a 3-year period. To minimise comorbidity effects only samples taken in GP-Practices were used and for untreated patients only those who had single tests results were used. For treated patients, median value across all results was used.
Results
Total data included 290,000 tests for 130,000 patients. However, the FT4/TSH results were used from 12,006 (F 9,231/M 2,775 & (age <60 5,850 & age $>=60$ 6,567)) treated patients with 43,846 actual test results. These were compared to the single results for 43,394 untreated patients (F 24,386/M19,008 & Age <60 32,537/Age $>=60$ 10,857). Cluster analysis showed overall for untreated patients, median values for TSH $=1.8$ mUnits/l and FT4 $=15.5$ pmol/l, with 24% patients falling outside the 5%/95% limit, while for treated patients median TSH $=3.6$mUnits/l ($+100\%$ vs untreated) and FT4 $=18.9$ pmol/l ($+22\%$), with 22 % of treated patients falling outside the treated 5%/95% percentile boundary. When considered against the **untreated boundary, 75% of treated results fell outside;** by sex females 78%, males 68%; by age <60 73%, $>=60$ 74%.
Conclusion
The current treatment regimens being applied of either low or high dose levothyroxine are not delivering the expected laboratory TFT profiles, with significant numbers of treated individuals being well outside expected values - both TSH/FT4 being significantly higher. This effect seems to be more prevalent in women than men - more concerning given the higher number of women requiring thyroid-hormone replacement.

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P10

A rare case of primary adrenal malignant melanoma masquerading as metastatic adrenocortical cancer

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Introduction
Melanoma is predominantly a skin malignancy, originating from melanocytes. We present a rare case of metastatic primary adrenal melanoma (PAM) mimicking adrenal cortical carcinoma (ACC).
Case report
A 36-year-old male presented with right flank pain, vomiting, pyrexia & 15kg weight loss. CT revealed 6cm adrenal mass; initially treated as an abscess. Despite normal adrenal screening biochemistry & prolonged antibiotics, the mass grew to 8cm, prompting suspicion of ACC. 18^{F}-FDG PET showed high uptake in adrenal mass with multiple lung & peritoneal deposits. Given adrenal biopsy contraindicated, lung biopsy was undertaken; histology indicated ACC: malignant epithelioid cells with pleomorphism & nuclear inclusions. The patient was informed of metastatic ACC diagnosis & Etoposide-Doxorubicin-Cisplatin-Mitotane (EDP-M) chemotherapy was planned.
Progress
Biopsy immunohistochemistry contradicted histology, demonstrating classic features of melanoma (cytoplasmic staining: MelanA, HMB45 & S100) & absence of adrenal markers; molecular test revealed the most common melanoma mutation: BRAF V600. No evidence of melanoma elsewhere noted. Urine steroid profile ruled out ACC. Melanoma MDT confirmed metastatic PAM & combination immunotherapy of Ipilimumab and Nivolumab was initiated. The patient is doing well on immunotherapy and heading towards disease remission.
Discussion
This case highlights diagnostic challenges of a) benign vs malignant adrenal mass, b) primary ACC vs secondary adrenal metastasis & c) malignancy type identification. Adrenal gland is a recognized metastatic site for melanoma [1] , but primary site for melanoma origin is exceptionally rare; 23 cases reported in literature.
Possible explanation
Adrenal medullary blasts & melanoblasts have a common embryological origin from neural crest.
Learning points
1. PAM should be considered as differential diagnosis in unilateral adrenal mass mimicking ACC. 2. To await immunohistochemistry & molecular test results before administering cancer-specific treatment. 3. Urine steroid metabolomics is useful in differentiating ACC from other malignancies/pathologies.
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P11

Salivary cortisol vs serum cortisol in the overnight dexamethasone suppression test: results of a service evaluation at one centre

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Introduction
Saliva hormone measurements are increasingly being applied in every day clinical practice. In relation to salivary cortisol/cortisone measurement there is a particular advantage, with minimal chance of cross reaction with prescribed glucocorticoids. We here evaluated the utility of these measurements in patients undergoing an overnight (1 mg) dexamethasone suppression test (ONDST).
Methods
A service evaluation of salivary cortisol/cortisone in vs serum cortisol in ONSDT was undertaken. Patients underwent ONDST, with parallel measurement of serum cortisol and salivary cortisone, by electrospray positive ion mode liquid chromatography tandem mass spectrometry. The cut point for adequate suppression of salivary cortisone was <2.7 nmol/l; serum cortisol was <60 nmol/l.
Results
Results for 32 individuals (23% men (median age 62) and 77% women (median age 59) were analysed. In 40% of individuals an adrenal adenoma was present; in 53% Cushings Syndrome was suspected. Serum cortisol failed to suppress in 50% of cases: 8 definite and 8 indeterminate. We found a strong correlation between 0900 salivary cortisone and serum cortisol after 1 mg ONDST beta $=29.2$ (95%CI 8.91, 49.7) $P = 0.008$. Performance of post-dexamethasone salivary cortisone (<2.7 nmol/l) alone in relation to suppression of serum cortisol (<60 nmol/l) was analysed. Concordance was 100% between tests: Cohens Kappa 1.0 $P < 0.0001$. For both tests a definite Cushings Syndrome diagnosis the concordance was 75% Kappa $=0.5$ $P = 0.01$. The sensitivity of both tests for Cushings was 100% with a positive predictive value of 50%.
Conclusion
We have demonstrated test reliability and clinical utility in substitution of salivary cortisone for serum cortisol in the ONDST (post-midnight Dexamethasone). Salivary cortisone could therefore be used as an alternative sampling method which does not require venepuncture or attendance at hospital. Application of the test has the potential for significant savings of money and time.

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P12

Exploring patient and caregivers' perceptions and experiences of administering hydrocortisone injection during an adrenal crisis: a mixed-methods cross-sectional study

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Background
Patients with AI and their caregivers face significant challenges during adrenal crises, particularly with hydrocortisone injections often requiring up to 20 steps to administer, which impedes effective self-treatment.
Aim
To explore the perceptions and experiences of patients with AI and their caregivers regarding the administration of hydrocortisone injections during an adrenal crisis.
Methods
Participants were recruited through two USA-based patient advocacy groups: Adrenal Insufficiency United (AIU) and the CARES Foundation. An online survey, incorporating both quantitative and qualitative questions, was administered to gather data on demographic information and specific challenges encountered with the hydrocortisone injection process. Free-text comments were analysed using content thematic analysis to generate themes, which were quantitatively analysed using SPSS descriptive statistics.
Results
The survey included 688 participants, mainly parents of children with adrenal insufficiency (62.7%), with a mean patient age of 20.8 years (SD = 18.0), and 29.5% of patients being under 7 years of age. Most hydrocortisone injections were administered by healthcare professionals or parents. Vomiting was the primary trigger for adrenal crises. Fifteen themes, categorized into Device Factors, External Factors, and Emotional Factors, explain the barriers and enablers of administering hydrocortisone during an adrenal crisis. The most prevalent barrier was the complexity of the injection process (n = 277; 44%), while the most helpful factor was the portability and convenience of the all-in-one powder and solution Act-o-Vial preparation (n = 221; 38%). Other key factors included the effectiveness of the hydrocortisone injection in treating adrenal crisis, the need for assistance to inject, and anxiety related to injections.
Conclusion
This study underscores the necessity for a simpler injection device to enhance patient self-confidence and self-administration ability. Heightened awareness among healthcare professionals and the public regarding adrenal crisis is imperative for timely management and prevention of avoidable hospital admissions.

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P13

Conn's syndrome, where is the lesion?

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Primary Aldosteronism (PA) can be due to a variety of underlying pathologies, predominantly aldosterone-producing adenomas and adrenal hyperplasia. PA is one of the leading causes of secondary hypertension in young patients. We describe the case of a young male presenting with a stroke in 2012, six years later he had a second ischaemic event and was noted to have treatment resistant hypertension. This constellation of symptoms prompted an investigation revealing hypertension, hypokalemia, and elevated aldosterone:renin ratios, culminating in a diagnosis of PA. However multiple imaging modalities including CT, MRI, PET-CT across a 6 year period were unable to identify any adrenal adenoma/ hyperplasia. Nine years after his initial stroke this patient was found to have mildly enlarged bilateral adrenal glands, with micronodular appearance, this was reported as a 12mm left adrenal lesion with 77% absolute washout on CT imaging. Subsequent adrenal vein sampling (AVS) revealed lateralisation to the **right** adrenal gland, adding complexity to the diagnostic puzzle. Here we have a case where the aldosterone secreting lesion was initially unable to be localised, then contradictory data between imaging and AVS. In this case PET-CT did not demonstrate an adrenal lesion. Recent Nature research has demonstrated non-inferiority between Metomidate PET-CT and AVS; however the access to such imaging techniques is a challenge. This case poses questions for Endocrinologists due to standard diagnostic techniques giving seemingly contradictory localisation of the lesion. Moreover, the chronology of the events in this case creates another unanswered question: whether this gentleman had two subsequent pathological processes (one being micro-tumours followed by an unrelated adrenal lesion) or whether we were simply unable to identify where the tumour was initially. These uncertainties underscore the complexities of diagnosing and managing PA, urging further exploration into novel diagnostic approaches and refining existing methodologies to improve patient outcomes.

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P14

Adrenal cushing syndrome presenting as type 2 diabetes

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Background
Cushing syndrome is caused by chronic, autonomous excess cortisol and causes a wide range of clinical manifestations. Impaired glucose metabolism which often leads to diabetes is a common complication of long-term exposure to both exogenous and endogenous glucocorticoid and plays a vital role in contributing to morbidity and mortality in patients with Cushing syndrome. The prevalence of diabetes in Cushing syndrome varies between 20 and 50% and the overall prevalence of impaired glucose metabolism reaches nearly 70%. We present a case of Adrenal Cushing Syndrome which initially presented as newly diagnosed diabetes.
Case presentation
A 48-year-old woman was referred to the Diabetes clinic in Hong Kong with new diabetes and paraesthesia in her hands. Further tests suggested adrenal Cushing (ACTH undetectable, 24-hour UFC 583 nmol/l (11.9-485), ODST 516 nmol/l (<50 nmol/l)). On returning to the UK, she was referred to the Endocrinology clinic for further evaluation. She was found to have Cushingoid features including thin skin, easy bruising, and facial plethora. Repeat biochemistry strongly supported the diagnosis of adrenal Cushing-(ODST cortisol 561 nmol/l (<50 nmol/l), 24-hour UFC 701, and ACTH 5 ng/l (0 - 46)). CT Abdomen showed a left adrenal adenoma. Repeat HbA1c was 47 mmol/mol with a fasting plasma glucose 6 mmol/l, therefore she was advised to continue with lifestyle adjustment. She subsequently had laparoscopic adrenalectomy (Weiss score 0/5, KI 67 2%) with postoperative good glycaemic control (HbA1c 40).
Conclusion
This case highlights the common association between Cushing syndrome and impaired glucose metabolism and diabetes. Early diagnosis and treatment of diabetes can reduce overall cardiovascular morbidity and mortality in patient with Cushing syndrome. Although fasting blood glucose and HbA1c may be normal in some patients, they may still have post prandial hyperglycaemia. Therefore, an OGTT should be considered in all patients with Cushing syndrome to identify glucose metabolism abnormalities.

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P15

Histopathological reporting of pheochromocytomas and paraganglioma (PPGLs)

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PPGL's are tumours arising from adrenomedullary and extra-adrenal chromaffin cells. The Royal College of Pathologists (RCPath) has issued updated guidance on the minimum dataset requirements in the histopathological reporting of PPGLs. The datasets enable pathologists to grade and stage cancers in a consistent manner and provide prognostic information, to facilitate the highest standard of care for patients. This retrospective analysis was conducted to assess if PPGL histopathological reports from within a model 4 hospital in Ireland would be in compliance with updated guidance. Data was reviewed from all specimens coded as adrenal in the laboratory information system for a period of 10-years. The RCPath dataset outlines 16 core items that should be included in each report and 5 non-core items that may be included to provide a comprehensive report or to meet local clinical or research requirements. A total of six histopathological specimens were reported as containing phaeochromocytoma. None of these reports met the RCPath updated minimum dataset requirements. The results [case 1 (12/16 core, 3/5 non-core), case 2 (10/16 core,1/5 non-core), case 3 (11/16 core, 1/5 non-core), case 4 (12/16 core, 2/5 non-core) case 5 (12/16 core, 2/5 non-core) and case 6 (11/16 core, 2/5 non-core)] show variable levels of compliance. All histopathological reports predated the updated RCPath recommendation, despite this on average 70% of core dataset items were reported. It is recommended that at least 95% of reports on cancer resections record a full set of core items. At present there is a narrative structure to reporting at our institution, this may account for the omission of core items, presumably as they were absent. However, the implementation of reporting templates should promote compliance with the minimum data-set, while retention of a narrative descriptive field allows reporting pathologists to include any surplus information or context they feel is required.

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P16

A forgotten relation between adrenal insufficiency and auricular petrification

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Background
Calcification or ossification of the auricular cartilage, known as "petrified ears," is a rare condition typically linked to local trauma, frostbite, or inflammation. Endocrinopathies, especially adrenal insufficiency, has been historically linked with this condition. There are several reports of its association with different causes of primary adrenal insufficiency but only a very few reported cases of secondary adrenal insufficiency leading to bilateral auricular calcification [1–4]. We are highlighting a case of hypopituitarism resulting in bilateral auricular calcification.
Case Report
This 31-year-old gentleman had a history of suprasellar germinoma diagnosed at the age of 15. He underwent surgery and radiotherapy in 2009 and developed panhypopituitarism soon afterwards treated with hydrocortisone, levothyroxine, testosterone and desmopressin. He was also on growth hormone replacement until his early adulthood. Over the last year, he started noticing both ears were getting hard and felt stony causing severe pain. He underwent a CT temporal bone which showed extensive calcification of both auricular cartilages. His adjusted calcium and phosphate levels were within normal range.
Discussion
The exact pathophysiological mechanism of hypocortisolism related calcification of the elastic cartilage remains uncertain. Barkan *et al*., previously have shown the association of hypopituitarism with auricle ossification and they proposed that the ossification was the result of endogenous cortisol deficiency [5]. Alteration in calcium homeostasis has also been suggested to contribute to ectopic calcification in cortisol deficiency, but calcium level was normal in our patient [6]. Bilateral involvement is more frequent than unilateral involvement, and petrified ears are more commonly encountered in males than in female [7].
Learning Points
1. Petrified ears encountered in clinical practice without a clear aetiology should prompt consideration of possible undiagnosed endocrinopathies, especially adrenal insufficiency.

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P17

WES as a tool for differential diagnosis of adrenal insufficiency in sudanese children

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Studies of adrenal insufficiency (AI) in African children are rare and diagnosis is challenging, especially in resource limited settings where biochemical and genetic testing are restricted. We describe the genetic characterisation of a cohort of Sudanese children, identifying founder effects and commonly mutated genes that will improve their treatment, expand our knowledge of AI, and expedite diagnosis of future patients. 48 patients from 43 families (31M:17F) with presentation of AI paired with biochemical finding of low cortisol ± high ACTH were included in this study. Exclusion criteria were clinical and/or genetic diagnosis of CAH or Triple A syndrome. Additional co-morbidities observed in some patients included white matter changes, muscular dystrophy, gait abnormalities, cataracts, obesity, and deafness. Whole exome sequencing (WES), copy number variation analysis (CNV), variant prioritisation (Exomiser/QCI) and splice predictions (SQUIRLS) were performed as a genetic diagnostic pipeline. Variants were confirmed by Sanger sequencing and possible splicing mutations were functionally assessed using the Exon Trap vector (MoBitech). *Genetic diagnosis was achieved for 26/43 families, with mutations in ABCD1* (7), *NNT* (5), *AIRE* (3) the most affected genes. CNV analysis identified a *CYP11B1-2 fusion event and a deletion incorporating 5-exons of AIRE*, and 2 downstream genes. This *AIRE* deletion was identified in 2 unrelated families and 3 patients from 2 families had a splicing defect in *NNT* (c.9193G>A) which resulted in partial exon skipping. Incidental findings in *MC4R, ADGRV1*, and *CNDP1* are likely to be causative of the obesity, cataracts and deafness, and abnormal gait respectively observed in patients. This study has not only diagnosed 60% of our Sudanese cohort but also identified commonly mutated genes and 2 possible founder effects. Sanger sequencing of bespoke candidate genes might provide a cheaper alternative, increase, and hasten the diagnosis rate of at-risk patients in resource limited settings.

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P18

Adrenal insufficiency associated with mutations in haem biosynthesis genes, is it a coincidence?

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Primary adrenal insufficiency (PAI) is associated with mutations in more than 25 genes, in our cohort, most commonly the melanocortin receptor gene (*MC2R*), its accessory protein (*MRAP*), steroidogenic enzymes (*STAR* and *CYP11A1*), and a gene involved in mitochondrial anti-oxidant defence (*NNT*). While mutations in haem biosynthesis genes have only ever been implicated as pathogenic in a group of diseases known as porphyria, over the years, tantalising case reports have linked the two conditions. We found 7 families (11 individuals) with defects in haem biosynthetic enzymes that have flagrant AI with or without porphyria; 1) a kindred ($n = 4$) from Egypt with biallelic mutations in the protoporphyrinogen oxidase (*PPOX*) gene p.(Glu339Lys), who have a spectrum of symptoms ranging from failure to thrive, focal neurology, cutaneous lesions of variegate porphyria along with severe AI. 2) Three kindreds with mutations in coproporphyrinogen oxidase (*CPOX*), (i) a preterm female of Asian descent homozygous for p.(Pro367Ala) mutation, who presented with anaemia, jaundice, focal neurology and cutaneous manifestations of Hereditary Coproporphyria (HCP) along with AI, (ii) siblings of Kurdish descent homozygous for p.(Ser28*) mutation, the boy had HCP along with AI and Disorder of Sex Development, while the girl has no clinical manifestations of HCP but has severe AI, and (iii) a patient with HCP from France who presented with AI aged 64, this patient had a urinary steroid metabolome that showed elevated levels of 11-deoxycorticosterone and 11-deoxycortisol. 3) Three adult patients with mutations in Hydroxymethylbilane Synthase (*HMBS*) gene who presented with AI during acute hepatic porphyria attacks. The evidence linking mutations in porphyria genes with PAI is ever-growing suggesting that testing adrenal function might be beneficial for these patients and that the causal genes should be considered for inclusion in gene panels for AI.

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P19

Pheochromocytoma presenting as cardiac emergencies

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Case 1
A 65 year-old lady presented to ED with chest pain and collapse. Her PMH includes hypothyroidism and gastritis.
Results and management
Her ECG was normal. Her troponin levels were raised at 48 and 70.6. CTPA which was requested as her D-dimer was high (1034), showed no PE but showed hypodense lesions in liver. In view of this, CT TAP was done which showed benign liver cysts, and a 2.6 cm adrenal mass. She was treated for ACS. Her ECHO and Angiogram were unremarkable. No clear underlying cause for her ACS was identified and was concluded that she had probable Type 2 MI secondary to cardiac arrthymia. Cardiac MRI showed a small inferolateral wall infarction. Further adrenal workup showed raised plasma metanephrine of 1249 pmol/l (Normal: <510 pmol/l), and plasma normetanephrine of 1456 pmol/l (Normal: <1180 pmol/l). CT adrenals showed benign right adrenal adenoma. MIBG scan showed right adrenal phaeochromocytoma. Subsequently she underwent laparoscopic right adrenalectomy.

Case 2
Whilst awaiting investigations for a right adrenal incidentaloma, a 76-year-old gentleman admitted to ITU following out of hospital cardiac arrest. His PMH includes hypertension and hyperlipidaemia.
Results and management
His ECG was unremarkable apart from old RBBB. His bedside ECHO was normal. CT PA showed no evidence of PE. His troponin was raised at 109 which subsequently normalised. No clear underlying cause for his cardiac arrest was identified. Adrenal workup showed raised plasma metanephrine of 548 pmol/l (Normal: < 510 pmol/l) and plasma normetanephrine of 1724 pmol/l (Normal: < 1180 pmol/l). MIBG scan showed 3.4cm right adrenal phaeochromocytoma. He later underwent laparoscopic right adrenalectomy.
Discussion
Phaeochromocytoma is a rare cause of secondary hypertension and cardiac complications. No clear cause has been identified for the acute presentations apart from phaeochromocytoma in our patients. Our cases illustrate the need for considering phaeochromocytoma in patients presenting with unexplained cardiac emergencies.

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P20

Primary aldosteronism in a patient with cushing's disease in remission

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A 47-year-old man attending with a history of Cushing's disease in remission following transsphenoidal surgery in 2013 continued to experience resistant hypertension which warranted further investigation. Postoperatively he was prescribed hydrocortisone 10 mg twice daily and desmotab 0.2 mg nocte for ACTH deficiency and diabetes insipidus. Over the course of six years antihypertensive therapy escalated until he required five agents – ramipril 10 mg, amlodipine 10 mg, bisoprolol 10 mg, spironolactone 100 mg, doxazosin 8 mg. He had ambulatory blood pressure monitor daytime average of 142/85mmHg and nighttime average of 150/88mmHg with episodes of spontaneous hypokalaemia and symptoms suggestive of obstructive sleep apnoea. Initial investigations ruled out Cushing's disease recurrence, cortisol 11 nmol/l post-1 mg overnight dexamethasone suppression test. Biochemical work-up revealed elevated aldosterone 877 pmol/l, and a fully suppressed renin <5mIU/l, normal potassium 3.9 mmol/l and normal plasma metanephrines, taken whilst off beta-blockers. Aldosterone-renin ratio was 175.4 suggestive of primary aldosteronism. Difficult-to-control hypertension significantly compromised the interpretability of biochemical workup. Equally, a saline suppression test was not suitable. Cross-sectional imaging revealed a 1.2cm left adrenal nodule (35 Hounsfield units). On the first attempt of adrenal vein sampling, there was a failure to cannulate the right adrenal vein. Repeat testing was successful and lateralized to the left adrenal gland, with a lateralization index of 39.5 and a contralateral suppression index of 0.18. He underwent robotic-assisted left adrenalectomy in March 2024, histology confirmed a 9mm adrenocortical nodule. He was discharged home on amlodipine 10 mg and bisoprolol 10 mg with excellent blood pressure control. Key learning points from this case centre around the diagnostic workup of primary aldosteronism including the interpretability of biochemistry during antihypertensive agent use, and the interpretation of adrenal vein sampling results. It also highlights the importance of considering alternative endocrine diagnoses in patients attending the outpatient clinic.

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P21

Impaired 11β-hydroxysteroid dehydrogenase type 2 activity in chronic kidney disease disrupts 11-oxygenated androgen biosynthesis

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In vitro data highlight a potential role for 11β-hydroxysteroid dehydrogenase type 2 (HSD11B2) in 11-oxygenated androgen biosynthesis, converting 11β-hydroxyandrostenedione (11OHA4) to 11-ketoandrostenedione (11KA4), the direct precursor of the potent androgen 11-ketotestosterone(11KT). As the kidney is the major site of HSD11B2 expression, we hypothesized that patients with chronic kidney disease (CKD) would have reduced 11-oxygenated androgen biosynthesis due to impaired HSD11B2 activity. In this cross-sectional multicentre cohort study of patients with CKD and healthy controls, serum concentrations of 11-oxygenated androgens, classic androgens and glucocorticoids were measured by tandem mass spectrometry. Cortisol (F)/cortisone (E) ratios, validated surrogate markers of HSD11B2 activity, were calculated. A computational model of peripheral 11-oxygenated androgen biosynthesis was fitted to the serum data to calculate relative HSD11B2 expression levels for each participant. We included 85 patients with CKD [65% male, median age 64 years, median eGFR 22ml/min] and 56 healthy controls [11% male, median age 34 years, median eGFR 103ml/min]. HSD11B2 activity declined with eGFR, with higher F/E ratios in CKD patients than controls [serum F/E 10.7 vs 5.8; urinary F/E 0.8 vs 0.6 ($P < 0.01$)]. Serum concentrations of E, 11KA4, 11KT and 11β-hydroxytestosterone (11OHT) were significantly lower in patients with CKD compared to controls ($P < 0.01$ for each). Patients with CKD had an increased ratio of 11OHA4/(11KA4+11KT+11OHT), reflective of reduced HSD11B2-mediated activation of 11-oxygenated androgens. A computational model based on enzyme kinetic parameters of HSD11B2, 11β-hydroxysteroid dehydrogenase type 1, 17β-hydroxysteroid dehydrogenase type 2 and aldoketoreductase 1C3 accurately predicted HSD11B2 as the key enzyme responsible for reduced 11-oxygenated androgen biosynthesis in CKD. Predicted HSD11B2 expression correlated with eGFR. This is the first *in vivo* study to confirm a central role for renal HSD11B2 in the peripheral activation of 11-oxygenated androgens. Further research is required to determine the clinical implications of this observation for patients with CKD.

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P22

Functional imaging in primary aldosteronism: a useful tool in a complex case

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A 39 year-old man was referred with resistant hypertension from the nephrology service. Diagnosis was at 26 years and associated with hypokalaemia, left ventricular hypertrophy and proteinuria. Initial results (on amiloride) were: Aldosterone (A) 1900 pmol/l, direct renin (R) 10.2mU/mL and Aldosterone:Renin Ratio (ARR) 186. Saline suppression testing off interfering medications confirmed primary aldosteronism (PA): Aldosterone 1050 pmol/l, Renin 4.1uIU/mL and ARR 256 at four hours. Adrenal CT demonstrated bilateral adrenal abnormalities including right-sided (21mm) and left-sided (12mm) lesions. Adrenal vein sampling was suboptimal with incomplete cannulation of the right adrenal vein, but showed suppression on the left [Aldo/Cortisol (A/C) ratios: inferior vena cava 6.1 and left adrenal vein 0.9]. He was initially managed with four agents at high doses, including spironolactone. After MDM discussions, C^{11}-metomidate PET scan was performed. This demonstrated bilateral focal uptake, albeit with the highest uptake in the 21mm right sided nodule with an SUV max ratio of 1.44:1 compared to the left adrenal nodule. After counselling, the patient underwent right laparoscopic adrenalectomy for disease control rather than with curative intent. Surgery was complicated by transient mild hypotension and acute kidney injury. Four weeks later biochemistry had normalised (A 294 pmol/l, R 16.0 mU/ml, ARR18). At eight weeks postoperatively, he required two anti-hypertensives at lower doses with

BP 127/85. He therefore currently demonstrates complete biochemical cure and partial clinical cure (PASO criteria). However close surveillance is planned given the potential for the unmasking of left-sided disease. This is the first patient at our Regional Centre where C11-metomidate PET scanning was used to investigate PA with bilateral lesions. Molecular imaging may, in the future, replace rather than supplement dynamic testing in these complex cases and may open the door to selective nodule ablation or debulking surgery in bilateral disease.

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P23

Management and outcomes of patients treated with mitotane for adrenocortical carcinoma in a tertiary adrenal tumour centre in Ireland

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Adrenocortical carcinoma (ACC) is a rare aggressive tumour with median overall survival of 3-4years. Mitotane may be recommended for use in ACC in an adjuvant or palliative setting. It requires close clinical surveillance and therapeutic drug monitoring due to adverse effects and toxicity potential. This audit reviewed the management practices in patients with ACC prescribed mitotane therapy from 2010 to 2023 in Beaumont Hospital compared to the 2018 ESE/ENSAT clinical practice guidelines. The cohort consisted of 24 patients (54% female), with a median age at diagnosis of 32years (IQR 33-60) and median follow up 5.5years (IQR 2-8) receiving adjuvant (75%) and palliative (25%) mitotane therapy. Median tumour size at presentation was 10cm (IQR 6.4-17.2). Ki67 index was $<10\%$ in 56%, median Weiss score was 5/9 (IQR 4-7). Therapeutic target range mitotane was reached in 88% of patients for a median time of 7months (IQR 2-11), with median duration of therapy 16months (IQR 9-25). Treatment-related adverse events included abnormal thyroid function (83%), nausea (67%), diarrhoea (46%) and dyslipidaemia (92%) with 41% requiring statin therapy. Mitotane was transiently paused during the treatment period in 67% of patients due to adverse effects and discontinued completely in 17% due to hepatotoxicity. Median maximum total daily dose of mitotane was 6 mg (IQR 4.75-6). Median total daily dose of hydrocortisone was 50 mg (IQR 50-60). Of patients who completed mitotane therapy, adrenal function recovered in ($n = 7/13$) 54% after a median time of 13 months (IQR 11-36). Progressive disease occurred in 5 patients and 5 patients died during follow up. Disease stage at diagnosis was predictive of mortality [ENSAT stage IV HR 41.8 (CI 2.6–4008)]. Recommended standards are being met in the management of ACC with mitotane in Beaumont Hospital. This audit highlights the challenges and need for close monitoring of patients with ACC on mitotane.

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P24

The aldosterone renin ratio – high rates of positive tests, low rates of onward referral; a single centre quality improvement project

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The Endocrine Society Guidelines 2016 recommend the Aldosterone Renin Ratio (ARR) to screen for Primary Hyperaldosteronism (PHA), yet we perceive low rates of referral to our service for such patients. Here we report a retrospective audit of ARR measurements requested through Regional Hospital Mullingar 01/01/2023 – 31/12/2023. ARR results were obtained directly from the referral laboratory. An assay specific ARR threshold >25 (ARR+) indicates possible PHA. We reviewed patient records for all ARR+ patients. A unified Excel database, including 144 consecutive ARR measurements from 139 patients, was created and interrogated using basic functions. Mean ($\pm$ standard deviation) patient age was 45.9 ($\pm$15.7) years, 67/139 (48.2%) were female. Most ARR requests originated from secondary care (110/144, 76.4%). ARR+ was observed in 34/144 (23.6%) of samples, representing 34 unique patients. The indication for testing was evident for 19/34 (55.9%) ARR+ patients; resistant hypertension (9/19, 47.36%), early onset hypertension (6/19, 31.57%), adrenal adenoma (3/19, 15.78%) and hypokalaemia (1/19, 5.26%). Simultaneous serum potassium measurement was available for only 111/144 (77.1%) ARR measurements, with concomitant hypokalaemia observed in 6/144 (4.2%) instances. Medication records were available for 18/34 ARR+ patients with concomitant interfering Anti-Hypertensive therapy noted in 11/18 (61.1%) measurements, including 5/18 (27.8%) and 1/18 (5.6%) measurements on Beta Blockers and Spironolactone respectively. Only 8/34 (23.5%) ARR+ patients had attended the Endocrinology service. In total, these data indicate low rates of referral for ARR+ patients, high rates of ARR measurement on interfering medications, and suboptimal correction of hypokalaemia prior to testing. Twenty-six ARR+ patients have been identified for early assessment in the Endocrinology Clinic. These data will be disseminated to service users in both primary and secondary care. Going forward we will circulate to memorandum to service users advising of the assay specific ARR reference range and offering guidance regarding confounding by Anti-Hypertensive Medications and Hypokalaemia.

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P25

Comparison of a morning serum cortisol concentration against a morning salivary cortisone concentration to predict the outcome of a short synacthen test

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The short synacthen test (SST) is a well-established method to assess adrenal function. Recent data has suggested a waking salivary cortisone may be a more convenient alternative to serum cortisol testing to predict SST outcome. This study compares the performance of a 9am serum cortisol sample to a simultaneous 9am salivary cortisone sample to predict SST outcome, to establish which method results in a greater reduction in SST requirements. We recruited 122 participants to undergo an SST with paired baseline serum cortisol, salivary cortisone, ACTH and DHEAS concentration. Receiver-operating characteristics (ROC) curve analysis demonstrated that both serum cortisol and salivary cortisone are good predictors of SST response (AuROC 0.96 and AuROC 0.92, respectively). All participants with a morning serum cortisol <117 nmol/l failed the SST (100% specificity, 42% sensitivity). All those with a morning serum cortisol >266 nmol/l passed the SST (100% specificity, 71% sensitivity). If SST were performed only when morning serum cortisol was indeterminate (117-266 nmol/l), 64% of SSTs could be avoided. All participants with 9am salivary cortisone concentration <8.58 nmol/l failed the SST (99% specificity, 45% sensitivity) and all those with 9am salivary cortisone >41.1 nmol/l passed the SST (100% specificity, 29% sensitivity), reducing SST requirements by 34%. Where serum cortisol concentration was indeterminate (117-266 nmol/l) ($n = 42$), the addition of a morning salivary cortisone concentration did not significantly reduce the need for SST compared with serum cortisol concentration alone ($P = 0.68$). Participants with a low morning cortisol (<266 nmol/l) and low DHEAS concentration were more likely to fail the SST than those with a low cortisol alone (RR 3.54, $P = 0.004$). Serum cortisol (9am) resulted in a much greater potential reduction in SST requirement than salivary cortisone (9am). The timing of sample collection appears to be a key determinant in the use of salivary cortisone to predict SST outcome.

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P26

Case report: congenital adrenal hyperplasia or adrenal hypoplasia congenita

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Adrenal hypoplasia congenita (AHC) is a rare and potentially life-threatening disorder of adrenal gland development, resulting from deletion or mutation of the DAX-1 gene. DAX-1 is located on the short arm of the X chromosome, and mutations result in X-linked primary adrenal hypoplasia, hypogonadotropic hypogonadism, and azoospermia in men. During the neonatal period, male

patients present with signs and symptoms often indistinguishable from those seen in salt-losing 21-hydroxylase deficiency and are frequently misdiagnosed with congenital adrenal hyperplasia (CAH). We present the case of a 45-year-old gentleman, referred for management of steroid and androgen replacement therapy after recently moving from South Africa to Ireland. His past medical history included congenital adrenal hyperplasia, diagnosed at birth, and primary hypothyroidism. He was treated with hydrocortisone 10 mg twice daily, fludrocortisone 0.1 mg once daily, intramuscular testosterone 200 mg twice per month (last dose 4 months previously) and levothyroxine 200 mg daily. His only brother died from an adrenal crisis age 4 years. He had no other family history of endocrinopathy and no biological children. On examination, he was tall and measured 2.02metres. Secondary sexual characteristics were normal (axillary and pubic hair Tanner stage 5); however, his testes were rudimentary. Biochemistry revealed hypogonadotropic hypogonadism, LH <0.3IU/l (1.2-8.6), FSH $<$ 1.2IU/l (1.3-19.3) and testosterone <1.39 nmol/l (6.07-27.10). Samples have been sent for DAX-1 genetic analysis. This case highlights the importance of critical assessment of biochemical and genetic studies in patients with adrenal insufficiency to determine the cause. Establishing the correct aetiology of adrenal insufficiency is vital for identifying potential associated comorbidities, inheritance, and optimal management.

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P27

Diagnostic and therapeutic challenges of metastatic pheochromocytoma; case series

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Introduction
We present cases of metastatic pheochromocytoma highlighting diagnostic, management, and therapeutic challenges.
Case-1
69 Female, presented with breathlessness, palpitations, and sweating of 4 months. Panic attacks of 10 years. Imaging confirmed left-sided pheochromocytoma, bone, liver, and pulmonary metastases. Plasma metadrenaline (MT) 4471 pmol/l (0-510), normetadrenaline (NMT) >25000 pmol/l (0-1180) LVEF 30%, global LV hypokinesia. Decompensated heart failure, LVEF 5-10%, non-sustained VT despite blockade. Following MDT discussion, left adrenalectomy, splenectomy, and liver resection with Impella (extracorporeal LVAD) support completed, with subsequent gradual cardiac improvement. Large, right humeral metastasis required resection, without mechanical cardiac support for symptom management. Awaiting MIBG-therapy. Genetics negative.
Case-2
69 Male, b/g Parkinson's disease, resistant hypertension, CKD 4. Admitted with acute STEMI, and significant blood pressure fluctuations. Plasma metanephrines were raised given caveats of co-beneldopa and acute MI repeat confirmed plasma NMT >25000. Imaging confirmed left phaeochromocytoma (100x115x80mm) with liver and bilateral lung metastases. Detailed pre-operative assessment and MDT discussions agreed that major debulking surgery, chemotherapy or MIBG therapy were not in patients' best interest. Currently awaiting SSTR PET CT to assess suitability of Somatostatin analogue (SSA) therapy. Genetics pending.
Case-3
63 Female, right pheochromocytoma (MIBG avid) 2014, presented with collapse, multi-organ dysfunction, Tukotsubo-cardiomyopathy, LVEF 8% requiring ECMO. Underwent right adrenalectomy (2015). Genetics negative. Recurrent symptoms and raised metanephrines in 2019; ^{68}Ga-DOTATATE scan confirmed kidney, liver, pelvis, spine, and lung metastasis. SSA therapy commenced 2022. Ga-DOTATATE updated scan 2023 (UK) confirmed avid progressive bone metastases with reduction of soft tissue disease. Plasma MT >25000, NMT 18500. Oral prednisolone 20 mg daily for ITP treatment precipitated pheochromocytoma-crisis with, with severe constipation (extreme faecal loading, dilated small and large bowel). Admitted to ITU for stabilisation. Patient awaiting MIBG therapy.
Conclusion
Management of metastatic pheochromocytoma in dedicated centres with multidisciplinary team, tailoring care to patients is required.

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P28

Assessing the adverse health impacts of glucocorticoid therapy in obstructive lung disease (AHEIGHT Study)

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Background
Oral and inhaled glucocorticoids are commonly used medications in the treatment of obstructive lung disease, and both are associated with glucocorticoid-induced adrenal insufficiency (GIAI) (1). However, the prevalence and clinical consequences of GIAI in this population are incompletely understood.
Aims/Methods
We aimed to assess the prevalence of undiagnosed GIAI in an unselected cohort of patients with asthma attending secondary care, and compare cardiometabolic risk profiles and health-related quality of life (HRQoL) in patients with and without GIAI. Forty-seven participants were recruited prospectively to attend a single study visit which included a short synacthen test (SST), assessment of glucocorticoid exposure over previous 12 months, body composition analysis, markers of metabolic health and HRQoL questionnaires.
Results
The prevalence of undiagnosed GIAI in our cohort was 38%(18/47). The risk of GIAI varied according to glucocorticoid exposure. Three-quarters of participants (12/16) on regular oral and inhaled glucocorticoids failed the SST, compared with 19% (6/31) of those on regular inhaled glucocorticoids and intermittent oral exposure only. There was no difference in markers of asthma control between those who passed or failed SST. Weight-adjusted cumulative prednisolone exposure was significantly higher in those with GIAI than those without, driven by maintenance prednisolone use (34 mg/kg vs. 6.5 mg/kg, $P = 0.001$). There was no significant difference in markers of cardiometabolic health between the two groups. While participants with GIAI reported HRQoL scores suggesting greater physical limitations and poorer physical function than those with intact adrenal function, when age, lung function and participant sex was accounted for, there was no clear association between HRQoL and baseline serum cortisol concentration.
Conclusion
Undiagnosed GIAI is very common in patients with asthma attending secondary care, but the risk varies according to pattern of glucocorticoid exposure. The full extent of the clinical implications of this diagnosis beyond adrenal crisis risk remain incompletely understood.

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P29

Implementing the study into the health status in adults with CAH in the UK and ireland - CAHASE2

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Congenital adrenal hyperplasia (CAH) occurs with an incidence of about 1 in 15,000. Several studies highlighted the suboptimal health status and care provision in adults with CAH that were associated with significant co-morbidities in relatively young adults. In 2023, we implemented CaHASE2 to develop a strategy for prospective collection of longitudinal health data of patients with CAH. Our recent CAH service evaluation suggested significant differences in the approach to CAH patients. The key aim of the current study is the identification of specific unmet needs in patients with CAH, through standardised phenotyping across all participating centres. In September 2023, PIs agreed a minimal dataset for the collection of real-world data in participating centres. The data will be collected using the international CAH registry (I-CAH; https://sdmregistries.org/). CaHASE2 was launched in November 2023. By May 2024, 20 centres from the UK and Ireland have been participating and have provided data into I-CAH. In total 334 adults (201 females, 130 males) with CAH have been recruited. Longitudinal data are available in 149 cases. We aim to recruit at least 400 adults with CAH by November 2024 with a first set of clinical data plus longitudinal data. The data will be analysed after the first completed 12 months cycle, and annually thereafter to assess the current level of care provision and inform the development of national CAH standards. In addition, we will establish a report that will provide participating centres with information about their local care provision in relation to other centres. This project will provide important information about the health status of CAH patients and how this might be related to differences in health care provision. Ultimately, such national data should lead to a higher degree of equality of service provision in all parts of the UK and Ireland.

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P30

Audit of short synacthen® test results in a university teaching hospital

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Introduction
Short synacthen® test (SST) is widely used to assess adrenal function. Controversy remains concerning sample timing and diagnostic cut-offs.
Methods
A retrospective analysis of SST results over 48-month period (1/1/2020 - 31/12/2023) was undertaken. Our protocol involves sampling cortisol at times 0, 30 and 60 minutes post Synacthen® 250 mg IM. Normal SST response was peak cortisol (assayed using Abbott Architect i2000) concentration of $\geq$470 nmol/l at 30 or 60 minutes. The aim of this audit was to assess protocol adherence, and to determine test outcomes and referral patterns.
Results
Of 343 total SSTs, 26 were excluded due to missing time-point data. Of 317 SSTs analysed, 51.1% were female. Median age in females was 53 years (range 17-90 years); in males 59 years (range 17-94 years). 257 tests (81.1%) occurred before 12pm, 60 tests (18.9%) occurred after 12pm. Test requests per speciality were Endocrinology 135 tests (42.6%), Medicine 162 tests (51.1%), of which Oncology had the highest number and Surgery 17 tests (5.3%). Indications for testing were collapse (12.3%), fatigue (11.6%), postural hypotension (9.4%), low AM cortisol (8.2%) and hyponatraemia (6.6%). Of 317 SSTs, 234 (73.8%) passed. Of the 83 (26.2%) who failed, 100% had cortisol level of $<$470 nmol/l at both 30 and 60 mins. Median cortisol at 60 mins was 314.8 nmol/l (range $<$28-467 nmol/l). No patient passed at 30 mins and failed at 60 mins. 47 patients (14.8%) achieved a pass at 60 mins but failed at 30 mins. Of those patients, seven were re-tested with four subsequently passing. One patient had no clinical data available.
Conclusion
The majority of tests were performed correctly as per protocol. Further data interrogation is required to investigate the utility and retention of the 60 min sample timing in our protocol.

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P31

A case of biochemically silent pheochromocytoma masquerading as adrenal incidentaloma

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Introduction
Pheochromocytomas are rare catecholamine-secreting tumors, primarily arising from the adrenal medulla, typically presenting with hypertension, palpitations, and headaches. Diagnosis involves hormonal evaluation and CT imaging with a washout of $<$40-60%. Recent studies show exceptions, with some tumours mimicking non-functional adenomas, displaying $>$60% washout. We present a case exemplifying this, where a symptomatic patient had normal initial biochemical tests but a CT washout of 64%, initially diagnosed as an 'adrenal incidentaloma', later proven otherwise.
Case Presentation
A 29-year-old female presented with dizziness, headaches, and palpitations for 3-4 months. Initial investigations, including plasma and urinary catecholamines and vanillylmandelic acid levels, were normal. Two years later, she presented with vague abdominal pain. CT scans revealed a 32 x 36 x 51 mm lesion in the right adrenal gland with 64% washout, suggesting a non-functional adenoma. One year later, she was admitted to another emergency department with typical presentation of pheochromocytoma - intractable vomiting, palpitations and hypertension. Plasma metanephrines and cortisol levels were markedly elevated. After treatment with alpha blockade, she symptomatically recovered following a one-week in-patient stay. Echocardiography during in-patient stay showed stress-induced cardiomyopathy which fully recovered on cardiac MRI performed a week later. Metaiodobenzylguanidine scan demonstrated intense radiotracer accumulation in the right adrenal lesion, increased in size up to 6.0 cm, confirming the diagnosis of pheochromocytoma. The patient subsequently underwent a successful laparoscopic adrenalectomy. Cytology was positive for pheochromocytoma. Genetic testing was negative for familial catecholamine secreting syndromes. Postoperative recovery was uneventful, with adrenalectomy leading to normalization of metanephrines.
Discussion
Despite normal early biochemistry and a non-typical CT scan for pheochromocytoma, our patient's symptoms recurred, eventually showing biochemical and radiological evidence in line with pheochromocytoma. This case emphasizes the importance of monitoring symptomatic patients for pheochromocytoma despite atypical CT findings. Prompt identification and treatment are crucial to prevent serious morbidity and mortality.

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P32

Hyperthermia-induced cell death in adrenocortical carcinoma: efficacy and mechanisms beyond caspase 3 apoptosis

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Adrenocortical carcinoma (ACC) is a rare, aggressive cancer with notable resistance to conventional therapies. Despite advancements in medical research, understanding the mechanisms behind ACC's resilience and exploring novel therapeutic strategies remain underdeveloped. Hyperthermia, the exposure of body tissue to high temperatures, is a potential treatment. However, the fundamental principles of how hyperthermia induces cell death in ACC are not well understood. This study aimed to address this gap by investigating hyperthermia's effectiveness in inducing cell death in ACC cells and examining the potential role of Caspase-3 mediated apoptosis.
Methods
The ACC cell lines (H295R and HAC15) and the non-cancerous HUVEC endothelial cell line were treated with hyperthermia at 42°C, 45°C, 48°C, and 50°C using temperature-controlled water baths. Cell viability was assessed using Annexin V/Sytox blue (flow cytometry), Calcein/Propidium iodide (confocal microscopy), and the xCELLigence Real Time Cell Analyser. The involvement of Caspase-3 mediated apoptosis was evaluated through western blotting.
Results
Significant reductions in cell viability were observed in H295R and HAC15 cells at 48°C and 50°C, both immediately and 24 hours post-treatment, defining these temperatures as 'lethal' for ACC cells. HUVEC cells were more robust at all treatment temperatures, indicating varied cellular sensitivities to hyperthermia. At 45°C, ACC cells initially showed decreased viability, with less cell death seen 24 hours post-treatment, suggesting an adaptive response to sublethal hyperthermic stress. Results from Annexin V/Sytox Blue staining and Caspase-3 western blotting indicated that Caspase-3 mediated apoptosis was not the primary pathway for hyperthermia-induced cell death in ACC cells.
Conclusion
Hyperthermia at temperatures $\geq$48°C is lethal to ACC cells, presenting new therapeutic possibilities. However, ACC cells show resilience at 45°C, suggesting alternative mechanisms beyond Caspase-3 mediated apoptosis in hyperthermia-induced cell death.

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P33

A case of secondary adrenal insufficiency related to long term steroids

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Background
Topical corticosteroids are frequently prescribed by dermatologists and primary care physicians. They are the most commonly prescribed medications in dermatology practice due to their anti-inflammatory and immunosuppressive properties. If used within a therapeutic window they are safe and effective, and their adverse effects are rare. Prolonged use even with topical agents can result in both local and systemic side effects. However, patients are often unaware of their serious and potentially fatal systemic side effects if used incorrectly. Our patient illustrates the dangers of using topical steroids for prolonged periods particularly if applied over a wide surface area.
Clinical case
The Patient is a 52-year-old female who had been diagnosed with Steroid dependent Pemphigus Foliaceus since October 2020 and was on long term topical

steroids and intermittent courses of oral steroids. In January 2022, she developed an Addisonian crisis which was treated and managed at Nottingham University Hospital. She had a Cushingoid appearance with thinning of the skin, BMI 28.2 kg/m2 but a normal blood pressure. Her 9AM cortisol was low with suppressed ACTH level suggesting that the patient had been receiving supraphysiological doses of steroids. To prevent adrenal crisis and to treat secondary adrenal insufficiency, the patient was on replacement doses of oral hydrocortisone (10 mg/5 mg/5 mg). Advice was given to wean off topical steroids whilst on the physiological doses of steroids. She was started on Tacrolimus instead of steroids for Pemphigus Foliaceus.
Conclusion
Primary care physicians and dermatologists usually warn patients about the potential side effects if used excessively or incorrectly in order to avoid the occurrence of local and systemic side effects, which could be fatal. However, the hazard of using topical steroids in dermatological conditions with a greater absorption if applied over a wide area of skin which can increase the risk of systemic effects can be overlooked.

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P34

An evaluation of the current protocol for short synacthen tests in a single hospital centre

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The short synacthen test (SST) is the most commonly performed investigation to assess adrenal function. We retrospectively audited the SSTs performed by the endocrine department in University Hospital Limerick between 2022 and 2024. The SST was performed as per our hospital protocol. A post-adrenocorticotropic hormone (ACTH) cortisol response of 450 nmol/l (using Roche Elecsys Cortisol III immunoassay) at any time point was considered adequate to rule out adrenal insufficiency. The data were analysed to ascertain the proportion of patients who achieved this level at 30 and/or 60 min. Patients taking the oral contraceptive pill were excluded from analysis. All tests were performed in the morning between 9.00 and 11.00. Eighty patients (61 female) underwent a short synacthen test in the day ward in this time. The Median age was 49 years, range 17-89 years. The most common indication was patients on long term steroids, receiving prednisolone treatment ($n = 23$). 61/80 (76.25%) patients passed the short synacthen test on the 30 minute sample. The median baseline cortisol in the patients who passed the short synacthen test was 319 nmol/l (range: 107-1068). A further 5 patients (6.25%) passed the short synacthen test on the 60 minute sample but not the 30 minute. The median 30 minute cortisol for these patients was 413 nmol/l (403-430 nmol/l). The protocol for short synacthen tests and the cut-off values for normal response varies in different hospitals. In our centre, the SST has previously been performed with both the 30 minute and 60 minute samples. However, using the 30 min cortisol sample post-Synacthen administration alone identifies clinically relevant adrenal insufficiency in the majority of cases. Sampling at 60 minutes should be reserved for patients who have borderline cortisol response at the 30 minute sample.

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P35

An audit of sick-day rule management of adrenal insufficiency in a single centre

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Patients with adrenal insufficiency should be prescribed stress dose steroids in acute settings to avoid adrenal crisis. Adrenal crisis is life-threatening if not recognized and if treatment is delayed. This audit aimed to identify the current practice of sick-day rule management in University Hospital Limerick of admitted patients with adrenal insufficiency. A cross-sectional analysis was conducted on inpatients referred for endocrinology consultation for adrenal insufficiency from January 2023 to December 2023. 59 patients had a diagnosis of adrenal insufficiency. 64.4% female ($n = 38$). The majority (52.5%, $n = 31$) had glucocorticoid-induced adrenal insufficiency, 25.4% ($n = 15$) had known primary adrenal insufficiency, 18.6% ($n = 11$) had ACTH deficiency. Aetiology was unknown in 2 patients. 45.8% ($n = 27$) of patients were on hydrocortisone and 37.3% ($n = 22$) were on prednisolone. Glucocorticoid replacement therapy was not specified in 10 patients. 86% ($n = 51$) of patients had more than one hospital admission per year. Initial blood pressure was noted in 40 patients. 17.5% ($n = 7$) of patients had systolic BP of <100mmHg. Only 17% ($n = 10$) received stress dose in the emergency department before referral to the medical/surgical service for admission. This was administered within 1 hour in 4 patients. 6 patients received the stress dose after an hour. The median time for glucocorticoid administration was 2 hours and 37 mins (Range, 12 mins - 7 hours and 22 mins). 37.3% ($n = 22$) had required stress dose due to concurrent infection, 27.1% ($n = 16$) due to surgery, and 27.1% ($n = 9$) due to non-specific acute illness. 8.5% ($n = 5$) were deemed not to require stress dose. 16.8% ($n = 10$) had required admission to HDU. 50.8% of patients had a length of stay of >14 days. The audit showed suboptimal inpatient sick day rule management. It highlights the need for more education for NCHDs and nursing colleagues on the importance of sick day rule management in patients with adrenal insufficiency.

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P36

Uptake of K20-coated iron oxide nanoparticles by adrenocortical carcinoma cells

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Adrenocortical carcinoma (ACC) is a rare cancer with a poor prognosis, typically resulting in a survival rate of up to 24 months. Treatment options include surgery, chemotherapy, and radiation, but the high recurrence rate underscores the need for new therapies. Magnetic iron oxide nanoparticles (IONP) are emerging as promising tools for cancer treatment due to their customizable size, shape, and surface properties for targeted cellular uptake. Our initial study investigated the uptake of IONP by ACC cells (H295R, HAC15, and MUC1), HUVECs, and primary monocytes, after incubation with 0, 5, 10, 20, and 50 μg/ml of IONP for 24 hours. The results indicated that nanoparticle uptake was both concentration and time-dependent and affected cellular viability. The optimal IONP concentration was found to be 10 μg/ml, which was then used to examine the uptake rate and intracellular distribution. Importantly, IONP did not affect metabolic respiration or steroidogenesis when ACCs were stimulated. The uptake efficiency of IONP by ACC cells decreased when primary monocytes and an HUVEC layer were present, as shown by a Transwell migration system. This study highlighted that ACC cells exhibit non-specific IONP uptake primarily through macropinocytosis. These initial findings provide a basis for future research aimed at enhancing specific uptake by ACC cells, potentially improving applications like magnet-induced thermal ablation or nanobiocontrast.

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P37

11β-hydroxysteroid dehydrogenase type 1 inhibition unmasks multiple pathways that may mitigate the adverse effects of prescribed prednisolone

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Background
Prednisolone is the most prescribed exogenous glucocorticoid (GC) and its use is frequently associated with iatrogenic Cushing's Syndrome. Once administered, prednisolone is converted to inactive prednisone by renal 11β-hydroxysteroid dehydrogenase type 2(11β-HSD2) and reactivated by 11β-HSD1. We have shown previously that 11β-HSD1 inhibition (with the selective 11β-HSD1 inhibitor, AZD4017) mitigates prednisolone-induced adverse effects. The role of other enzymes, including Carbonyl reductase 1 (20β-hydroxylase, CBR1) in prednisolone and prednisone metabolism are unexplored.
Aims
To describe the patterns of unique plasma metabolites associated with prednisolone and prednisone clearance, define the impact of 11β-HSD1 inhibition and assess correlations between plasma metabolites and clinically significant outcomes.
Methodology
Retrospective analysis of detailed 8-hour assessment period of 2-hourly plasma samples after administering prednisolone (20 mg) with either placebo or AZD4017. Plasma metabolites were quantified using LC-MS/MS. Specific enzyme activity was inferred using the ratio of target metabolite/substrate levels.
Results
Following oral prednisolone administration (20 mg), prednisolone (AUC = 820 ± 213 ng/mL) and prednisone (AUC = 154 ± 50 ng/mL) were the most abundant metabolites, followed by 20β-OH metabolites ($AUC_{20β\text{-}OH\text{-}prednisolone}$ = 69.5 ± 71.2; $AUC_{20β\text{-}OH\text{-}prednisone}$ = 24.8 ± 16.8 ng/mL). Inhibition of 11β-HSD1 activity with AZD4017 decreased prednisolone availability by 59% ($p < 0.001$). Interestingly, AZD4017 did not increase prednisone availability (Δ_{AUC} = -38.67, 95%CI -84.42;7.08, $p = 0.113$). Furthermore, 8h after prednisolone administration, prednisone levels were lower in the AZD4017 treated group (Δ-14.88 ng/mL, 95%CI -18.94;-10.83, $P < 0.001$). This observation was driven through increased (+93%, $p = 0.007$) CBR-1 activity assessed by 20β-OH prednisone/prednisone concentrations. Logistic regression identified 20β-OH-prednisone(4h) as the only predictor of higher glucose disposal ($B = 0.382$, $p = 0.017$) and osteocalcin levels ($B = 0.727$, $p = 0.006$) after prednisolone, indicative of less significant adverse effects.
Conclusions
11β-HSD1 significantly regenerate active prednisolone. Preferential prednisone clearance by CBR1 limits reactivation, mitigating adverse effects of prescribed GCs. Finally, 20β-OH-prednisone may predict prednisolone-related adverse effects, suggesting a more precise prescribing approach.

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P38

Peri-operative challenges in adrenalectomy for pheochromocytoma with severe catecholamine induced cardiomyopathy

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Introduction
Pheochromocytoma is a rare catecholamine-secreting tumour that commonly arises from the adrenal medulla. In addition to the episodic cardiovascular complications leading to severe hemodynamic disturbances perioperatively, it has been increasingly recognised that catecholamine-related cardiomyopathy is a life-threatening condition. Our case highlights the complexities and risks involved in the perioperative management of adrenalectomy.
Case Report
A 60-year-old man had a finding of a large mass with central cystic necrosis measuring 9.0/8.4/8.2 cm involving the left adrenal gland after presenting with a CAP. Further investigations showed raised plasma metanephrines (metanephrine at a maximum of 12707 pmol/l and normetanephrine at 48024 pmol/l) to confirm the diagnosis of pheochromocytoma. During preparation for surgery, the patient suffered an acute embolic infarct in the right temporoparietal region and subsequent haemorrhagic transformation. He was then readmitted with shortness of breath, ankle swelling and pulmonary oedema. An echocardiogram showed severe left ventricular dysfunction with an EF of 18%; his BNP was 604pg/ml. A diagnosis of catecholamine induced cardiomyopathy (CICMP) with severe left ventricular failure was made.
Discussion
Surgical excision was deemed the only option and co-ordinated efforts between specialities were made to prepare the patient for surgery. His predicted P-POSSUM scores for mortality and morbidity were 10.2% and 77.9% respectively. Pharmacological preparation required a fine balance between pheochromocytoma, LVF and stroke management as an inpatient. Once optimised, the patient had a successful open left adrenalectomy. Since surgery, the patient has remained symptom free and repeat plasma metanephrines eight weeks post operatively showed normal levels.
Conclusion
Whilst surgery remains the definitive treatment for pheochromocytoma, it is accompanied by significant risks, particularly in the presence of CICMP, LVF and recent stroke. Careful pre-operative assessment and preparation by multi-disciplinary teams prior to theatre are essential to reduce the incidence of mortality and morbidity associated with this challenging condition.

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P39

Diuretic induced flaccid paralysis as first presentations of primary aldosteronism

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Introduction
Hypokalaemia related flaccid paralysis is a rare condition of transient, severe muscle weakness caused by temporary muscle excitability loss due to low plasma potassium concentrations. We present two patients who were diagnosed with primary aldosteronism after developing profound muscle weakness, following initiation of diuretics.
Case 1
A 35-year-old European male presented to the Emergency Department with severe limb pains, weakness and evidence of leg oedema. He had commenced thiazide diuretics six weeks previously. Serum potassium was low; 2.1 mmol/l (3.5-5.2 mmol/l) with elevated creatine kinase; 9067 U/l (<308U/l). Despite five antihypertensive agents, blood pressure was 173/112mmHg. Primary aldosteronism was suspected and then confirmed with elevated aldosterone concentration of 1331 pmol/l following saline suppression testing. Imaging demonstrated a unilateral 21mm adrenal lesion consistent with an adenoma. The patient underwent adrenalectomy, achieving biochemical and clinical cures.
Case 2
A 55-year-old Irish male with a 28-year history of hypertension was suspected to have a secondary aetiology. To complete biochemical assessment, his usual aldosterone antagonist was discontinued and substituted for indapamide. Four weeks later, he had developed profound lethargy and progressive muscle fatigue. He was unable to walk due to lower limb weakness. Blood results revealed potassium of 1.6 mmol/l, resultant myositis and ECG features consistent with severe hypokalaemia. He required prolonged management in Intensive Care. After medication substitution and an appropriate time interval, primary aldosteronism was suggested by direct renin of 8mU/l and elevated plasma aldosterone of 1730 pmol/l. Adrenal Vein Sampling demonstrated lateralisation of aldosterone production correlating with CT imaging. The patient underwent adrenalectomy with complete biochemical and partial clinical response.
Discussion
Primary hyperaldosteronism rarely presents with hypokalaemic paralysis, particularly in the context of thiazide treatment. Given these medications form part of hypertension management guidelines, it is crucial to be cognisant of this risk, especially when aldosteronism is suspected.

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P40

Things that go bump in the night: phaeochromocytoma a cause of nocturnal headaches

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Phaeochromocytoma is rare and can be challenging to diagnose. The classic triad of paroxysmal headache, palpitations and pallor is not seen in most cases and the presentation can be more unusual. We describe a case of chronic nocturnal headaches caused by Phaeochromocytoma. A 58-year-old man with a PMHx of Essential Hypertension and Diabetes Mellitus Type 2 presented overnight to the Emergency Department with a sudden and severe "thunderclap headache". The patient described a history of nocturnal headaches over several years and stated that his symptoms had been worsening, increasing in frequency and severity, over

the few months leading up to presentation. He had been investigated as an OP and had a normal MRI brain. He had recently been started on Ramipril and his DM2 was diet controlled. Palpitations and pallor had not been described but patient and wife recounted a "funny turn" episode years before: he had a minor bang to abdomen, felt very unwell, collapsed before having a seizure. Initially, SAH was the concern but was ruled out by CT brain and lumbar puncture. Neurology review was sought and a primary headache disorder, Hypnic Headache, was suspected but features were atypical. He was found to be hypertensive, especially overnight, and ECG revealed an LVH pattern. HS-Troponin was raised but he had never had chest pain. He was investigated for secondary hypertension and Phaeochromocytoma was confirmed biochemically and radiologically: plasma metanephrines revealed normetanephrine >25000 pmol/l, metanephrine 23300 pmol/l, 3-methoxytyramine 1320 pmol/l with CT and MIBG showing a large left Phaeochromocytoma with possible metastasis to liver and pelvis. The patient was quickly medical managed with alpha and then beta blockade before he underwent a successful adrenalectomy. His symptoms have now resolved and he remains under MDT F/U and is planned to have MIBG therapy.

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Bone & Calcium

P41

Parathyroid adenoma revealed by recurrent acute pancreatitis: a case report

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Acute pancreatitis is a common etiology of acute abdominal pain, it has multiple causes including hypercalcemia. It is a rare manifestation of primary hyperparathyroidism, reported only in 3-15% of cases which can lead to a diagnostic and therapeutic delay. This is a case of a 76-year-old patient who presented with acute CTSI-3 pancreatitis and severe hypercalcemia at 153.09 mg/l (3.82 mmol/l). Despite the regression of the signs of pancreatitis with treatment, his general condition remained altered with signs of dehydration and diffuse bone pain. The patient developed a second episode of acute pancreatitis 2 months later. The malignant origin was suspected following resistant hypercalcemia and the presence of vertebral nodular images on MRI. However, this hypothesis was ruled out after multiple investigations in favor of primary hyperparathyroidism with degenerative bone lesions. The PTH was high at 758, 8 pg/ml, cervical ultrasound showed a right cervical image with parathyroid scintigraphy confirming the diagosis of right parathyroid nodule. The patient underwent an adenomectomy inducing a peroperative reduction in the PTH level to 92.7pg/ml after thirty minutes. The histological study found a 33mm encapsulated parathyroid adenoma with principal cells, and a KI67 estimated at 2%. Postoperatively, we noted a return to normal of serum calcium and PTH as well as a good clinical evolution of the general condition and disappearance of the pain. The control CT was without abnormalities apart from a few non-infected peripancreatic collections. Furthermore, we did not find any lesions suggestive of MEN or other cases in the patient's family. In case of acute pancreatitis without a history of cholelithiasis or alcoholism, rare causes, particularly hyperparathyroidism, must be sought. Early diagnosis and adenomectomy allow definitive managment and prevent recurrence of acute pancreatitis.

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P42

Assessment of bone mineral metabolism in patients with differentiated thyroid cancer

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In 2022, the 5-year prevalence of thyroid cancer in Romania was 2.1/100.000. Differentiated thyroid cancer (DTC), the predominant form, often necessitates surgery and TSH suppressive therapy (TST). If severe and prolonged, this may accelerate bone remodelling, resulting in osteoporosis and increased fracture risk. This retrospective study aimed to assess the impact of TST on bone metabolism in a cohort of DTC patients. We analyzed: age, menopausal status, degree, and duration of TST, lumbar spine and hip bone mineral density (BMD), lumbar spine TBS, and FRAX fracture risk. We reviewed 148 DTC patients admitted between 2018-2023, followed up for 4.60 ± 3.46 years, out of which 62 underwent a bone density (DXA) scan, 27 having multiple examinations. 82% were overweight or obese, with a mean age at DTC diagnosis of 55.61 ± 12.11 years. 92% were women, 44 being postmenopausal (PM). 66% had osteopenia or osteoporosis and 7 had prior fragility fractures. Additionally, 46% exhibited low lumbar spine TBS, indicating compromised bone microarchitecture. The PM group has significantly lower mean BMD($P = 0.004$) and T score($P = 0.008$) in the femoral neck compared to premenopausal women. Dynamic evaluation revealed that higher TSH levels correlated with increased BMD in the lumbar spine ($P = 0.026$) and femoral neck($P = 0.028$). Patients with TST had significantly lower mean BMD($P = 0.008$), T($P = 0.012$) and Z scores($P = 0.007$) in the lumbar spine compared to those without suppression. Similar trends were observed in the femoral neck for the group with TSH<0.1mIU/l compared to those with moderate($P = 0.052$) or without suppression($P = 0.047$). We found negative correlations between the duration of TST and most DXA parameters in the femoral neck, while in the lumbar spine only with TBS. In conclusion, TSH suppression may impact bone metabolism, particularly in postmenopausal patients or those already having osteoporosis. Future prospective studies with larger patient cohorts could optimize patient care.

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P43

A unique case of primary hyperparathyroidism remission post FNAC and literature review

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Iatrogenic remission of Primary Hyperparathyroidism (PHPT) is a rare phenomenon. We report a unique case of PHPT remission post FNAC. A 64-year-old gentleman was referred to endocrine clinic with incidental finding of hypercalcemia (Adjusted calcium 2.77 mmol/l and PTH 8 pmol/l). He was diagnosed with PHPT and was a candidate for surgical intervention. Sestamibi scan and ultrasound parathyroid were done to localise the adenoma. However, these two scans had conflicting results. Sestamibi scan showed two parathyroid adenomas postero-inferiorly, in contrast, ultrasound parathyroid showed thyroid nodule postero-inferiorly with benign features. Ultrasound guided FNAC of the probable thyroid nodule was done in the same setting by the radiologist, however the cytology was inconclusive. His calcium and PTH levels subsequently normalised (Adjusted calcium 2.5 mmol/l and PTH 3 pmol/l) for the first time in a year. The repeated Sestamibi scan 8 months post FNAC, surprisingly showed no scintigraphy evidence of parathyroid adenoma. Serial monitoring of calcium and PTH levels has been normal. In literature, 7 cases of PHPT remission post FNAC have been reported. Parathyroid adenoma could undergo haemorrhage or infarction post FNAC. Of these cases, three patients had recurrence of PHPT from 45 days to 4 months post procedure. Although this patient is currently in remission, he will require long term monitoring of bone profile due to the risk of recurrence. It is reported that FNAC of suspected parathyroid lesion has low sensitivity if it is done without PTH washout. Hence, in this unique instance of conflicting results of Sestamibi scan & Ultrasound Parathyroid, we suggest not to routinely perform FNAC for the diagnosis of PHPTH as patient may require long term monitoring post procedure. If FNAC is considered, then it should be done with PTH washout to improve sensitivity.

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P44

Identification of novel GPCR targets for the treatment of osteoporosis

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G-protein coupled receptors (GPCRs) are transmembrane proteins whose surface expression and extracellular activation make them desirable drug targets. Approximately 35% of approved drugs target GPCRs, including osteoporosis treatments such as Teriparatide. Despite the ageing population resulting in increased osteoporosis diagnoses, current treatments lack long-term efficacy, highlighting the need to identify new drug targets. Using RNA-sequencing we identified multiple GPCR genes to be highly expressed in human primary osteoclasts and these could provide novel drug targets for osteoporosis. To assess how these GPCRs affect osteoclast differentiation and activity, we designed a pipeline of assays amenable to high-throughput, automated analyses. These comprise: nuclei staining to assess osteoclast differentiation; TRAP enzyme activity; and high-content imaging of NFAT nuclear translocation to measure osteoclast signalling. These were compared to bone resorption assays that are the current gold standard technique to assess osteoclast activity, despite their low efficiency and potential for bias in data interpretation. We first demonstrated the utility of these methods using GIPR as a positive control, and showed GIPR activation reduced bone resorption, TRAP activity, mature osteoclast number and NFAT nuclear translocation, all of which were prevented by pre-treatment with GIPR antagonist. We then chose six GPCRs to assess in detail. Using our assay pipeline with receptor-specific agonists and antagonists we showed that no receptors affected osteoclast differentiation, and SUCNR1 and GPR84 did not affect activity. In contrast, FFAR2 reduces bone resorption, TRAP and NFAT nuclear translocation, while FFAR4, FPRs and GPR35 reduced bone resorption and TRAP. Thus, we identified four GPCRs that reduce osteoclast activity and could represent novel targets for osteoporosis. Moreover, we demonstrated that high-throughput assays, which measure multiple compounds in hundreds of cells in a single experiment using automated analyses, can accurately assess osteoclast activity, reducing observer bias and increasing efficiency of target detection for future osteoporosis therapies.

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P45

Influence of ethnicity and deprivation on occurrence of paget's disease in greater manchester, uk (population 2.85 million)

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Introduction
There is variation in Paget's disease occurrence in different regions/populations. We looked at Paget's occurrence (GP-coded diagnosis) in a large UK urban conurbation and explored the influence of age/gender/ethnicity on occurrence. We also looked at the impact of Paget's disease on the severity of COVID-19 infection.
Methods
We undertook an anonymised search using an integrated primary/secondary care-based database in Greater Manchester (GMCR), covering a population of 2.85million people. We looked at the occurrence of clinically diagnosed Paget's disease in January 2020 in men/women over 60 years old by age/gender/deprivation level (assessed using the Townsend-Index and expressed in quintiles), and ethnicity (based on self-report).
Results
We identifed 534,571 people aged $\geq$60years on 1January 2020. The majority were white (84%): 4.7% describing themselves as Asian/Asian British; 1.27% Black/Black British. There were 931 with clinically diagnosed Paget's disease. Overall prevalence in the GM area was 0.174%. Prevalence was higher in menvswomen (0.195vs0.155%). Compared to the prevalence of Paget's in whites (0.179%) the prevalence was lower in those of Asian/South Asian descent (0.048%) and higher in those of Black/Black British descent (0.344%). Prevalence increased with increasing deprivation. After adjustment for age/gender/deprivation the risk of disease remained lower in Asians (OR = 0.36) and higher in Black British (OR = 2.13). Among those with a positive COVID-19 test those with Paget's disease were more likely to require hospital admission within 28-days. However confidence intervals embraced unity (OR1.37; 95% CI (0.94,1.95).
Conclusion
Clinically apparent Paget's disease is uncommon affecting less than 2 per thousand men/women over 60-years old. Within GM, it is more common in those of Black-British descent and less common in those of South-Asian descent. Further research is required to determine whether such differences are due to variation in disease occurrence or disease presentation.

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P46

Two cases of pseudohypoparathyroidism type 1B presenting to a tertiary dublin hospital

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Pseudohypoparathyroidism (PHPT) is a very rare disorder characterised by a lack of response to parathyroid hormone at the level of the proximal tubule. In the absence of the classical features of Albright Osteodystrophy, the diagnosis can be missed. We present two cases of type 1B PHPT. The first case was of a 39 year old man presenting with non-specific abdominal symptoms and was found to have a corrected calcium of 1.89 mmol/ (2.21-2.52 mmol/l) with a paired PTH of 734pg/ml (15-65pg/ml) but normal phosphate and a slightly raised alkaline phosphatase (ALP). Vitamin D level was 17 nmol/l (>50 nmol/l). He had a normal phenotype. He was treated with intravenous calcium and transitioned to oral calcium, Vitamin D and active vitamin D. Coeliac screen was negative. Three months later calcium normalised to 2.24 mmol/l and vitamin D had climbed to 65 nmol/l. PTH level had fallen but remained significantly raised at 334pg/ml. Genetic testing confirmed a diagnosis of pseudohypoparathyroidism Type 1B due to partial loss of the maternal methylation pattern at the GNAS locus. The second case was of a 22 year old man presenting to his GP after experiencing tetany while abroad, necessitating IV calcium replacement. Corrected serum calcium was low at 1.63 mmol/l with a raised serum phosphate of 1.63 mmol/l with normal ALP and vitamin D and a PTH of 308pg/ml. He had a normal phenotype. Genetic testing diagnosed PHPT Type 1B due to loss of the maternal methylation pattern at the GNAS locus. His calcium normalised on oral calcium with 1600 units of Vitamin D daily and 1 mg of one alpha. PTH remained elevated at 138pg/ml. Pseudohypoparathyroidism should be suspected in individuals with hypocalcaemia, raised PTH and hyperphosphatemia especially if the PTH level remains raised despite correction of calcium and vitamin D deficiency.

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P47

Out of place, out of sight: a case report of ectopic parathyroid adenoma in primary hyperparathyroidism

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Introduction
Primary hyperparathyroidism (PHPT) involves excessive secretion of parathyroid hormone (PTH), leading to elevated serum calcium levels. Ectopic parathyroid adenomas, constituting 10-22% of cases, arise due to abnormal embryonic migration and can be located from the mandible to the pericardium. This complicates their localization and diagnosis. Parathyroidectomy, with a success rate over 90%, remains the treatment of choice. This case report discusses the diagnostic challenges and management in a PHPT patient with an ectopic parathyroid adenoma.
Clinical Case
A 61-year-old male was referred to our endocrinology service in March 2017 for persistent, asymptomatic hypercalcemia, with levels between 2.76 and 2.86 mmol/l and elevated PTH levels. The patient, on active surveillance for prostate cancer, had no significant past medical or family history. Ultrasound kidneys

showed no stones, and a DEXA scan revealed normal bone density. He was advised to increase fluid intake, avoid calcium supplements, and monitor calcium levels biannually with his GP. By July 2022, his calcium levels had risen to 3.06 mmol/l, necessitating further investigation. A SESTAMIBI scan indicated increased uptake in the right posteroinferior thyroid lobe, but a parathyroid ultrasound did not confirm an adenoma. The SESTAMIBI uptake was located inferiorly for neck ultrasound localization, suggesting a retrotracheal position. Consequently, a 4DCT scan was performed, revealing an 11x20x32 mm lesion in the posterior mediastinum, lateral to the oesophagus, consistent with an ectopic parathyroid adenoma. The patient underwent a successful parathyroidectomy with postoperative normalization of calcium levels.

Conclusion

This case illustrates the necessity of a systematic approach in managing PHPT with atypical presentations like ectopic adenomas. Effective diagnosis and management involve a multidisciplinary team (endocrinologists, radiologists, and surgeons). The successful surgical intervention not only normalized the patient's calcium levels but also demonstrated the effectiveness of targeted surgery in managing complex hypercalcemia cases due to ectopic parathyroid adenomas.

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P48

Hypoparathyroidism audit

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Objectives

Improving the management of chronic hypoparathyroidism is crucial for enhancing the quality of life and reducing morbidity and mortality. Our audit assessed the effects of introduction of a dedicated specialist nurse led hypoparathyroidism clinic.

Methods

During 2022 we developed an SOP and undertook training to enable the provision of an endocrine specialist nurse led chronic hypoparathyroidism clinic. The clinic commenced in November 2022 providing protocol driven, consultant supervised, specialist nurse delivered clinical care to a cohort of chronic hypoparathyroidism patients in our large teaching centre service. After the service had been running for 14 months we performed an audit of outcomes in this service. Four treatment standards and nine monitoring standards were used. These standards were derived from the 2015 EJE chronic hypoparathyroidism guidelines as described in our previous national audit of chronic hypoparathyroidism management (Kiam *et al* 2022).

Results

Over 14 months, 24 individual patients were seen in the service. Each Patient had at least one annual face to face appointment plus remote contact by phone and/or letter as necessary in between appointments. The mean age of patients was 50.25 years and the commonest cause of hypoparathyroidism was post-surgical (100%). Compliance with the audit standards varied between 100% and 63% for the treatment standards and between 96% and 12% for the monitoring standards. Some of the areas of weakness revealed included low rates of 24 h urinary calcium excretion monitoring, serum magnesium monitoring and low rates of renal imaging. In addition, and importantly, 14% of subjects had experienced at least one hospital admission during the audit.

Conclusion

This is a novel model of service delivery for a traditionally under-served population of patients and initial audit outcomes suggest delivery of care standards which are already higher than those seen in our previous national audit of chronic hypoparathyroidism.

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Diagnosing william-beuren syndrome in a patient with primary hyperparathyroidism

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Williams-Beuren syndrome (WBS) is a rare multisystem genetic disorder, with an estimated prevalence of 1:7500 live births. WBS is characterised by distinctive facies, mild intellectual disability, cardiovascular disease, and endocrine disorders including hypothyroidism, hypercalcaemia, and diabetes. Hypercalcaemia is seen in 5 to 50% of individuals with WBS. It is usually identified in infancy and resolves during childhood. The first case report of WBS with primary hyperparathyroidism (PHPT) was published in 2017. Our report describes a patient with PHPT, where the diagnosis of WBS was established on genetic testing undertaken as part of the workup for PHPT. A 35-year-old gentleman has a history of mild intellectual disability and type 2 diabetes. He is investigated for persistently elevated serum calcium levels. The tests report an elevated parathyroid hormone level and a sestamibi scan is positive for a left inferior parathyroid adenoma. His Z score is less than -2. He undergoes a parathyroidectomy of the isolated gland and the histology is consistent with a parathyroid adenoma. He has been normocalcaemic one year postoperatively. He underwent genetic testing, which reported a heterozygous deletion of the long arm of chromosome 7, as seen in WBS. A review of his notes highlighted that WBS was suspected in infancy by a paediatrician and paediatric cardiologist, given his distinctive facies, hyperactivity, and presence of a cardiac murmur, but genetic testing was not performed at that time. The mechanism of hypercalcaemia with WBS is not fully understood. Various mechanisms have been proposed, including the potential role of transient receptor potential C3 (TRPC3) channels in increasing calcium absorption. The American Academy of Paediatrics recommends that patients with WBS have 2-yearly calcium checks from age 6, and more frequently at younger ages. Hypercalcaemia in individuals with WBS should be investigated, to ensure that alternative aetiologies are diagnosed and managed appropriately.

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Cost-effectiveness and societal burden implications of opportunistic screening for low bone density using wrist radiographs in a UK general radiography setting

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Background

Fragility fractures lead to considerable societal costs and individual suffering. Despite the availability of cost-effective treatments for high-risk patients, a significant treatment gap exists, with many high-risk individuals remaining unidentified and untreated. The aim of this study was to evaluate the cost-effectiveness and impact of opportunistic screening for bone health with IBEX BH, a software solution that provides areal bone mineral density from wrist Digital Radiographs, in a United Kingdom general radiography setting.

Methods

The study used a health economic model that compared the health outcomes and costs of screening with IBEX BH vs usual care for men and women aged 50 and older who had a forearm radiograph for any reason at Royal Cornwall Hospitals NHS Trust. The model incorporated data on fracture incidence, fracture risk reduction, mortality, quality of life, and fracture and treatment costs from published sources and extracts from the Royal Cornwall Hospitals NHS Trust database. Costs and health outcomes in terms of quality-adjusted life years were simulated over the lifetime of patients. The analysis took an NHS and personal social services perspective.

Results

The results showed that screening with IBEX BH was associated with a gain of 0.004 quality-adjusted life years and a cost saving of £63 per patient compared with usual care, making it a dominant (cost-saving) strategy. Sensitivity analyses confirmed the robustness of the results under various assumptions.

Conclusions

IBEX BH could be a cost-effective tool for early identification and prevention of fragility fractures at Royal Cornwall Hospitals NHS Trust, potentially addressing the current challenges of low provision of fracture risk assessment and, therefore, the osteoporosis treatment gap.

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A rare case of 1,25 - dihydroxyvitamin d mediated severe hypercalcaemia due to polyethelene hip prosthesis

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Background
Calcitriol-induced hypercalcemia is uncommon posing diagnostic dilemma. This case report describes a patient with severe hypercalcemia due to granulomatous changes around a polyethylene wear hip prosthesis.
Case Report
An 80-year-old woman presented with hypercalcemia and stage 3 acute kidney injury. Serum calcium was 3.9 mmol/l, Parathyroid hormone 0.2 pmol/l(1.3 - 9.3), confirming PTH-independent hypercalcemia. CT and MRI imaging, tumor markers and bone marrow biopsy did not reveal a neoplastic process. FDG PET-CT indicated increased uptake around the left hip prosthesis, suggesting inflammation and mild to moderate FDG avidity in left external iliac and common iliac lymph nodes. No bone lesions identified. Lymph node biopsy was attempted but failed. There was no convincing evidence for lymphoma. MRI of the hip showed features of a pseudotumor around metal debris. Metal on Nonmetal prosthesis was evident. She had significantly Elevated 1,25-dihydroxyvitamin D at 282 pmol/l (55-139). Blood tests were negative for Angiotensin converting enzyme and PTH related peptide. Histological diagnosis was avoided due to surgical risk. The diagnosis of calcitriol mediated hypercalcemia secondary to granulomatous inflammation around polyethelene wear was considered in the context of previous hip surgery and the absence of other obvious causes. She was initially managed with hydration and Denosumab; followed by oral prednisolone 20 mg daily which was tapered off over a course of year with satisfactory response.
Conclusion
Calcitriol-induced hypercalcemia due to granuloma, though rare, can be severe and associated with renal injury. Vitamin D metabolite levels are crucial for diagnosis, and steroid therapy is promisingly effective.

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Vitamin D replacement in primary hyperparathyroidism – friend or foe?

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Local and national guidelines for post- hip fracture bone protection in an elderly population, advise vitamin D replacement and IV bisphosphonate. We report the case of an 82 year old man who underwent left hemiarthroplasty after low-trauma neck of femur fracture. He received a loading dose of Vitamin D (150,000 units over six days) and followed by IV Zolendronic Acid 5 mg on day nine of admission. On admission the serum calcium was elevated (2.63 mmol/l), on repeat it was within range for intervention (2.59 mmol/l). He promptly developed PTH dependent hypercalcaemia (corrected Ca 3.19 mmol/l; PTH 31 pmol/l Phosphate 0.68 mmol/l) which was resistant to conventional management. Subsequent investigations showed; Vitamin D 25 nmol/l, eGFR >60 ml/min/1.73m^2, Calcium/Creatinine Ratio 0.0287. A DEXA scan showed osteopenia (T score Hip -1.6, T score spine 0.2). A Technetium-99m (sestimibi) scan reported tracer activity in the right mid pole of the thyroid likely parathyroid adenoma. Calcitriol (1, 25 OH Vit D) level was 66 pmol/l, 8 days after loading with Vitamin D. Hypercalcaemia was resistant to multiple lines of medical management, despite IV normal saline, IV furosemide, cinacalcet and prednisolone over nine days of, in addition to the recent IV Zolendronic acid given before this. Calcitonin stabilised the serum calcium for 48 hours. He had proximal myopathy, peripheral oedema, anorexia, nausea, vomiting and constipation. The serum calcium continued to rise to a maximum of 3.51 mmol/l, Denosumab 120 mg was given, a good response was achieved over 72 hours, the serum calcium normalised (2.5 mmol/l). Once normocalcaemic, he symptomatically improved before discharging. Controversy exists about the role of Vitamin D replacement in primary hyperparathyroidism. This case highlights the potential impact of high-dose Vitamin D exposure and the difficulty in correcting consequent hypercalcaemia in patients with primary hyperparathyroidism.

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Relative energy deficiency in sport in female gaelic athletic association players and the impact on bone health and growth and development

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Relative Energy Deficiency in Sport (RED-S), a potential consequence of low energy availability (LEA) can impact athletic health and performance. Bone health, growth and development can be adversely impacted. The 2023 International Olympic Committee Consensus Statement on RED-S recommends assessment for impairment of bone health, growth and development with DXA scanning and measurement of growth hormone (GH) and insulin-like growth factor 1(IGF-1). We aim to investigate if elite female Gaelic Athletic Association (GAA) players are at risk of RED-S using bone health and growth and development markers. We recruited 44 intercounty GAA players, who underwent extensive blood testing panels including the following: bone profile, 25-hydroxyvitamin D, parathyroid hormone (PTH), GH, IGF-1 and bone turnover markers. Thirty players had DXA scans to assess bone density. These have been completed pre-season to assess the baseline levels and will be repeated mid-season and end-season to evaluate the impact of intense training. Preliminary results from our study include the following. All 30 participants who underwent a DXA scan had normal bone density, with an average T score of 1.1 (17 participants $>$ 20 years old) and average Z score of 0.9 (13 participants $<$ 20 years old). Bone profile and PTH for the 44 participants were within the appropriate reference intervals. 12 (27%) participants were vitamin D insufficient (25-50 nmol/l). The mean GH was 274ng/ml (range 178-362) and IGF-1 was 5.02 ng/ml (range 0.05 – 17.52). This is the first study evaluating the bone health of female GAA players. The preliminary results from the suggested indicators for monitoring are unremarkable to date. We await the analysis of the bone turnover markers and further interval evaluation, to assess the impact of the playing season. We hope that our study will lead to improved education and ultimately better health, performance and safe participation for women in sport.

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Vitamin D insufficiency in parathyroid bone disease

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Background
Vitamin D insufficiency and low bone mineral density (BMD) are common in primary hyperparathyroidism (PHPT). The relationship between Vitamin D status and parathyroid bone disease is worthy of investigation.
Aim
Our aim was to review the medical management of PHPT in an Irish university hospital and perform a sub-group analysis on people with low BMD and vitamin D insufficiency – serum 25OH vitamin D $<$75 nmol/l (Evaluation and Management of PHPT: Guideline - Fifth International Workshop).
Methods
A retrospective electronic search using the laboratory information system (iSOFT Telepath®) was performed over a 12 month period (2022). We collected clinical, biochemical and radiological data on 58 subjects (43 female). Approval granted from institutional audit committee. Statistical analysis was performed using GraphPad Prism.
Results
Median (SD) adjusted serum calcium was 2.65 mmol/l (0.1); 19% (11/58) had a calcium level $>$2.85 mmol/l. Median (SD) PTH and serum 25OH vitamin D levels were 10.1 pmol/l (4.1) and 61 nmol/l (35.7) respectively. The results demonstrated that 76% (44/58) of patients had vitamin D insufficiency and 76% (44/58) had low BMD, of which 50% (22/44) had osteoporosis. 59% (13/22) were on treatment for osteoporosis. Following statistical analysis, there was no association between vitamin D status (deficient/sufficient) and low BMD. Furthermore, there was no statistical relationship between BMD and serum adjusted calcium, PTH or vitamin D concentration. 36% (21/58) of patients with vitamin D insufficiency were on

vitamin D replacement. Of those with low BMD, 77% (34/44) had a three-site DEXA (including radius). Fracture was recorded in 14% (8/58) - three wrist, three ankle and two miscellaneous - all of whom had a low BMD.
Discussion
Vitamin D insufficiency and low BMD were common in Irish patients with mild PHPT. Parathyroid bone disease is a complex condition. The role of vitamin D deficiency and supplementation to reduce fracture risk require further investigation.

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An exploratory study of bone turnover markers in autoimmune pulmonary alveolar proteinosis

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Autoimmune pulmonary alveolar proteinosis (aPAP) is a disease whereby antibodies to granulocyte macrophage colony stimulating factor (GM-CSF) cause dysfunction of alveolar macrophages, leading to surfactant accumulation and respiratory failure. GM-CSF has a role outside the lung; promoting fusion of prefusion osteoclasts into multinucleated osteoclasts capable of bone resorption. Osteopetrosis is a disorder of reduced osteoclast function, causing failure of osteoclast-mediated resorption of the skeleton and increased fracture risk. We hypothesised that patients with aPAP may have low osteoclast activity as a result of GM-CSF dysfunction, mimicking osteopetrosis. This exploratory study phenotypes bone turnover in a cohort of patients with aPAP. Serum samples from 34 patients with aPAP from the Ruhrlandklinik, Essen were analysed for N-propeptide of type 1 collagen (P1NP) and C-terminal crosslinking telopeptide of type 1 collagen (CTX-1). 19 were male. Median age was 47.5 years (IQR 38.75-54). 8 patients were current smokers; 17 patients had previously smoked. 2 patients had a diagnosis of osteoporosis and 1 of myelodysplastic syndrome. 1 patient was on bisphosphonate therapy, 2 on hormone replacement therapy, and 5 were taking corticosteroids. P1NP levels in all participants with aPAP were within normal gender-specific reference ranges. Median P1NP in female patients was 41.60 mg/l (IQR 34.90-49.85 mg/l) (reference range 17.3-83.4 mg/l). Median P1NP in male patients was 39.2 mg/l (34.7-52.9 mg/l) (reference range 22.1-96.2 mg/l). The majority of the aPAP cohort demonstrated CTX-1 levels within normal reference ranges. Median CTX-1 in female patients was 0.22 mg/l (IQR 0.080-0.320 mg/l) (reference range 0.025-0.573). Median CTX-1 in male patients was 0.291 mg/l (0.205-0.380) (reference range 0.016-0.584). There was no difference in bone turnover markers in the aPAP cohort compared to 11 healthy controls (P1NP p-value = 0.56, CTX-1 p-value = 0.67). Bone turnover markers were normal in this cohort of aPAP patients. Further studies are required to establish if a relationship exists between aPAP and osteoclast dysfunction.

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Pseudohypoparathyroidism – an atypical cause of hypocalcaemia

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Pseudohypoparathyroidism is a group of rare genetic disorders characterised by end organ PTH resistance in the body. It is a rare cause of hypocalcaemia. We present the case of a thirty-eight-year-old lady with no past medical history who presents for the first time to her general practitioner for a general check up and is incidentally found to have hypocalcaemia with a level 1.70 mmol/l. She was referred to hospital for the work up and treatment and was found to be hypocalcaemic on repeat testing. She was generally asymptomatic but complained of occasional spasms of the hand. On examination she had short stature and truncal obesity. As part of the initial management, calcium was replaced intravenously. Vitamin D deficiency was excluded (vitamin D level 80 nmol/l). Her magnesium was also normal. PTH was elevated at 171 ng/l and phosphate was elevated at 1.70 mmol/l. Her blood work was consistent with a diagnosis of pseudohypoparathyroidism. Based on these results, a genetic test was sent which confirmed a diagnosis of pseudohypoparathyroidism type 1 b. We commenced our patient alfacalcidol 0.5 mg twice daily and followed up in the endocrine clinic with improved calcium levels (2.02 mmol/l). Her first-degree relatives have been asked to attend for calcium measurements. The reported incidence of pseudohypoparathyroidism is 0.3 – 1 in 100,000 depending on the population however its exact incidence is unknown in Ireland. The clinical picture of pseudohypoparathyroidism includes hypocalcaemia, hyperphosphatemia, raised parathyroid hormone (PTH) levels and features of Albrights Hereditary Osteodystrophy (if type 1a or 1c) such as short stature, brachydactyly, obesity and intellectual impairment. Resistance to other hormones such as TSH, GHRH, FSH, LH can also occur depending on the subtype. This is usually a sporadic genetic disorder that occurs due to STX16 deletion leading to abnormal methylation of GNAS but can rarely be inherited.

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Different pattern of association between body composition parameters and surrogate markers of bone quality, in patients with overweight or obesity

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Background
Body composition parameters might be determinants of bone strength and we aimed to investigate the relationship between body composition variables and surrogate parameters of spine and hip bone quality.
Patients and methods
235 patients with overweight or obesity (mean age= 50.12 ± 14.2 years, mean BMI $= 35.04 \pm 6.65$ kg/m^2) were included. DXA whole-body scans were conducted, using a DEXA Prodigy®, GE machine. Measurements included total and regional fat and lean mass, total and lumbar BMD. Trabecular bone score (TBS) measurements were performed using TBS iNsight. Proximal hip DEA scans were analysed for bone geometry by use of the HSA programme and cross-sectional area (CSA), section modulus (SM), and cross-sectional moment of inertia (CSMI) were included in the analysis.
Results
There was no significant difference in TBS values between men and women, but men showed higher values of CSA, CSMI and SM. In univariate analysis, TBS negatively correlated with age (r = -0.421, $P < 0.001$) and positively correlated with BMI, total bone mass ($r = 0.394$, $P < 0.001$), total fat ($r = 0.210$, $P < 0.001$) and total lean mass ($r = 0.188$, $P = 0.004$). In a linear regression model, age and total fat mass, but not total lean mass remained independently associated with TBS. Hip geometry parameters showed no association with BMI but positively correlated with total BMD ($P < 0.001$ for all), total lean mass ($r = 0.583$ for CSMI,0.615 for CSA, 0.683 for SM, $P < 0.001$ for all)and negatively correlated with t%at mass (r = -0.317 for CSMI, -0.262 for CSA, -0.382 for SM, $P < 0.001$ for all). In regression models, lean mass retained its positive association with all HSA parameters, while %fat mass remained negatively correlated.
Conclusions
Bone quality surrogate parameters show a different pattern of association with body composition variables; while total fat mass was an important determinant of TBS, lean mass proved to be the strongest factor associated with hip strength parameters.

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Efficacy of vertebral fracture assessments in detecting osteoporotic fractures: a comparative audit of local and ISCD criteria

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Introduction
Osteoporosis is a significant health concern in Ireland, with 6.2% of men and 20% of women over 50 affected in 2021. Vertebral fractures, the most common type of osteoporotic fracture, often go undiagnosed, with 70% remaining undetected. Vertebral Fracture Assessments (VFAs) during routine DXA scans enable early detection of low bone density and timely intervention, using low doses of ionising radiation. The International Society for Clinical Densitometry (ISCD) provides guidelines for identifying patients who would benefit most from VFAs.
Aim
This audit aimed to evaluate the effectiveness of VFAs performed at our local test centre, assessing whether they met both local and ISCD criteria and identifying the impact on clinical outcomes.

Methods
We reviewed the local DXA database and analyzed the last 50 patients who had VFAs based on local indication criteria. We assessed whether the VFAs met local and ISCD criteria, identified new fractures, and noted any changes in clinical treatment.
Results
All 50 patients who underwent VFAs met local criteria, with 37 also meeting ISCD criteria. New vertebral fractures were identified in 21 patients (42%). Additionally, three patients who met local but not ISCD criteria had new fractures detected, leading to recommended treatment.
Conclusion
VFAs are effective in detecting new vertebral fractures, with a high yield of 42% at our centre. The local criteria were more comprehensive than ISCD standards, significantly influencing treatment outcomes.

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A very rare presentation of severe hypercalcemia due to sarcoid like granulomatous myositis

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Introduction
Granulomatous myositis (GM) is a very rare inflammatory condition and can cause PTH- independent hypercalcemia. The hypercalcaemia is due to the elevated levels of extrarenal 1,25 dihydroxy vitamin D produced by activated macrophages due to granulomatous inflammation. We present a case of very severe hypercalcemia due to GM.
Case presentation
An 82-year-old lady presented to the emergency department due to deterioration in renal function and 4 months history of lethargy, constipation, and reduced mobility. Initial investigations showed an adjusted serum calcium of 4.33 mmol/l, parathyroid (PTH) hormone of 1.5 nmol/l, vitamin D of 81 nmol/l and creatinine of 217 micromole/l. Intravenous fluid treatment followed by empirical Zoledronic acid normalised the calcium transiently and then rose back to 2.64 mmol/l. On further investigation, serum ACE was normal at 23 U/l (20-70) and serum 1,25 dihydroxy vitamin D was elevated at 189 pmol/l (20-120). PET CT showed intense uptake in the lower limb muscles and left biceps, and a targeted muscle biopsy confirmed Sarcoid-like granulomatous myositis. Serum creatine kinase was normal. This patient responded well clinically and biochemically to Prednisolone 30 mg daily. The calcium remains normal on a reducing dose of steroids, and she has returned to her previous level of independence.
Conclusion
The presence of very severe hypercalcemia and very low PTH in an elderly person usually suggests malignancy but was not the case here. The case is very unusual in that serum ACE level was normal unlike most other similar cases of isolated GM. It is also unusual to have a severe myositis with normal CK levels. We had a high degree of suspicion for other causes of PTH-independent hypercalcaemia, resulting in a PET scan request. We recommend considering PET scan in unexplained PTH independent hypercalcaemia, even with normal serum ACE level.

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Familial hypocalciuric hypercalcaemia (FHH) type 3: a rare case requiring cinacalcet therapy

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Familial hypocalciuric hypercalcaemia consists of 3 subtypes which are all inherited in an autosomal dominant manner and caused by inactivating mutations. FHH type 1 is most common (>65%) and is due to mutation in the calcium sensing receptor gene (CaSR), FHH2 due to GNA11 mutation and FHH 3 due to AP2S1 gene mutation (has been found in both kindreds from Oklahoma and Northern Ireland). FHH results in hypercalcaemia and hypocalciuria. It is usually asymptomatic, requiring no treatment. However FHH 3 is clinically the most severe form, and cases of osteomalacia, pancreatitis and nephrolithiasis have been reported requiring treatment with cinacalcet therapy.
Case
A 37 year old woman was referred for incidentally detected hypercalcaemia. Adjusted calcium 2.94 mmol/l, PTH 97ng/l, vitamin D 14 nmol/l and 24 hour urinary calcium (when vit D deficient) 3.28 mmol/ 24 hours. She had 1 previous adjusted calcium checked 2 years prior to referral at 2.91 mmol/l. A maternal aunt had a history of parathyroidectomy. Her parathyroid ultrasound and sestamibi scan were both negative for parathyroid adenoma. Due to her young age she had genetic analysis performed confirming pathogenic AP2S1 missense variant. Subsequent adjusted calcium levels rose to 3.08 mmol/l with symptoms of constipation and fatigue, therefore cinacalcet 60 mg od was commenced which successfully alleviated her symptoms and lowered her adjusted calcium to 2.34 mmol/l. Our patient now desires pregnancy and has been referred to clinical genetics with withdrawal of cinacalcet therapy.
Learning points
1. FHH rarely requires treatment, if end organ damage due to hypercalcaemia occurs then treatment is with cinacalcet as parathyroidectomy is not curative. 2. Only 4 cases of FHH in pregnancy have been reported with no maternal pregnancy complications, however neonatal biochemistry will depend on the fetal genotype and referral to genetic counselling is recommended.

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Diabetes & Metabolism

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Enhancement of adipose hypoxial inducible factor-1α by probiotics alleviates metabolic disturbance in experimentally induced pcos

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Background
Polycystic ovarian syndrome (PCOS) is critically characterized with metabolic and endocrine dysfunctions, precipitating metabolic syndrome and infertility in reproductive aged women. Adipose tissue dysfunction has been implicated in the pathogenesis of metabolic syndrome, including in PCOS individuals. Probiotics are healthy bacteria in the gut that regulate metabolic health. However, the impact of probiotics on adipose-driven metabolic syndrome has not been reported. The present study therefore hypothesized that probiotics would attenuates metabolic disturbance in experimental PCOS rat model, probably by modulation of HIF-1α.
Materials and methods
Eight-week-old female Wistar rats were randomly allotted into four groups ($n = 5$). Administration of letrozole (1 mg/kg *p.o*) for 21 days induced PCOS, thereafter the animals were treated with $2x10^7$ CFU (*p. o*) of probiotics for six weeks.
Key findings
Letrozole-induced PCOS rats were characterized with elevated circulating testosterone, and multiple ovarian cysts. In addition, rats with PCOS developed increased body weight, which was also accompanied with insulin resistance, hyperinsulinemia, and increased leptin, and decreased adiponectin, adipose TG, as well as elevated adipose lipase. Inflammatory markers (NF-kB, TNF-α) and macrophage inhibitory factor were elevated, while antioxidant defense (GSH) was depleted in PCOS animals. A significant increase in adipose TGF-β1, caspase-6 and HDAC2 levels was observed in PCOS rats when compared with the control. Immunohistochemical evaluation of adipose tissue also showed severe expression of NLRP3 in PCOS rats and these changes were accompanied by decreased expression of HIF-1α. However, treatment with probiotics reversed these aberrant systemic and adipose tissue change in PCOS model.
Significance
The present results suggest the therapeutic benefit of probiotics, against adipocyte dysfunction in PCOS rat model, through modulation of HIF-1α/MIF-dependent pathway.
Keywords
Adipose; HDAC2; HIF-1α; Inflammation; PCOS; Probiotics.

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A quality improvement project to improve statin prescription in eligible patients with type 1 diabetes mellitus

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Background
Type 1 diabetes mellitus (T1DM) is associated with high cardiovascular risk. Statins reduce the risk of non-fatal myocardial infarction when used as a primary prevention in selected patients with T1DM. A 2020 audit of statin prescription in our department showed 28.3% of patients who met criteria were on statin therapy. The aim of this quality improvement project was to improve statin prescription in eligible patients presenting to our outpatient diabetes department.
Methods
A printed proforma based on NICE 2023 guidelines was introduced to accompany patient diabetes data records. Clinical staff were educated on how to use the proforma and there was an accompanying supplementary tool with further instructions if required. We then prospectively collected data over two cycles from July to August 2023 and January to April 2024. Results of the first cycle were presented at departmental meetings prior to cycle two.
Results
Overall, 155/363(42%) of patients were already on statin therapy. Over the two cycles, 33/248 (13%) of patients were commenced on statin therapy. 110/248 (44%) were not started on a statin, this was appropriate in 88/110 (80%) patients. Therefore 33/55 (60%) patients meeting criteria were started on cholesterol lowering therapy. The most common reasons for not starting statin therapy were not meeting clinical criteria 50/108 (46%), patient declined 26/108 (24%) and planning pregnancy/childbearing age 7/108 (6%). There was an increase in incomplete forms of (11/113) 10% from cycle 1 to (44/250) 18% in cycle 2.
Conclusion
This QIP led to an increase in statin prescription among eligible patients with T1DM in our department. While effective in achieving our aim, there were limitations (i) Not all patients meeting criteria were commenced on treatment (ii) the number of unfilled forms increased between cycles. Electronic records and mandatory completion may improve this.

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Abstract withdrawn

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Knowledge of type 2 diabetes patients about hypoglycemia

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Background
Hypoglycemia is a common but preventable complication of type 2 diabetes. Knowledge of its causes and what patients should do is essential. The main objective of our study was to describe the level of patients' knowledge about hypoglycemia. The secondary objective was to study the factors influencing this knowledge.
Methods
This was a cross-sectional observational study over a period of 3 months including patients followed for type 2 diabetes at the the Internal Medicine department of El Razi Hospital. The evaluation was carried out by a questionnaire in dialect Arabic relating to the value of hypoglycemia, its physical signs, the situations that favor it, its correction and actions to avoid it. A sufficient level of knowledge was determined by a score greater than or equal to 60%.
Results
The average age of our population was 65 years with female predominance. The rate of professional inactivity and illiteracy were high at 51.1% and 31% respectively. Only 31.6% had benefited from therapeutic education. A third of our population had an insufficient level of knowledge. Sixty-six percent of the population did not know the threshold for hypoglycemia and 38% defined it as a value less than 1g/l. Ninety-five percent of patients could correctly name 2 clinical signs of hypoglycemia. A third of patients thought that lack of insulin can be responsible for hypoglycemia. Only 74 patients corrected hypoglycemia by combining a fast sugar with a slow sugar. Ninety-eight percent of the population on insulin therapy did not master the adaptation of insulin doses according to needs. The factors that most influenced knowledge were professional activity ($P = 0.001$), secondary or higher education level ($P = 0.00$) and therapeutic education ($P = 0.047$).
Conclusion
Our study revealed a lack of patient knowledge of hypoglycemia. Repeated therapeutic education adapted to patients is desirable in order to reinforce their knowledge.

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P65

Case: the glycaemic effect of GLP-1 receptor agonist semaglutide as an adjuvant therapy in HNF1-α MODY

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MODY as a result of a genetic variant in the HNF1-α gene is traditionally treated with sulphonylureas, often with eventual progression to insulin use due to the loss of beta cell function. We present the case of a 58-year-old female who attended the diabetes service for many years for a genetically confirmed diagnosis of HNF1-α MODY. She was originally diagnosed with pre-diabetes at the age of 16 and eventually commenced on oral hypoglycaemic agents (OHAs) at the age of 23, with transition to insulin at 29. At routine diabetes review at the age of 57, Semaglutide was offered as an adjuvant to basal-bolus insulin in light of suboptimal glycaemic control with HbA1c ranging between 57 – 74 mmol/mol. There were no microvascular complications of diabetes. After 12 months of Semaglutide therapy, her HbA1c had improved to 46 mmol/mol. Dexcom G7 data revealed an improvement in time in range (TIR) from 70% preceding Semaglutide use to 78% after Semaglutide use for 12 months. Total daily dose (TDD) of basal insulin reduced by 42% (25 to 14 units) with a reduction in regular prandial insulin with all meals to PRN Novorapid with high-glycaemic-index foods. There are few case reports surrounding the use of GLP-1 receptor agonists in HNF1-α MODY. One report has shown glycaemic benefit with the addition of Liraglutide when compared with pioglitazone and insulin detemir alone, with another case showing a reduction in HbA1c from 63 to 49 mmol/mol with a switch from Glimepiride to Dulaglutide. We report the safe and efficacious use of Semaglutide in a case of HNF1-α MODY resulting in improved TIR and reduced insulin TDD. The use of GLP1-receptor agonists in HNF1-α MODY have been shown in few case reports to produce beneficial glycaemic outcomes with further evidence required to determine their safety and efficacy.

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P66

Abstract withdrawn

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P67

Specific diet and exercise patterns exert discernible effects on acute ketone metabolism in healthy adults: a cross-over observational study

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Physiological ketosis may play an important role in human health. We sought to describe, using point of care blood ketone measurements, the time to onset of ketosis (plasma beta-hydroxybutyrate (BHB) ≥ 0.5 mmol/l) when fasting, and in response to various exercise and dietary scenarios following 12- and 24-hour fasts. Ten healthy female adults had BHB concentrations measured continuously over three hours during three dietary scenarios on separate mornings, after a 12-hour fast: no breakfast, standard carbohydrate breakfast and an isocaloric low carbohydrate breakfast. On a fourth morning, they performed a supervised 60-minute bout of moderate intensity aerobic exercise at 70% of their estimated maximal heart rate. Separately, four healthy participants (2 female) underwent precisely the same set of

diet and exercise scenarios, but after a 24-hour, and with the addition of 50% and 90% exercise intensity scenarios. Exercise was associated with a higher ketone concentration area under the curve (AUC) compared to fasting (68 ± 21 mmol•h/l vs 48 ± 16, mmol•h/l, $p = 0.019$), low carbohydrate breakfast (43 ± 14 mmol•h/l $p = 0.039$) and to standard carbohydrate breakfast (41 ± 11 mmol•h/l $p = 0.002$) following the 12 hour fast. An intensity-dependent inverse effect of aerobic exercise was found with lower ketones at higher intensities, with significant differences observed at high intensity (90% HRmax) to moderate intensity (70% HRmax) exercise (89 ± 20 mmol•h/l vs 183 ± 62 mmol•h/l $p = 0.027$) following a 24 hour fast. Exercise and dietary scenarios influence circulating ketone concentrations in healthy individuals following either 12 or 24 hours of fasting to an extent that is discernible and detectable with repeated point-of-care measures of blood BHB. Whether quantification of fluctuations in BHB concentrations over time could provide meaningful feedback on diet and physical activity behaviours for people with obesity and related disorders remains to be determined

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P68

A review of hyperglycaemia management in a Model 4 hospital Emergency Department in the Republic of Ireland

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Background
Diabetic ketoacidosis (DKA) and Hyperglycaemic Hyperosmolar State (HHS) are serious emergencies with clear management guidelines, requiring early recognition and treatment. There are limited recommendations for uncomplicated hyperglycaemia management in the ED.
Aim
To review current practices regarding management of emergency and non-emergency presentations of hyperglycaemia to St. James's Hospital ED.
Methods
A retrospective review was carried out. All adults presenting to St James's Hospital ED from 1/4/23 to 31/9/23 with 'hyperglycaemia' or 'diabetes' as their coded presenting complaint were included. Their notes were examined for those with DKA or HHS and compliance to guidelines was assessed. The management of non-emergency hyperglycaemia presentations were also studied.
Results
66 patient encounters were included. 27% had type 1 diabetes mellitus. 63% had type 2 diabetes mellitus and 10% had a new diagnosis. 24% ($n = 16$) of the presentations were DKA. Just over 80% of DKA patients had appropriate initial and maintenance fluids prescribed in accordance with electrolyte levels. All DKA patients had a fixed rate insulin infusion started. Only 1 of those pre-established on insulin had their long-acting insulin prescribed. 62% had IV Dextrose prescribed pre-emptively resulting in initiation in all those whose blood sugar level (BSL) dropped below 15 mmol/l. No one without a pre-emptive prescription had Dextrose started when BSLs fell. 69% had hourly BSLs checked while only 56% had hourly ketone checks. 3 patients presented in HHS. 2 were managed with fluids, however one was immediately started on an insulin infusion. Of the remaining 47 patient encounters 19 were discharged. Of the 28 admitted only 13 were given treatment in ED.
Conclusions
We highlight the strengths and weaknesses of hyperglycaemia management in our department. Management guidelines of DKA and HHS increase compliance but cannot guarantee it. The management of non-emergency hyperglycaemia is highly variable depending upon patient factors and physician experience.

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P69

Glycaemic status, length of stay and mortality in acute pancreatitis patients admitted to intensive care

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Background
Severe acute pancreatitis (SAP) has a high rate of mortality and complications. We evaluated the association between glycaemia, length of stay (LoS) and mortality in SAP patients admitted to our intensive care unit (ICU).
Methods
Data from 91 patients admitted to ICU between December 2018 and June 2022 with a primary diagnosis of SAP were retrospectively analysed. Blood glucose levels were measured as per local standard practice. Percentages of readings above range (PAR; >10 mmol/l) and below range (PBR; <3.9 mmol/l) were calculated. Patients with overall PAR >25% were categorised into a hyperglycaemia group or a non-hyperglycaemia group otherwise. Patients with PBR >4% were categorised into a hypoglycaemia group or a non-hypoglycaemia group otherwise. Further analysis was also performed based on pre-existing diagnosis of diabetes. An unpaired t-test was used to compare normally distributed variables. Non-normally distributed variables were compared using a Mann-Whitney U test. Association between categorical variables was assessed using Chi-Squared test of independence. All p-values are two-tailed and values less than 0.05 were considered statistically significant.
Results
The overall mean number of glucose tests per day was 5.1.

Table of median LoS for hyperglycaemia/non-hyperglycaemia:

Group	n	Median (IQR) ICU LoS (days)
PAR >25% (Hyperglycaemia)	39	10.0 (4.4-36.1)
PAR <25% (Non-hyperglycaemia)	52	8.0 (3.2-17.9)

Median ICU LoS was 2 days higher in the hyperglycaemia group compared to the non-hyperglycaemia group ($P = 0.16$), however this did not reach statistical significance. No significant difference in ICU LoS or mortality was found in the hypoglycaemia group compared to the non-hypoglycaemia group. LoS and mortality were comparable in those with or without pre-existing diabetes.
Conclusion
In SAP patients admitted to ICU, we found no significant association between glycaemic status and LoS or mortality. Glucose level above 10 mmol/l was however associated with tendency for higher LoS and this may merit further exploration.

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P70

Association between impaired awareness of hypoglycaemia and psychological outcomes in people living with insulin-treated type 2 diabetes

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Background
Impaired awareness of hypoglycaemia (IAH) is associated with impaired psychological health in people living with type 1 diabetes (T1D). We explored the differences in anxiety, depression and diabetes distress according to hypoglycaemia awareness in people living with insulin-treated type 2 diabetes (T2D).
Methods
This analysis included 321 T2D participants from the Hypo-METRICS study. Participants completed the General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9) and Problem Areas In Diabetes (PAID) questionnaires at the baseline visit. IAH was defined as GOLD score >4. Chi-squared and Mann–Whitney U tests were used to examine between-group differences.
Results
27% of participants had IAH. For those with IAH vs intact hypoglycaemia awareness (NAH), median [IQR] age was 61[52-66] vs 64[56-70] years (p-value=0.02), 61% vs 65% were men (p-value=0.7), 43% vs 40% were using routine continuous glucose monitoring (p-value=0.8) and median HbA1c was 7.5% [6.8-8.5] vs 7.4% [6.8-8.2] (p-value=0.6). Participants with IAH had higher anxiety (GAD-7: 5 [2-7.5] vs 2.5 [0-6], p-value= 0.004) and depression scores (PHQ-9: 6 [3-10] vs 4 [2-8], p-value=0.017). There were no significant differences in diabetes distress scores (PAID: 20 [9-40] vs 19 [9-36], p-value= 0.5).
Conclusion
IAH in people with insulin-treated T2D is associated with higher scores of generalised anxiety and depression, as in IAH in people with T1D, but not diabetes-specific distress. While there may be confounding factors, people with T2D and IAH could be at higher risk of anxiety and depression. It is therefore important to clinically assess psychological health outcomes.

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P71

Assessing medication adherence and identifying barriers to adherence among patients with type 2 diabetes mellitus in uzbekistan

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Introduction
Diabetes mellitus (DM) significantly impacts health in Uzbekistan, with a 7% prevalence among adults aged 20-79, affecting over 1.3 million people in 2021. The disease contributed to 16,670 deaths and incurred healthcare costs of approximately 277.6 million USD, projected to rise by 25% by 2030. Poor medication adherence can lead to severe complications such as hyperglycemia and cardiovascular diseases, making it essential to understand and improve adherence rates.
Objective
The objective of the research is to measure medication adherence levels among DM patients in Uzbekistan using the Morisky Medication Adherence Scale (MMAS) method and to identify factors contributing to non-adherence.
Methodology
The 8-item MMAS was administered to patients to assess adherence over the past month, with scores ranging from 0 to 8. Additional data on sociodemographic characteristics, medical history, and barriers to adherence were collected through structured questionnaires.
Results
The study involved 121 participants with DM, predominantly aged 60 years or older (51%), with a slight majority of females (55%). Most had a high school education (67%) and were non-smokers (82%). Hypertension was common (74%) , followed by heart disease (33%) and obesity (29%). Adherence levels were high in 17% of participants, medium in 30%, and low in 53%. Common reasons for non-adherence included forgetting medication (77%), being too busy (40%), and medication delivery issues (28%). Financial constraints (28%) and the perception of taking too many medications (19%) were also significant factors. Finding prescribed medications at local pharmacies was challenging for 44% of the respondents, and 56% reported receiving insulin injections.
Conclusion
Understanding medication adherence patterns is crucial for effective management of DM. This research may inform the development of targeted interventions to improve adherence rates and enhance patient outcomes in Uzbekistan.

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P72

Impact of new start hybrid closed loop (HCL) insulin pump therapy on glycaemic control, diabetes distress and hypoglycaemia awareness in tallaght university hospital (TUH)

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Background
Diabetes nurses and dietitians, with support from the endocrinology team, led a restart of the insulin pump service for pump-naïve patients in TUH in May 2023.
Aim
To compare glycaemic control, diabetes distress and hypoglycaemia awareness pre and post HCL system use in the first 6 months.
Research Design
Patients who had completed BERGER carbohydrate counting course, attended a carbohydrate counting refresher. Food and insulin diaries, HbA1c and retinal screening results were reviewed to ensure safe and accurate HCL system settings. Patients who started HCL therapy (Medtronic 780G pump with Guardian 4 CGM) from May to October 2023 were evaluated using GOLD hypoglycaemia awareness screening tool and Diabetes Distress Scale (DDS-17) or PAID. HbA1c and CGM data were compared.
Results
Table 1. Comparison of glycaemic control in patients with data both pre and post HCL therapy.

	Pre			Post		
	n	Mean	SD	n	Mean	SD
HbA1c mmol/-mol (%)	16	64.7 (8.1%)	10.3	16	56.1 (7.3%)	6.9
Percentage Time in Range	18	41.7	18.1	18	72.6	9.8

Table 2. Proportion of patients meeting time in range targets and Diabetes Distress and Hypoglycaemia Awareness pre and post HCL Therapy. *Meeting all CGM Targets: Time in range>70%, Low<4%, very low<1%, very high<5%

	Pre		Post	
	No.	%	No.	%
Time in Range >70%	2	11.11	12	66.67
Meeting All CGM Targets*	1	5.56	7	38.89
Severe Diabetes Distress	5	31.25	4	25.00
Moderate Diabetes Distress	8	50.00	5	31.25
No Diabetes Distress	3	18.75	7	43.75
Impaired Hypoglycaemia Awareness	6	37.50	5	31.25
Normal Hypoglycaemia Awareness	9	56.25	10	62.50
Undetermined Hypoglycaemia Awareness	1	6.25	1	6.25

Conclusion
Restart of the TUH insulin pump service for pump naïve patients enabled 24 patients to successfully start HCL therapy in this 6 month period. Glycaemic control (HbA1c and time in range), diabetes distress and hypoglycaemia awareness improved.

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P73

Advanced diabetes technologies for management of type 1 diabetes mellitus (T1DM) in a visually impaired person

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Background
The leading cause of visual impairment among individuals with diabetes is diabetic retinopathy. Hybrid closed-loop (HCL) therapy has revolutionised diabetes care, offering a more automated and precise approach to insulin delivery. However, these technologies can inadvertently marginalise individuals with disabilities, including those with visual impairment.
Case
We present the case of a legally blind 70-year-old female with a 60-year history of T1DM and proliferative diabetic retinopathy. Other medical history includes ischemic heart disease, chronic kidney disease with microalbuminuria, hypothyroidism, dyslipidaemia, and hypertension. Since 2003, she has been managed with insulin-pump therapy, and more recently with sensor-augmented pump therapy,

using the Medtronic MiniMed Paradigm Veo 754 with Guardian 2 sensor. Due to difficulties with the Guardian 2 application, it was replaced by Dexcom G6. Her baseline HbA1c was 7.5% (58 mmol/mol). She has impaired hypoglycaemia awareness and experienced recurrent hypoglycaemia. Upon pump renewal, she chose the mylife Ypsomed pump with Dexcom G6 and CamAPS FX, as it allowed her to use a visual aid to view a smartphone screen.
Intervention
In-person training was conducted at the Diabetes Day Centre. Although she has limited carbohydrate counting skills, a consultation with the dietitian led to the creation of a meal chart. The bolus advisor was configured with small, medium, and large meal options.
Outcome
Over nine months, she showed significant improvement in glycaemic control: time-in-range increased from 55% to 67% and time-below-range decreased from 10% to $<1\%$. Self-reported hypoglycaemia awareness improved from <2.5 mmol/l to 3.9 mmol/l with a Gold score of 1. She expressed satisfaction with the system, noting significant reduction in the overall burden of managing diabetes.
Conclusion
HCL therapy can enhance glycaemic control and quality of life in visually impaired individuals. This case emphasises the need for individualised diabetes management strategies and the benefits of advanced technologies in complex clinical scenarios.
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P74

A challenging case of adult-onset non-diabetic hypoglycemia: unveiling glycogen storage disease type vi (hers disease)
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Introduction
Glycogen Storage Disease Type VI (GSD VI), typically diagnosed in childhood, is rarely identified in adults. This case highlights a 48-year-old woman with adult-onset non-diabetic hypoglycemia, who was ultimately diagnosed with GSD VI.
Case Description
A 48-year-old woman presented with a ten-year history of intermittent, episodic symptoms including overnight sweating, cramps, morning fatigue, mood swings, and worsening migraines. Initial investigations in primary care failed to identify a cause. Hypoglycemia was confirmed using a Libre sensor, revealing primarily nocturnal and fasting episodes, unrelated to food timing or type. The patient had no significant weight changes and denied alcohol or tobacco use. Her medical history included migraines, managed with naproxen and sumatriptan. She had no history of gastric surgery, diabetes, or a family history of similar conditions. Extensive testing at our clinic included normal HbA1c, 9 am cortisol level, kidney and liver functions, and pituitary profile. Sulfonylurea screening was negative. C-peptide and insulin responses during a prolonged fasting test were appropriate, and the IGF-2:IGF-1 ratio was normal. Further fasting tests revealed elevated free fatty acids, beta-hydroxybutyrate, and some urinary organic acids, with normal carnitine and CK levels. Imaging studies, including a CT abdomen and pelvis (CTAP), were unremarkable. These findings excluded hyperinsulinemia-related causes such as insulinoma and pointed towards a possible metabolic cause related to glycogen utilization. Our endocrine MDT recommended a workup for GSD. Despite no pathogenic variant detected in genetic analysis for GSD, enzymatic analysis revealed abnormal kinetic activity in the glycogen phosphorylase enzyme, leading to a diagnosis of GSD VI (Hers disease).
Conclusion
This case underscores the complexity of diagnosing adult-onset non-diabetic hypoglycemia and highlights the importance of comprehensive metabolic evaluation and enzyme activity analysis in identifying the cause. The diagnosis in this patient suggests that mild variants of GSD VI may be underdiagnosed in the adult population.
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P75

An adipose organoid model for investigating adipose health and function
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Background
In obesity the relationship between white adipose tissue expansion and neovascularisation becomes uncoupled leading to inadequate perfusion of adipose tissue. Under these circumstances the secretory profile of adipocytes becomes metabolically unfavourable and pro-atherosclerotic. Therefore, targeting white adipose tissue may provide a potential therapeutic strategy to combat the negative metabolic and cardiovascular consequences of obesity. Here, we validated a murine adipose organoid model, which mimics adipose function including vascularisation.
Methods
To culture adipose spheroids, stromal vascular fraction cells were isolated from epididymal adipose tissues from C57BL/6 mice and seeded in a low adhesion 96-well plate. Adipose differentiation was initiated with differentiation media. Following initiation of adipose differentiation, adipose organoids were maintained in growth media for 8 days. To confirm different cell types were present in cultured organoids, gene expression of various cell-specific markers was quantified using real-time PCR. 3T3-L1 fibroblasts and whole adipose tissue from wild-type mice served as negative and positive controls respectively. To assess the vascular phenotype of the adipose organoids, organoids were fixed for immunofluorescence.
Results
Data was presented in fold changes relative to 3T3-L1 fibroblasts. Gene expression studies revealed cultured adipose spheroids expressed adipocyte markers *Adipoq* (3600-fold increase), *Fabp4* (1200-fold increase) and *Hoxc8* (16000-fold increase); endothelial cell markers *Cdh5* (100-fold increase), *Kdr* (200-fold increase) and *Pecam1* (20-fold increase); immune cell markers *Cd14* (6-fold increase), *Cd68* (100-fold increase), *Csf2ra* (1000-fold increase), *Fcgr2b* (barely detected in 3T3-L1 fibroblasts but expressed at comparable level to adipose tissue) and *Icam1* (1500-fold increase). In addition, using immunofluorescence, cultured adipose spheroids present vessel-like structures stained with isolectin B4.
Conclusion
Here, we demonstrate that this adipose organoid model displays markers of diverse cell types. Immunofluorescence analysis reveals the presence of vessel-like structures within these cultured organoids. These findings demonstrate the suitability of our model for advancing studies on adipose health and function.
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P76

Investigative approach using smart insulin pens in a young person with type 1 diabetes and recurrent prolonged hypoglycemic episodes
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This is a case of an 18-year-old person living with Type 1 Diabetes, presenting with unusual severe hypoglycemic episodes, on insulin Detemir twice daily and insulin Aspart with meals. Episodes appeared prolonged in duration requiring IV glucose infusions with a total of four inpatient admissions. Intentional overdose was recurrently denied, and smart insulin pen downloads confirmed normal expected insulin dosing. Investigations included a Short Synacthen Test with a stimulated 30-minute cortisol of 678 nmol/l, negative insulin antibodies, suppressed insulin and c-peptide levels, a plasma 3 hydroxybutyrate level of 0.2 mmol/l and a potassium of 3.0 mmol/l on admission. Antibodies for coeliac were also negative and both IGF-1 and IGF-2 levels were in normal range. Eventually a second pen was found and downloaded, showing significant amounts of insulin dialed, including 309.5 units and 570 units on two separate occasions. The second dose had been administered during a hospital admission for severe hypoglycemia. He then admitted administering the above amount of insulin on a background of significant life stressors and history of self –harm. Samples stored for analogue insulin measurement in Cologne were no longer required with financial savings. This case highlights, how the smart insulin pen technology can be a tool in intentional insulin overdoses. Mental health support was the key to prevent an impending medical emergency in this scenario.
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P77

Characteristics of hypoglycaemia and its outcomes in people with continuous glucose monitoring (CGM) devices: pilot data from the DEKODE hypoglycaemia study
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Background
Continuous Glucose Monitoring (CGM) devices are increasingly used to track blood glucose levels in individuals with diabetes. Despite widespread agreement on their benefits, limited information exists regarding the characteristics and clinical outcomes when these individuals experience hypoglycemia.
Objective
To investigate the characteristics of hypoglycaemia and its outcomes in people using CGM devices.
Methods
This retrospective study was conducted across five hospitals in the UK between October 2023 and January 2024. Participants included those using CGM devices who experienced hypoglycemia during the study period and were treated for it in the five hospitals. Data collected encompassed sociodemographic information, precipitating factors, management strategies, outcomes, and the total duration of hypoglycaemia. Data analysis was performed using SPSS 29.0.
Results
A total of 104 hypoglycaemic episodes (96 with type 1 diabetes, 8 with type 2 diabetes) were identified, with 69 occurring in an inpatient setting. Among the participants, 50% were male. The median age was 35.5 years (interquartile range [IQR] 34.0-50.0 years), and the median Charlson comorbidity index was 5 (IQR 4-6). The median HbA1C level before admission was 75 mmol/mol (IQR 60-98 mmol/mol). Hypoglycaemia episodes were classified as follows: 61.5% at level 1, 31.7% at level 2, and 6.7% at level 3. The median duration of hypoglycaemia was 69 minutes (IQR 22-110 minutes). The primary precipitating factor was missed meals (42.3%), and the others included incorrect insulin dosage (1.9%), intercurrent illness (3.8%), multiple factors (30.8%), and other unclear reasons (21.2%). During these episodes, 7.2% patients received glucagon, but only 1.9% were prescribed glucagon upon discharge.
Conclusion
Missed meals were the most common precipitating factor for hypoglycaemia. Notably, only a small percentage of patients were prescribed with glucagon upon discharge. These findings emphasise the need for improved education for healthcare professionals on preventative strategies of hypoglycaemia in patients using CGM devices.

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P78

Audit on recognition and management of steroid-induced hyperglycemia in tipperary university hospital

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Introduction
Glucocorticoid use is well-known to exacerbate uncontrolled blood sugar levels in patients with known diabetes and worsen glycemic control in non-diabetics. Steroid induced hyperglycemia (SIH) is one of the most prevalent side effects with approximately 18-52% of patients experiencing it following steroid initiation [1]. There is a lack of guidance for SIH in Tipperary University Hospital (TUH) which prompted this audit. Our aims were to identify whether SIH was being screened for and recognize what treatment plans were being initiated.
Methods
Patients treated with steroids were identified via the TUH Hospital in-patient Enquiry (HIPE) database, between September 2021 and 2022. The charts were examined retrospectively to evaluate whether these patients were identified and subsequently managed for SIH. We audited the patient notes, drug and insulin prescribing charts, to establish their diabetes status, treatments given, whether blood glucose levels (BGL) were monitored, and if endocrine services were consulted. No personal identifiers were recorded.
Results
Twenty-six patients' charts were recruited. Thirteen people had pre-existing diabetes, who were predominantly (77%) type-2 diabetics. Only fourteen (54%) patients on steroids had their BGL monitored whilst their steroids were initiated, with ten of them (71%) developing SIH. Among the diabetics, all received BGL monitoring after steroids were initiated, while only one non-diabetic had their BGL monitored. Pre-meal insulin supplementary scale was the most common intervention employed, with only twelve (46%) patients being referred to endocrine.
Conclusion
SIH is common but often missed. Its diagnosis is potentially harmful as it leads to poor wound healing, increased rates of hospital-based infections and mortality, which should motivate healthcare workers to monitor its occurrence and manage it appropriately. Deviation in practice exists due to lack in formal local guidance, and this audit provides a starting point for further quality improvement projects.

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P79

A retrospective look at HBA1C levels in type 1 diabetes patients in GUH pre- and post-initiation of hybrid closed loop pump therapy

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Aim
To evaluate HbA1c values in patients attending the diabetes service at Galway University Hospital before and after initiating hybrid closed loop pump therapy.
Background
Advancements in the treatment of Type 1 diabetes mellitus, especially the development of hybrid closed loop pump systems, have greatly improved blood glucose management. These systems automate insulin delivery based on real-time glucose readings, enhancing glycaemic control, and alleviating the self-management burden for patients. Consequently, an increasing number of patients are starting on hybrid closed loop pump therapy.
Methods
We reviewed our patient cohort who began hybrid closed loop pump therapy, including within the last three years, assessing their HbA1c levels both before initiation and at least three months post-therapy. This allowed us to evaluate the impact of the pump on long-term glycaemic control.
Results
We analysed 278 patients: 225 using Medtronic 780G, 49 with the Tandem T-slim X2, and 4 with the Ypsomed Cam APS. Among these patients, 144 exhibited improvements in their HbA1c levels with improvements ranging from a minimum of 2.9% to a maximum of 48%. 87 patients either had no HbA1c data post pump therapy or had been on pump therapy for only 1-2 months. The remaining 48 patients experienced no change or a deterioration in their HbA1c levels following the initiation of pump therapy.
Conclusion
This audit demonstrates that the majority of patients experienced an improvement in HbA1c levels following the initiation of hybrid closed-loop therapy. Cases where HbA1c levels remained unchanged or worsened were mainly attributable to technical issues or user errors. Overall, the findings suggest that hybrid closed-loop therapy is associated with enhanced glycaemic management in patients with type 1 diabetes mellitus.

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P80

Monitoring and management of inpatients on systemic glucocorticoids – quality improvement for inpatient care

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Background
Blood glucose monitoring for inpatients on systemic glucocorticoids is recommended by The Joint British Diabetes Societies for Inpatient Care, due to increased insulin resistance. Stress dosing of steroids during acute illness is recommended by the Society of Endocrinology in patients taking long-term systemic steroids due to the increased likelihood of suppressed hypothalamo-pituitary-adrenal function.
Aims
We aimed to determine whether capillary blood glucose (CBG) and HbA1c were measured in inpatients on systemic steroids, with and without a diagnosis of diabetes. We also assessed whether stress doses of steroids were given to inpatients on long term steroids admitted with acute illnesses.
Methods
A cross-sectional study was carried out in adult medical, surgical, and critical care wards in Midlands Regional Hospital Portlaoise in early May 2024.
Results
9 of 81 inpatients (11%) were on systemic (oral and IV) glucocorticoids on the day of the study. Mean age of inpatients on steroids was 72.7 ± 14.3 years. Of those on steroids, 78% had no known pre-existing diabetes. CBG monitoring was

not performed in any of the inpatients on systemic steroids with no known diabetes. CBG monitoring was performed appropriately on all patients with known diabetes ($n = 2$). 22% of inpatients on systemic steroids had HbA1c measurements within a 3-month timeframe. Patients on long term steroids ($n = 2$) did not receive stress dose steroids during admission.

Conclusion

This study demonstrated blood glucose monitoring was not performed on inpatients on steroids without pre-existing diabetes although this cohort of patients were at risk for steroid-induced diabetes due to their age and co-morbidities. This audit also identified the knowledge gap among the hospital staff to administer stress doses of steroids for patients on long-term steroid therapy during acute illness. This highlights a need for ongoing education to staff and implementation of local policies together with the hospital pharmacy department.

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P81

Assessing the prevalence of MASLD in a cohort of patients attending the diabetes clinic in a single centre - using the fibrosis-4 (FIB-4) index for liver fibrosis

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The prevalence of Metabolic Associated Steatotic Liver Disease (MASLD) is approximately 55% in patients with Type 2 diabetes (T2DM). The EASL-EASD-EASO guidelines recommend screening patients with T2DM for MASLD. Fibrosis-4 Index (FIB-4) is a simple tool used to screen for MASLD in T2DM. FIB-4 scores are characterised as; low (<1.3), moderate (1.3 – 2.67) or high risk (>2.67). The aim of the audit was to screen a consecutive number of patients attending the out-patient clinic with T2DM with the FIB 4 score to determine risk of MASLD.

Methods

Consecutive patients attending the out-patient clinic in April 2024 were included. Data including demographics, year of diagnosis, medications, body mass index, haemoglobin A1C and laboratory values were collected using the Beaumont Hospital electronic patient record (CELLMA) and laboratory database. FIB-4 score was calculated using the age adjusted formula, age $\times$ AST (IU/l)/platelet count ($\times 10^9$/l) $\times \sqrt{}$ALT (IU/l).

Results

49 patients were included. Average age was 66 years; one third were female. BMI was 29.97kg/m^2 $\pm$5.54; 40% had a BMI greater than 30kg/m2. The average FIB-4 score was 1.33 $\pm$0.8. 29 patients were low risk, 17 were moderate and 6 were high risk.

	Low risk ($n = 29$)	Moderate to high risk ($n = 20$)
Percent of total (n 49)	59	41
Age (mean)	62	72
BMI (mean, in kg/m2)	29.9$\pm$4.9	30$\pm$6.7
Duration of diabetes (years)	15.18	14
Metformin (%)	90	90
Sulphonylurea (%)	45	40
SGLT2i (%)	66	50
DPP4i (%)	38	40
Pioglitazone (%)	3	0
GLP1RA (%)	41	30
Insulin (%)	31	15

Comparison between risk groups and their baseline characteristics

Conclusion

This audit demonstrates that 40% of patients with T2DM merited referral for fibroscan or to hepatology. Changes are needed to encourage the routine use of the FIB-4 scoring system in patients with T2DM, in particular now that medications such as GLP-1RA therapy may benefit patients with MASLD.

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P82

Monogenic diabetes screening in the midwest of ireland

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Monogenic diabetes is estimated to account for as much as 4% of childhood and adolescent diabetes. Positive test rates for monogenic diabetes in the UK have been reported as 23%[1]. The aim of this study was to determine positive testing rates among adults within the University of Limerick Hospital Group catchment population of approximately 413,000 people. Adults (age $>$16years) who underwent screening for monogenic diabetes over a 24 month (January 2021 to December 2022) were identified from biochemistry laboratory records and included in the study. Hospital records were used to acquire clinical and biochemical data. Twenty-two adults underwent screening for monogenic diabetes during the study period. The mean$\pm$SD age at the time of screening was 47.3$\pm$18.1 years. 86.4% of this group underwent proband screening with the remainder having a relative with a known monogenic diabetes diagnosis. Nine adults (41%) tested positive for monogenic diabetes, seven for pathogenic *GCK* mutations and two for mitochondrial diabetes. There was no significant difference in mean$\pm$SD age of those testing positive (45.4$\pm$19.9years) vs testing negative (48.5$\pm$18.3years), $P = 0.35$. The positive testing rate among probands and relatives was 36.8% and 66.7% respectively. Islet antigen antibody testing and c-peptide measurement are considered a pre-requisite to genetic testing. However, $n = 3$(13%) had no previous antibody testing and c-peptide levels were not measured for $n = 8$(35%). When measured, c-peptide was detectable in all. A MODY probability score was not recorded for any patient yet was only applicable in $n = 4$ due to age $>$ 35 or missing biochemical data. To conclude monogenic diabetes testing rates among adult probands is 2.3/100,000 per year in the Midwest of Ireland. Rates of monogenic diabetes detection among adults within this region exceed the average reported across the UK[1].

Reference

1. Pang, L. *et al.* (2022). *Diabetes Care*, 45(3), pp. 642–649. doi:10.2337/dc21-2056.

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P83

Diabetic ketoacidosis, urosepsis and emphysematous osteomyelitis in a patient on an SGLT2 inhibitor

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Emphysematous osteomyelitis (EO) is a rare, potentially fatal infection caused by gas forming organisms. It is characterized by the presence of intraosseous gas. Diabetes is a predisposing condition. SGLT2 inhibitors increase the risk of urinary infection and Diabetic Ketoacidosis (DKA). A 78-year-old man presented with a one-week history of flu-like symptoms and lower back pain. He had a history of type 2 diabetes, and had been started on an SGLT 2 inhibitor. He was found to be in DKA, with raised inflammatory markers. *Klebsiella pneumoniae* was isolated in blood and urine cultures. Imaging was performed to investigate the lower back pain. Computed Tomography showed extensive pockets of air on the L4 and L5 vertebral bodies, with extension into the iliopsoas muscles bilaterally and the anterior epidural space. Magnetic resonance imaging showed an epidural abscess along the posterior body of L5. Findings were consistent with EO and an iliopsoas abscess. Urosepsis with lymphovascular drainage to the lumbar region is considered the likely route of transmission. *Klebsiella Pneumoniae* is not commonly associated with osteomyelitis. However, a literature review of EO identified *Klebsiella Pneumoniae* as the causative agent in 20% of all reported cases in the literature. Diabetes was a predisposing factor in 34% of cases. In recent years, hypervirulent strains of *K pneumonia* have been identified, causing invasive infections including liver abscesses and necrotizing fasciitis. Diabetes is reported to predispose to this syndrome. Though it is not clear the degree to which the SGLT2 inhibitor contributed to the development or course of this infection, the case emphasizes the importance of considering the increased risk of urinary infections when prescribing SGLT2 inhibitors to patients with diabetes, given their predisposition to aggressive infections. It also highlights the role for cross sectional imaging in patients with diabetes and *klebsiella* bloodstream infection.

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P84

Implementation of diabetic ketoacidosis guidelines and its impact on patient outcomes

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Introduction
Revised guidelines by the Joint British Diabetes Society-Inpatient (JBDS-IP) recommend reducing the fixed rate intravenous insulin infusion (FRIII) from 0.1 to 0.05 units/kg/hour and starting 10% glucose at 125 ml/hour when blood glucose levels fall below 14 mmol/l.
Aim
This study evaluates trends in implementation, associated outcomes with the revised JBDS-IP guidelines for DKA management in the UK.
Methods
A retrospective review of DKA admissions from October 2021 to March 2023 was conducted across five UK hospitals. The uptake of FRIII reduction was monitored, the time between blood glucose reaching 14 mmol/l, initiation of 10% dextrose, FRIII reduction was analysed.
Results
We observed 753 DKA admissions across five hospitals, with a gradual uptake of the guidelines for reducing FRIII prescriptions, reaching 49.7% over 18 months. In episodes where FRIII rate reduction guidelines were followed, a significant delay was noted between initiating 10% Dextrose and reducing FRIII when blood glucose dropped below 14 mmol/l (median [IQR] hours – all episodes: 0.5 (0.1 – 1.8) vs 3.2 (0.7 – 6.5), $P = .00001$). The reduction in hypoglycaemia was not significant (16.5% vs 13.8%, $P = .344$), except in one hospital, a higher hypoglycaemia frequency was observed (18.2% vs 7.8%, $P = .016$). There was a trend towards longer DKA episodes [hours] (23.7 (13.6 – 31.8) vs 16.2 (10.8 – 24.4), $P = .060$), higher total units of FRIII administered (152.7 (81.3 – 254.3) vs 115.8 (64.7 – 192.8), $P = .085$). No significant differences were found in hypokalaemia (33.5% vs 30.7%, $P = .448$), hyperkalaemia (29.4% vs 29.9%, $P = .881$), DKA duration (17 (12-25) vs 17 (11-27), $P = .750$), length of stay (3.4 (2.4-5.6) vs 3.4 (2.1-6.8), $P = .753$) between the groups.
Conclusion
The study reveals suboptimal adoption of the revised JBDS-IP guidelines for FRIII rate reduction in DKA management, with no significant improvement in outcomes. Further efforts are needed to address barriers to effective guideline implementation.

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P85

A novel bipyrazole compound as a potential therapeutic agent for diabetes mellitus through PGK1/AKT activation

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Background
Diabetes mellitus type 2 (T2D) is a prevalent metabolic disorder characterized by insulin resistance and high blood sugar levels. Existing treatments focus on managing these symptoms, but there is an ongoing need for more effective interventions. Our study explores the potential of 2′,3,3,5′-Tetramethyl-4′-nitro-2′H-1,3′-bipyrazole (TMNB) in this context, based on its presumed impact on oxidation, glycation, and insulin resistance processes.
Aims/Purpose
The primary objective of this research was to investigate the efficacy of TMNB as an intervention for T2D. We aimed to understand its effects on insulin sensitivity, blood glucose levels, and molecular pathways involved in glucose metabolism.
Methods
Our study employed both *in vitro* and *in vivo* models. We induced T2D traits in mice using a high-fat diet (HFD) and streptozotocin (STZ) injections. These mice were then treated with TMNB at a dosage of 10 mg/kg daily for 12 weeks. Parallel to this, *in vitro* experiments were conducted using HepG2 cells, a human liver cell line integral to glucose metabolism, to assess the impact of TMNB on oxidative and glycative stresses.
Results
in vitro studies revealed that TMNB significantly reduced oxidative and glycative stresses in HepG2 cells, leading to increased insulin sensitivity. In the *in vivo* mouse model, TMNB treatment resulted in a decrease in fasting glucose levels and an improvement in insulin responsiveness. At the molecular level, TMNB was observed to activate phosphoglycerate kinase 1 (PGK1), enhancing the AKT signaling pathway, which is crucial for glucose uptake and counteracting insulin resistance.
Conclusion
Our findings suggest that TMNB holds significant potential as a therapeutic agent for managing T2D, primarily through its action on PGK1 and the AKT signaling pathway, highlighting the importance of targeting molecular pathways to improve glucose metabolism and insulin sensitivity.

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P86

Audit on diabetic ketoacidosis (DKA) management in county hospital navan

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Introduction
DKA is a fatal complication of diabetes mellitus, if not treated appropriately. In hospital guideline on management of DKA has been developed in Our lady's hospital Navan and updated last in 2019.
Aim
To assess the adherence of DKA guideline in our hospital and to assess the complexity of medical admissions with DKA in our hospital.
Methods
We collected retrospective data for our audit and prospective data on our re-audit with the help of hospital records, analyzed the data on excel. Audit was presented in hospital grand-rounds and re-audit conducted post education.
Results
Audit was conducted on retrospective data of inpatients between 1st of January 2023 to 31st December 2023, Re-audit was conducted prospectively between 15th of January 2024 to 15th of April 2024. In the audit 30 patients were included, with mean age of 38.5 ± 22.4 years, average length of stay of 4.5 days, with mean blood glucose levels of 24.5 ± 9.21 mmol/l, mean ketone levels of 5.2 ± 1.2 mmol/l, mean HCO3 of 14.6 ± 4.6 mmol/mol, and mean Ph of 7.21 ± 0.13. Compliance with guidelines on fluid replacement was 95%, with insulin dose was 91% and with K replacement was 91%. In the Re-audit, 3 patients were included, with a mean age of 25 ± 4.5 years, average length of stay was 3.3 days, mean glucose of 19.4 ± 6.5 mmol/l, mean ketone of 6.1 ± 0.5 mmol/l, mean HCO3 of 17.4 ± 3.6 mmol/mol, and mean Ph of 7.2 ± 0.01. Overall compliance rates with fluids, insulin and K replacement in the re-audit was 100%.
Conclusion
We have highlighted the importance of completing an audit cycle with education of doctors on management of DKA in a county hospital.

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P87

Clinical audit on awareness among doctors of a county hospital navan on diabetes and rules of driving

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Introduction
Hypo-glycaemia awareness and education on rules of driving are paramount in patients who are on regular insulin and are driving currently. It is the responsibility of the prescribing physician to make sure that patients who are prescribed insulin are educated on the rules of driving.
Aim
To assess and educate the doctors of a county hospital, on implications of hypo-glycaemia on driving and to update them on the national driving licence service's (NDLS) guidelines in Ireland.
Methods
We designed a questionnaire, based on the NDLS guidelines for recognition and management of hypo-glycaemia, and asked all the doctors in the hospital to answer the questionnaire, then educated them in the grand rounds of the hospital. We then requested them to fill the questionnaire again after a month of education to assess for improvement.
Results
Audit was conducted in November 2023, in which 42 doctors participated, with an average score of 70% correct answers, in which the medical department had an average score of 72%, surgical department of 64% and emergency department of 70.6%. Post education in December 2023, we conducted a re-audit in January 2024. 39 doctors participated in the re-audit and scored an average of 72%, with medicine departments average score of 72.9%, surgical departments score of 67.9% and emergency departments score of 75.3%.
Conclusion
This audit demonstrated an improvement in knowledge around educating patients on hypo-glycaemia and driving with a simple once off intervention of education

of one hour in grand-rounds of a county hospital, highlighting the need for continual education around this topic.

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P88

Insulin-releasing and glucose-lowering effects of gallic acid in cellular and high fat-fed mice models of type 2 diabetes

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Aim
Gallic acid is one of the major bioactive phenolic compounds that have been isolated from several plant extracts with reported antidiabetic actions. However, insulinotropic effects and mechanisms underlying antidiabetic actions of garlic acid is poorly understood. This study investigated insulin-releasing and glucose-lowering effects of gallic acid.
Methods
Glucose-stimulated insulin secretion in BRIN-BD11 cells were examined in the absence or presence of graded concentrations of gallic acid or in combination with modulators of insulin secretion. Cytotoxic effects in cells and effects of garlic acid on glucose tolerance in mice with diet-induced obesity-diabetes were also examined.
Results
Gallic acid (0-10μM) stimulated significant ($P < 0.01$ -0.001) and non-toxic dose-dependent secretion of insulin release from BRIN-BD11 cells with the highest stimulatory effect (2.1-fold, $P < 0.001$) at 10μM. Chronic (24 h) exposure of BRIN-BD11 cells to gallic acid produced enhanced insulin secretion (0-10 μM, 1.2- to 1.5-fold, $P < 0.001$-0.05). Insulin-release stimulatory actions of gallic acid increased with increasing glucose concentration (1.1mM to 5.6mM = 33%, $P < 0.001$; 5.6mM to 16.7mM = 11%, $P < 0.01$) and in the presence of stimulators (30mM KCl = 4.6-fold, $P < 0.001$; tolbutamide = 200μM, 2.4-fold, $P < 0.01$). Reduced effects were observed in incubations lacking calcium (44%, $P < 0.01$) and in the presence of verapamil (50nM, 31%, $P < 0.01$) and diazoxide (300μM, 27%, $P < 0.01$). Garlic acid increased intracellular calcium concentration (24%, $P < 0.05$) and membrane potential (20%, $P < 0.05$) in BRIN-BD11 cells as well as glucose tolerance (22%, $P < 0.05$) and plasma insulin (23%, $P < 0.05$) in high fat-fed mice.
Conclusion
These results encourage the investigation of long-term effects of garlic acid in animal models of type 2 diabetes.

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P89

Outcomes of real-time continuous glucose monitoring in adults with type 1 diabetes - quality improvement in diabetes care in a regional diabetes service in Ireland

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Background
NICE 2022 updated guidelines and the updated Irish guidelines (launched on 10th May 2024) in type 1 diabetes (T1D) in adults recommend the use of continuous glucose monitoring (CGM) based on individual preferences and needs. This study aimed to evaluate the outcomes of Dexcom real-time CGM (rt-CGM) in adults with T1D attending our regional diabetes service.
Methods
A retrospective data analysis was conducted from the Dexcom Clarity platform for adults with T1D (≥16 years), who were sharing the data with our service up to April 2024.
Results
rt-CGM metrics data from 173 adults with T1D were studied. The median age of the cohort was 38 years (IQR = 22), with a gender distribution of 98 males and 75 females. 18% used Dexcom G6 and 82% were on Dexcom G7. Median Time in Range (TIR) was 43% (IQR = 31), Time Below Range (TBR) was 1% (IQR = 3), Glucose Management Indicator was 8% (IQR = 1.5), glycaemic variability was 35% (IQR = 8.2) and Time CGM Active was 97% (IQR = 6.4). High engagement with rt-CGM was observed with 96% regularly wearing their devices (>70% active CGM time). However, only 12% met the recommended target TIR >70%. When the study cohort was categorized into three age groups, 4.9% (16-25 years), 16.9% (25-45 years), and 10.9% (>45 years) achieved the recommended TIR > 70%. Conversely, 82.9% (16-25 years), 77.9% (25-45 years) and 76.4% (>45 years), maintained TBR <4%.
Conclusion
Our study revealed a strong adherence to rt-CGM use among adults with T1D. Majority of rt-CGM users achieved TBR targets, indicating the benefit of reduced hypoglycaemia likely due to rt-CGM hypo alerts. However, only a small proportion of rt-CGM users met the recommended TIR target. Enhanced patient education, continuous provider training, and improved integration of CGM data into clinical practice are recommended to optimize diabetes care outcomes.

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P90

CCR5 activation stimulates adipocyte differentiation through ERK-dependent pathway

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Obesity is associated with low-grade chronic inflammation. Studies demonstrated that RANTES and CCR5 mRNA levels were significantly increased in visceral adipose tissue of obese patients compared with lean control. However, the role of CCR5 activation on pathogenesis of obesity is not clear. The purpose of this study is to explore the effects of CCR5 activation on adipogenesis and its underlying regulatory mechanisms. 3T3-F442A preadipocytes and primary preadipocytes isolated from wild type (WT) and CCR5 knockout ($CCR5^{-/-}$) mice were used to explore the role of CCR5 activation on adipocyte differentiation. To investigate the role of CCR5 on obesity *in vivo*, male C57BL/6J WT mice and $CCR5^{-/-}$ mice were fed a normal chow (NC) or a high-fat diet (HFD) for 2 months, and plasma RANTES, the fat pad weight, adipocyte size of adipose tissues, and adipose CCR5 expression were measured. Results were showed that treatment with RANTES stimulated intracellular triglyceride accumulation and the expression of adipogenic transcription factors, such as PPARγ and C/EBPα, and adipocyte-specific protein a P 2 during the process of adipocyte differentiation. These findings suggested RANTES stimulated adipocyte differentiation. Pretreatment with CCR5 inhibitor maraviroc and ERK inhibitor PD98059 significantly inhibited RANTES-stimulated adipocyte differentiation. Besides, RANTES also stimulated adipocyte differentiation in the primary preadipocytes isolated from wild type mice but not CCR5 knockout ($CCR5^{-/-}$) mice. Furthermore, compared with NC feeding, elevated plasma RANTES level and adipose CCR5 expression, and obesity were observed in WT mice fed with HFD, but not $CCR5^{-/-}$ mice. In conclusion, CCR5 activation by RANTES stimulated adipocyte differentiation via ERK-dependent pathway. CCR5 plays an important pathogenic role in the development of obesity.

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P91

Characterization of plasma free amino acid profile in patients with type one diabetes in jordan

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Type 1 diabetes mellitus (T1DM), typically emerging in childhood, is an autoimmune condition where T cells destroy insulin-producing islet β cells in the pancreas. Chronic hyperglycemia from diabetes results in significant organ damage, including the kidneys, eyes, nerves, heart, and blood vessels. The study of plasma-free amino acids (PFAA) profiles in T1DM within the Jordanian population is scant and not well-documented. This research analyzed the PFAA profiles in Jordanian children with T1DM, involving 100 people with T1D and 100 control participants. Analytical assessments covered various amino acids (acidic, basic, aromatic, branched-chain, glucogenic, and ketogenic). Clinical examinations included BMI, blood pressure, fasting blood sugar (FBS), glycosylated hemoglobin (HbA1c), and lipid profiles. Results indicate significant differences in FBS, HbA1c, LDL-c, and total cholesterol between diabetic and non-diabetic groups. Diabetics displayed elevated branched-chain amino acids

(Ile and Leu), methionine, and arginine, while levels of glutamic acid, histidine, and phenylalanine were lower compared to non-diabetics. The analysis also revealed notable variations in other amino acids such as aspartic acid, serine, alanine, cysteine, tyrosine, phenylalanine, histidine, lysine, and arginine between groups, indicating altered amino acid metabolism associated with diabetes. Moreover, glucogenic and ketogenic amino acids significantly increased in the diabetic group, suggesting shifts in metabolic pathways. The study found strong positive correlations of specific amino acids with key clinical indicators. For instance, HDL levels correlated positively with isoleucine, cholesterol with tyrosine, and HbA1c with both isoleucine and histidine. These findings underscore the potential of PFAA profiling not only in understanding metabolic alterations in T1DM but also in enhancing early diagnosis and management of the condition. This expanded insight into the amino acid profiles provides a deeper understanding of the biochemical impacts of T1DM and offers avenues for targeted therapeutic strategies.

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P92

Investigation of the mechanism underlying the antidiabetic actions of extracts of *Ocimim basilicum*

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Aim
Ocimum basilicum extract is used traditionally for type 2 diabetes treatment in developing countries. Studies have reported antidiabetic properties of aqueous and methanolic extracts of *O. basilicum* but mechanisms underlying these actions are not fully understood.
Methods
Insulin-releasing effect of *O. basilicum* extract (0.1 – 1000μg/ml) were investigated using BRIN-BD11 cells. Effects of the extract (100μg/ml) on insulin secretion at various glucose concentration, presence of established modulators of insulin secretion and in the absence of extracellular calcium were also investigated. Insulin concentrations were measured by ELISA. Total flavonoids and phenolics content, phytochemicals, Cytotoxicity, protein glycation and intracellular calcium concentration were investigated.
Results
O. basilicum extracts stimulated non-toxic insulin secretion at concentration $\geq$0.1 mg/ml in a dose-dependent manner. Insulin secretion increased by 2.95-fold at 1000 μg/ml and the lowest stimulation of insulin was observed at 10 μg/ml (0.5-fold, $P < 0.001$) compared to glucose (5.6mM) control. Insulin-release increase with increasing glucose concentration (1.1mM to 5.6mM, 10%, $P < 0.05$, and 5.6mM to 16.7mM, 13%, $P < 0.05$). Actions of the extract was reduced in the presence of diazoxide (300μM, 30%, $P < 0.01$), verapamil (50 μM, 29%, $P < 0.01$) and in the absence of extracellular calcium (29%, $P < 0.05$). Enhanced insulin secretion was observed in incubations containing KCl (30mM, 3.2-fold, $P < 0.001$) and IBMX (200μM, 2.1-fold, $P < 0.01$). Intracellular calcium concentration significantly improved on exposure to *O. basilicum* by 24% ($P < 0.01$). Preliminary screening of phytochemicals shows presence of alkaloids, flavonoids, tannins and saponins. *O. basilicum* shows significant concentration of both total flavonoids and phenolics content, improved protein glycation.
Conclusions
These results suggest that the anti-diabetic properties of *O. basilicum* extract may involve the $K_{AT\ P}$ -dependent pathway and motivate future investigation of its *in vivo* effects.

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P93

Role of cannabinoid type 2 receptor in white adipocyte browning

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The browning of white adipocytes can increase energy expenditure through the activity of uncoupling protein 1 (UCP1) located on the mitochondrial inner membrane. The endocannabinoid (EC) system, composed of endogenous cannabinoids and cannabinoid receptors, has been shown to regulate energy balance in the body. A previous research has demonstrated that blocking the cannabinoid type 1 receptor (CB1R) causes white adipocyte browning. However, the mechanism of the EC system regulating white adipocyte browning was still not elucidated. 2-Arachidonoylglycerol (2-AG), one of the endogenous endocannabinoids, can activate CB1R and CB2R. Our results showed that treatment with 2-AG in 3T3-L1 adipocytes could increase expressions of adipocyte browning markers, including UCP1, PRDM16, and PGC1α. The 2-AG-induced upregulation of browning markers was substantially abolished by pretreatment with a CB2R antagonist. These findings suggested that CB2 activation could induce white adipocyte browning. JWH133, a CB2R agonist, also decreased lipid droplets' diameter in 3T3-L1 adipocytes. Based on the results of Seahorse XF Mito stress test, we found that the mitochondrial respiration function of 3T3-L1 adipocytes was increased when treated with JWH133. Furthermore, one-week JWH133 subcutaneously infusion (0.2 mg/kg/day) caused weight reduction in both epididymal adipose tissues (eWAT) and inguinal adipose tissues (iWAT) in mice. Additionally, a reduction in adipocyte size in iWAT was also observed. It also enhanced UCP1 protein levels and UCP1 immunoreactivity signal in iWAT. In coclusion, our studies demonstrated that activation of CB2 receptors could induce white adipocyte browning *in vitro* and *in vivo*. These finding provide a novel perspective for the clinical application of CB2 in promoting energy metabolism to treat obesity and associated diseases.

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P94

Does technology help? inpatient hypoglycaemia: potential benefits of an electronic insulin management solution

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Hypoglycaemia in hospitalised patients with Diabetes is common, confers higher morbidity/mortality, prolongs length-of-stay and increases re-admission rates. Previous audit identified adequate initial treatment of hypoglycaemia but poor subsequent management risking recurrent episodes. In March 2023, insulin prescribing moved from paper-based to an electronic medicines management process in line with other medication prescriptions in our institution. An alert for electronic prescription of a hypoglycaemia plan was created for all patients prescribed insulin and a "hypoglycaemia alert" for recurrent hypoglycaemia was incorporated. This audit aimed to clarify that introduction of an electronic insulin management solution did not negatively affect hypoglycaemia management in comparison to the previous paper-based system and to assess for potential benefits. Hypoglycaemia was defined as capillary blood glucose level (CBGL) < 4 mmol/l. Management of all episodes of hypoglycaemia in in-patients with Diabetes on medical and surgical wards over 14-days in January 2024 was reviewed and compared to results of a previous audit in 2019. 59 episodes of hypoglycaemia occurred in 27 patients. Recognition and initial treatment of hypoglycaemia with appropriate fast-acting carbohydrate was adhered to in 77.5%; repeat CBGL performed in 83%, with 25.4% tested within the recommended 15 minutes; 48% of patients had recurrent hypoglycaemia. These results were similar to the previous audit. Prescription of hypoglycaemia plans were present in 88% compared to 8% previously. Administration of long-acting carbohydrate post-hypoglycaemia was documented in 27% of cases, an improvement from 13%. In 44%, diabetes treatment was adjusted post hypoglycaemia, a 50% increase compared to the previous audit (44%vs 22%). This study confirms ongoing good compliance with initial management of hypoglycaemia. However, deficiencies remain in relation to monitoring patients post hypoglycaemia. The introduction of an electronic insulin management system has improved administration of long-acting carbohydrate and adjustments to diabetes treatment. Its potential to prevent recurrent hypoglycaemia needs further study.

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P95

Plasma free amino acids profiling in jordanian patients with hypertension and type 2 diabetes mellitus

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Lifestyle-related disorders such as metabolic syndrome, diabetes mellitus (DM), dyslipidemia, and hypertension are key contributors to cardiovascular diseases. The interplay of diabetes and hypertension significantly affects the progression of atherosclerotic cardiovascular disease. Amino acids vary chemically based on

their side chains, classifying them into acidic, basic, and neutral groups. Alterations in amino acid metabolism are critically involved in disease pathogenesis. This study aimed to assess the plasma-free amino acid (PFAA) profiles and other relevant indices for evaluating lifestyle-related disorders like type 2 diabetes mellitus (T2DM) and hypertension in the Jordanian population. We recruited 200 participants, half diagnosed with hypertension and T2DM, and half as healthy controls. A comprehensive panel of amino acids across various categories was analyzed using an amino acid analyzer. Clinical assessments included body mass index (BMI), blood pressure (BP), fasting blood sugar (FBS), glycated hemoglobin (HbA1c), total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Significant differences were observed in BMI, systolic blood pressure (SBP), HbA1c, FBS, LDL-C, and TG levels between the diseased and non-diseased groups. The PFAA profiling revealed elevated levels of branched-chain amino acids (BCAAs), aromatic amino acids (AAAs), acidic, basic, glucogenic, and ketogenic amino acids in the diseased cohort. Positive correlations were noted between BCAAs and markers like cholesterol, TG, and BMI, with negative correlations between BCAAs and LDL-C and FBS. Additionally, AAAs showed positive correlations with HbA1c and negative correlations with cholesterol and LDL-C. The findings underscore that elevated plasma concentrations of specific amino acids such as acidic, basic, AAAs, and BCAAs are linked with an increased risk of lifestyle-related diseases, particularly DM and hypertension. These amino acids could serve as novel biomarkers for identifying individuals at heightened risk of these conditions, enhancing early diagnosis and targeted intervention strategies.

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P96

A study of referral patterns and patient characteristics observed in Ireland's first fully functional community hub diabetes service during its inaugural year of operation

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Enhanced community care (ECC) for type 2 diabetes mellitus (T2DM) is a new initiative in Ireland. ECC involves episodic community-based consultant-led multidisciplinary care that supports general practitioner (GP)-delivered chronic disease management (CDM, available to patients with a medical or GP visit card). The Dublin North West (DNW) hub was the first fully operational hub. This study focuses on its inaugural year of activity. The study goals were to report on hub referral patterns, the characteristics of the patients referred, rates of eligibility for CDM and the impact of hub activity on acute hospital waiting lists. A retrospective analysis of patient charts and hospital databases was conducted for all patients referred to the DNW hub between March 2023-2024. Of the 204 referrals received 67% of patients were re-directed from acute hospital waiting lists, 22% were referred by GP's and the majority of other referrals were internal from other sources within the hub. The average wait time to be seen was 8.57 weeks and 19.6% of patients failed to attend their initial appointment. Of those patients who attended, 44% were female and 56% were male with an average age 56.2 years, and only 46% were eligible for CDM. The numbers of patients waiting for a diabetes appointment in Connolly Hospital decreased by 61% over the time period, with the average waiting time decreasing from 11 to 5 months. The study offers novel insights into community hub-delivered T2DM care in Ireland. It demonstrates a clear reduction in waiting times for the acute hospital diabetes clinic and faster access to specialist diabetes care. The greatest source of referral was the hospital waiting lists. Notably, a significant number of patients did not have eligibility for CDM which may over time lead to patients with uncomplicated T2DM remaining within acute hospital clinics for financial reasons.

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P97

Glucosamine increases FGF21 expression through Akt-mTOR-p70S6K axis-induced endoplasmic reticulum stress response in skeletal muscle cells

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Glucosamine (GlcN) is a common supplement that is widely used to improve osteoarthritis, but it would impair myogensis through endoplasmic reticulum (ER) stress eIF2α-ATF4 pathway. Fibroblast growth factor 21 (FGF21) is one of muscle-secreted cytokine that participates in the myogenic differentiation. The Akt-mTOR-p70S6K axis play a pivotal role in protein synthesis, while sustained activation in mTOR signaling that triggers ER stress and conducts FGF21 production in skeletal muscle. However, a relationship between GlcN and muscular FGF21 expression has not been established. The aim of this study was to determine whether GlcN induces FGF21 production in skeletal muscle cells, which could be involved in the activation of Akt-mTOR-p70S6K pathway and ER stress response. We found markedly increased levels of ATF4 and FGF21 in the soleus muscle from chronic GlcN-infused mice. In *in vitro* studies, treatment of GlcN stimulated FGF21 expression in C2C12 myoblasts. Treatment of cells with FGF receptor inhibitor significantly blocked myogenic differentiation. In addition, ER stress inhibitors reduced GlcN-induced FGF21 expression. Furthermore, inhibition of Akt-mTOR-p70S6K axis prevented the induction of GlcN in eIF2α-ATF4 signaling, resulting suppressed the GlcN-induced FGF21 up-expression. Together, our findings suggest that increased FGF21 levels could induce by the activation of Akt-mTOR-p70S6K signaling pathway and ER stress response, and may be involved in protecting from the GlcN-impaired myogenesis.

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P98

Changes in development and function of skeletal muscle in UCP-1 knockout mice

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Brown adipose tissue (BAT) and skeletal muscle are play vital roles in the regulation of thermogenesis. In addition to thermogenesis through muscle activity, heat can be produced by non-shivering thermogenesis of BAT to produce heat. The heat production of BAT is dependent on the activity of uncoupling protein 1 (UCP1), which generates heat by dissipating the mitochondrial proton gradient. Recent studies suggested that UCP1 deficiency might cause the compensatory thermogenesis in the skeletal muscle. However, the changes of development and function of skeletal muscle in UCP-1 knockout mice *in vivo* is not clear. Furthermore, whether the BAT UCP1 expression can affect development of skeletal muscle *in vitro* is need to be elucidated. Results of our study showed that the gastrocnemius weight in skeletal muscle and cross-sectional area of muscle fiber from UCP1 knockout mice was significantly decreased compared with that from wild-type mice. Compared control conditioned-medium derived from control WT-1 brown adipocytes, decreased expression of myosin heavy chain (MHC) and increased expressions of atrophy markers, such as atrogin-1, MuRF-1 and myostatin, were found in C2C12 myotubes treated with conditioned-medium derived from UCP1-knockdown WT-1 brown adipocytes. In conclusion, UCP1 deficiency in BAT might cause skeletal muscle atrophy via upregulating atrogin-1, MuRF-1 and myostatin.

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P99

Differential impact of GLP-1 and GLP-2 on beta-cell function, glucose metabolism, and appetite

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Background
Glucagon-like peptide-1 (GLP-1) and glucagon-like peptide-2 (GLP-2), are key products of the L-cell proglucagon-gene with diverse effects on metabolism. Whereas GLP-1 has been extensively studied, much less attention has been devoted to GLP-2. The current study directly compares the impact of GLP-1 and GLP-2 on pancreatic beta-cell function and turnover *in vitro*, as well as the effects on glucose tolerance and appetite suppression in mice.
Methods
Acute glucose-dependent (1.1, 5.6 and 16.7-mM) insulin secretion studies (10^{-12}-10^{-6} M; 20-min) were performed in BRIN-BD11 beta-cells. The influence of GLP-1 and GLP-2 (10^{-8} -10^{-6} M) on BRIN-BD11 cell proliferation was assessed

by Ki-67 staining, whereas protection against cytokine-induced (IL-1beta, TNF-alpha, IFN-gamma) apoptosis was determined by TUNEL-staining. Acute *in vivo* gluco-regulatory and satiety actions of the peptides (25 nmol/kg bw) were investigated in overnight-fasted C57BL/6 mice.
Results
As expected, GLP-1 significantly ($P < 0.001$ - $P < 0.0001$) enhanced insulin secretion from BRIN-BD11 cells at 1.1, 5.6 and 16.7-mM glucose, whereas GLP-2 lacked beta-cell secretory actions. However, both GLP-1 (36% and 50%) and GLP-2 (42% and 49%) enhanced ($P < 0.0001$) beta-cell proliferation at 10^{-8} and 10^{-6} M respectively. In addition, beta-cell protection against cytokine-induced cell stress was significantly ($P < 0.0001$) reduced by both GLP-1 (39% and 41%) and GLP-2 (36% and 40%). In mice, administration of GLP-1 or GLP-2 significantly suppressed food intake (50% and 40% respectively, $P < 0.001$ - $P < 0.0001$) at 30, 60, 120 and 180 mins. When the peptides were administered conjointly with glucose (2g/kg, ip), GLP-1 induced prominent ($P < 0.001$) reductions in blood glucose levels when compared to glucose control, with GLP-2 also decreasing blood glucose but to a lesser extent ($P < 0.01$).
Conclusion
Pancreatic beta-cell secretory actions of GLP-1 and GLP-2 are distinct. However, these proglucagon-derived products, secreted from intestinal L-cells in equimolar concentrations, share hitherto unappreciated similarities in terms of their effects on beta-cell turnover and metabolic control.

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P100

An audit of c-peptide testing in a university teaching hospital: are we meeting recommended standards?

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C-peptide is a marker of pancreatic beta cell function and is used to investigate hypoglycaemic disorders and aid diabetes classification. An international consensus report (ADA/EASD) on the management of type 1 diabetes recommends C-peptide (with concurrent glucose) measurement, in individuals 3 years after diagnosis where there is uncertainty about diabetes classification. We conducted a retrospective audit of C-peptide testing among adult patients in Galway University Hospitals. All relevant laboratory data for the calendar year 2023 were retrieved from the laboratory information system. Patient demographic and clinical data were retrieved from electronic medical records. 192 tests were undertaken on 181 adults with C-peptide results ranging 7-4199 pmol/l (ref. interval 370-1470 pmol/l) with a median of 754 pmol/l (IQR 404-1230 pmol/l). 18 patients had a C-peptide level <200 pmol/l; one was undertaken due to hypoglycaemia, 4 were conducted at the time of diagnosis and 13 patients were already on insulin therapy. Only 56% of samples had a concurrent glucose measurement to facilitate interpretation. 124 patients had a diagnosis of diabetes at the time of testing with 30 of these being a new diagnosis. The most common indication for testing was to determine diabetes classification ($n = 83$), only 28 took place a minimum of 3 years post-diagnosis, followed by hypoglycaemia workup ($n = 26$) and assessment of endogenous insulin production ($n = 25$). 92 samples were paired with islet autoantibody testing. Based on a combination of islet autoantibody and C-peptide results 15 patients (8.2%) had a diabetes reclassification. Appropriate use of C-peptide measurement can aid better diabetes classification with implications for patient self-management, education and risk counselling. Our findings highlight the importance of C-peptide as a diagnostic aid for classifying diabetes and calls for closer adherence to recommended guidelines for testing.

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P101

Validation of gestational diabetes mellitus diagnosis in electronic health records

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Objective
To assess the accuracy of gestational diabetes mellitus (GDM) diagnoses in electronic health records (EHRs) by comparing them to a real-time clinical team database maintained by the hospital.
Methods
The study employed a retrospective validation design to evaluate the accuracy of GDM diagnoses in the EHRs of The Coombe Hospital, Dublin. Patient IDs were matched between the EHR system and a real-time clinical team database (GDM Val) which recorded all GDM patients. Data were collected from 2018-2022 and included medical histories recorded by midwives. GDM in the EHRs were labelled as positive if "Diabetes developed during pregnancy" was noted, then matched with GDM diagnoses from GDM Val. The comparison yielded true positives, false positives, true negatives, and false negatives, assessing the EHR's reporting accuracy against GDM Val.
Results
The dataset included 37,651 EHRs from 31,100 patients, (mean $\pm$ SD: age, 32 ± 5 y; BMI, 26.2 ± 5.5 kg/m^2); 20.7% had a BMI over 30. GDM prevalence was 11.0% using EHRs and 10.5% using GDM Val. Of 3,952 patients with matching IDs, 3,388 were correctly identified with GDM in both EHRs and GDM Val (ground truth), while 564 lacked a corresponding GDM label in EHRs. Additionally, 771 patients were incorrectly diagnosed with GDM in EHRs without matching IDs in GDM Val. Overall, there were 32,928 true negatives (87.5%), 3,388 true positives (9.0%), 771 false positives (2.0%), and 564 false negatives (1.5%). Furthermore, GDM prevalence for both EHRs and GDM Val databases revealed a notable reduction in 2020 (EHR, 10.0%; GDM Val, 7.7%), indicating a deviation from the trend observed in other years.
Conclusions
The analyses revealed clinically meaningful discrepancies between EHR-recorded GDM diagnoses and the clinical team's database, highlighting a need for improved reporting accuracy in EHR systems if they are to be used for EHR trained machine learning models.

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P102

Histological analysis of debrided tissue from chronic ulcers in people with diabetes mellitus

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Chronic ulcers represent very common and serious complications of diabetes mellitus. Their persistence leads to repeated infections, often leading to amputation. The current state-of-the art treatment includes debridement which is aimed at preparing the wound bed and stimulating ulcer edges to trigger tissue regeneration. We aimed to test the hypothesis that features of the debrided tissue may be indicative of the natural evolution of the wound. As a first step for this characterization we examined, histologically, debrided tissue of 18 ulcers from 13 different people attending the podiatry clinic at Connolly Hospital for routine care of diabetes-related ulcers. Patients gave informed consent to the examination and this project was granted approval by the Connolly Hospital Ethics Committee. Samples were fixed in formalin immediately after collection and transferred to the Tissue Engineering Research Group Laboratory of RCSI for histological processing and analysis. Paraffin sections of 7 microns were prepared, stained with haematoxylin-eosin and examined using light microscopy. From a first analysis of these samples it appeared that, in general, all contained epithelial rests where tissue was clumped and appeared necrotic. In 2 samples a clear strong inflammatory infiltrate was observed, and in another a small area of cells presumed to represent inflammatory infiltrate was seen. Interestingly, in 4 of the samples, in addition to obviously necrotic clumps of tissue, it was possible to identify epidermal rests that resembled viable or normal tissue in appearance. However, we did not identify a specific correlation between these findings and clinical features suggestive of ulcers that were less severe or healing better. More detailed investigation of a larger number of samples with longer clinical follow up of the ulcers over time may provide additional insight into this important question.

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P103

No effect of liraglutide, dulaglutide or danuglipron on *in-vitro* aggregation and activation of platelets from healthy subjects

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Glucagon-Like Peptide 1 receptor agonists (GLP1RAs) have been shown to lower the risk of cardiovascular events and death in people with type 2 diabetes at high cardiovascular risk. Danuglipron, is a small molecule peptide agonist of the GLP1 receptor, a novel drug class of oral medication with promising effects on improving glycaemic control and promoting weight loss in people with diabetes or obesity. Due to the early cardiovascular risk reduction observed in some GLP1RA cardiovascular outcomes trials, we hypothesised that part of this risk reduction may be attributed to an effect on platelet aggregation and/or activation. The aim of this study was to measure aggregation and markers of platelet activation in platelets of healthy participants following *in-vitro* exposure to liraglutide, dulaglutide or danuglipron. Platelet aggregation was measured by light transmission aggregometry using healthy donor platelet rich plasma (PRP). PRP was incubated with vehicle control or liraglutide (20μM), dulaglutide (20μM) or danuglipron (30μM). ADP, arachidonic acid (AA), epinephrine and collagen were used as agonists for aggregation. Resting and AA or ADP-activated platelet surface expression of the activation molecules CD62P and PAC-1 were measured by flow cytometry. One-way repeated measures ANOVA and mixed effects analysis were used to compare control and treatment group means. No significant difference in final aggregation (n = 3-5, $P > 0.05$), resting and AA-activated expression of CD62P or ADP-activated PAC-1 expression were identified (n = 3/group, $P > 0.05$) in response to incubation with liraglutide, dulaglutide or danuglipron. In this *in-vitro* study of healthy donor platelets, treatment with liraglutide, dulaglutide or danuglipron did not alter measures of platelet aggregation or activation.

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P104

Planning for recruitment and retention in the D1 now randomised controlled trial -a re-audit of a young adult cohort with type 1 diabetes

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Introduction
The D1 Now study was established to improve outcomes for young people with type 1 diabetes. The D1 now intervention focuses on making the clinic visit more young person-centred through enabling young people to set their agenda, and use of a support worker as a liaison. An audit of the young adult cohort attending University Hospital Galway (UHG) in 2011 showed suboptimal glycaemic control and high rates of unscheduled emergency visits and non-attendance at outpatient clinics.
Aims
The aim of this study was to re-audit the young adult cohort in UHG to identify any changes over the last 10 years and to help develop strategies to recruit and retain young adults for a definitive randomised control trial (RCT) of the D1 Now intervention.
Methods
An audit of all young adults aged 18-25 years attending the type 1 diabetes service at UHG on 1st July 2021 was carried out over a 2-year period. Demographic, clinical, laboratory and clinic attendance data were gathered from hospital electronic record systems.
Results
148 young adults (55% female) were included with a mean age of 23 years. Non-attendance rates at outpatient clinics were high at 28% and 7% did not attend any clinic appointment over the 2 years. 11% had at least one hospital admission. Insulin pump usage was 26% compared to 4% in the 2011 audit. Mean haemoglobin A1c was 70 mmol/mol compared to 81 mmol/mol in 2011.
Conclusions
Glycaemic control has improved in this cohort since the 2011 audit, likely partly attributable to increased availability of diabetes technology. However clinic non-attendance remains high. This highlights the need to investigate new ways to improve young adult engagement in their diabetes care. The D1 Now definitive RCT is due to commence across Ireland and will explore this area further.

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P105

Management of enteral and parenteral nutrition in inpatients with diabetes in an Irish tertiary referral centre

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Introduction
Recent consensus guidelines for the Joint British Diabetes Societies and the Endocrine Society cover the common clinical scenario of optimising glycaemic control in patients receiving enteral (NG/PEG), and total parenteral nutrition (TPN), although the approach recommended differs. Here, we outline an Irish tertiary referral centre experience, and compare with international guidance.
Methods
We extracted data from our electronic referral system, which captures all inpatient consultations, from May 2018-May 2024. This includes demographics, patient diagnosis (ICD-10 codes), referral information (free text), HbA1c at referral, and specialist opinion (including regimen recommended). Data was extracted to Excel and analysed using Stata version 16.0, using simple descriptive statistics.
Results
Over the 6-year study period, the inpatient diabetes service received 215 inpatient referrals for patients on TPN (39%) or NG/PEG feeding (61%). Mean age was 68 years (SD 13.5), and median HbA1c at referral was 53 mmol/mol (IQR 46-64). Type 2 diabetes accounted for 67% of referrals, 15% had type 1 diabetes, 8% had another type, and 9% did not have a confirmed diagnosis of diabetes. Multiple daily injection (MDI) insulin was the most popular regimen, being used in 28% overall, followed by sliding scale insulin alone (22%), and basal plus correction insulin (19%). IV insulin use was less common (9%). 19% continued oral medication. Twenty-five percent of referrals were on the same patient, at different times during their admission.
Conclusion
Enteral and parenteral feeding is a common indication for inpatient consultation. Multiple referrals on the same patient are common, indicating the complex nature of the clinical situation. Multiple different regimens are in use, with subcutaneous basal insulin and MDI regimens being the most popular in both type 1 and Type 2 diabetes. Further study, examining glycaemic targets achieved, with a view to developing a definitive institutional protocol would be desirable.

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P106

An intentional overdose of ultra-long-acting insulin analogue complicated by treatment refusal in a patient with mixed personality disorder and type 2 diabetes mellitus

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Diabetes Mellitus is one of the leading causes of morbidity and healthcare costs internationally. Innovations in treatment options however, including insulin analogues, continue to emerge. While insulin therapy may be required for certain patients with Type 2 Diabetes Mellitus (T2DM), it bestows upon them the opportunity for potential harm, namely insulin overdoses, whether accidental or intentional. This case details an intentional ultra-long-acting insulin analogue overdose in a 44-year-old female with T2DM, known mixed personality disorder and previous deliberate self-harm. A total of 1500iu of insulin degludec were reported to be injected pre hospital, requiring 3L 10% dextrose, 200ml 50% dextrose 5 mg IM glucagon and 300 mg of IV hydrocortisone within the first 32 hours, resulting in a mean BGL of 7.6 mmol/l (fasting 4 mmol/l – 5.5 mmol/l) with 2 hypoglycemic events of 3.4 mmol/l and 2.9 mmol/l. Inpatient care was complicated by treatment and investigation refusal, with self-removal of IV access including CVC. The patient had a psychiatric review and the decision to treat the patient in her best interests was taken. She required decreasing amounts of IV dextrose boluses, glucagon, and hydrocortisone, and was transferred to the psychiatric ward on day 10 of her admission with a mean BGL of 11 mmol/l with a serum insulin level decreasing from a peak of 2802mIU/l to 105mIU/l (fasting < 25mIU/l). As increasing numbers of patients require and are prescribed insulin therapy, the risk of negative outcomes rises. In potential high-risk patient groups, including patients with suicidal ideation, the risks of insulin therapy may outweigh the potential benefit in their glycemic control. As diabetes continues to emerge as a condition requiring multidisciplinary-team input, this case demonstrates the need for the implementation of readily available psychology/psychiatric services, in community, outpatient and inpatient settings, to recognize, address and manage patients with behaviors concerning for potential insulin overdoses.

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P107

Introduction of an online glucose monitoring system for management of gestational diabetes in cork university maternity hospital – a pilot study

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The prevalence of gestational diabetes mellitus (GDM) is increasing worldwide and is currently 12% (appx. 800 women/annum) in our institution with 40% of the patients requiring treatment with insulin. The aim of this project is to assess if the use of an online glucose management platform in addition to usual care would improve patient satisfaction in women with GDM. Patients diagnosed with GDM were randomised to the use of Bluetooth enabled **Onetouch Verion** or **Accucheck Instant** glucometer-app for glucose monitoring. Glucose readings were visible to the patient via a smartphone app and to the healthcare practitioner via a virtual desktop platform. A 7-point questionnaire assessed overall satisfaction with care processes (part A), and a 5-point questionnaire assessed satisfaction with either app (part B). Narrative comments were also requested from patients. Over 90% of patients from both groups were happy with processes of care, understanding of GDM treatment, and interactions with the healthcare team. All **Onetouch** users ($n = 17$) agreed that the app had a fast response time, was useful, easy to use, created confidence and improved data interpretation (part B). Of those using **Accucheck** ($n = 10$), 80% users had a similar positive response. All participants would recommend **Onetouch** and 90% would recommend **Accucheck.** Narrative comments were generally positive. Negative comments highlighted technical issues. Use of an online glucose monitoring system is safe and is associated with increased patient satisfaction in women with GDM. Introduction of this virtual monitoring systems will negate the need for documenting glucose readings in a paper diary.

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P108

Exploring the role of mitochondria-endoplasmic reticulum contact sites in bile acid synthesis

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Mitochondria-endoplasmic reticulum contact sites (MERCS) play a key role in cholesterol metabolism and steroidogenesis by facilitating the efficient transfer and processing of cholesterol for steroid hormone synthesis. However, whether MERCS play a role in bile acid synthesis is completely unexplored. Here we begin to investigate a role for MERCS in bile acid synthesis using two alternative models of MERCS disruption. First, to reduce the total number of MERCS we performed siRNA knockdown of Ribosome binding protein 1 (RRBP1). Second, to increase the distance between ER and mitochondria at the contact sites we overexpressed the testis-specific protein (FATE1). The two models were validated by qPCR, western blot and electron microscopy. Gene expression studies were then conducted to assess the effects on bile acid synthesis. RRBP1 knockdown (KD) in human hepatoma cells decreased mRNA expression of CYP7A1 (1.66 ± 0.29 [SC] vs. 0.95 ± 0.09 [KD], $P = 0.002$), CYP8B1 (1.31 ± 0.16 [SC] vs. 0.68 ± 0.17 [KD], $P = 0.008$), and AKR1D1 (1.37 ± 0.23 [SC] vs. 0.80 ± 0.38 [KD], $P = 0.022$) and increased the expression of HSD3B7 (0.76 ± 0.16 [SC] vs. 1.20 ± 0.34 [KD], $P = 0.032$), while CYP27A1 expression remained unchanged. The expression of FXR and its target SHP were unchanged, suggesting these changes are not a result of altered bile acid levels or signalling via FXR. However, LXRβ expression was increased (0.925 ± 0.15 [SC] vs. 1.24 ± 0.26 [KD], $P = 0.047$), consistent with altered oxysterol signalling. In contrast, FATE1 overexpression had no effect on the expression of genes involved in bile acid synthesis or signalling. In conclusion, these data highlight the critical role of MERCS in BA synthesis. Our data would suggest that the regulation of the total number of MERCS, but not the distance between the ER and mitochondria, is associated with changes in the expression of genes involved in bile acid synthesis and signalling.

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P109

Corynebacterium sp. in diabetic foot ulcers – a retrospective, single-centre, observational descriptive study from a tertiary hospital

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Introduction
Corynebacterium sp. has long been understood to be a colonising bacteria in diabetic foot infections. We present a retrospective study to describe the experience of *Corynebacterium sp*. in a cohort of inpatients with active diabetic foot disease (DFD) in a tertiary referral centre.
Methods
We included all inpatients attending our tertiary referral centre who were admitted with a DFD-related complaint and who were seen on the multi-disciplinary diabetic foot round (DFR) over a 6-month period. The primary outcome of the study was the presence of *Corynebacterium sp.* growth in superficial, deep tissue and bone cultures. The secondary outcome was correlation of *Corynebacterium sp.* growth on bone/deep tissue samples with superficial samples.
Results
62 new patients were reviewed on the DFR in this 6-month period. 2 of these patients had a second admission for a DFD-related complaint within the study period, therefore 64 patient episodes were included. Of these patient episodes, 56 had samples sent for culture. 30 (54%) had superficial swabs, 5 (9%) had deep tissue samples and 21 (37%) had bone samples sent as their highest-quality sample. *Corynebacterium sp.* were cultured on 9 of 56 patient episodes with culture samples sent in the study period (16%). Of these, 8 were detected on bone (7 intra-operative samples, 1 bedside sample) and 1 on deep tissue; no superficial wound swabs grew *Corynebacterium sp.* during the study period. None of these positive culture results was consistent with growth from a superficial swab within 3 months of the positive sample.
Conclusions
In this cohort, *Corynebacterium sp.* were present only in bone or deep tissue samples with no superficial sample correlation. If we wish to adequately target potentially pathogenic microorganisms like *Corynebacterium sp.*, we must push for deep tissue samples to be sent in all of our patients with diabetic foot infections.

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P110

A case of insulin autoimmune syndrome (hirata disease) - a rare cause of hypoglycaemia

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Background
Insulin autoimmune syndrome (Hirata disease) is a very rare cause of hypoglycaemia; approximately 400 cases have been described. The presence of insulin autoantibodies leads to the formation of insulin-Ig complexes, with subsequent dissociation of insulin resulting in episodes of severe hypoglycaemia. The condition can present a diagnostic and management challenge.
Case Report
A 77-year-old man was attended by paramedics with a GCS of 8 and severe hypoglycaemia (capillary blood glucose 1.0 mmol/l) which responded well to initial treatment. He had no history of diabetes or exposure to exogenous insulin or antiglycaemic agents. On transfer to hospital, he had another severe hypoglycaemic episode. Blood samples sent two hours after the second hypoglycaemic episode showed an extremely elevated C-peptide (22,000 pmol/l) and insulin level (>6400 pmol/l). Differential diagnoses included insulinoma, antiglycaemic agent exposure or immune-mediated disease. Cross-sectional imaging did not identify any pancreatic lesions and there was no exposure to antiglycaemic agents; the extremely high C-peptide and insulin levels made these diagnoses less likely. Insulin autoimmune syndrome was confirmed with positive IgG against insulin and polyethylene glycol precipitation of insulin-Ig complexes. The patient was initially managed with regular complex carbohydrate meals, alongside prednisolone at night to reduce nocturnal hypoglycaemic episodes. B-cell depletion using rituximab resulted in reduced frequency of hypoglycaemic episodes and a marked improvement in insulin levels. Prednisolone was able to be discontinued. The patient is now well, with no recent hypoglycaemic episodes on flash glucose monitoring.
Discussion
Insulin autoimmune syndrome is a diagnosis to consider in cases of hypoglycaemia of unclear cause with very elevated insulin and C-peptide levels. Blood sampling during the hypoglycaemic episode is useful to aid the diagnostic

process. Management can be challenging, with limited evidence base. This patient had an excellent response to rituximab, with good biochemical and symptomatic outcomes.

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P111

GPR120/GPR40 agonism activates downstream signalling molecules that improve beta cell function and insulin resistance in type 2 diabetes

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Background
G-Protein Coupled Receptors-120 (GPR120) and GPR40 are of interest as targets for treating diabetes and obesity due to their involvement in incretin secretion. This study investigated the mechanistic function of dual agonism on regulating the regeneration of beta cell mass, proliferation, and the insulin secretory response, using CRISPR/Cas9 gene knockout cells and intracellular-signalling analysis.
Methods
Clonal pancreatic BRIN-BD11 cells and GPR120 K/O cells were treated with GPR120/GPR40 agonists to determine GPR120 and GPR40 expression by qPCR. Protein expression was assessed by immunocytochemistry; insulin secretion by radioimmunoassay at normoglycaemic and hyperglycaemic conditions; and cell toxicity by MTT analysis. Phosphorylated extracellular signal-regulated kinase 1/2 (ERK1/2) and protein kinase B (AKT1/2/3) were investigated in BRIN-BD11/GPR120 K/O cells by western blotting.
Results
qPCR demonstrated that the stimulatory effect of GPR120/GPR40 agonist Alpha-Linolenic Acid (A-LA) was completely abolished in GPR120 K/O cells, no GPR120 gene expression was observed at 5.6mM ($P < 0.001$) and 16.7mM ($P < 0.001$) glucose. Addition of A-LA resulted in upregulation of GPR40 gene expression in GPR120 K/O cells ($P < 0.05$) at 16.7mM glucose. Immunocytochemistry confirmed co-localisation of insulin/GPR120 in BRIN-BD11 cells, and lack of GPR120 expression in K/O cells. Agonists A-LA, Compound A and GSK137647 increased insulin secretion in a dose-dependent manner in BRIN-BD11 cells ($P < 0.05$- $P < 0.001$), with no cytotoxicity. Western blot showed GSK137647 increased AKT1/2/3 expression at 16.7mM glucose ($P < 0.05$). Dual agonism by A-LA resulted in upregulation of phosphorylated ERK1/2 in BRIN-BD11 cells (by 31%, $P < 0.05$) at 5.6mM glucose and a 54% reduction in expression ($P < 0.01$) in GPR120 K/O cells. A-LA had no effect on GLP-1R gene expression in K/O cells confirming the importance of GPR120/GPR40 agonism.
Conclusion
Dual activation of GPR120/GPR40 has an important role in regulating pancreatic islet growth and proliferation, mediating anti-apoptotic effects, and has significant potential for new drug development for diabetes treatment.

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P112

A real-world, single-centre experience of vascular specialist input on the multidisciplinary diabetic foot round in a tertiary hospital – an observational study

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Introduction
Multidisciplinary Foot Team (MDFT) input is a cornerstone of best-practice guidelines for the management of active diabetic foot disease (DFD). This study describes the experience of the inpatient multidisciplinary DFD ward round (DFR) in our hospital over two three-month periods, one year apart.
Methods
We prospectively captured data from the DFR in our hospital over two three-month periods, one year apart. This weekly DFR reviews inpatients with active DFD on a consults basis. During the earlier study period, no vascular surgical specialists were available to be in attendance at the time of the round. During the later study period, vascular surgeons were present on the DFR. The primary outcome measure was rate of amputation. Secondary measures included length of stay, microbiology and imaging investigations, vascular studies, HbA1c, diabetes classification and prior history of amputation and ulceration. Categorical data were compared using Chi-squared test. Numerical data were compared using Mann-Whitney U test.
Results
24 individual patients who were admitted with a primary DFD-related complaint were reviewed on the DFR in the first three-month period. In the second three-month period one year later, there were 23 such reviews. There was a statistically significant increase in amputation rates between the time periods. There were 3 minor and 2 major amputations in the earlier period (1 patient underwent both a minor and major amputation during the admission). There were 10 minor and 0 major amputations in the later period. Average length of stay was not significantly different between the two groups.
Conclusions
The presence of vascular input on the DFR was associated with a significantly higher rate of minor amputations. We believe this change reflects prompt vascular input leading to timely definitive management. This study highlights the powerful role that a comprehensive MDFT assessment plays in altering patient outcomes.

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P113

Relative energy deficiency in sport in female gaelic athletic association players

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Relative Energy Deficiency in Sport (RED-S) is a syndrome caused by low energy availability (LEA), where an athlete's energy intake is inadequate to match expenditure. In 2023 the International Olympic Committee released a consensus statement for REDS, with recommendations for studying health outcomes. [1] Our study aims to investigate if elite female Gaelic Athletic Association (GAA) players are at risk of LEA and RED-S. 44 female intercounty GAA players were recruited. Body composition was assessed with DXA scan and blood tests including FBC, renal profile, LFTs, TFTs, creatinine kinase (CK), lipid profile, glucose, insulin, c-peptide and micronutrients pre-season. Testing will be repeated mid-season and end-season. The following preliminary results are our baseline data set ($n = 44$). The average age was 23.5 years (range 18.8-33.9), BMI was 23.18 kg/m ^{2} (range 19.7-30.5) and body fat percentage was 25.17% (range 18-38%). Twenty-three (52%) players had a body fat percentage $< 25\%$. Twenty-eight players (64%) had an elevated CK. Eighteen (41%) participants had abnormal lipid profiles (high cholesterol and/or LDL). Eight (19%) players were iron deficient (< 10.7 umol/l). Completed LEAF-Q questionnaires (to date) suggest that 68.75% (11/16) are at risk of LEA. This is the first study evaluating the potential health outcomes of RED-S in female GAA players, a significant proportion of whom are at risk of LEA. The median body fat percentage observed in our group is less than that reported by Jakeman et al., who looked at the body composition of Irish 18 to 29 year -year-old females. Elevated CK may represent the effect of gym-based pre-season strength and conditioning training. Abnormal lipids and iron deficiency have been reported in RED-S but other suggested indicators for monitoring, such a low haemoglobin were not apparent. Planned further analysis will evaluate the impact of high intensity training over the playing season.

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P114

The importance of identifying the correct type of diabetes: a rare case of bardet-biedl syndrome type 3

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Bardet-Biedl affects 1/100,000 people. Biallelic loss of function pathogenic variants in over 26 genes may be due to autosomal recessive inheritance. Diagnosis is clinical, with genetic testing confirmation. Presenting features include retinal cone-rod dystrophy, obesity, polydactyly, cognitive impairment, hypogonadism, genitourinary abnormalities, monogenic diabetes, hypothyroidism, polycystic ovarian and metabolic syndrome. We present a rare case of Bardet-Biedl type 3, with compound heterozygous pathogenic ARL6 gene

variants. Initial genetics failed to identify an explanation with only one, classified benign variant, in exon 2 of the BBS10 gene identified. Further genetic investigation with a Bardet-Biedl and associated ciliopathy syndromes panel, identified two pathogenic variants in ARL6 gene. ADP Ribosylation Factor like GTPase 6 is a protein coding gene, associated with 5.1 % of all Bardet-Biedl cases. First presenting aged 16, with symptomatic hyperglycaemia, treatment was for presumed Type 1 diabetes. Other features however included polydactyly, central obesity, retinal dystrophy, intellectual disability, and PCOS. Referral to adult diabetes clinics age 29yrs allowed insulin discontinuation with dieting and metformin. Insulin reserve was confirmed (c-peptide 10.9 mg/l, negative anti GAD, IA2, ZnT8 antibodies). Endocrine referral in 2021 for secondary amenorrhea confirmed secondary hypogonadism from a partially empty sella on pituitary MRI. 63% of MRI pituitaries in Bardet-Biedl have abnormalities including pituitary hypoplasia, Rathke's cyst, enlarged glands secondary to hyperprolactinemia, with primary or secondary hypogonadism. A fibroscan due to deranged liver function tests confirmed NASH cirrhosis from obesity associated insulin resistance. This case highlights the importance of extensive genetic testing for the appropriate diagnosis, management and counselling of patients with Bardet-Biedl syndrome and of the importance of clarifying the type of diabetes present through c-peptide and Anti GAD, IA2 and ZnT8 antibodies testing.

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P115

AKR1D1 plays a critical role in the progression of MASLD: Evidence from *in vitro* and *in vivo* studies

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Bile acid (BA) homeostasis is disrupted in MASLD with characteristic changes in BA pool composition. BAs are signalling molecules that modulate hepatic lipid metabolism, inflammation, and cellular proliferation *via* the activation of nuclear receptors, notably FXR. Altered FXR activation has profound effects on the transcription of genes involved in hepatoprotection. We have previously shown that the hepatic enzyme 5β-reductase (AKR1D1), which catalyses a key step in the synthesis of primary BAs, is progressively downregulated with advancing MASLD and is a marker for advanced fibrosis and cirrhosis. We hypothesise that AKR1D1 downregulation plays a role in altering the BA pool with a consequent disruption of BA signalling, contributing to MASLD pathogenesis. In hepatoma cells, AKR1D1 knockdown increases hepatocyte triglyceride accumulation, induces apoptosis, and alters mRNA and protein expression in inflammation and p53 signalling pathways. To determine whether our *in vitro* observations are mirrored *in vivo*, we aged wild-type (WT) and AKR1D1 knock-out (KO) mice to 52-weeks on a normal chow diet. Intrahepatic triglyceride accumulation and gene expression were assessed by biochemical assays and qPCR, respectively. Endorsing our *in vitro* findings, liver triglyceride content was increased in AKR1D1 KO mice compared to WT. mRNA expression of NFkappaB1 was elevated (0.93 ± 0.17 [WT] *vs.* 1.19 ± 0.3 [KO], $P = 0.013$), suggesting an increase in inflammatory signalling. Increased expression of cell cycle regulatory and apoptosis genes was also observed (*Tp53*: 1.01 ± 0.12 [WT, $n = 15$] *vs.* 1.24 ± 0.18 [KO], $P = 0.0023$); *Casp3*: 1.12 ± 0.3 [WT] *vs.* 1.3 ± 0.25 [KO], $P = 0.046$; *Casp9*; 1.04 ± 0.13 [WT], *vs.* 1.24 ± 0.19 [KO], $P = 0.0053$). mRNA expression of the FXR-induced target gene small heterodimer partner (*Shp*) was upregulated ($1.27.85 \pm 0.5$ [WT,] *vs.* 1.7 ± 0.5 [KO], $P = 0.05$). In conclusion, disruption of BA synthesis following AKR1D1 deletion is associated with increased intrahepatic triglyceride accumulation and expression of inflammatory and apoptotic genes *in vivo*, suggesting a role in MASLD pathophysiology.

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P116

Semaglutide intervention in overweight people with schizophrenia: the road back to better physical health - preliminary results from a feasibility study

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Introduction
Weight gain and its associated adverse health consequences have become a significant aspect of the life experience of many people with schizophrenia and other severe enduring mental illnesses (SMIs). Glucagon-like peptide -1(GLP-1) receptor agonists could be of substantial value in addressing this unmet need. We aimed to determine whether semaglutide treatment is feasible and acceptable to individuals in an inpatient setting and successful in facilitating weight reduction in overweight individuals with schizophrenia.
Methods
10 people (6 men and 4 women) with a diagnosis of schizophrenia/schizoaffective disorder according to ICD-10 with a body-mass index (BMI) of at least 30 kg/m2 were commenced on the GLP-1 agonist semaglutide, administered as per BNF in increasing dose increments up to a maximum dose of 2.4 mg/week. Body mass index (BMI) and glycated haemoglobin (HbA1c) were assessed at baseline and 6-week follow-up. Concerning patient-reported outcome measures (PROMs), we assessed the quality of life using the EQ5D5L rating scale.
Results
Age range was 32-52 years. Baseline BMI was 33.5kg/m2 (range 30.5-38,8). At 6-week follow-up, there was a 6% (95% confidence interval (CI) 4.2-7.8%) reduction in BMI, $P = 0.009$. Mean HbA1c decreased from 42 mmol/mol (95% CI 40-45) to 40 mmol/mol (95% CI 38-43), $P = 0.01$. EQ5D5L visual analogue rating (VAR) scale showed a mean improvement from 52-61 (out of 100) with an improvement in the mobility domain score. All individuals stated that they wished to continue the treatment.
Conclusions
Already at 6-week follow-up, we have seen a reduction in BMI and HbA1c and improvement in self-rated overall quality of life in people with schizophrenia. While there are costs attached to the prescription of GLP-1 agonists in people with SMI, further evaluation including health economic assessment may support this treatment being offered more widely to improve cardio-metabolic profile and long-term health outcomes in people with SMI.

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P117

The challenges of managing type 1 diabetes mellitus in the presence of dercum's disease

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Although the prevalence and aetiology of Dercum's disease (Adiposis Dolorosa) are currently unknown, this condition is most commonly diagnosed between the ages of 35 and 50 years and more common in women than in men. We described the challenges of the glycaemic management of a 44-year-old male who was diagnosed with Dercum's disease about a decade after the diagnosis of Type 1 Diabetes Mellitus. Despite previous episodes of diabetic ketoacidosis, his Hba1c over the last five year has been reasonable on once daily degludec and pre-prandial aspart. He has neither microvascular nor macrovascular complications to date. According to him, multiple nodules started to appear throughout his body, particularly in the abdominal region about five years ago but the lipomas had only become painful several months after their appearance. The patient found it increasingly difficult to manage his insulin injections due to the numerous painful nodules especially in the abdominal region due to the limited sites for insulin injection. Consequently, he has undergone multiple surgical excisions of lipomas, primarily for pain management and to facilitate insulin injections. Despite these interventions, the lipomas have recurred, necessitating repeated surgeries. The histologies confirmed the presence of lipomas. This case highlights several challenges faced by people with Type 1 Diabetes Mellitus and Dercum's disease. In our case, he has limited sites for insulin administration due to extensive painful lipomas. He required multiple surgical resections for removal of the painful lipomas. This is complicated by the recurrence of lipomas at the resection sites. Other related comorbidities and its proposed management will be discussed. Clinical expertise from multidisciplinary team consisting of the diabetologist, diabetes nurse specialist, dermatologist, plastic surgeon, pain specialist and psychologist, is needed for optimal management of this complex case.

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P118

Fulminant type 1 diabetes and autoimmune thyroid disease during treatment with a checkpoint inhibitor

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Atezolizumab, a programmed death-ligand 1 (PD-L1) inhibitor, has been associated with development of several immune-related adverse events. Type 1 diabetes mellitus (T1DM) is considered a rare adverse event, described in 0.2-0.9% of patients treated with PD-L1 inhibitors. We present the case of a 67-year-old lady, who was diagnosed with extensive-disease small cell lung cancer. She received four cycles of carboplatin, etoposide and atezolizumab, and thereafter maintenance therapy of atezolizumab was initiated. Four months into treatment she was diagnosed with primary hypothyroidism due to auto-immune thyroiditis. Nine months after her first dose of atezolizumab, she presented to the emergency department with four days of polyuria, polydipsia, and abdominal pain. Laboratory investigations demonstrated hyperglycaemia (glucose 25 mmol/l), profound ketonaemia (ketones 7.7 mmol/l), and severe metabolic acidosis (pH 7.14, HCO3 11 mmol/l). Subsequent investigations revealed low C-peptide level (30 pmol/l) but only modest elevation of HbA1c (50 mmol/mol). Her presentation was consistent with rapid-onset diabetic ketoacidosis (DKA) as the presenting feature of auto-immune diabetes mellitus, akin to T1DM. DKA resolved with appropriate treatment, but she experienced rapid relapse with recurrent DKA 4 hours after IV insulin was stopped. She required prolonged IV insulin therapy, before transitioning to basal-bolus insulin treatment. Atezolizumab inhibits the binding of PD-1 to PD-L1. A rare side effect involves the activation of T-cells against pancreatic β-cells, leading to β-cell destruction. This can cause complete insulin deficiency, manifesting as fulminant T1DM. This subtype of T1DM is characterised by rapid onset ketoacidosis within days of development of hyperglycaemia symptoms, pronounced hyperglycaemia despite modest HbA1c elevations, and the near-complete destruction of β-cell at onset of disease evidenced by low C-peptide levels. When PDL1 inhibitors are administered, clinicians and patient should be aware of the potential for development of fulminant T1DM in addition to other auto-immune endocrine complications.

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P119

Lower urinary tract dysfunction in the diabetic population: diabetes specialist'sknowledge base, clinic practice patterns and patient survey

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Introduction
Patients with Diabetes have a higher risk of lower urinary tract dysfunction/-symptoms (LUTS) compared to those without diabetes. Causative factors include autonomic, detrusor, and urothelial dysfunction, microvascular ischaemic changes, and glycosuria. With a shift towards holistic diabetes management, this study examined whether urinary dysfunction is routinely addressed in outpatient settings and whether Diabetes speciality teams feel equipped to manage this issue. The prevalence of LUTS among patients was also surveyed.
Methods
A 10-question multiple-choice survey was emailed to all current Irish Endocrine Society (IES) members. Respondents ranked treatment options by preference. Data was aggregated, and mean values for each category were compiled. Subgroup analyses compared responses between consultants, trainees, and nurse specialists. A separate questionnaire was distributed to patients attending diabetes outpatient clinics at St James's Hospital.
Results
Responses were received from 43 diabetes specialist doctors and nurse specialists. Over 80% were aware that patients with diabetes experience more bothersome LUTS, yet only 18% routinely inquired about urinary dysfunction in clinic. About 51% had prescribed pharmacotherapy for LUTS, with alpha blockers being the most common. Nearly 80% cited clinic time constraints as the main barrier to assessing LUTS, and over 50% felt they lacked expertise in managing urinary dysfunction. A preliminary review of the first 40 patient responses revealed that 70% experienced LUTS, with 60% finding them bothersome. Less than 30% had discussed these issues with a healthcare provider, and only 15% had received medical treatment.
Conclusion
Despite awareness among diabetes specialist team that patients have a higher burden of LUTS, these issues are not routinely assessed or managed in outpatient settings. Clinic time constraints and a lack of expertise were identified as significant barriers. The patient survey underscores that LUTS is a common, yet under-addressed, issue in this population.

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P120

Switching to a hybrid closed-loop insulin system leads to reduction in mean hba1c levels in subjects with type 1 diabetes

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Objective
We examined our cohort of adults with type 1 diabetes who are using hybrid closed-loop (HCL) insulin delivery systems, to describe what proportion are meeting international targets of HbA1c, time-in-range, and time spent below range. We assessed longitudinal changes in HbA1c associated with switching from an open-loop to a HCL insulin pump.
Methods
We undertook a single-centre observational study of patients using Medtronic™ 780G insulin pump. Outcomes include sensor glucometrics and change in HbA1c.
Results
184 participants with type 1 diabetes were included (median age 42 [IQR 31-53] years, 50% [$n = 92$] female, median duration of diabetes 26 [IQR 15-35] years). Mean duration of HCL pump therapy use was 18 (IQR 11-26) months. The majority (92.4%, $n = 170$) of participants had been previously treated with open-loop pump systems; 14 participants (7.6%) were treated with multiple daily injections and so were not included in the analysis of HbA1c change. Mean baseline HbA1c was 61.5 mmol/mol ($\pm$12.6 mmol/mol), and reduced to 56.8 mmol/mol ($\pm$10.6 mmol/mol) following transition to HCL pump (at 4-12 month clinical follow up) (-4.7 mmol/mol reduction, $P < 0.001$). The proportion of individuals with HbA1c of $\leq$53 mmol/mol rose from 26.6% to 38.7% ($P = 0.001$). Subgroup analysis was performed on 104 participants for whom CareLink™ data was available. The mean time spent in closed-loop mode ('SmartGuard™') was 90.6% ($\pm$12.2). Mean time-in-range was 70.4% ($\pm$10.9), and 52% of patients achieved a target of $\geq$70% glucose time-in-range. Mean time spent below range was 1.7% ($\pm$1.7) and 88% of participants spent $<$4% time below range.
Conclusion
In this real-world analysis of adults with type 1 diabetes, switching to HCL therapy was associated with improved glycaemic control evidenced by significant reduction in HbA1c levels, with a greater proportion of subjects achieving the internationally recommended glycaemic target of HbA1c $\leq$53 mmol/mol.

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P121

Novel mutation in the SLC5AC gene causing renal glucosuria and hypoglycaemia

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Renal glucosuria is a rare cause of hypoglycaemia. We describe an 18-year-old female who presented with a 2-year history of recurrent episodes of light-headedness and headaches. Glucometer readings during these symptoms demonstrated hypoglycaemia as low 2.1 mmol/l. She also had a 4-year history of recurrent urinary tract infections. Multiple dipstick urinalyses with GP demonstrated glucosuria, which was quantified with a 24-hour urinary glucose elevated at 4g/1.73m^2 /day. Fasting glucose was 4.7 mmol/l and HbA1c 34 mmol/mol. Baseline pituitary function was normal and Fanconi syndrome was excluded (normal urinary phosphate, uric acid and amino acids). She underwent a 5-hour oral glucose tolerance test for evaluation of hypoglycaemia (results shown in Table 1). This demonstrated hypoglycaemia with an exaggerated insulin response to the glucose load. Symptoms provoked during hypoglycaemia at 180 min corresponded with the light-headed symptoms she had described over the previous 2 years. Genetic testing with mitochondrial genome and glycogen storage disorder panel identified a heterozygous novel missense mutation in the SLC5A2 gene, variant c.394C$>$A, p.(Arg132Ser). The subject's mother and sister did not demonstrate glucosuria, and no further family members are

Table 1

Time(mins)	Glucose(mmol/l)	Insulin(pmol/l)	C-peptide(pmol/l)
0	4.2	39	489
30	4.7	696	3182
60	3.0	218	2307
90	3.1	204	1213
120	3.8	195	1916
150	2.9	95	1496
180	2.8	27	708
210	3.5	23	495
240	3.8	19	400
270	3.8	23	397
300	3.9	27	387

available for screening. The subject responded to a low glycaemic-index diet. This case describes renal glucosuria with hypoglycaemia secondary to a novel mutation in the SLC5A2 gene, which encodes for sodium-glucose cotransporter-2 (SGLT2) protein. The association of renal glucosuria and hypoglycaemia has been rarely described, with only 3 case reports in the literature.

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P122

Case report: a case of severe insulin resistance due to antibodies specific for detemir

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Insulin antibodies were common when animal insulin was used given its high immunogenicity. The advent of recombinant DNA technology in insulin production has reduced the incidence of insulin antibodies and its presence is rarely considered clinically significant. Exogenous Insulin Antibody Syndrome (EIAS) describes the formation of insulin antibodies to exogenous insulin. We present a case of a 65-year-old gentleman who was diagnosed with diabetes mellitus secondary to pancreatectomy for acute pancreatitis twenty years prior. His insulin requirement reached 3.2 units/ kg eighteen years into his diagnosis, on insulin detemir, novorapid and metformin. Due to the large volume of insulin per injection, insulin detemir was switched to equivalent dose of Insulin glargine. He was admitted to the hospital with severe hypoglycaemia two weeks later, necessitating insulin dose reduction to 1.3 units/kg. He was tested for antibodies specific for detemir and antibodies to human insulin. The results showed a very high amount of antibodies specific for insulin detemir at 41.9%. The high titre of insulin detemir-specific antibodies reduced insulin activity by competing for the insulin receptor, hence reducing insulin action and triggering hyperglycaemia and insulin resistance; a high affinity/low-capacity phenomenon. The absence of antibodies to insulin glargine in this patient's case resulted in hypoglycaemia with equivalent dose. This case demonstrated a case of antibodies specific for detemir resulting in severe insulin resistance in pancreatectomy-related DM. Albeit rare, EIAS should be considered a differential diagnosis in patients with suboptimal glycaemic control and severe insulin resistance.

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P123

The NONcNZO10/ltJ polygenic mouse is ideal model to study de novo lipogenesis and modeling type 2 diabetes remission by weight loss

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Background and aims
Understanding the mechanisms that lead to remission of type 2 diabetes (T2D) after weight loss is critical to develop novel therapies. We hypothesized that weight loss decreases hepatic de novo lipogenesis (DNL), a primary mechanism expected to modulate T2D remission.
Methods
24 mice (NONcNZO10/ltJ) at age 5-6 weeks were placed for 12 weeks on high sucrose diet (HSD: 60% sucrose/20% fat). After 12 weeks, 6 mice were placed on calorie restriction (CR) (30% of total calorie intake), and another group ($n = 6$) continued the HSD for up to 24weeks. Deuterated water (^2H2O) and 13 ^{C} -labelled palmitic acid were used for tracing DNL and dietary fatty acids, respectively. Fat and lean mass were assessed and OGTT was performed at baseline, 12, and 24 weeks. Stable isotopes were analysed by high resolution LC–MS.
Results
HSD increased body weight and total fat mass but decreased lean mass ($P < 0.0001$ for all). CR had the opposite ($P < 0.05$). After 12 weeks, mice on HSD developed impaired glucose tolerance which exacerbated further at 24 weeks. However, CR brought about significant improvement in glucose tolerance ($P < 0.001$), and insulin sensitivity ($P < 0.01$) as assessed by OGTT. There was major decrease in hepatic lipid deposition after CR. The pro-lipogenic effect of HSD is supported by expression of DNL related genes. This was translated by higher incorporation of deuterium in the plasma and liver tissues. At 24 weeks, deuterium-labelled palmitic acid/octadecanoic acid had decreased in CR group ($P < 0.05$, $P < 0.0001$, respectively). Finally, HSD was associated with high leptin and low adiponectin levels.
Conclusion
Our data suggest an important role of DNL on restoration of normal glucose tolerance and resolution of T2D. In addition, the NONcNZO10/ltJ exhibits a unique metabolic phenotype similar to that of human, making it the ideal model to study T2D remission with specific emphasis on DNL pathway.

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P124

Protocol divergence in the management of diabetic ketoacidosis

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Diabetic Ketoacidosis (DKA) is a life threatening emergency and its management is frequently protocolised. Adherence to protocols has been shown to shorten the time to DKA resolution however the management recommendations outlined in most DKA protocols is based on weak evidence and/or consensus. The aim of this study was to evaluate the frequency with which divergence from local DKA protocol was observed at our institution. A retrospective review of medical records was conducted of adults presenting with DKA to our institution over a three month period. Data collected included intravenous fluid (IVF), insulin and potassium requirements based on the protocol as well as intravenous fluid, insulin and potassium prescribed and administered to individual patients. A total of ten DKA patients were identified and included in this study. The mean $\pm$ SD of hours patients spent on the DKA protocol was 9.3 ± 3.9 hours. A mean $\pm$ SD volume of IVF of 4.4 ± 2.1L was required as per the protocol however 50% of patients were prescribed IVF in excess of that recommended. A fixed rate insulin infusion was prescribed in all patients. 40% of patients received a lower dose of insulin than was specified in the protocol. Although basal insulin was recommended in all cases, it was only prescribed in 50% of the patients. Based on the serum potassium levels and DKA potassium replacement policy, the mean $\pm$ SD of replacement patients should have received was 84 ± 45 mmol however potassium was under-prescribed in 60% of patients. Potassium was <3.5 mmol in 40% of patients. This study illustrates that divergence from the DKA protocol was common. Trends towards insufficient insulin and potassium replacement were observed with IVF frequently exceeding recommendations. Assessment of individual patient data is needed to determine if the observed divergence was premeditated.

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P125

Unveiling hidden diabetes: a neuropathic foot ulcer as the first sign of type 2 diabetes mellitus in a post-menopausal woman

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Diabetes mellitus (DM) is a prevalent chronic disease often diagnosed through routine screening or the manifestation of typical symptoms like polyuria and polydipsia. However, it is rare for diabetic neuropathic complications, such as foot ulcers, to be the initial presentation, especially in the absence of other medical conditions. This case report discusses a 53-year-old female who presented with a neuropathic foot ulcer, leading to the diagnosis of Type 2 Diabetes Mellitus (T2DM). A 53-year-old female was referred by her general practitioner (GP) to a diabetic foot clinic for evaluation of a neuropathic foot ulcer. The patient's HbA1c level was measured for the first time following this referral and found to be 120 mmol/mol (13.1%), confirming a diagnosis of diabetes. The patient reported no significant past medical history or alcohol intake. She had experienced vague symptoms of polyuria for about a year but attributed them to post-menopausal changes and did not seek medical attention. Given the unusual presentation of T2DM with a neuropathic ulcer as the first symptom, differential diagnoses were thoroughly explored. Exclusions included vitamin B12 and folate deficiencies, anaemia, hypothyroidism, and autoimmune diseases, none of which were present. This case underscores the necessity for heightened public awareness regarding the early symptoms of diabetes to prompt

timely medical consultation. Early detection and management are crucial to prevent severe complications. The case is particularly notable due to the rarity of a neuropathic ulcer being the initial presentation of T2DM in the current era of advanced medical screening and public health awareness. It highlights a gap in patient education and awareness about diabetes symptoms. This case advocates for enhanced public health initiatives to educate individuals on recognizing early diabetes symptoms, encouraging timely medical evaluation to prevent end-organ damage and improve long-term outcomes.

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P126

Novel unimolecular peptides targeting GLP-1 and APJ receptors exert potent satiety inducing effects in mice

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Incretin mimetics and associated hybrid co-agonist peptides remain a driving force in improving metabolic control and managing type 2 diabetes and obesity. Additionally, the adipokine apelin which targets the APJ receptor, has displayed positive anti-diabetic and obesity effects in pre-clinical trials. To harness these beneficial effects, two novel dual-agonist unimolecular peptides were developed based on the amino acid sequence of GLP-1 and apelin and named Exendin-Linker-Apelin (ELA) and Apelin-Linker-Exendin (ALE). Of these two hybrid peptides, ELA proved more efficacious in all pre-clinical trials and was used going forward alongside a range of acylated analogues to prolong therapeutic effects. Cumulative food intake was measured in 21 h fasted trained normal (n = 8) mice at 30, 60, 90, 120, 150, and 180 min following i.p. injection of saline vehicle (0.9% w/v NaCl) or test peptides (each at 25 nmol/kg bw). ELA and associated Lys ^{12}, Lys ^{27} and Lys ^{38} hybrid peptides resulted in an immediate reduction in food intake compared to saline controls ($P < 0.001$). Furthermore, when test peptides were administered at t=-6 h, whilst ELA significantly inhibited food intake ($P < 0.001$), the acylated analogues had a greater satiety inhibiting effect compared to non-acylated ELA ($P > 0.001$). ELA, Lys ^{12} and Lys ^{38} maintained their satiety inhibiting effects when peptide administration was delayed by 21 h ($P < 0.001$). Finally, Lys ^{38} maintained this satiety reducing effect up to 63 h post injection ($P < 0.05$), thereby demonstrating that these acylated analogues may be protected from elimination and display improved plasma stability. In conclusion, hybrid co-agonist acylated and non-acylated ELA peptide analogues, demonstrated significant reductions in food intake that may suggest application for the treatment of obesity, or obesity-related forms of metabolic dysregulation such as type 2 diabetes.

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P127

Healthcare costs and utilisation for diabetes mellitus among hospitalised patients in ireland: the national kidney disease surveillance system

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Background
Understanding the frequency, length of stay, and costs of inpatient hospitalization for diabetes mellitus (DM) is crucial for effective healthcare planning. This study examines these factors for diabetes-related hospitalisations in Ireland.
Materials and Methods
A retrospective observational study was conducted using the National Hospital In-Patient Enquiry (HIPE) database. Non-coded hospitalisations and patients < 1 year were excluded. All ICD-10 hospital admissions with a principal or additional diagnosis of diabetes (E10, E11, E13, E14, O24) in 2022 were included. Hospitalisation rates, length of stay, and costs were analysed by demographic factors, Charlson comorbidity score (0, 1-2, and ≥3), and region. Age-standardised rates were determined using the European Standard Population from 2012.
Results
In 2022, 8.6% of all coded hospitalisations in Ireland (146,362 out of 1,711,564) recorded diabetes as a principal or additional diagnosis, costing €601 million. Of the 10,511 hospitalisations with diabetes as the principal diagnosis, 58.5% were due to type 2 diabetes, 28.4% to type 1 diabetes, 12.7% to gestational diabetes, and 0.2% to other or unspecified diabetes. The average length of stay was 4.9 days, increasing from 3.9 to 9.2 days with rising Charlson Comorbidity score. Hospital admissions, length of stay, and costs rose with increasing comorbidity burden. Common complications included kidney, eye, neurological, and circulatory issues. Males had higher complication rates than females: 1.9 times higher for kidney, 1.8 times for eye, 3.6 times for circulatory, and 1.9 times for neurological complications. DM hospitalisation rates were higher in males and increased with age. Rates varied significantly across regions, being lowest in the South West and highest in the Midland region ($P < 0.01$).
Conclusion
Diabetes mellitus significantly impacts healthcare utilisation and costs in Ireland. Older patients with higher comorbidity burdens have longer hospital stays and higher resource use. Demographic and regional disparities highlight the need for targeted health planning and interventions.

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P128

Role of FKBP51 on the development of obesity-associated metabolic disorders

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Abnormal adipogenesis and adipocyte dysfunctions have been suggested to be important mechanisms underlying the development of metabolic syndrome. Obesity is associated with a chronic, low-grade inflammation status. The pathogenic mechanisms at the molecular level in obesity-associated inflammation and insulin resistance are not fully understood and need to be elucidated. The 51 KD FK506-binding protein 51 (FKBP51), encoded by *Fkbp5* gene, is one of the of immunophilin family members. *Fkbp5* gene is highly expressed in adipose tissues and FKBP51 expression is most abundant in adipose tissue. Previous study indicated that FKBP51 expression progressively increases during 3T3-L1 adipocytes differentiation and play an important regulator of cellular adipogenesis. In addition, FKBP51 expression in human adipose tissue increases following dexamethasone exposure and is associated with insulin resistance. Therefore, we hypothesize that FKBP51 is a mechanism linking obesity-associated inflammation and insulin resistance. The results showed that high-fat diet (HFD) feeding induced adipose *Fkbp5* mRNA up-regulation in wild-type (WT) mice. Global *Fkbp5*-knockout (KO) can ameliorate the obesity, insulin resistance and inflammation induced by HFD feeding in mice. We also demonstrated that *Fkbp5* regulated adipocyte differentiation *in vitro*. For example, Fkbp5 overexpression promoted adipogenic differentiation in 3T3-F442A preadipocytes. Suppression of endogenous FKBP51 expression by transfecting *Fkbp5* shRNA suppressed adipogenic differentiation in 3T3-F442A preadipocytes. Besides, bone marrow *Fkbp5* deficiency is successful to protecting against HFD-induced obesity, insulin resistance and inflammation in WT mice transplanted with bone marrow from *Fkbp5*-KO mice. These results suggested that FKBP51 is a novel link between obesity, adipose inflammation and insulin resistance.

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Endocrine Cancer & Late Effects

P129

IGF-2 mediated hypoglycemia in adrenocortical carcinoma: a case series

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Non-islet cell tumor hypoglycemia (NICTH) is a rare phenomenon that is likely mediated by insulin growth factor 2 (IGF-2). IGF-2 excess results from tumor overproduction of either mature IGF-2 or incompletely processed IGF-2 ("big IGF-2"), which binds to the insulin receptor causing hypoglycemia. We present a case of IGF-2 mediated hypoglycemia secondary to adrenocortical carcinoma, as well as a series of 8 previously published cases. An 83-year-old male with a history of prostate cancer and arrythmia presented to the emergency department for confusion, weight loss, and abdominal distension. Blood glucose was 1.3 mmol/l (3.3-11.0 mmol/l), and treatment with dextrose lead to improved mentation. Imaging showed a 17cm L adrenal mass, and adrenal workup showed non-suppressed cortisol after 1 mg dexamethasone suppression test (DST), elevated DHEAS and elevated estradiol. IGF-1 was low-normal, and IGF-2 was normal. Ratio of IGF-2: IGF-1 was 10.8, which is diagnostic of IGF-2 mediated hypoglycemia. A combination of dexamethasone and uncooked corn starch was effective in managing hypoglycemia, allowing for discontinuation of IV dextrose. We identified 8 additional cases of IGF-2 mediated hypoglycemia secondary to ACC. The median age at diagnosis was 41. Most (n = 5) cases had stage IV disease at presentation. The median glucose for the critical sample was 1.8 mmol/l. All insulin and C-peptide levels were either normal or suppressed. Serum IGF-1 was suppressed in 89%, and IGF-2 was elevated in 42%. Every case had an

IGF-2: IGF-1 ratio of >10, with a median ratio of 27.8 (range 10.8-84). Death was reported in most ($n = 6$) cases; median time between diagnosis and death was 17.5 (range 3 - 48) months. Medical management for hypoglycemia involved glucose administration, corticosteroids, octreotide, diazoxide, recombinant growth hormone, and everolimus with varying efficacy. IGF-2 mediated hypoglycemia in the setting of ACC is generally associated with advanced disease and poor prognosis.

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P130

Detection of BRAFV600E in thyroid cancer tissue using digital droplets PCR and whole exome sequencing

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Introduction
The BRAF ^{V600E} mutation has been reported in 27– 90% of Papillary Thyroid Carcinoma (PTC). BRAF ^{V600E} may be associated with adverse outcomes in PTC. It is unknown if detection of BRAF ^{V600E} can play a key role in prognosis, and can be used as a surrogate-marker of poor outcomes in PTC.
Objectives
• To investigate prevalence of BRAF ^{V600E} mutation in TC using digital droplet PCR (ddPCR).
• To use Whole Exome Sequencing (WES) of tumour DNA to validate ddPCR methodology.
• To determine whether BRAF ^{V600E} is associated with adverse outcomes in TC.
Methods
Patients were recruited from University Hospitals of Leicester NHS Trust thyroid cancer service (March 2022 – April 2023). Formalin-fixed, Paraffin-Embedded (FFPE) tissue blocks were obtained from archival stores. DNA was isolated using the Qiagen GeneRead Kit and quantified using Qubit 2.0 HS Kit. BRAF ^{V600E} was detected using Bio-Rad assay on QX200 ddPCR system. WES was performed at Novogene Lab (UK). Follow-up was for 12 months at intervals in line with routine clinical reviews. Adverse outcomes were recorded using clinical and radiological findings.
Results
Twenty-three patients (14 males and 9 females) had accessible tumour FFPE blocks. Mean age was 54 years (range 26 – 84) across four subtypes: (PTC $n = 12$), follicular (FTC $n = 5$), medullary (MTC $n = 3$), anaplastic (ATC $n = 3$). BRAF ^{V600E} was detected in 5/12 (41.6%) PTC and 1/3 (33.3%) ATC. 8/17 of the BRAF ^{V600E} -negative and 0/6 BRAF ^{V600E} -positive patients developed recurrence and/or metastases. WES results confirmed the presence of BRAF ^{V600E} in 5/12 (41.6%) PTC and 1/3 (33.3%) ATC.
Discussion
Both ddPCR and WES were concordant for BRAF ^{V600E} presence, with prevalence figures consistent with previous data. During 12-month follow-up, BRAF ^{V600E} did not appear to drive adverse outcomes in TC. It is therefore likely that other mutations were driving disease progression in the BRAF ^{V600E} -negative cohort. We plan to investigate what those driver mutations are.

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P131

A decade of abdominal paragangliomas in the northern ireland regional referral centre

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Background
Paragangliomas are rare neuroendocrine tumours of the sympathetic and parasympathetic paraganglia. Optimal outcomes are dependent on careful investigation, management and follow-up.
Aim
The aim of this audit was to review clinicopathological characteristics of a cohort of operated abdominal paragangliomas in Northern Ireland.
Methods
This is a retrospective audit of abdominal paragangliomas from the Northern Ireland regional service operated 01/01/2014-31/12/2023. Cases were identified by searches of SNOMED codes in histopathological archives. Clinical and laboratory data were collected from retrospective electronic chart review.
Results
A total of 26 patients were operated for abdominal paraganglioma. Twelve (47%) patients were female, median age 55 years (range 18-72). At presentation 10/19 (53%) had documented classical symptoms of headache, sweating or palpitations and 5/20 (25%) were detected as incidentalomas. There was a formal diagnosis of hypertension in 15/23 (65%) pre-operatively and 15/20 (75%) had preoperative evidence of functionality (elevated urine or plasma normetanephrines or metanephrines $\geq$2x upper limit of reference range requiring pre-operative alpha blockade). Six patients not tested pre-operatively were diagnosed intraoperatively or postoperatively on histological assessment. Median radiologically reported maximum tumour diameter was 49mm (range 20-185). Genetic testing results were available in 22 patients, of whom 12 (55%) had *SDHA*, *SDHB*, *SDHC* or *VHL* variants. Median follow up was 40.2 (range 0.2-109.7) months. Two patients had metastatic paraganglioma and one had synchronous paraganglioma and phaeochromocytoma at diagnosis. Metastatic disease management included surgery, somatostatin receptor ligand, tyrosine kinase inhibitor, stereotactic radiotherapy and peptide receptor radionuclide therapy. Three patients were deceased at follow up.
Conclusions
Multidisciplinary care of abdominal paraganglioma in Northern Ireland demonstrates good clinical outcomes. In this cohort, albeit modest follow up, there was no local recurrence. Future work will expand this dataset and utilise it to continue enhancing the care of patients living with paragangliomas in the region.

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P132

Multiple endocrine dysfunctions associated with immune checkpoint inhibitors treatment: case report

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Background
Immune checkpoint inhibitors (ICI) are anti-cancer drugs associated with adverse events that results from releasing the immune system against self-antigens while attacking cancer cells. Multiple endocrine dysfunctions have been associated with administration, including hypophysitis, thyroid disorders and diabetes.
Case report
We report the case of a 57-year-old female, diagnosed with melanoma of the left arm Barlow Depth 2 mm, receiving treatment with combined therapy (nivolumab and ipilimumab) from March 2023, who presented in the Emergency Department with nausea, vomiting, and low blood pressure (BP 90/70 mmHg). Blood tests showed TSH 33.6 mUi/ml (<3.6), ft4 0.2 ng/ml (0.8-1.7), ACTH <1.5 pg/ml, plasmatic cortisol level 8 am 0.6 mg/dl. Pituitary MRI showed no tumoral mass and normal visual field. Rapid volemic correction and hemisuccinate hydrocortisone iv were started with improvement of symptomatology. After two days, oral treatment with prednisone and levothyroxine substitution treatment, with immediate improvement. After four months, the patient presents to the Emergency Department for vomiting and diarrhea. Blood tests showed increased glucose level (523 mg/dl), ketoacidosis (pH 7.1, HCO3=9.3 nmol/l, Peptid C <0.03 ng/ml, HBA1c 9%, anti-GAD antibodies < 5 UI/ml). Insulinotherapy was initiated, with rapid improvement of her state.
Conclusion
ICI-related fulminant diabetes is associated with an incidence of <1% in PD1 inhibitors. Rapid elevation of HBA1c and the presence of ketoacidosis, even in the presence of negative anti-GAD antibodies in this patient, were suggestive of ICI diabetes. The particularity of the case is the presence of secondary cortical insufficiency, primary hypothyroidism, and diabetes induced by ICI.

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P133

Prevalence of hypopituitarism in survivors of adult onset, primary, non-pituitary, brain tumours treated with intensity-modulated radiotherapy

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Background
Intensity-modulated radiotherapy (IMRT) precisely delivers radiation to brain tumours while partially sparing surrounding structures like the hypothalamic-pituitary axis. The risk of hypopituitarism in survivors of adult-onset, primary, non-pituitary brain tumours following IMRT is poorly understood.
Methods
We conducted a retrospective cohort study of brain tumour survivors undergoing endocrine surveillance in Beaumont Hospital. Patients with an adult-onset, non-pituitary, brain tumour who received IMRT were included. Endocrine surveillance typically consisted of annual pituitary profiles and either a synacthen or dynamic growth hormone (GH) and cortisol assessment depending on whether patients were GH replacement candidates.
Results
Sixty-nine patients (26 women) were identified with a median age of 38.0 (IQR 30.0-46.2) years at radiotherapy completion. Gliomas were the most common neoplasm ($n = 38$), followed by meningiomas ($n = 17$), pinealomas ($n = 6$), medulloblastomas ($n = 5$) and 'other' brain tumours ($n = 3$). Median radiotherapy treatment dose was 54 (IQR 54-60) Gray. Hypopituitarism was diagnosed in 38% (26/69) of patients after a median of 50 (IQR 29-76) months follow up. Among the 30 patients who underwent dynamic GH testing, 63.3% ($n = 19$) had GH deficiency. The prevalence of ACTH, gonadotropin, and TSH deficiency was 24.6%, 14.5% and 8.7%, respectively. Panhypopituitarism developed in 7.2% ($n = 5$) of patients. Linear regression analysis revealed a significant association between time following radiotherapy and the likelihood of developing hypopituitarism (OR 1.29 95% CI 1.06-157, $P = 0.01$), gonadotropin (OR 1.41 CI 1.12-1.34, $P < 0.01$) and TSH deficiency (1.27 95% CI 1.01-1.63, $P = 0.05$) but not ACTH (OR 1.12 95% CI 0.93-1.33, $P = 0.23$) or GH deficiency (OR 1.12 95% CI 0.84-1.49, $P = 0.43$).
Conclusion
These findings demonstrate a high prevalence of hypopituitarism in survivors of adult-onset brain tumours treated with IMRT; almost two-fifths of patients were affected by 50 months. Long-term systematic endocrine surveillance is essential for early diagnosis and treatment of hormone deficits to potentially improve quality of life and prevent hypopituitarism-related complications.

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P134

Evaluating human monocyte migration and co-culture with adrenocortical cancer cells

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Adrenocortical carcinoma (ACC) carries a 5-year prognosis of <10%. Therapeutic options are limited including surgery and mitotane – a poorly tolerated and efficacious insecticide. Recent data have demonstrated that the immune environment of ACC is deficient in lymphocytes while demonstrating a relative rich monocyte/macrophage population in the tumour microenvironment. We have investigated the migration of circulating monocytes to ACC. ACC cells were seeded in the bottom chamber of the transwell system. Monocytes were isolated from human fresh blood using magnetic beads with high purity (>95%) and quality. Migration of monocytes at 24/48h was evaluated by identifying those remaining in the top chamber, the floating fraction in the bottom chamber and those adherent to ACC cells in the bottom chamber. Analysis of monocyte/macrophages was undertaken by flow cytometry. At 24h, when compared to control conditions, more monocytes had migrated to the ACC cells seeded lower chamber and attached to the bottom. Similar results were observed in migration at 48h. Predominantly Classical monocytes (CD14++CD16-HLA-DR+) migrated to metastatic cancer cells (MUC1), and Non-Classical monocytes (CD14+CD16+HLA-DR+) migrated to primary cancer cells (H295R/ HAC15) at 48h. We then investigated the polarization cytokine profile of migrated monocytes with or without ACC cells at 72 h by multiplex bead-based assay. Migrated monocytes indicated a significant shift toward the M2 phenotype in the presence of H295R or HAC15. The production of the pro-inflammatory factors of IL-6, TNF-alpha, etc. decreased and immunosuppressive factors of IL-10, TARC, etc. increased. MUC1 didn't increase M2 or M1 cytokine secretion. Moreover, surface markers of migrated monocytes were evaluated at 72h by flow cytometry. All ACC cell lines switched macrophages into M2 phenotype, as evidenced by the decrease in the expression of the M1 marker CD86 and the increase in the expression of the M2 markers CD163 and CD206.

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P135

Successful pregnancy after radioiodine treatment for differentiated thyroid carcinoma - a case series

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Background
Pregnancy outcome after radioiodine treatment for differentiated thyroid carcinoma (DTC) is debated. Some studies found a 23% infertility rate after radioiodine treatment. On the other hand, postoperative radioiodine therapy for DTC had no significant effect on spontaneous abortion, premature, stillbirth and congenital malformation.
Aim
To access pregnancy outcome in a series of women with DTC treated with radioiodine postoperatively.
Subjects and methods
Seven women with pregnancies after radioiodine treatment for DTC were retrospectively reviewed. Average age at DTC diagnosis was 24 ± 6.5 years.
Results
Median maximum tumor diameter at diagnosis was 1.5 cm (25 th percentile: 1 cm, 75 th percentile: 2 cm). Pathology revealed one papillary thyroid carcinoma, 4 follicular variant of papillary thyroid carcinomas and 2 diffuse sclerosing variant of papillary thyroid carcinomas. Thyroid carcinomas were multifocal in 4 cases. Mean radioiodine dose administered was 164.4 ± 57.7 mCi ^{131}I. Median interval between last radioiodine dose and baby delivery was 57 months (25 th percentile: 23.25 months and 75 th percentile: 110 months). One patients had 2 spontaneous abortions before successful pregnancy. All babies are in good health.
Conclusions
Pregnancy outcome is favorable in young patients treated with radioiodine for differentiated thyroid carcinomas when conception occurs at least 12 months after treatment.

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P136

Efficacy and safety of RET-kinase inhibitors in RET-altered thyroid cancer: A single arm meta-analysis

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Background
RET proto-oncogene that encodes receptor tyrosine kinase is responsible for the pathogenesis of most of the thyroid cancer subtypes. Selpercatinib and pralsetinib, both specific RET-kinase inhibitors, are the only two FDA-approved drugs for RET-altered thyroid cancer. We aimed to evaluate the safety and efficacy of these two drugs.
Methods
We searched PubMed, Embase, Cochrane and Clinicaltrials.gov databases for RCTs and observational studies published up to March 28, 2024 and included the ones that saw the efficacy of RET-kinase inhibitors in RET-altered thyroid cancer and reported any one of the desired endpoints. The primary endpoint was 1-year progression free survival (PFS) and objective response rate (ORR). The quantitative analyses were done using R programming language. Heterogeneity was examined with I^2 test.
Results
We included 4 studies with 560 patients, of them, 510 had RET-mutant and 50 had RET-fusion thyroid cancer. The 1-year PFS was 0.84 (95% CI=0.79-0.88, I^2=43%), ORR was 0.69 (95% CI=0.65-0.73, I^2=0), progressive disease was 0.02 (95% CI=0.01-0.03, I^2=0), stable disease was 0.24 (95% CI=0.20-

0.29, I^2 = 39%). Some important adverse events were hypertension 0.35 (95% CI = 0.29-0.42, I^2 = 53%), diarrhoea 0.20 (95% CI = 0.15-0.26, I^2 = 56%), increased ALT 0.28 (95% CI = 0.24-0.32, I^2 = 23%), increased AST 0.32 (95% CI = 0.23-0.41, I^2 = 78%), Electrocardiogram QT prolongation 0.14 (95% CI = 0.11-0.18, I^2 = 0).
Conclusion
These findings suggest that selpercatinib and pralsetinib are efficacious and safe to use in RET-altered thyroid cancer. However, more randomized trials are needed to prove our findings.

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P137

Using a combination of bulk and single cell RNA sequencing to identify transcriptomic differences in metastatic vs non-metastatic phaeochromocytomas and paragangliomas

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Introduction
Phaeochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumours that are inherited in at least 40% of cases. The most common pathogenic germline variants (PGVs) implicated in the development of PPGLs are in genes coding for the subunits of succinate dehydrogenase (SDH). PPGLs are heterogenous tumours that have a variable clinical phenotype. Rates of metastatic disease varies from 5-40%. This variability is not currently understood. All patients identified with a PPGL related PGV are therefore offered screening that involves annual clinical review and a whole-body MRI every 2-3 years. With patient numbers increasing a more appropriate means of triage is needed. In this study we will use bulk and single cell RNA-sequencing (ScRNA-seq) to identify transcriptomic differences in metastatic vs non-metastatic SDH related PPGLs. Here we will discuss our approach to successfully extracting RNA from fresh as well as archived PPGL tissue samples for both bulk and ScRNA-seq.
Methods
104 PPGL samples have been collected. Samples were provided in either formalin fixed paraffin embedded (FFPE) blocks or fresh frozen tissue (FFT) stored at -80°C. We have performed RNA extraction on 52 SDH related PPGLs ($n = 39$ FFPE, $n = 13$ FFT). RNA was successfully extracted from FFPE samples that were surgically resected up to 23 years previously (average = 11 years). A DV200 of >35% in these samples indicated sufficient RNA integrity for successful sequencing in cases of FFPE stored tissues. A subset of tumour samples collected directly from the operating theatre were processed for immediate single cell dissociation using a bespoke protocol that has resulted in successful ScRNA-seq in 2 PPGL samples.
Results
Bulk-sequencing data is now available for 32 SDH related PPGLs. Utilising archived tissues allows us to increase the number of confirmed metastatic cases for our downstream analysis. ScRNA-seq reveals the distinct cellular populations present in PPGLs.

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Neuroendocrinology

P138

Treatment resistant cushing's disease following standard and novel multi-modal therapy in the setting of a constitutional pathogenic MSH2 variant

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We report the long-term progress of a 51-year-old female with Lynch syndrome, who presented in 2015 with Cushing's disease secondary to a constitutional pathogenic *MSH2* splice site variant. [1] Transsphenoidal surgery was followed by gamma knife radiotherapy 6 months later due to persistent hypercortisolism. Radiotherapy resulted in remission, with adrenocorticotrophic hormone (ACTH) deficiency noted 2 years postoperatively. MRI pituitary 3.5 years after surgery showed a small amount of stable residual tissue. By June 2021 she reported increased weight gain. Adrenocorticotrophic hormone was detectable and associated with resumption of adrenal cortisol production. A watchful waiting approach was adopted. Follow-up pituitary MRI in June 2021 was unchanged and 24-hour urinary free cortisol concentrations were normal (121-188 nmol/24 hours, reference range <210 nmol/24 hours). She presented in September 2021 with a left sixth nerve palsy, optic neuropathy and an orbital apex mass. Recurrence of hypercortisolaemia and elevated ACTH were noted. She recommenced a block and replace regime with metyrapone and dexamethasone in November 2021. Further pituitary radiotherapy and/or bilateral adrenalectomy were considered by the multidisciplinary team, but were deemed high risk in the setting of severe hypercortisolaemia-induced comorbidity and frailty. She continued with medical therapy. Her condition progressed with ongoing hypercortisolism and deteriorating vision. Immunotherapy with the PD-1 inhibitor nivolumab was ineffective. Cabergoline was similarly unsuccessful. A 6-month trial of pasireotide titrated to 30 mg monthly did not result in biochemical or tumoral response. Following preoperative optimisation of her physiology she underwent bilateral adrenalectomy with adjunctive radiotherapy. Follow-up MRI to monitor for corticotroph tumour progression after bilateral adrenalectomy is awaited. This is a rare case of an aggressive pituitary neuroendocrine tumour resistant to multi-modal therapy occurring in an individual with Lynch syndrome.
Reference
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P139

Progressive neurosarcoidosis presenting as idiopathic hypopituitarism with atypical radiological features for 13 years

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Background
Sarcoidosis is an immune-mediated multisystem condition of unknown etiology, characterized by non-caseating granulomatous inflammation. While it commonly affects lungs and the reticuloendothelial system, it can affect any organ. Central nervous system involvement is found in 5-15% of cases, with less than 1% experiencing symptoms related to hypothalamic-pituitary dysfunction. Neurosarcoidosis primarily targets the leptomeninges, leading to infiltration of the hypothalamus and pituitary gland by granuloma with deficiencies in LH, FSH and GH being common. Most patients suffering from sarcoidosis develop neurological manifestations within two years of diagnosis and can present with inflammation in the pituitary gland which can mimic infiltrative pituitary lesions.
Case Report
We present a 54-year-old male patient, who initially presented with infertility, hypothyroidism and growth hormone deficiency due to presumed idiopathic hypopituitarism. He had two children following gonadotropin therapy, and was maintained on pituitary hormone replacement. After 13 years, he developed further symptoms of Neurosarcoidosis including cerebellar infarction, optic neuritis and paralysis in lower limbs, and later developed systemic sarcoidosis including erythema nodosum, and cervical lymphadenopathy. Initially, his MRI brain showed a decrease in the size of the pituitary gland in 2004, and there were no other features to suggest a systemic illness. Repeat MRI Brain in 2019 showed an empty sella. His chest x-ray was normal, T-spot was negative and serum ACE was undetectable, but eventually a lymph node biopsy confirmed features of sarcoidosis. Unfortunately, his condition has progressed despite high-dose steroid therapy and methotrexate.
Conclusion
This case emphasizes the need for thorough re-examination for features of Neurosarcoidosis in cases of apparently idiopathic panhypopituitarism, to identify patients developing further complications, even after many years. Obtaining a tissue diagnosis is often difficult, and systemic features may be absent. Prospective studies are needed to establish a more uniform strategy for managing hypothalamic pituitary Neurosarcoidosis and identifying factors that predict treatment outcomes.

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P140

Screening for carcinoid heart disease (CaHD): an audit of practice and assessment of deprivation index in sheffield NET centre, a european neuroendocrine centre of excellence

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Aim of the audit
Guidelines recommend screening for carcinoid heart disease (CaHD) in patients with carcinoid syndrome (CS) using 5-hydroxyindoleacetic acid (5HIAA), NT-pro BNP and Echocardiogram. We audited patients with CS for these parameters and gathered information related to social deprivation.
Objectives
To ensure that the CS diagnosis was confirmed biochemically, assessment of social deprivation, review of waiting times, audit of echocardiogram requests when 24-hour urinary 5-HIAA >300 µmol/l.
Methodology
The Sheffield NET database was interrogated retrospectively to review patients with and without CaHD who had been referred to neuroendocrine MDT. Data was collected for 50 patients.
Results
62% of patients were females, mean age 65 years. 96% had $<$ 2 weeks waiting period between referral and MDT discussion. 90% had 24-hour urine 5HIAA to confirm the diagnosis biochemically. Assessment of NT-Pro BNP was low at 20%. 50% of patients were found to have severe CS with 24-hour U5HIAA $>$ 300 µmol, of whom 92% had echocardiography performed. 34 out of 49 patients with CS were in the 1 – 6 most deprived areas as per the index of multiple deprivation deciles ranking in comparison to 14 out of the 17 patients who had both CS and CHD.
Conclusion
Sheffield NET Centre has a short waiting time from referral to MDT review for CS patients, appropriate biochemical and echocardiography were requested. Improvements in NT pro-BNP requesting could be made. Here we highlight 82 % of the patients with severe CS and CaHD live in the most socially deprived areas. These findings might be helpful to facilitate strategies to aid early diagnosis and management of patients with CS/CaHD where it is needed most. To our knowledge this is the first association of deprivation and CaHD. Further national study could lead to improvement in morbidity and mortality.

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P141

Efnb2 controls pituitary development by regulating the pituitary stem cell niche

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Efnb2 plays an integral role during mouse development, specifically in angiogenesis and stem cell regulation. *Efnb2* encodes for Ephrinb2 ligand that binds to Eph receptor. Preliminary data suggest implications of *Efnb2* in pituitary tumors. The involvement of Eph:Ephrin signaling pathway in pituitary development is currently unknown. Better knowledge of Efnb2 in the pituitary will improve the understanding of endocrine disease. Therefore, a pituitary-specific Cre-driver ($Hesx1^{Cre}$) was used to genetically delete *Efnb2* in early pituitary progenitors *in vivo*. Our experiments show that *Efnb2* recapitulates the expression of pituitary stem cells (PSCs) during embryogenesis. Deletion of *Efnb2* leads to abnormal morphology of the gland, specifically impacting the niche of PSCs which suggests its involvement in PSCs maintenance. We then performed mRNA sequencing during early pituitary development stages to elucidate the molecular role of *Efnb2* in the pituitary. This transcriptomic analysis revealed novel functions of *Efnb2* in cell proliferation, epithelial integrity and cell lineage commitment. Validation experiments of transcriptomic analyses confirm that *Efnb2* negatively regulates PSC proliferation *in vivo* and *in vitro*. *Efnb2* mutants exhibit increased mitotic index, hyper-proliferating in the niche of PSC. Additionally, *Efnb2* mutants present down-regulation of epithelial integrity leading to abnormalities in epithelial-mesenchymal transition (EMT) of the PSC niche. Moreover, mutant mice present a significant reduction in the expression of pituitary lineage commitment markers (Pit1, Pomc1 and Gsu). These results demonstrate that *Efnb2* is critical for pituitary development and further regulates the niche of PSC.

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Kisspeptin does not induce anxiety in humans

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Background
The neuropeptide kisspeptin is a critical endogenous activator of the reproductive system, with escalating clinical interest as a novel therapeutic agent for reproductive and psychosexual disorders. However, conflicting animal data suggest that kisspeptin can have anxiolytic, neutral, or anxiogenic effects. Given the rapid development of kisspeptin-based therapeutics, it is important to clarify kisspeptin's effects on psychometric measures of anxiety and associated circulating cortisol levels in humans.
Methods
Ninety-five eugonadal participants ($n = 63$ men, $n = 32$ premenopausal women) completed a double-blind, randomised, placebo-controlled, crossover study (mean age $\pm$SEM 30.9$\pm$0.9yrs, BMI 24.0$\pm$0.4kg/m ^{2}). Participants attended for a 75minute intravenous kisspeptin-54 infusion (1nmol/kg/h) and again for a rate-matched placebo. Blood was sampled at 15-minute intervals throughout the infusions for circulating kisspeptin, LH, sex-steroid levels, and cortisol. Participants completed a state anxiety questionnaire ('STAI Y1-State') before and at the end of the infusions to assess for any dynamic effects of the infusions on anxiety.
Results
Intravenous kisspeptin significantly increased serum LH to similar levels previously described using this administration protocol, confirming that the dose was biologically active ($P < 0.001$). As expected, kisspeptin had no significant effects on downstream sex-steroid levels during the 75minute study period, thereby excluding these as possible confounders. State anxiety was not significantly altered by kisspeptin, compared to placebo (mean difference in 'STAI Y1-State' scores during the infusions: kisspeptin -0.4$\pm$0.8, placebo 1.3$\pm$0.8, $P = 0.09$). Moreover, kisspeptin had no significant effects on circulating cortisol compared to placebo ($P = 0.73$).
Summary
This is the largest study demonstrating that a biologically active dose of kisspeptin to humans does not affect psychometric measures of anxiety and associated cortisol levels. Given that animal studies have yielded conflicting results, this provides important clinical data and reassurance that kisspeptin does not induce anxiety in humans and so informs the rapid development of kisspeptin-based therapeutics for reproductive and psychosexual disorders.

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P143

Clinical complexities of adipsic arginine vasopressin deficiency

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Introduction
Adipsic arginine vasopressin deficiency (AAVP-D) is rare, accounting for ~100 cases in literature. It poses multiple therapeutic challenges, with increased morbidity and mortality. We discuss an interesting case of AAVP-D, and the importance of careful management and follow-up.
Presentation
24-year-old female underwent debulking of recurrent central neurocytoma. Post-operatively, she developed new confusion with hypernatraemia (171 mmol/l) and increased urine output (~354mls/h). Plasma osmolality was raised (346 mmol/kg) , with low urine osmolality (142 mmol/kg) and adipsia. Transient AAVP-D was suspected; successfully treated with IV Desmopressin. Her symptomatic hypernatraemia resolved (133 mmol/l), and she was discharged. One week later, she re-presented with worsening confusion and agitation. Admission bloods showed hypernatraemia (170 mmol/l), raised osmolality (329 mmol/kg), acute kidney injury (urea 10.0 mmol/l, creatinine 104 micromol/l), alongside increased urinary frequency (80-355mls/h). Permanent AAVP-D was suspected; regular Desmopressin 50 micrograms/day was thus commenced. Desmopressin has since been titrated according to plasma sodium levels (currently 150 micrograms/day) in outpatient Endocrinology clinic, alongside fixed oral fluid intake of 2L/day.

Discussion
AAVP-D poses multiple clinical challenges. Thirst sensation secondary to increased osmolality is lost, complicated by confusion associated with hypernatraemia. Variations in fluid intake can result in catastrophic fluctuations in sodium and osmolality levels. Management thus includes calculating a fixed fluid goal daily and titration with desmopressin to ensure consistent urine output, patient weight, and plasma sodium level. Historically morbidity was associated with confusion regarding previous nomenclature of 'diabetes insipidus'; mistaken for more common 'diabetes mellitus'. Change in nomenclature to 'arginine vasopressin deficiency' in 2022, allows further clarification on pathophysiology of this complex disease.
Conclusion
AAVP-D is a rare clinical dilemma. We wish to highlight from our patient's case the pathophysiology of AAVP-D, and the importance of careful fluid balance and medical management, and emphasise why alternative nomenclature was necessary.

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P144

Case: recurrent vaginal paraganglioma with hypertension in pregnancy

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Paraganglioma is a rare neuroendocrine tumour. There are few case reports in the literature describing vaginal paraganglioma to date. We present the case of a 37-year-old female referred to endocrinology services with symptomatic hypertension, initially noted during her first pregnancy three years prior. This was on a background of a vaginal paraganglioma diagnosed in 2006 which was excised by gynaecology services without complication. Her first pregnancy in 2021 was notable for symptoms of palpitations and headache with an episode of hypertension at 39/40 gestation requiring a short course of labetolol. This was deemed to be as a result of gestational hypertension. She reported hyperhidrosis and anxiety post-partum with further symptoms of hypertension 6 months after delivery. Symptoms were again noted at 37/40 gestation during her second pregnancy in 2023 with documented hypertension. A C-section was performed at 38/40 due to reduced foetal movements with subsequent large post-partum haemorrhage. Cross-sectional imaging revealed pelvic lymphadenopathy at that time, presumed to be reactive secondary to intra-abdominal haemorrhage. An MRI pelvis was arranged 6 months post-partum due to persistent hypertension and elevated urinary normetadrenaline and noradrenaline, which revealed a right-sided 1.2cm vaginal vault lesion with persistent pelvic lymphadenopathy. Her case was discussed at the gynaecology-oncology and neuroendocrine multi-disciplinary team meetings with subsequent FDG-PET-CT confirming MRI findings without distant metastases. The patient awaits surgical debulking and a gallium-PET scan and has been commenced on Doxazosin peri-operatively while breastfeeding. There are few case reports in the literature of vaginal paraganglioma with a review in 2022 citing only eleven cases, one of which was associated with a SDHB genetic variation. This case highlights the importance of lifelong surveillance in patients with paraganglioma.

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P145

Panhypopituitarism secondary to CVST with dominant posterior pituitary symptoms

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22 yr old male pt known case of ulcerative colitis and CVST, presented with diarrhoea, abdominal pain and left lower limb swelling. DVT was confirmed on doppler. During admission he suffered from UC flare up and developed toxic megacolon with perforation. An emergency laparotomy was performed, also an IVC filter was placed due to ongoing DVT. Medication history includes sertraline, clexane, fostair, adalimumab. During ITU admission, Pt was found to have increased urine output (>3l/24hr) post op., ongoing hypoglycaemia (bm< 3) and hypotension and required ionotropic support. He was receiving continuous IV dextrose (5 – 6 litres) daily. Blood work showed Serum osmolality=342, Urine osmolality=484 mOsmol/Kg, Urine Na <20 mmol/l. Na dropped from 159 to145 mmol/l was noted (after switching noradrenaline to vasopressin trial and stopped due to sudden drop). Initial blood test showed Sodium levels varying between 150-159 with normal potassium. Random cortisol 203 done at midnight. C peptide > 1000, Adj calcium- 2.42. Endocrinology review suggested full pituitary profile, MRI pituitary and short synacthen test. SST showed normal response. ACTH<1.5, IGF1 14.9, 9AM Testosterone levels were low at 0.4, TSH, FSH, LH and prolactin were normal. MRI showed the pituitary is small volume for patient's age. No adenoma. Diagnosis of Pan-hypopituitarism secondary to extensive CVST, with dominant posterior pituitary symptoms was made after MDT discussion. He was commenced on IV hydrocortisone as ACTH being <1.5 confirms secondary adrenal suppression. Desmopressin was started at 100 mg TDS. Diazoxide 5 mg/kg daily in 2-3 divided dose as per response for intractable hypoglycaemia. Testosterone replacement in the form of Testogel starting from 40.5 mg OD. Due to intractable hypoglycemia and borderline low IGF-1 pt had glucagon stimulation test and that confirmed insufficient GH and was started on GH to improve hypoglycaemia. It was noted that patient did not receive any check point inhibitor for his treatment of Ulcerative colitis since his diagnosis.

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P146

Transformation of non-functioning pancreatic neuroendocrine tumours into insulinomas in multiple endocrine neoplasia type 1: a case report

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Duodenopancreatic neuroendocrine tumours (dpNETs) affect more than 90% of patients with Multiple Endocrine Neoplasia type 1 (MEN1) by age of 70. Insulinomas are the second most common functioning dpNET encountered in this setting. We present the case of a 56 year-old woman with genetically confirmed MEN1 in whom non-functioning pNETs transformed into insulinomas, seven years after being diagnosed with MEN1 syndrome and pNETs. The patient was referred to the neuroendocrine clinic following the detection of an incidental pancreatic lesion on abdominal imaging. This occurred on a background of primary hyperparathyroidism, previously managed by parathyroidectomy. At the diagnosis, Endoscopic ultrasound (EUS) confirmed multiple small pNETs, one located in the head of the pancreas and several in its body and tail with multiple areas of enterochromaffin-like cell (ECL) hyperplasia. Surveillance EUS was performed 2-yearly over a 6 year period and showed stable pNETs. There were no symptoms to suggest a functioning pNET over this initial time period. The following year however, the patient was admitted to hospital following a severe hypoglycaemic episode (capillary blood glucose <2 mmol/l), and commenced diazoxide. A 72-hour fast showed a nadir serum glucose of 2.5 mmol/l (insulin and c-peptide results were non-diagnostic as performed shortly after stopping diazoxide). Interval EUS showed an 11mm pNET in the isthmus and 2 smaller pNETs in the body and tail of the pancreas with multiple areas of ECL hyperplasia. Selective intra-arterial calcium injection test was positive and localised to the proximal gastroduodenal and proximal splenic arteries. 3 pNETs were successfully enucleated, 2 of which were histologically proven insulinomas. This resulted in a significant reduction in the burden of hypoglycaemia. Although uncommon, non-functional pNETs have the potential to transform into a functional syndrome in MEN1. Further research is required to predict risk factors and mechanisms of transformation in pNETs.

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P147

Assessing biological stress markers in the hair of individuals at ultra-high risk for psychosis using a novel method of extraction

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Background
The hormone cortisol is both induced by and is a biomarker of stress. However, its long-term measurement in blood and urine is limited by feasibility of collection.

Hair is a novel matrix to measure long-term steroid levels. We developed a liquid chromatography-tandem mass spectrometry (LC/MS) method to assess hair cortisol in individuals at ultra-high risk (UHR) for psychosis as a biomarker of stress.
Method
Hair samples from 10 UHR individuals (3M/7F, mean age 23.0) and 12 age-matched controls (2M/10F) were analysed by LC/MS. 3cm-long hair samples from the proximal vertex region of the scalp were pulverised under liquid nitrogen. Steroid extraction was carried out using Methyl tert-Butyl Ether (MTBE) and water, before evaporation under a nitrogen stream. Samples were reconstituted in 50:50 methanol and water and run by LC/MS (Waters Acquity with Xevo-XS) using a validated method. Absolute steroid levels and ratios were correlated with measures of self-reported stress.
Results
15 steroids were isolated, including cortisol and cortisone. We observed a reduced relative standard deviation (RSD) in the cortisol/cortisone (f/e) ratio compared to cortisol alone (f/e RSD 11.35, IQR 25.42, cortisol RSD 17.44, IQR 45.06) and proceeded with f/e ratio as a measure of biological stress. We observed no difference in the hair f/e ratios of UHR individuals compared to control participants, nor did we observe correlations between severity of positive symptoms or self-reported stress levels and f/e ratio.
Conclusions
Whilst we successfully developed a novel method of steroid extraction from hair in individuals at UHR for psychosis, f/e ratios from this group did not significantly differ from healthy controls or correlate with self-reported stress. Further research is now needed to validate hair f/e ratio measurements as a biological stress marker in a larger high-stress population.

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P148

Effect of endoscopic transsphenoidal surgery on pituitary function – preliminary report from a tertiary referral centre

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Limited data are available on the effect of transsphenoidal surgery using the endoscopic method on pituitary function. In this preliminary report we retrospectively evaluated the frequency of pituitary failure and recovery in a population of patients who underwent this procedure over a 12 months period. 42 (21 women) consecutive adult patients were included. 29 patients had non-secretory pituitary neuroendocrine tumours, the rest had secretory tumours and other non-adenomatous pituitary region masses. 29 patients had optic chiasma compression. Pituitary function was assessed using baseline and dynamic testing. Of the 35 patients who had full gonadal function assessment, 20 had preoperative deficiency with six showing recovery and four developing new deficiencies postoperatively. 23 patients had dynamic hypothalamo-pituitary-adrenal (HPA) axis assessment with three showing preoperative deficiency, six developing postoperative deficiency and none showing recovery. 10 of 40 patients assessed showed preoperative TSH deficiency with two developing new deficiency and four showing recovery postoperatively. Four patients had preoperatively AVP deficiency with no recovery and no new cases postoperatively. GH deficiency was assessed in only four patients preoperatively and persisted in all four patients postoperatively. This preliminary report showed that a minority of patients develop pituitary deficits following endoscopic transsphenoidal surgery while some recover. These data will help to counsel patients undergoing this procedure. Larger study is necessary for definitive conclusions.

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P149

A case report of an FSH-producing pituitary macroadenoma presenting with panhypopituitarism in a male

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Functioning gonadotroph adenomas (FGAs) are rare pituitary tumours which express and secrete biologically active gonadotrophins or their subunits. The exact prevalence is unknown. Several syndromes have been recognised in different subgroups including hypogonadism, precocious puberty, ovarian hyperstimulation, and elevated serum testosterone with testicular enlargement. Transsphenoidal surgery is the treatment of choice and definitive diagnosis is made on subsequent histopathological assessment and immunohistochemical analysis. We present the case of a 55 year old Irish male, referred to endocrinology services following an episode of severe hypoglycaemia (serum glucose 1.1 mmol/l [3.5-7.7]). He had a history of alcohol excess, portal hypertensive gastropathy, cardiac arrest secondary to ventricular fibrillation necessitating ICD placement. He described a history of fatigue, erectile dysfunction and decreased libido. Initial investigations demonstrated a morning cortisol of 30 nmol/l (166-507) and ACTH 13.7pg/ml (7.2-63.3); discordant thyroid function with TSH 1.56 mU/l (0.27 – 4.2) and FT4 8.99 pmol/l (12 – 22); elevated FSH 14.1 IU/l (1.5 – 12.4), within range LH 2.6 IU/l (1.7 – 8.6) and low testosterone of 6.35 nmol/l (6.7-31.3). A CT pituitary revealed a 2.2cm pituitary adenoma. He was treated with hydrocortisone, levothyroxine and testosterone replacement. 1 year later he developed new visual disturbance with visual fields demonstrating a bitemporal hemianopia. He underwent transsphenoidal resection with histopathological examination demonstrating a pituitary adenoma with positive immunostaining for Chromogranin, Cam5.2, FSH, LH and SF1 consistent with a diagnosis of a gonadotroph pituitary adenoma. Post operatively his FSH had normalised to 7.3IU/l. FGAs represent a rare subset of pituitary tumours with distinct immunohistochemical profiles and varied clinical presentations. These tumours should be considered in patients with impairment in one of more pituitary axes and elevated gonadotrophins.

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P150

Ectopic adrenocorticotropic hormone secretion in metastatic small cell lung cancer

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We describe the presentation of a 65 years old lady with upper gastrointestinal bleed to Altnagelvin Area Hospital in April 2023, eventually diagnosed with Cushing's syndrome due to ectopic ACTH secretion from a high grade neuroendocrine tumor. Acute presentation was preceded by three months of general decline, weight loss, poor appetite and a history of smoking 20 cigarettes per day for more than 20 years. On examination, she was cachectic and delirious with cutaneous nodules in the thorax, anterior abdominal wall and the left gluteal region. Hypertension noted with systolic blood pressure measuring above 150 mm Hg. Endoscopy showed three duodenal ulcers. Baseline investigations showed a potassium of 2.8 mmol/l with refractory to intravenous replacement. Above combined with bicarbonate was 40 mmol/ L and hyperglycemia without pre-existing Diabetes prompted endocrine investigations. Renin was 51.21 u IU/ml and Aldosterone was 106 pmol/l. Cortisol at six am came back significantly elevated at 4381 nmol/l with a repeat reading of 4068 nmol/l. ACTH levels were 480 ng/l-527ng/l . CT imaging revealed an infiltrating mass within the mediastinum involving the right main pulmonary artery, the SVC, extending to the right lung. Bilateral adrenal masses, liver lesion, ascites and multiple subcutaneous deposits were noted through the thorax and upper abdomen. Imaging of the brain showed a metastatic lesion in the left parietal lobe. Core biopsy results from cutaneous nodule, were suggestive of a high grade neuroendocrine/small cell lung carcinoma. Despite management in ICU with Metyrapone and Dexamethasone the patient deteriorated further and was deemed not fit for chemotherapy from the Respiratory MDM. Sadly, she passed away 32 days after the initial presentation, in the palliative care ward in Omagh Hospital.

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P151

The pre- and perioperative management of pheochromocytomas and intraabdominal paragangliomas- service evaluation at the tertiary centre

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Background
Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumours managed with pre-operative alpha+/- beta blockade prior to surgery. These patients are at risk of intra-and postoperative haemodynamic instability. The aim of this project was to review the outcomes of PPGL patients operated on between 2018-2023 at Cardiff and Vale UHB.
Methods
Retrospective case notes ($n = 29$) review for data collection on baseline demographics, presentation, metanephrines results, pre-operative pharmacotherapy (duration, type, dosage), surgical outcomes and length of stay.
Results
Twenty-one patients had pheochromocytoma, 7- paraganglioma and there was 1 benign tumour (M=18, F=12, mean age 57.1 years old (SD=16.63)). The most common presenting complaint was either hypertensive episodes, headaches, palpitations, or a combination of the 3. All pheochromocytoma patients and 6 (85%) paraganglioma patients had abnormal pre-operative urine/plasma metanephrines. Higher baseline urinary normetadrenalines correlated with a longer length of hospital stay ($P = 0.04$). Twenty-eight patients were started on alpha-blockade (Phenoxybenzamine (PBZ) $n = 23$; doxazosin $n = 5$). The median pre-operative systolic BP was 128mmHg lying and 113mmHg standing. Within the PBZ cohort, 4 patients were also managed with bisoprolol prior to surgery. These patients required higher doses of PBZ preoperatively (median total daily dose 80 mg ranging from 30 mg BD to 60 mg TDS) compared to those on PBZ alone ($P = 0.0063$) Additionally, the combined alpha and beta-blocked patient cohort ($n = 6$, PBZ=4, doxazosin $= 2$) was also found to be more haemodynamically unstable intraoperatively requiring significantly more metaraminol boluses (6.3) compared to the non-beta blocker cohort (3.4 boluses) ($P = 0.0260$). Interestingly, amongst those 6 alpha- and beta-blocked patients, 4 (67%) were also treated with a calcium channel blocker.
Discussion
In our cohort, PPGL patients on combined alpha- and beta-blockade experienced a higher number of hemodynamic intraoperative instability. Larger prospective studies would be beneficial to establish an up to date evidence-based approach regarding optimal pre-operative preparation of the PPGL patients.

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P152

A review of outcomes following outpatient alpha-adrenoceptor blockade preoperatively in patients with pheochromocytoma and paraganglioma in a single tertiary centre

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Phaeochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumours, the majority of which secrete excess catecholamines resulting in significant hypertension and tachycardia. Pre-operative blood pressure control with alpha-adrenoceptor blockade is therefore implemented. The aim of the study was to assess the pre-, intra- and post-operative outcomes of patients undergoing outpatient alpha-blockade in our centre. A retrospective chart analysis was conducted on patients who underwent surgical resection of PPGL between 2015 and 2023. Parameters assessed included patient demographics, genetic mutations, pre-operative alpha-blockade agent, total daily dose (TDD), intra-operative blood pressure, length of stay and post-operative complications. To date, data have been collected from charts of 28 patients; 82% had phaeochromocytoma resection; 18% had paraganglioma resection; mean age at surgery 49.6 years. Of 24 patients who had genetic testing in our centre, a genetic mutation was not identified in 74%; SDHB 8%; VHL 8%; MEN2A 4%. Pre-operative functionality assessment revealed secretion of one catecholamine ($n = 10$), and two or more catecholamines ($n = 14$). Alpha blockade agent was documented in 26/28 patients. Phenoxybenzamine was the preferred pre-operative alpha blockade agent in 81% ($n = 21/26$) with a mean TDD of 67 mg, and doxazosin in 19% with a mean TDD of 11 mg. Mean nadir and peak blood pressures were 76/44mmHg and 151/84mmHg, respectively. Median length of stay was 5 days (IQR 2.5-7). There were no blood pressure-related complications. Post-operative complications included fever secondary to atelectasis, hospital acquired pneumonia and intra-operative ureteric injury with post-operative intra-abdominal haematoma. Overall, preliminary data suggest that our local alpha-blockade protocol prior to PPGL resection results in satisfactory intra-operative blood pressure control with few post-operative complications. Data collection is ongoing in our cohort of patients with PPGL.

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P153

Pheochromocytoma and takotsubo cardiomyopathy: a case report

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Introduction
Pheochromocytoma is a rare neuroendocrine tumour, commonly diagnosed between ages 40 and 50, typically presents with hypertension, palpitations, and episodic headache. We would like to report a patient diagnosed through an uncommon presentation -cardiomyopathy.
Case report
A 49-year-old female with hypertension, T2DM and obesity, presented to the emergency department with shortness of breath. Although her CXR & ECG were normal and CTPA excluded PE although showed an incidental lung nodule. Her echocardiogram showed global severe systolic dysfunction, Ejection Fraction 30%, with normal valves. The CT coronary angiogram showed normal coronary arteries and lung function tests also were normal. Interval chest CT scan for the lung nodule revealed right adrenal incidentaloma (4.5 x 2.6 cm heterogeneous attenuation (part-cystic part-soft tissue density, no fat). During the endocrinology consultation, she was noted to have a year history of frequent palpitations, sweating, and dizzy spells. Adrenal investigations revealed normal 1 mg overnight dexamethasone suppression test. Her plasma Normetadrenaline level was 8350 pmol/l (120 - 1180), and Metadrenaline 1250 pmol/l (80 - 510). Repeated metanephrines yielded similar results. Confirming pheochromocytoma. Dedicated adrenal MRI showed right-sided 4cm heterogenous cystic adrenal lesion, lacking signal drop-out on out-of-phase, making adenoma unlikely. Interestingly, MIBG scan didn't show any abnormal uptake. The patient underwent uneventful laparoscopic right adrenalectomy, which confirmed histologically benign pheochromocytoma, PASS score of 5/20 and low level of SDHB expression. Patient also had incidental U2 thyroid nodule – however calcitonin levels came back normal and genetic testing for MEN was negative. Her 6-months postoperative echocardiogram showed recovery from cardiomyopathy (EF 55-59%), and cardiac medications were withdrawn.
Conclusion
Thorough history taking, and careful investigations are crucial in diagnosing the underlying cause of unexplained cardiomyopathy. Although uncommon, recognizing Takotsubo cardiomyopathy in pheochromocytoma is vital for improving the clinical outcomes.

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P154

Primary hyperparathyroidism in multiple endocrine neoplasia type 1 (MEN1): the northern ireland (NI) experience

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Primary hyperparathyroidism (PHPT) is commonly the first and most frequent clinical manifestation in MEN1 occurring in up to 95% of patients. Clinical course differs to that of sporadic PHPTH in terms of complications, surgical management and recurrence rates. This study aims to review the challenges of PHPT in MEN1. Retrospective analysis of patients attending a dedicated MEN1 clinic, under long-term review was carried out ($n = 26$). 85% had PHPT ($n = 22$; male:female 9:13; age 49.9: range 28-70 years); the most common manifestation. It was the initial presentation in 17 of these 26 patients. Average age at diagnosis of PHPT was 31 years. Calcium was 2.86 mmol/l and PTH 106 pg/mL at diagnosis. Fourteen patients had DEXA scan; all had either osteopenia (43%) or osteoporosis (57%). Renal calculi occurred in 22.7%. All patients underwent parathyroidectomy. Main surgical technique used in the first operation was subtotal parathyroidectomy (3 or 3.5 gland removal) (20 of 22 patients). Limited parathyroidectomy (2 gland removal) was employed in 2 patients. 9% and 54.5% had persistent and recurrent disease, respectively, after first surgery. Recurrence was on average 13 years after first surgery. Rate of remission after first surgery was low at 36.3%. 5 patients required a second surgery (3 achieved remission) and 1 patient required a third operation (now in remission). 31.8% developed hypoparathyroidism post-operatively. The experience in NI of MEN1-related PHPT is similar to other studies. This is a multi-glandular disease of which management is challenging. Recurrence rates are much higher compared with sporadic disease (54.5% vs 1-15%). Effects on bones are more severe in MEN1 (57% vs 40% in sporadic PHPT). Renal effects are similar. The timing of surgery requires multi-disciplinary involvement with close and long term follow up at a dedicated clinic to allow optimal outcomes.

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P155

Fertility outcomes following transsphenoidal surgery for pituitary tumours at the university hospital of wales, cardiff

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Background
Fertility outcomes following transsphenoidal surgery (TSS) for pituitary adenoma are unclear, meaning decision-making regarding management options and peri-operative patient counselling is challenging.
Objective
To identify the implications of TSS pituitary adenoma resection on the hypothalamic-pituitary-gonadal (HPG) axis and evaluate longer-term fertility outcomes to identify the burden of post-operative infertility.
Design
Retrospective Analysis
Population
The population consisted of 236 patients (females >50y were excluded) diagnosed with a non-functional adenoma (NFA), Cushing's disease or acromegaly who underwent transsphenoidal pituitary surgery at the University Hospital of Wales (UHW) between 2011-2019.
Method
Retrospective analysis of patients' electronic records was conducted via Welsh Clinical Portal and Cardiff and Vale Portal.
Results
n = 236. Sex: 173 (73%) male, 63 (27%) female. Mean age: 48(15-81)y male and 35(15-50)y female. Diagnosis: 138 NFA, 31 Cushing's, 67 acromegaly. Post-operatively – New hypogonadism: 13 (7.5%) males and 1 (1.6%) female. HPG axis restoration: 14 (8.1%) males and 7 (11.1%) females. Fertility – Males: 4/173 (2%) desired fertility, 1 (0.6%) of whom started gonadotrophin therapy; we were unable to determine whether successful conception occured for male patients. Females: 13/63 (20.6%) desired fertility. 6/13 (46.2%) (diagnosis: 2-NFA, 2-Cushing's, 2-acromegaly) conceived naturally. 7/13 (53.8%) were referred to fertility services. 3/7 declined and 4/7 underwent fertility treatment, resulting in a birth in 1/4 (25%) (Diagnosis: acromegaly) but had failed to be successful in 3/4 (75%) (diagnosis: 1-NFA, 1-Cushing's, 1-acromegaly) prior to our data collection: 1 of these went on to conceive naturally but miscarried.
Conclusion
A desire for fertility was more commonly expressed by female patients post-TSS in our case series. Around half of females desiring fertility in this retrospective review were able to conceive naturally. Of those referred for fertility treatment, 1/4 had treatment resulting in a live birth. Our analyses are limited by small case numbers and limited duration of follow-up.

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P156

Using transcriptomics to refine the subtypes of non-functioning pituitary neuroendocrine tumours

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Background
Transcription factors *TPIT*, *SF-1* and *PIT-1* correlate to differentiation of the pituitary cell lineages. In 2017 the World Health Organisation updated the classification of pituitary neuroendocrine tumours (PitNETs) to include transcription factor immunohistochemical (IHC) staining. This has been reiterated in the 2022 classification of PitNETs.
Aim
To further refine the diagnostic classification of non-functioning PitNETs using transcriptomics.
Methods
Clinicopathological data were extracted from a retrospective pseudoanonymised database of 350 non-functioning PitNET patients who underwent surgery in Northern Ireland. Ethical approval for access to and use of corresponding PitNET samples in research was granted by the Northern Ireland Biobank. RNA extraction was performed with Illumina's TruSeq RNA exome from formalin-fixed paraffin-embedded tissue samples. RNA-seq was aligned to hg38 and sequenced on the Illumina NovaSeq 6000 system. The World Health Organisation 2022 classification of pituitary tumours was used to inform transcript selection, namely of *TPIT*, *SF-1* and *PIT1*. Two hundred and fifty-seven nonfunctioning PitNETs successfully surpassed sequencing QC thresholds. Transcriptomic data was analysed using Bioconductor's DeSeq2 Package for differential gene expression analysis and Pheatmap for data visualisation.
Results
TPIT, *SF-1* and *PIT1* concurred with 18/21 (90%) of the ACTH positive, 50/51 (98%) of the gonadotrophin positive and 3/11 (27%) of the growth hormone, thyrotrophin and prolactin positive tumours as described by IHC. Twenty-two hormone-negative tumours were reclassified as corticotrophinoma, 141 hormone-negative tumours were reclassified gonadotrophinomas, and 10 hormone-negative tumours were reclassified as *PIT1* lineage. Hormonal-IHC and RNA-seq were discordant on three samples.
Conclusion
The results are proportionally equivalent to the literature, with *SF-1* (199 (77%)) the most prevalent subtype, followed by *TPIT* (44 (17%)) and the *PIT1* lineage (14 (4%)). This method refines the non-functioning PitNETs diagnosis in this Northern Ireland cohort, most notably reclassifying 22 tumours as the high risk silent corticotroph subtype that have a higher risk of recurrence.

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P157

A case of panhypopituitarism due to a rathke's cleft cyst in a 32-year-old male with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED)

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Background
Autoimmune polyendocrinopathy-candidiasis–ectodermal dystrophy (APECED) is a rare monogenic disorder characterized by various loss-of-function mutations in the AIRE gene. Clinical manifestations in this case included chronic mucocutaneous candidiasis, hypoparathyroidism, primary adrenal insufficiency, type 1 diabetes, and vitiligo. Additionally, the patient had a history of primary hypothyroidism and epilepsy.
Clinical Case
Hypopituitarism was first suspected based on routine follow up bloods showing a low TSH (0.01 mU/l) with stable free T4 (14.50 pmol/l) on unchanged thyroxine dose and low ACTH (3.6 pg/ml) with no clinical evidence of glucocorticoid over-replacement. A subsequent pituitary panel revealed hypogonadotropic hypogonadism, with FSH 0.3 IU/l (1.5 - 12.4), LH 0.3 IU/l (1.7 - 8.6), and testosterone levels at <0.09 nmol/l (7.98 - 29.14). Additionally, growth hormone of 0.5, and IGF-1 68 µg/l (88.3 - 246) and a prolactin of 343 mU/l (86 - 324). The patient reported low energy, low libido and erectile dysfunction. Visual field testing revealed a left eye temporal hemianopia, however this was complicated by a right vitreous haemorrhage due to diabetes, causing a near complete loss of vision in the right eye. MRI of the pituitary gland revealed a 2.9 cm T1 bright, non-enhancing cystic lesion extending from a normally sized pituitary fossa into the suprasellar cistern, with signal characteristics suggestive of proteinaceous material. Review of historical record revealed an MRI brain done 5 years previously which did not show any obvious pituitary abnormality. Given visual fields defect, the patient underwent transphenoidal resection. Histological diagnosis confirmed a Rathke's cleft cyst. High index of suspicion is required to diagnosed hypopituitarism in patients with multiple endocrinopathies on long term hormonal replacement.

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P158

Acute haemorrhagic stroke in a young patient: unusual presentation of cushing's disease

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Background
Haemorrhagic stroke below age 45 is often associated with hypertension and warrants additional investigations. We describe a young patient presenting with acute intracerebral haemorrhage, and how further investigations led to the underlying endocrine diagnosis.
Case
A 43-year-old female patient with no past medical history presented with facial weakness, speech difficulties and systolic blood pressure above 200mmHg. Brain CT and MRI scans revealed acute intracerebral haemorrhage. Additionally, there was evidence of old intracerebral haemorrhages. She required glyceryl trinitrate infusion. Subsequently three different antihypertensive agents failed to achieve control. HbA1c was elevated at 79 mmol/mol (diabetes > 48), and metformin started. Young stroke investigations were unremarkable. She was referred to Endocrinology for further assessments. On examination the patient had proximal myopathy, purple striae, central adiposity, interscapular fat pad, plethoric round facies, hirsutism, skin thinning and spontaneous bruising suggesting Cushing's syndrome. Overnight 1 mg dexamethasone suppression test failed to suppress cortisol to < 50 (690nmo/l), leading to 48hr Low dose (LDDST) and 48hr high dose dexamethasone suppression tests (HDDST). Post-LDDST cortisol was unsuppressed at 390 nmol/l; pre-test ACTH of 82.1ng/l (normal < 46.0) reduced to 65.4ng/l confirming hypercortisolism. 24-hour urinary free cortisol was elevated at 330nmol/24h (normal < 140). Post-HDDST cortisol was 94 nmol/l; ACTH suppressed from 98.9 to 24.0 pointing to pituitary Cushing's disease. Other endocrine tests were normal. MRI pituitary demonstrated a 2.5mm microadenoma on the right of the gland. Inferior petrosal sinus sampling to confirm source (due to corticotrophin releasing hormone shortage) and transsphenoidal surgery is planned.
Discussion
This patient's presentation and the sequence of events serve as a gentle reminder to consider endocrine hypertension in young stroke patients. Our patient had the classical phenotype of Cushing's syndrome, including refractory hypertension and diabetes. A high index of suspicion is essential for prompt diagnosis in such situations where patients present with complications of severe hypercortisolism to the acute medical take.

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P159

Hiding in plain sight: pitfalls in the evaluation of cushing's syndrome

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A 58-year-old woman was referred for a short synacthen testing (SST) prior to discontinuing oral prednisolone (up to 10 mg/day), which had been administered for over several years for management of COPD. Her primary team noted features of presumed iatrogenic Cushing's syndrome, including cervicodorsal fat pad, type 2 diabetes, dyslipidaemia, hypertension, osteopenia, NAFLD and anxiety, and sought to wean her off glucocorticoids to minimise further adverse effects. On examination, she had significant proximal myopathy, increased BMI and marked cervicodorsal fat pad which interfered with her ability to dress unaided. Unexpectedly, she passed the SST [baseline cortisol 211 nmol/l, ACTH 41pg/ml (15-65) and 30-minute post-synacthen cortisol concentration 607 nmol/l (> 430 nmol/l)]. She subsequently failed the 1 mg overnight dexamethasone suppression test, (137 nmol/l) and a 48-hour dexamethasone suppression test (171 nmol/l), suggesting endogenous ACTH-dependent hypercortisolaemia. The interpretation of these results was complicated by concomitant carbamazepine use. Investigations were repeated with paired dexamethasone measurements, confirming endogenous cortisol excess. A CRH test supported pituitary-dependent Cushing's disease and an MRI pituitary was unremarkable. However, 24hr urinary free cortisol and several midnight salivary cortisol concentrations were normal. Her symptom pattern also suggested an element of cyclicity to her Cushing's. Due to her anaesthetic risk from a respiratory perspective and patient preference, further investigations were paused and a therapeutic trial of metyrapone was commenced. After initial difficulties with glucocorticoid-withdrawal symptoms, ultimately requiring a "block and replace" regime of metyrapone and hydrocortisone, she is doing well, with improved energy, mood, glycaemic control, blood pressure and reduction in facial plethora and cervical adiposity. This case is the exception that proves the rule. Patients with iatrogenic Cushing's syndrome should be considered to have glucocorticoid-induced adrenal insufficiency unless proven otherwise, both arising from exposure to excess exogenous glucocorticoids. A robust synacthen response in a clinically cushingoid patient on exogenous steroids should prompt consideration of an endogenous source.

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P160

An unusual presentation of macroprolactinoma

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Background
Patients with macroprolactinoma commonly manifest with symptoms attributable to hyperprolactinemia and/or mass effect. Seizures are a rare presenting feature. We report a case of a male patient who presented with seizures and was subsequently diagnosed with cystic prolactinoma, with favourable response to dopamine agonist therapy.
Case description
A 29-year-old man initially presented with generalized tonic-clonic seizures. MRI brain revealed a 5.7x2.4x2.1 cm pituitary macroadenoma with suprasellar extension and cystic degeneration, without any evidence of hydrocephalus. Visual field assessment showed bitemporal hemianopia. Hormonal evaluation indicated a significantly elevated prolactin level of over 42,000 mIU/l, along with secondary hypogonadism. Cabergoline and Levetiracetam were initiated, resulting in notable clinical, biochemical improvement and near-complete radiological resolution; however, he was subsequently lost to follow-up. He presented again with similar seizure episodes five years after the initial presentation. Investigations revealed a recurrence of the partially cystic pituitary adenoma measuring 5.4x2.4x2.1 cm, with bitemporal hemianopia and prolactin levels of 84,821 mIU/l. The patient was treated mirroring the initial approach, supported by family involvement ensuring compliance. He exhibited a favourable response with respect to both his prolactin levels and visual symptoms. A follow-up MRI after six months of treatment showed significant tumour regression with residual changes, and the patient has remained free of seizures.
Conclusion
In the context of macroprolactinomas, seizures are occasionally observed as a complication of medical management, typically due to hemosiderin deposition in the medial temporal lobe following intra-tumoural haemorrhage. However, seizures as an initial presentation in patients with macroprolactinoma are rare. Our patient presented with seizures on both occasions, which were attributed to the large prolactinoma. Medical management, including dopamine agonists, remains the primary treatment approach, often resulting in documented tumour regression and subsequent reduction in seizure frequency, allowing for the gradual tapering and cessation of anti-epileptic treatment.

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P161

Challenges of treatment of metastatic insulinoma- case series

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Introduction
Marked heterogeneity has been noted in clinical phenotypes of metastatic insulinomas. We present a case series highlighting heterogenous clinical presentations, radiological features, and treatment modalities.
Case-1
55 Male, chronic diarrhoea, weight loss of 18months, with severe hyper-insulinemic hypoglycaemia (HH) of few weeks. 37 mm pancreatic body tumour with multifocal liver metastases; one with marked peri-lesional steatosis (PS). Grade 2 (G2) well differentiated (WD) neuroendocrine tumour (NET), Ki-67 8%, focal insulin positivity.

Case-2
46 Male, abdominal pain, vomiting, diarrhoea, weight loss of 1 month. 6 cm pancreatic tail tumour, nodal and multifocal liver Metastases; one with PS. Histology favoured acinar cell carcinoma. Strong synaptophysin/chromogranin positivity noted. Disease progression despite palliative chemotherapy. Refractory HH after 2yrs, repeat liver biopsy G2 WD NET, Ki-67 11%.
Case-3
47 Male, symptomatic HH with unifocal (<2cm) insulinoma. Partial pancreatectomy, Indeterminate-grade NET, Ki-67 <5%, focal insulin positivity. Recurrence of HH after 10yrs, two liver Mets with PS, no uptake in ^{68}Ga-DOATATATE scan.
Case-4
18 Female, MEN 1, severe HH with multifocal insulinoma. Distal pancreatectomy; G2 WD NETs, 17 mm(Ki-67 2%, insulin negative), 11mm(Ki-67 4%, insulin positive). New nodal and liver Metastases in 1 year, without HH. Nodal (Ki-67 10%) and liver (Ki-67 3%) resection. Bi-lobar liver metastases in ^{68} Ga DOTATATE scan.
Case-5
39 Male, MEN-1, severe HH with multifocal insulinoma, partial pancreatectomy. New nodal and single liver metastases after 28 years, with no recurrence of HH. Pancreatic lesions remained stable.
Management
Cases 1-3 had liver lesions with marked PS which can be helpful in radiological diagnosis of insulinoma metastases. Cases 1,2,4 treated with multi-modal therapy including PRRT. Case-3 treated with liver-directed therapy. Case-4 developed DOTATATE-induced mylodisplasia requiring bone marrow transplant.
Conclusions
Diagnosis, management and predicting metastatic behaviour of insulinoma remain a clinical challenge. PS is a useful radiological feature of insulinoma metastases.

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Defining food intake and body fat accumulation in an MC4R zebrafish model

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Introduction
Obesity is a global epidemic that involves environmental and genetic factors. In humans, loss-of-function mutations in the melanocortin-4-receptor (MC4R) is the most common cause of monogenic obesity. MC4R is one of the five melanocortin receptors known to regulate appetite and nutrients metabolism. Different animal models exist to study the role of MC4R in appetite and metabolism. Here we study a zebrafish model of MC4R loss of function (sa122 mutant line) to define food intake and body fat accumulation.
Methods
We utilized IVF to rederive the MC4R sa122 mutant zebrafish line generated with TALEN technology by the Sanger Institute. The zebrafish was genotyped with a PACE assay. We quantified food intake using DiA;4-Di-16-ASP-stained paramecium and fluorescence was measured with FLUOstar Omega Microplate Reader at 7 dpf (days post fertilization). To study fat accumulation, at 5 dpf, before oral nutrition starts, we performed Oil Red O staining to identify adipose tissue and quantified with ImageJ. Statistical analysis was undertaken using Prism 9.
Results
At 7 dpf, MC4R sa122 zebrafish mutants showed no significant difference in food intake when non-fasted compared to wild-type (WT) controls ($P = 0.99$). However, food intake assessment following fasting was increased compared to WT-controls ($P = 0.02$). At 5 dpf, fat accumulation was not statistically different ($P = 0.82$) between MC4R sa122 mutants and WT zebrafish.
Discussion
The MC4R sa122 mutant line shows a difference in food intake under fasting conditions but no difference without fasting. We showed no difference in fat accumulation between MC4R sa122 and WT.

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P163

A case of atypical presentation of macroprolactinoma in young female

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Background
Prolactinoma is the most common of all the pituitary tumours (40-60%) requiring medical attention. Most Premenopausal women with prolactinoma usually present with menstrual irregularities, galactorrhoea, and infertility (85-90%) rather than symptoms due to the tumor's size. In contrast, men typically seek help for symptoms related to the tumor's mass effect, such as visual impairment (80%), along with less specific symptoms of hypogonadism.
Case description
We report the case of a 33-year-old female with Turner's mosaic variant, initially presenting with primary amenorrhea and later diagnosed with dyspraxia, dyslexia, and dyscalculia. A routine optician check-up revealed visual abnormalities, and when reviewed by the ophthalmology team she was confirmed to have dense bilateral hemianopia. An MRI pituitary showed a 4 x 2.4 x 3.6 cm partly cystic sellar mass with suprasellar extension compressing the optic chiasm. She was referred to the endocrinology team and diagnosed with a raised prolactin level (16789 mIU/l) without macroprolactin interference, along with biochemical evidence of hypopituitarism (low FT3 and FT4, suboptimal SST response). She was started on cabergoline along with levothyroxine, and hydrocortisone replacement. The treatment plan included close visual field monitoring, interval MRIs, and consideration of transsphenoidal surgery if medical treatment failed.
Conclusion
This young female with a macroprolactinoma presented unusually with bitemporal hemianopia. Due to her Turner syndrome and non-adherence to oestrogen therapy for the past decade, typical symptoms like amenorrhea and galactorrhoea were absent, leading to a delayed diagnosis and mass effect. The co-occurrence of Turner syndrome and pituitary macroadenoma is rare; only nine cases are reported in the literature, with six having a functioning pituitary adenoma and three a non-functioning one. Our case highlights this uncommon occurrence.

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P164

Multidisciplinary management of aggressive corticotroph pitnets. a case series

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Background
Aggressive PitNETs require multidisciplinary management. Cushing's disease (CD) poses specific challenges regarding biochemical control and management of complications.
Aim
To describe management of a series of aggressive corticotroph PitNETs.
Patients
Six patients (2F/4M, 46-75 yo), managed through the pituitary MDT.
Results
At diagnosis all patients had overt CD due to macroPitNets (2-3.8 cm diameter), with suprasellar extension (2), cavernous (4) and sphenoid sinus (3) invasion. Initial manifestions included diabetes mellitus (100%), hypertension (83%), obesity (100%), optochiasmatic syndrome (83%), thyrotroph (83%) and gonadotroph (83%) failure. 4 patients had oculomotor palsy: 3 at onset (1-tumour invasion, 2-apoplexy), 1 later, through cavernous invasion. 3 patients had pituitary apoplexy: 2 at onset (one recurred), 1 during follow-up. 2 patients presented nonfatal pulmonary thrombembolism. Median follow-up was 31 months (0-191). 2 patients died: M, 75 yo, before PitNET treament, due to respiratory sepsis and M, 67 yo, treated multimodally, 31 months after diagnosis, due to septic lower limb ulcers.
Treatment
Transphenoidal surgery: 4 patients (1-3 interventions/patient), subsequently irradiated: 3 fractionated radiotherapy (RXT), 1 gammaknife. The patient with recurrent apoplexy underwent RXT and medical treatment only. Pathology ($n = 4$): ACTH+, Ki-67 = 10-80%, small cell tumours (2), frequent mitoses (2), necrosis (1), Crooke cell tumour (1). 5 patients achieved tumour control initially, 4 escaped, after 15-132 months. Presently 2 patients have tumour control, the 2 others are undergoing radiotherapy (1) and chemotherapy (1). 3 patients achieved

biochemical/clinical control, following surgery and RXT (1), metyrapone (1, postoperatively) and relacorilant (1). 1 patient with rapid tumour regrowth following 3 operations and RXT (last Ki-67 = 80%) is receiving temozolomide and capecitabine, uncontrolled biochemically on 1000 mg/day ketoconazole. No patient developed PitNET metastasis.
Conclusions
Aggressive corticotroph PitNETs require complex multidisciplinary management and close follow-up to detect relapse, which is frequent. Pituitary apoplexy is frequent and oculomotor palsy portends poor prognosis.

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P165

A case series of insulin-mediated hypoglycaemia in older adults

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Introduction
Unexplained falls are a common rationale for emergency presentations amongst older adults. Admissions are associated with significant morbidity. We present a case series of two older adults presenting following collapse, with resultant diagnosis of insulin-mediated hypoglycaemia.
Case 1
79 year-old woman presenting following a presyncopal event. In the weeks preceding admission, described lethargy and weight loss, with associated palpitations and tremor. TSH was <0.01mu/l and fT4 60 pmol/l. Random serum glucose was 2.9 mmol/l, without associated symptoms. TSH-Receptor antibody was positive, and a diagnosis of Graves thyrotoxicosis made. Carbimazole 20 mg BD was commenced. A 72-hour fast was undertaken (Table 1), with serum glucose nadir 1.9 mmol/l. Endoscopic ultrasound identified a pancreatic head insulinoma. Diazoxide was commenced, with surgical input and successful resection.
Case 2
87 year-old woman admitted with an intertrochanteric fracture following a nocturnal fall. Random capillary glucose was 2.7 mmol/l. Notable symptoms included recurrent episodes of diaphoresis and presyncope requiring use of dextrose tablets in the years preceding admission. Fasting serum glucose was 3.5 mmol/l, with normal serum cortisol and HbA1c of 30 mmol/mol. 72-hour fast identified serum glucose of 1.7 mmol/l at 14 hours, with hyperinsulinaemia(Table 2) and full ketone suppression. CT pancreas was unremarkable, however there was subsequent diagnosis of small-cell lung cancer. Diazoxide was commenced. Diagnosis was of presumed insulinoma, given biochemistry and symptom chronicity. IGFII:IGFI ratio was preserved. Further work-up was deferred given prognosis.
Discussion
This case series describes two unexpected diagnoses of insulin-mediated-hypoglycaemia in older adults, as a causative factor in falls presentations. This highlights an unusual underlying pathology of syncopal events, with significant associated morbidity.

Table 1. Summarised results of 72h fast in Case 1.

	T = 29
Glucose(mmol/l)	1.5
Insulin(mU/l)	21
C-peptide(ug/l)	4.47

Table 2. Summarised results of 72hour fast in Case 2.

	T = 14
Plasma glucose(mmol/L)	1.7
Insulin(mU/L)	6.4
C-peptide(ug/L)	1.56

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P166

Physiological growth of the pituitary gland or hypophysitis - difficult differential diagnosis of pituitary enlargement in adolescence. report of two cases

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The increasing availability of MR imaging has led to a rise in the number of referrals of children with pituitary abnormalities to endocrinologists. We are presenting the cases of two female teenagers who underwent pituitary MRI in the context of an intensive headache without associating symptoms suggestive of pituitary insufficiency.
Case 1
12.5 yo girl admitted in neurology clinic due to an episode of lipotimia associated with intense headache; the MRI showed enlargement of the anterior pituitary and a stalk of 6.5 mm; a trial of glucocorticoid before an extensive hormonal workup (normal prolactin and thyroid function tests). Her visual field assessment was normal, and she had normal urinary output. 2 weeks after the glucocorticoid was started, the stalk decreased to 3.6 mm and continued to improve with normal MRI appearance 1.5 years after the first description of global; her headache decreased gradually; a full pituitary workup showed a normal range for pituitary hormones. Tumor markers were negative, as well as markers for hypophysitis.
Case 2
A 15-year-old girl had a pituitary MRI due to intense headaches that showed an enlarged pituitary with a craniocaudal diameter -16 mm abutting the optic chiasm and normal stalk. Her previous history is positive for autoimmune hepatitis under azathioprine since the age of 5 yo. Pituitary hormones and visual field were normal at the presentation and in the follow-up visit with spontaneous partial regression of the pituitary enlargement and evident distance until the optic chiasm.
Discussion
The diagnosis of hypophysitis has a big probability in both cases: first case because of the stalk enlargement and response to glucocorticoid; the second case because of her autoimmune history and spontaneous reversal of pituitary enlargement. This should be considered, due to the need for follow-up for the occurrence of isolated corticotrope insufficiency – following regression of inflammation.

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P167

DNA methylation via nanopore sequencing: will it be the future biomarker of the neuroendocrine tumour?

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Background
DNA methylation analysis has been proven useful biomarker in patients with colon (1-3), breast (4), and lung cancer (5). However, the clinical utility of this method in neuroendocrine neoplasms (NENs) is limited. Our research group has previously worked on the role of circulating cell-free tumour DNA (ctDNA) in neuroendocrine tumours (NETs) and thyroid cancers. Preliminary findings showed that this is a potentially useful clinical tool (6). We are expanding our research project to investigate the role of ctDNA methylation via nanopore sequencing in the detection and surveillance of NETs.
Subject and Methodology
We have already recruited patients 9 patients with NENs and will recruit more patients with germline mutation and unknown primary origin (total n-17). We are conducting this research with the collaboration of the genetics department of the University of Leicester. This is a retrospective, longitudinal, observational, pilot study.
DNA methylation analysis via nanopore sequencing
Methylation is a process that can silence the promotor areas of tumour suppressor genes and methylation of the gene itself can cause mutational events (7). Nanopore sequencing allows the investigation of methylation changes on a genome-wide level (8). The Ligation Sequencing Kit will be used to prepare the sheared DNA which will be loaded onto a MiniION Flow Cell. We will use the MinKNOW software to collect raw data from the device. The "REMORA" tool will be used for methylation analysis (9).
Conclusion
Successfully managing NENs relies on timely detection and diligent monitoring of treatment responses. We will investigate methylation analysis of the target genes identified in our group as pathogenically significant and to see if methylation of these and other genes are responsible for tumorigenesis in NENs. If successful, this work will progress to a larger comparative study to investigate the utility of ctDNA methylation analysis as a biomarker of neuroendocrine tumours.

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Nursing Practice

P168

How text messaging can improve the management of nurse-led clinics: a trial of direct messaging in a hyperthyroid telephone clinic

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Introduction
Managing a nurse-led Hyperthyroid Telephone Clinic with over 700 patients is challenging. If thyroid function blood test results are not available for review, telephone appointments are cancelled, resulting in empty clinic slots. A trial using direct messaging software in DrDoctor was initiated to improve clinic utilisation. This substituted best practice 14-day appointment reminder messages with two-way messaging between patients and nurses.
Method
All patients who had already consented to receive messages from DrDoctor were included in the trial. Blood test reminder messages were sent with the option for patients to reply with the date of a blood test or rearrange appointments.
Results
Before the trial, 109 patients were called over a 6-week period out of a possible 384 appointments. Comparatively, 274 patients were called out of a possible 384 appointments after direct messaging was implemented. Patient replies allowed nurses to rearrange appointments and fill empty clinic slots at short notice. The nurse prescriber was made aware of last-minute blood results to avoid cancellations. Patients were able to request alternative appointments, improving attendance during the clinic. Clinic preparation time reduced as template messages could be sent to multiple patients at once. Appointment availability improved with less overbooking required. Early feedback from a small sample of patients is positive overall.
Conclusion
Initial data suggests direct messaging can improve clinic utilisation and management of follow-up clinics, with wider implications for Endocrinology. Communication between patients and nurses improved and as a result clinic utilisation improved. More data is needed over a longer period of time to determine any variable factors not accounted for in the current trial period. Following this trial, the nursing team will pilot sending direct messages instead of making telephone calls for hyperthyroid follow up. If successful, this will have potential for monitoring appointments in other areas of Endocrinology.

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Other (E.g. Education, Teaching)

P169

Ensuring sustainability in diabetic retinopathy screening

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Fixed annual interval screening for referable diabetic retinopathy (RDR) irrespective of the calculable risk of it developing is wasteful and unsustainable in the era of Precision medicine. Prediction models exist that can identify the **at-risk** and **low-risk** subgroups and assign screening intervals based on that risk. Using data on 2770 participants followed for a mean of 3.5 years of annual retinopathy grading results combined with twice yearly systemic risk factor measurements; we identified and published the biomarkers most correlated with progression to referable retinopathy status in an Irish population for the first time. The strongest association was PRIOR RETINOPATHY SEVERITY (HR 4.02) followed by most recently recorded SYSTOLIC BP (HR 1.29)/HbA1c (HR 1.22) SERUM TRIGLYCERIDES (HR 1.10). Furthermore, we carried out the first external validation of prediction models developed using similar data assembled in England. Its accuracy of prediction was evaluated by comparing predicted with observed outcomes. Its predictive accuracy was compared with the commercially available RETINARISK app which empowers users with the means of tracking their own disease progress. Whilst the recently introduced Irish screening algorithm which assigns biennial screening intervals using retinopathy screening results alone; our analysis demonstrates that precision of prediction and hence risk stratification are enhanced by inputting values on a limited series of systemic risk factors relevant to the population of study. A ten-fold difference in risk stratification between lowest and highest risk groups was found in the English models. We demonstrate that there would be a $>70\%$ probability that a randomly selected subject from the screening cohort who did in fact develop RDR would have been allocated to the higher risk score category by the models tested. This means that their next scheduled screening appointment would not be extended from 1 to 2 years based on advice from the prediction model.

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P170

A unique presentation of thauvin-robinet-faivre syndrome (TRF) in association with androgen insensitivity syndrome (AIS)

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Thauvin-Robinet-Faivre (TRF) syndrome is a rare autosomal recessive condition characterised by excessive fibroblast proliferation and only 4 cases from two families have been reported in the literature to date. It is typified by a gene mutation of the FGF-1 intracellular binding protein (FIBP) and its full phenotype is still being characterised. We present a case history of a patient who had TRF associated with androgen insensitivity syndrome (AIS). A 22 years old male was referred to the endocrinology clinic by his dermatologist, who noticed profound furrowing of the forehead and wondered about a diagnosis of acromegaly. Tests on referral revealed an elevated serum testosterone of $>$ 35 nmol/l with inappropriately normal gonadotrophins. On review the patient reported excessive sweating, excessive hair growth, bilateral gynaecomastia, headaches, joint pains. A background of autistic spectrum disorder, atrial and ventricular septal defects, Chiari malformation, hypermobility and macrocephaly were noted. Examination revealed normal secondary sexual characteristics, euthyroid state, and bilateral gynaecomastia. Testicular examination was normal. Repeat pituitary profile revealed IGF-I level of 51.8 nmol/l (normal 14.2-61.4 nmol/l) excluding a diagnosis of acromegaly. MRI pituitary was normal. Repeat serum testosterone was within normal limits and ultrasound of testes was normal. A diagnosis of pachydermatoperostosis was entertained. The patient was referred to the clinical genetics clinic in a tertiary centre but molecular testing for pachydermatoperostosis was negative. A trio whole genome sequencing revealed a homozygous gene mutation of FIBP, confirming a diagnosis of TRF syndrome but also a hemizygous mutation of the androgen receptor gene resulting in mild AIS. This to our knowledge, is the first described case of TRF presenting in conjunction with AIS. AIS could be part of the phenotype for TRF but other cases will need to be identified to confirm this. A lower threshold of screening for AIS may be required to identify cases earlier.

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P171

Effectiveness of a bespoke educational video for healthcare professionals (HCPs) on arginine vasopressin deficiency (AVP-D) and desmopressin in sheffield teaching hospitals NHS foundation trust (STH NHS FT)

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Background
AVP deficiency (AVP-D) or cranial diabetes insipidus (CDI) is a rare condition treated with Desmopressin. A patient safety alert was issued in 2016, following mortalities, with recommendations to implement: Desmopressin as a critical drug, raise awareness among healthcare professionals (HCPs) and has driven the name change.
Aim
To assess healthcare professionals' knowledge on AVP-D and Desmopressin. To evaluate the effectiveness of a bespoke educational video.
Methods
90 HCPs from STH NHS FT participated in this 10-point questionnaire. They were randomly allocated to two groups: the intervention group who watched the educational video upon completion of the survey and the control group who did not. The same survey was sent to all participants via email one week later. 35 responses were received.
Results
At baseline, 91% of the responders, mainly doctors and nurses, recognized this condition although 54% were unaware of the new term, AVP-D. 88% demonstrated good awareness on the importance of Desmopressin as a critical drug. However, only 47% were aware of potential complications following Desmopressin omission and 28% were familiar with the various preparations available. Interestingly, only one responder answered all questions correctly. From the subsequent 35 responses received, the control group had a better initial overall knowledge with a mean total score of 58% compared to that of the intervention group, whose mean total score was 46%. The intervention group showed substantial improvement (mean overall score 83%) after the educational video while the control group returned a relatively similar performance (mean overall score 65%).

Conclusion
Over half of HCPs were unaware of the name change. Knowledge on AVP-D and Desmopressin among HCPs requires further improvement. We have demonstrated a trend towards enhancing knowledge by utilizing our bespoke educational video. A larger study involving multiple centers could be conducted to ascertain the significance of our findings.

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P172

Case report: nephrons, neurons and too much urine — the highs and lows of lithium-associated arginine vasopressin resistance (AVR) in bipolar affective disorder (BPAD)

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Background
Arginine vasopressin disorder (previously diabetes insipidus (DI)) can be distinguished clinically into a relative deficiency of, or resistance to anti-diuretic hormone. Lithium is the mainstay of therapy for patients with bipolar affective disorder (BPAD), 40% of whom will go on to develop arginine vasopressin resistance (previously nephrogenic DI). We present a challenging case of an elderly gentleman receiving long-term lithium therapy who developed a hyperosmolar, hypernatremia with significant polyuria.
Case report
An 81 year-old man presented to the Emergency Department with dyspnoea and cough. He was treated for pneumonia with IV antibiotics. He had a background of COPD, laryngectomy for previous laryngeal cancer and BPAD taking 800 mg of Lithium Carbonate daily. As his pneumonia improved, he exhibited persistent low mood, oppositional behaviour towards staff and frequently declined oral intake. On Day 12 of admission his sodium acutely rose from 152 mmol/l to 161 mmol/l. His Corrected Ca2+ was $>$ 2.7 mmol/l. His urea and creatinine were also acutely elevated and serum osmolality was 351mOsm/kg (275-295mOsm/kg). He was clinically dehydrated on hydration assessment. Fluid balance assessment revealed a polyuria of $>$4L in 24 hours, with a urine osmolality of 543mOsm/kg ($<$ 800mOsm/kg). He was treated with 2L of 5% dextrose. His lithium was held and serum lithium levels were shown to be 0.47 mmol/l (NR 0.6-1.0 mmol/l) two days later. Psychiatry reviewed remotely and advised cessation of lithium until biochemistry normalised. Desmopressin 0.1 mg PO was then administered. Over several days his sodium levels normalised and polyuria resolved. Although his mood remained an issue, he was discharged home on day 19 with plans to closely monitor.
Conclusion
This case not only highlights the complexities of lithium induced AVR but also the compounding systemic challenges of managing such cases in a regional model-three hospital, without psychiatry services and with extended wait times for specialised tests.

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P173

Evaluating the introduction of a practical thyroid ultrasound teaching session for 3rd year medical students

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Background and Aims
The use of thyroid ultrasound is gaining in popularity at undergraduate level, this can help augment students understanding of both anatomy and endocrinology. We aimed to embed a weekly one hour thyroid ultrasound practical teaching session as part of the QUB (Queen's University Belfast) 3 rd year medical student's endocrine and diabetes rotation. Students completed a questionnaire on the effectiveness of the teaching.
Methods
Fifty consecutive third-year medical students completed a questionnaire (n = 15 questions) assessing various aspects of teaching effectiveness. Mean Likert scale scores ranging from 1 (very good) to 5 (very poor) were calculated for each of the questions to gauge perceptions of competence, relevance, and alignment of assessments with learning objectives. Thyroid ultrasound was performed using a GE Vscan Air wireless handheld ultrasound.
Results
Mean scores across the questionnaire ranged from 1.18 to 3.79, reflecting diverse perceptions among students. Notably, students initially reported low confidence levels in their clinical knowledge of thyroid ultrasound indications (mean score: 3.10) and in using the ultrasound machine (mean score: 3.79). However, following the session, the mean confidence level in using the ultrasound machine significantly improved to 1.96. Positive scores were noted for the clarity of learning objectives (mean score: 1.50) and opportunities for practice (mean score: 1.74). Instructor competence and approachability received relatively favourable scores (mean score: 1.65), and students felt they had sufficient opportunities to ask questions (mean score: 1.18). The course's relevance to students' future careers was also rated positively (mean score: 1.24).
Conclusion
This initial analysis provides valuable insights into thyroid ultrasound teaching effectiveness. The significant improvement in students' confidence levels in using the ultrasound machine suggests the session was effective in enhancing practical skills. However, opportunities for further improvement exist, a longer session could allow for adequate assessment of students and subsequent feedback.

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P174

Design, build and implementation of a solution for prescribing, monitoring and administration of insulin within an inpatient electronic patient record – the st james's hospital experience

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Background
Insulin is a high-risk medicine that was involved in just under 20% of all medication safety events causing harm following a local audit that reviewed data over a 2.5 year period. Insulin was one of the only licensed medicine remaining that was managed via a paper process in inpatient areas at St James's Hospital as it was excluded from the initial implementation of electronic medicines management processes due to the significant amount of additional design features needed to safely manage this high-risk drug. Medication safety data indicated the separate paper process created clinical risk. Expert opinion, and the literature suggested migration to a digital solution would deliver safety, effectiveness and efficiency benefits.
Aims/objectives
Design and implement a custom digital solution in the EPR for insulin management in collaboration with multiple clinical disciplines.
Methods
An agile, iterative design and collaborative approach was adopted throughout the 6-month project period. Over 50 workshops and meetings with stakeholders in informatics, endocrinology, medicine, nursing, pharmacy and operations were organised to identify requirements, make design decisions and plan the implementation.
Results
The custom insulin management solution design and build included 11 clinical decision support tools and 10 prescribing plans with additional configuration to support prescribing, administration and monitoring/review in patients with DKA/HHS. A usability score of 81% was calculated following an assessment of perceived usability of the insulin solution following implementation across the nursing, pharmacy, clinician, clinical nutrition disciplines. There have been no reported insulin-related medication safety events causing harm since implementation in March 2023.
Conclusion
The critical success factors to the safe and effective custom insulin management solution implementation project include the clinical collaboration, multidisciplinary input. Project success has been demonstrated by the high usability score, assessed using a validated usability tool and the lack of events causing harm.

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P175

Empowering young people with diabetes: co-researching interventions for improved diabetes management

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Research shows that young people with diabetes often have poor attendance rates in clinical settings and increased presentations of DKA at hospitals. Clinical settings may not adequately support young people in managing all aspects of their diabetes. Engaging young co-researchers in research design, implementation, and dissemination provides invaluable insights into the unique challenges of managing diabetes in adolescence and young adulthood. The D1-Now study aims to be one of the first studies designed by, with, and for young people with diabetes. Reflecting on our 2018 IES conference abstract, which detailed the successful formation and replicability of the Young Adult Panel (YAP), the current study focuses on co-designing and evaluating pilot and effectiveness trials with YAP. D1-Now uniquely included 8-10 young people with diabetes who informed, designed, and refined an intervention aimed at young adult diabetes clinics across Ireland. This intervention comprised three key elements: an SMS app, an agenda-setting tool for clinic visits, and a key support worker for each young person. The pilot trial, conducted over 12 months across 4 diabetes centres, demonstrated the transformative impact of involving young people in research, highlighting the need for patient-centred interventions. Findings suggests that the approach is both feasible and acceptable with a few changes. Building on the success of the pilot trial, the upcoming effectiveness trial will include a YAP mentor panel and a YAP panel, sustaining and elevating young adults' engagement over the years while incorporating necessary updates to their representation. This co-designed study demonstrates the importance and transformational impact of including young people in research development and evaluation. By amplifying their voices, researchers gain a deeper understanding of the complexities of diabetes management, leading to more effective, patient-centred interventions. Therefore, involving young people as co-researchers in diabetes studies enhances the relevance and acceptability of interventions, promoting empowerment and self-advocacy.

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P176

5 year analysis of profound hyponatraemia: single centre experience

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Background
Hyponatremia is the most encountered electrolyte abnormality and is associated with high morbidity and mortality rates. An accurate diagnosis requires careful clinical and biochemical assessment. Due to patient safety incidents a retrospective 5-year audit was undertaken to study current management of acute profound hyponatremia (Na < 125 mmol/l) at our institution compared to European consensus guidelines.
Methods
All patients with acute Na < 125 were identified from biochemistry records from 2017-22. Case note review, investigations, management and outcome was reviewed.
Results
A total of 121 patients were identified (56% female). Mean age was 65 years (range 23-97). Mean Na was 111.9, with 3 cases of Na < 100 (analytical limit of assay). 47% were asymptomatic, 37% moderately symptomatic and 15% severely symptomatic. The most common symptoms were confusion (31%), seizures (16%) and vomiting (12%). Volume status wasn't determined in 12%; 35% were deemed hypovolaemic, 33% euvoleamic and 20% hypervoleamic. As far as investigations are concerned 43.8% had none, 23.9% had incomplete and 32.2% had complete investigations. No cases of hypoadrenalism or hypothyroidism were identified. 1.8% hypertonic saline was used in 23 patients on the wards, and one received 3% hypertonic saline in ITU (8 severe symptomatic, 14 moderate symptomatic, 2 asymptomatic). 11 severely symptomatic patients were not given hypertonic saline despite being indicated. The data also reveals 66% of the patient who had received hypertonic saline had no indication. 9% of patients overcorrected at either 24 or 48 hours. Of these, 63% had hypertonic saline and 37% had 0.9% saline. However, none developed symptoms of osmotic demyelination. Mortality was 26% at 30 days and 52% at 1 year.
Conclusion
Investigation and appropriate management of hyponatremia remains a challenge despite international consensus guidelines. Mortality remains elevated but in line with previous studies. Further work is needed to reduce the risk of harm to this patient group.

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P177

Defective anti-tumour functionality and metabolism in MAIT cells from patients with obesity undergoing bariatric surgery

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Introduction
MAIT cells are a unique subset of T-cells, that have been conserved throughout 150 million years of mammalian evolution. They can contribute to rapid pathogen control, tissue repair and anti-cancer immunity, but can also cause inflammation and tissue damage in diseased settings. Previously, we have reported dysregulated peripheral blood MAIT cells in children and adults with obesity, highlighting altered cellular metabolism as the causative mechanism. However, there is a paucity of evidence regarding the impact of obesity on the anti-cancer functions of MAIT cells and their behaviour in different adipose tissue depots.
Methods
We sought to evaluate the immuno-metabolic phenotype of MAIT cells in the blood, subcutaneous and omental adipose tissue of patients with obesity undergoing bariatric surgery using flow cytometry, killing assays and single cell metabolic analysis.
Results
We detailed significant alterations in the phenotype, effector function (including the ability to kill cancerous targets) and metabolism of peripheral blood MAIT cells in patients with obesity (mean BMI of 38.73) compared to controls (mean BMI of 25). Additionally, in the patients with obesity there were no differences in MAIT cell frequency, phenotype, cytokine profile or metabolism between omental and subcutaneous adipose tissue highlighting the relevance of subcutaneous adipose tissue as a less invasive site for evaluating immunologic health in obesity.
Conclusion
Our data indicates that MAIT cells are significantly dysregulated in people with obesity, with a loss of protective functions, including the ability to kill cancerous targets. Furthermore, we demonstrate that subcutaneous adipose tissue is quantitatively and qualitatively similar to omental adipose opening up the ability to longitudinally assess adipose tissue MAIT cells in both people with obesity and control groups.

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Pregnancy & Lactation

P178

Knowledge of iodine requirements in pregnancy remains low in NI despite two educational interventions: time for a radical rethink

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Iodine surveys in pregnant women in UK and Ireland have consistently demonstrated iodine deficiency since the 1990s (nine cohorts) but there remains no fortification program. In its absence education and supplementation are key. Knowledge scores have been low across the UK. However, since the last report from NI 10 years ago, the NI antenatal "Pregnancy Book" provided at booking has a new iodine entry. Recently the British Dietetic Association (BDA) have published a two-page Iodine Fact Sheet; however, it is cautionary rather than encouraging regarding supplementation in pregnancy. We explored the knowledge of a cohort-subset of 118 pregnant women from NI recruited to a randomised controlled intervention: milk provision plus BDA factsheet vs BDA factsheet provision alone. An iodine knowledge questionnaire was completed before and after intervention. Separately, semi-structured interviews were conducted in six pregnant women and 10 midwives (including two lecturers) from across the UK. Of the 118 cohort, 71% reported taking an iodine-containing supplement. At baseline 84 women completed the questionnaire and 39% confirmed that they were aware that iodine requirements increased in pregnancy. Only 21% recognised milk as a good source of iodine. At study end, of 46 participants, 67% were aware of increased requirements but there was no improvement in recognition of dietary iodine sources. Midwives reported poor iodine knowledge with nutrition education a low priority during training. Their focus during antenatal care was on relevant food avoidance and multivitamin use. Interviewed women had low iodine knowledge and lacked confidence in their ability to

achieve their iodine requirements. In the UK, midwives are reported as the primary source of dietary advice during pregnancy and so need to be a focus. Educational strategies may include changes in midwifery curriculum, pregnancy-specific fact sheets, social media campaigns and clearer messaging around supplementation.

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P179

Improving iodine status in pregnancy: a randomised controlled trial (RCT) of milk provision for pregnant women in NI – bring back the milkman?

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Iodine status surveys in pregnant cohorts in the UK and Ireland have demonstrated deficiency since 1990s, but there is no nationwide fortification program unlike many other European countries. Therefore, dietary modification and supplementation are key. Milk/dairy products are the main dietary sources of iodine locally. One previous RCT of milk provision in non-pregnant women in NI reported improved iodine status after 3L/week milk. We recruited 118 women at booking. Each received the British Dietetic Association iodine fact sheet. Those randomised to intervention also received 4L/week milk (or yoghurt) for 12-weeks. Cohort median urinary iodine concentration (mUIC) for sufficiency in pregnancy is >150 µg/l. Mean maternal age was 32 years (range 21 – 45 years), gestational age 12.1 weeks, BMI 27.5 kg/m2 and deprivation scores were in moderate range. Use of an iodine-containing supplement was reported in 71.4%. The intervention group mUIC was 53.8 µg/l at baseline and 120.7 µg/l after 12-weeks while the control group had mUIC 52.5 µg/l and 105.7 µg/l respectively (mean change 81.8 vs 44.5 µg/l, $P = 0.27$). Urine samples from 55 infants had mUIC 125 µg/l (sufficiency >100 µg/l) with no difference between groups. Food Frequency Questionnaires showed a trend towards increased milk consumption ($P = 0.06$) in the intervention group. In the intervention group, 10.2% were sufficient at baseline rising to 37.2% after 12-weeks (27% improvement) vs control group 22.0% to 32.4% respectively (10% improvement) ($P = 0.08$ and $P = 0.66$ between groups). The study was underpowered to detect this magnitude of difference. This is the fourth consecutive pregnant cohort on the island of Ireland to demonstrate iodine deficiency since 1997 despite high levels of supplementation. We believe this is the first milk provision RCT in pregnancy and, in the absence of any prospects of a fortification program, further dietary trials are worthwhile.

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P180

A case of severe hypertriglyceridemia in pregnancy and review of the literature

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Introduction
Pregnancy is associated with physiological rise in triglyceride level and there is increasing evidence that high levels of cholesterol are associated with adverse pregnancy outcomes, including gestational diabetes, pre-eclampsia, fetal growth restriction, large for gestational age, preterm labour, acute pancreatitis, hyperviscosity syndrome; cardiovascular risk to the women such as myocardial infarction in pregnancy and increased atherosclerosis in later life and in offspring.
Case
36-year-old woman, primigravida, presented at 24 weeks' gestation with rupture of membrane, was found to have lipemic serum. She got pregnant through IVF in Iraq. She had a history of PCOS, prediabetes, hypertension, and hypertriglyceridemia. There was no family history of dyslipidemia. She was not on dietary fat restriction or lipid-lowering therapy prior to pregnancy. Her pre-pregnancy average fasting triglyceride level was 10 mmol/l. Prior to admission she was on Labetalol, Folic acid, and Aspirin. Upon presentation she had elevated blood glucose (14 mmol/l), plasma triglyceride of 40 mmol/l and total cholesterol of 13.6 mmol/l with normal liver enzymes and amylase. Obstetrical ultrasound showed normal fetal growth but showed anhydramnios. She was managed with a low saturated fat diet ($<20\%$ of total calories from fat/day), intravenous insulin and 5% dextrose infusion. Within 72 h of admission, her plasma triglyceride level had reduced by almost 50%. However, due to fetal compromise urgent C-section was required, and a preterm stillborn baby was delivered. Following delivery, insulin infusion was continued, Atorvastatin 40 mg OD and Fenofibrate 200 mg OD were added, and patient was discharged with a Triglyceride level of 9.3 mmol/l, lipid clinic follow up was arranged.
Conclusion
Severe gestational hypertriglyceridemia necessitates preconception planning, regular monitoring during pregnancy, prompt recognition and management to prevent maternal and fetal morbidity and mortality. We discuss the most appropriate approach, safety and role of pharmacological agents and role of plasmapheresis.

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Comparison of gestational diabetes one-step and two-step screening methods: incidence of gestational diabetes and associated pregnancy outcomes

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Introduction
Gestational diabetes mellitus (GDM) is a common condition of pregnancy, associated with significant maternal and fetal complications. Debate surrounds screening practices, without worldwide consensus on the optimal screening method. Both the one-step (a fasting two-hour 75g oral glucose tolerance test) and two-step (a non-fasting one-hour 50g glucose challenge test followed, if positive, by a fasting three-hour 100g glucose tolerance test) methods are internationally acceptable screening tests.
Methods
We evaluated incidence of GDM alongside maternal and fetal pregnancy outcomes in two centres where risk-factor based GDM screening is performed using these different methods.
Results
963 participants were recruited and underwent screening for GDM using the one-step ($n = 531$) and two-step methods ($n = 432$). Mean ($\pm$SD) age was slightly lower in the one-step group at 33.9 (4.9) years vs 36.1 (4.8). In both groups, most participants were Caucasian (80% and 86%). Mean BMI was 28.6kg/m^2 (6) and 27.4 (6.2). The incidence of GDM was higher in the one-step group (19.0% vs 13.7%, $P = 0.027$). Data collection is in progress, with completed outcomes data available on 240 and 350 participants in the one-step and two-step groups, respectively. On review of preliminary data, mean delivery gestation was 38.7 (1.5) and 38.7 (1.7) weeks. Pre-term birth rates (delivery before 37 weeks' gestation) were 4.6% and 7.7%. Rates of Caesarean section did not differ, at 44.2% and 44.3%. Mean birth weights were similar; 3.52kg (0.53) vs 3.52kg (0.55). The incidence of macrosomia (defined as birth weight >4kg) was also comparable, at 17.1% in both groups. Rates of small for gestational age (birth weight $<10^{th}$ centile) were 4.6% and 3.4%. Fetal complications were very rare in both groups.
Conclusion
In our study population, the incidence of GDM was higher in those tested using the one-step method. Maternal and fetal outcomes were similar between groups.

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Abstract withdrawn

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P183

Spontaneous bilateral adrenal haemorrhage: 2 cases occurring in pregnancy

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Bilateral adrenal haemorrhage (BAH) is uncommon in pregnancy; most cases are thought to be secondary to trauma, anti-coagulation, pre-eclampsia, tumour or sepsis, rather than spontaneous. Management is usually conservative, but adrenalectomy may be required in uncontrolled haemorrhage. We discuss two cases of spontaneous BAH presenting in the third trimester.

Case 1

A 23-year-old female with BMI 33kg/m ^{2} presented at 37 weeks' gestation with a two-week history of worsening right flank pain. Renal ultrasound revealed a 5.5x2.3x5.1cm complex mass superior to the right kidney. She underwent an emergency caesarean section for foetal distress at 37+4, blood pressure was normal throughout. Post-natally CT demonstrated sub-acute spontaneous BAH and hydrocortisone was commenced. Functional testing including plasma catecholamines, aldosterone, renin, androgen screen, urine 5-HIAA and pituitary function tests were normal. She has required glucocorticoid and mineralocorticoid replacement and follow-up MRI confirmed no underlying adrenal lesion.

Case 2

A 24-year-old female with BMI 37 kg/m ^{2} and diet-controlled gestational diabetes presented with severe abdominal/chest pain and vomiting at 30+4 weeks gestation. Contrast CT was performed due to haemodynamic instability to exclude aortic dissection, revealing markedly enlarged adrenal glands with adjacent stranding. Elevated blood pressure settled with analgesia and pre-eclampsia screening was negative. Cortisol was 269 nmol/l and she was commenced on intravenous hydrocortisone. Functional testing was otherwise normal. Spontaneous BAH was confirmed on MRI adrenals three days later and she went on to have a spontaneous vaginal delivery at term. She remains glucocorticoid-dependent two months post-partum, with follow up imaging awaited. Spontaneous BAH in pregnancy is rare and has only been described in the literature as case reports, with true incidence unknown. Increased BMI and gestational diabetes have been suggested as potential additional risk factors in these cases. It remains an important consideration in the differential diagnosis of abdominal pain in pregnancy, particularly in the third trimester.

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P184

Lactation induction: a protocol for women with endocrine conditions, surrogate mothers and same-sex couples

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The benefits of breastfeeding for infant and lactating mother are undisputed. Lactation induction is increasingly sought by women with endocrine conditions or by parents who have not been pregnant themselves. We developed a protocol for breastfeeding support and lactation induction in women under the care of our tertiary antenatal endocrine clinic. These women typically have premature ovarian insufficiency on HRT, or hypopituitarism. A separate cohort of women who do not have an endocrine condition (surrogate mothers, or the non-pregnant woman in a same-sex couple) seek referral for lactation induction. Lactation induction uses medication to stimulate breast milk production in individuals lacking the physiological capacity to produce colostrum and mature breast milk. In surrogate and adoptive mothers and non-pregnant mothers, the objective is to facilitate physiological changes akin to pregnancy, enabling women to breastfeed their child. Women with hormonal deficiencies have the physiological potential to breastfeed, but require bespoke hormonal supplementation. In all cases, women need multi-disciplinary input from the Specialist Infant Feeding Team. We retrospectively reviewed the case series of patients undergoing lactation induction in the preceding 5 years. In this small cohort (10 pregnancies), women received individualised care from an endocrinologist and a specialist midwife. Hormonal treatment with progesterone and/or oestrogen, and treatment with dopamine antagonist domperidone is used. Women follow either a bespoke HRT regimen, or a protocol for lactation induction. This protocol offers an accelerated regimen and a standard protocol, initiated 6 months before baby's anticipated due date. The majority of women (8/10) did achieve breastmilk production; the duration of feeding varied between 24 hours to > 12 months. 2/10 women could not initiate breastmilk production (> 40 years, non-pregnant and without a preceding endocrine diagnosis). Effective lactation induction and breastfeeding support requires intensive input from a multi-disciplinary team that can provide tailored hormonal treatment and practical support.

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Reproductive Endocrinology

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Abstract withdrawn

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Case of young man with waardenburg and kallmann syndromes with unexpected reversibility of hypogonadism- a SOX 10 story

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Waardenburg syndrome type-II is characterised by sensorineural deafness and skin/ hair hypopigmentation due to pathogenic variants in SOX10 gene. SOX10 protein is a transcription factor regulating early neural crest-cell development. Recently SOX10 pathogenic variants have been described in a small number of patients with both Waardenburg and Kallmann Syndrome (hypogonadotropic hypogonadism (HH), anosmia) indicating co-pathogenicity. An 18 year old male presented with delayed puberty. He was diagnosed with bilateral sensorineural deafness at three months and had cochlear implants. He had severe nasal polyposis, wide nasal bridge, hypo-pigmented patches of hair, learning difficulties and physical tics. His mother has mild hearing loss and maternal grandfather had heterochromia. On examination his height was 170cm (mother 167cm, father 180cm) and weight 86Kg with under-androgenised features and anosmia. Morning results demonstrated HH: testosterone 1.3 nmol/l (8.6-29), LH 3.7 IU/l (1.7-8.6), FSH 3.2 IU/l (1.5-12.4). Bone age was 14.5 years (chronological age 18.5 years). MRI was contraindicated because of cochlear implants but CT pituitary fossa was unremarkable. After counselling regarding possible behavioural change, he was started on escalating doses of testosterone treatment. On return for assessment his testosterone treatment had been stopped for 12 months (unplanned) after 12 months treatment. Morning bloods demonstrated repeatedly normal gonadal function e.g. testosterone 13.7 nmol/l, LH 9.1 IU/l, FSH 6.8 IU/l. SOX10 gene sequencing should be considered in patients with sensorineural hearing loss who develop HH. Also, detection of SOX10 mutations in new-borns with deafness and hypopigmentation should prompt hormone testing for HH during mini-puberty (first six-months). This would allow timely treatment for some, to maximise secondary characteristics and fertility potential. The natural history of patients with SOX10 pathogenic variants is not fully understood. One similar case of reversibility has been reported and suggests that re-evaluation of hypogonadism might be considered at intervals.

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Unusual endocrine end organopathy in primary haemochromatosis

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Background

Hereditary Haemochromatosis causes iron build up in various organs. Endocrine organs are a known target for iron accumulation, secondary only to the liver. Hypoparathyroidism from parathyroid involvement is a rarely recognised entity with its mechanism still not fully understood.

Case Description
We report a case of a 38-year old, otherwise fit and well, male diagnosed with hereditary haemochromatosis due to family screening managed with regular venesections, which kept his iron levels well controlled. Upon his endocrine referral for hypogonadal symptoms 7-years after diagnosis of HH, work up revealed an isolated central hypogonadism picture with a pituitary MRI that was within normal limits. Incidentally, he had a background of unexplained and longstanding paresthesia of his upper limbs that had been deemed to be anxiety related after neurology review and work up. In the context of this and low normal serum calcium over many years and with a previous renal work up for mild Chronic Kidney Disease returning inappropriate and low PTH, a clinical diagnosis of primary hypoparathyroidism was considered. He was empirically supplemented with activated vitamin D, which improved his biochemistry and paresthesia symptoms. Given the absence of any previous neck surgery or clues to etiology, primary haemochromatosis was speculated as the underlying cause of his primary idiopathic hypoparathyroidism.
Conclusion
This case highlights the incidental presence of two endocrinopathies in a patient with hereditary haemochromatosis, with otherwise well controlled iron. This reminds clinicians that well controlled haemochromatosis still leaves people with unmet needs, which should prompt us to look for concomitant pathologies. Hypoparathyroidism is one of the pathologies that is not recognised as a haemochromatosis relation.

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The neural bases underlying distressing low sexual desire is sex specific

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Background
Hypoactive Sexual Desire Disorder (HSDD) affects 10% of women and 8% of men. In women, the 'top-down' neurofunctional HSDD model suggests that hyperactivation of higher-level cognitive brain regions suppresses lower-level sexual brain activity in response to erotic cues, impairing sexual function. Conversely, the neurodysfunction in men with HSDD is not fully characterised and unlike in women where therapies exist, there are no licensed pharmacotherapeutics. Here, we present the first direct comparison of the neural bases between women and men with HSDD.
Methods
Thirty-two premenopausal women and 32 men with HSDD underwent task-based functional MRI (fMRI) measuring sexual brain activity during erotic vs control (exercise) videos. Participants completed psychometric questionnaires, providing behavioural relevance for brain-activity changes.
Results
Women exhibited greater activation in higher-level cortical (e.g., inferior frontal gyrus) and lower-level limbic regions (e.g., amygdala) in response to erotic videos compared to men. These findings, coupled with inverse correlations between limbic-region activation and HSDD severity, support the 'top-down' mechanism underlying HSDD in women. Conversely, men exhibited lower activation in both higher-cortical and lower-limbic regions, alongside heightened visual cortex activity compared to women, suggesting a disconnect between visual sensitivity to erotic cues and the limbic system, serving as an underlying mechanism for HSDD in men. Moreover, women who had greater hypothalamic activation in response to erotic videos, displayed improved psychometric scores in the evaluative ($r = 0.55$, $P = 0.001$), motivational ($r = 0.56$, $P = 0.003$), and physiological ($r = 0.57$, $P = 0.0006$) domains of sexual desire/arousal.
Discussion
This is the first direct comparison of the neural bases of HSDD between women and men. While supporting the 'top-down' mechanism in women, it suggests different neurodysfunctional processes in men, highlighting a potential functional disconnection between sensory/attention and sexual centres. Identifying sexual dimorphisms in low sexual desire has key clinical implications relevant to the development of therapeutics for people living with HSDD.

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Is there an association between daylight hours and serum testosterone levels in men?

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Introduction
Studies assessing variability of serum testosterone levels associated with seasonal environmental factors have been contradictory. We assessed associations between the seasons and changes (δ) in seasonality indices and male serum total testosterone (δTT) variability.
Methods
Data were collected in 144 men with paired serum TT samples (126 non-fasting/18 fasting) analysed at Walsall Manor Hospital, UK (52.3 degrees North). Seasonal factors (ambient temperature within 15 minutes of sampling, humidity, precipitation, duration of daylight on the day of sampling, monthly average ambient temperature, and precipitation) were obtained from local weather-station archives. Sign-rank test determined inter-sample differences between TT and seasonality indices. Linear regression analyses studied associations between δTT and δ seasonal indices in the total cohort and subgroups (stratified by medians of age, TT and men with paired non-fasting samples). Sign-rank determined whether serum TT differed between the seasons.
Results
Median inter-sample interval was 63 days. No significant inter-sample differences were evident regarding serum TT levels and seasonality indices. No associations were noted between δTT and δ seasonality indices in the total cohort and subgroups stratified by age and TT. Interestingly, δ ambient temperature ($P = 0.012$) and daylight duration ($P = 0.032$) were inversely associated with δTT in the 126 men in the non-fasting group (dependent variable). Only a small degree of the variability in the δTT was accounted by the above-mentioned independent variables. The seasons did not appear to influence serum TT values.
Conclusions
No relation was shown between seasonality and serum TT in the total cohort, thus possibly eliminating a confounding variable that could affect laboratory and clinical practice. It may be that seasonal variation in length of day is too modest at this location to demonstrate significant associations, hence our findings are latitude specific. We suggest that further data analysis to address this question in areas with greater seasonal variation would be appropriate.

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Leveraging genomic-based machine learning to discover bioactive molecules that alleviate symptoms of polycystic ovary syndrome

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The pathophysiology of Polycystic Ovary Syndrome (PCOS) is multifactorial, therefore discovering effective treatments is challenging. Bioactive food molecules are a potential avenue for PCOS treatment; however, they often lack robust evidence. Applying machine learning (ML) to a genomic dataset may provide accelerated discovery of molecules and drugs that potentially alleviate symptoms through interactions with PCOS-related genes. 17,600 genes, 2,100 bioactive molecules found in foods, and 1,508 clinically available drugs were collected from open-source datasets. 13 genes associated with PCOS (*AMH, AMHR2, AR, FSHR, GNRHR, CYP21A2, LMNA, INSR, DNAH11, BMP15, GDF9, LHB, DLK1*) were considered as targets to determine the interactivity between PCOS and identified molecules. A higher ranking implied greater interaction between pathways associated with target genes and bioactive molecules (or drugs). Fisher's exact test assessed whether the molecule rankings were better than a random baseline. Findings were validated using prior literature regarding molecules, foods, or drugs identified to significantly improve PCOS symptoms in women. A higher proportion of beneficial targets were in the top 10 compared to the bottom 10 of 2,100 molecules ($P = 0.0031$). Of the top 10, isoflavones were predicted to interact with *AR* and reported to possess

antiandrogenic properties. Furthermore, levoglutamide and anthocyanidins demonstrated anti-inflammatory properties in animal studies. Newly identified molecules included epicatechin-3-gallate (found in green tea) and 24-methylenecycloartan-3-ol (a triterpenoid found in almonds), recognised to reduce androgens and inflammation. The identified pharmacological agents in the top three drug classes acted on *GNRHR, AR,* and *INSR,* which are known to be important in the pathophysiology of PCOS, thus validating the reliability of the algorithm. Our findings show scope in rapid hypothesis generation for nutritional interventions, or clinical drug repurposing, targeted at PCOS. This ML pipeline can be utilised in other polygenic reproductive and/or metabolic disorders to aid in the identification of novel targets.

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Impact of synthetic estrogen ethinylestradiol on endometrial morphology and function in diet-induced obese mice

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Background/aims
Obesity is a major risk factor for endometrial cancer with estrogens in combined oral contraceptives enhancing the severity of the disease. This study aims to explore the effect of synthetic estrogen ethinylestradiol (EE2) commonly used in oral contraceptives, on endometrial morphology and regulatory markers in diet-induced obese mice.
Methods
Female TO mice were on a high-fat diet (HFD) for 27 weeks. Three groups ($n = 5$) were given different concentrations of EE2 (3.5ng/ml, 88ng/ml or 4000ng/ml) for 28 days. Estrous cycling and metabolic parameters were measured at regular intervals. UTH tissues underwent H&E and immunohistochemistry staining for analysis.
Results
HFD significantly ($P < 0.01$) increased body weight while high-dose EE2 significantly ($P < 0.01$) decreased body weight compared to HFD. High-dose EE2 significantly ($P < 0.05$) decreased blood glucose compared to ND mice. HFD and all EE2-doses significantly increased cumulative energy intake ($P < 0.01$ and $P < 0.001$). Medium-dose EE2 significantly reduced gland number in UTH compared to ND ($P < 0.05$). HFD and all EE2-doses significantly ($P < 0.001$) increased gland diameter compared to controls. HFD, medium and high-dose EE2 significantly ($P < 0.05$ and $P < 0.01$) decreased epithelium thickness compared to ND and HFD groups. Myometrium thickness also decreased ($P < 0.05$ and $P < 0.01$) after medium and high-dose EE2 compared to ND and HFD mice. Low and medium-dose EE2 significantly increased CTCF of FOXA2 compared to HFD ($P < 0.01$) and medium and high-dose increased compared to ND ($P < 0.05$). Medium and high-dose EE2 significantly decreased CTCF of SOX-9 compared to ND and HFD ($P < 0.05$, $P < 0.01$ and $P < 0.001$). All EE2-doses significantly decreased CTCF of ZO-1 compared to HFD ($P < 0.05$, $P < 0.01$ and $P < 0.001$) and medium-dose compared to ND ($P < 0.001$).
Conclusion
This data highlights the impact of estrogen in the regulation of endometrial health and its possible contribution to the development of endometrial cancer. Further understanding of mechanistic effects of EE2 might help in the treatment of estrogen-dependent endometrial cancers.

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Diabetes as an independent risk factor for endometrial carcinoma

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Introduction
Diabetes mellitus (DM) has become a global health concern, associated with increased mortality and morbidity rate. The escalating incidence of DM, particularly type 2 DM (T2DM), aligns with the rising rates of various cancers, hinting at a plausible direct connection between DM and cancer. Mounting evidence suggests that DM may contribute to the heightened incidence of endometrial cancer (EC) and underscores its correlation with poor prognosis. Individuals with DM face double the risk of progressing to EC, possibly due to the conducive environment for the growth and invasiveness of EC cells in high-glucose conditions. Given the inadequacy of existing treatments to prevent or delay EC progression, early and effective prevention through glucose metabolism interventions remains as promising approach.
Materials and Methods
A comparative analysis published data from MEDLINE, EMBASE, PubMed, and Research Gate was conducted through the systemic search over the past 2 years.
Results
Most epidemiological studies highlight association between EC and T2DM. Analysis of T2DM's impact on cancer risk unveils a significant increase in both morbidity and mortality for EC. Early-stage DM, besides T2DM patients, exhibits a 4.9% heightened risk of EC. T1DM also correlates with an elevated risk of EC. Additionally, DM emerges as an independent risk factor for EC mortality. Biological Mechanisms: Mounting evidence suggests that insulin resistance (IR) and hyperinsulinemia, mediated by insulin and insulin-like growth factors, influence endometrial cells and signaling pathways such as PI3K, MAPK/ERK, and VEGFR, thereby promoting angiogenesis and EC occurrence. Chronic inflammation factors like TNFα, IL-6, and COX-2 contribute to carcinogenesis.
Conclusion
This study enriches the comprehension of the intricate relationship between DM and EC, providing a global outlook on the effects of DM on EC through diverse mechanisms. It underscores the clinical potential of antidiabetic medications for EC, furnishing invaluable insights for future research and therapeutic strategies.

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Association of PCOS related metabolite glycoprotein acetyls with gestational diabetes and preeclampsia in the born in bradford study

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Introduction
Glycoprotein Acetyls (GlycA), is a marker of systemic inflammation, we have recently shown its association with pregnancy in Polycystic Ovary Syndrome (PCOS). This study aims to investigate the association between GlycA levels and the risk of gestational diabetes mellitus (GDM) and preeclampsia in the Born in Bradford (BiB) cohort.
Methods
The Born in Bradford study is a UK-based longitudinal birth cohort. We performed profiling of circulating lipids, fatty acids, and metabolites using a high-throughput targeted NMR platform (Nightingale Health, Helsinki, Finland), providing quantitative data on 227 metabolites. GlycA levels were compared between women with GDM and preeclampsia and those without these conditions using a t-test.
Results
The study included 10,608 women with a median age of 28 years (IQR: 25-31). The cohort comprised predominantly English, Welsh, Scottish, Northern Irish, or British participants (37%), followed by Pakistani (40%), Indian (3%), and African (1%) ethnicities. Metabolomics analysis revealed that GlycA levels were significantly higher in women with gestational diabetes (mean 1.68 vs. 1.52, $P < 0.0001$) but not in those with preeclampsia.
Conclusion
Elevated GlycA levels are significantly associated with an increased risk of gestational diabetes in the Born in Bradford cohort but not with preeclampsia. These findings highlight the potential of GlycA as a biomarker for gestational diabetes and warrants further investigation for other complications during pregnancy.

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P194

Multi-receptor activation by (GIP-GCG-GLP-1) triple agonist regulates female reproductive function in diet induced obese mice

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Background/Aims
Emerging evidence suggests that gut hormones interact with the reproductive axis and impact fertility in females. Here we combine three major gut hormones glucose-dependent insulinotropic peptide (GIP), glucagon (GCG) and glucagon-like peptide-1 (GLP-1), as a triple-agonist (TA) to elucidate its effects on female reproductive function.

Methods
Female Swiss TO-mice ($n = 6$) on high-fat diet (HFD) or normal diet (ND) for 18-weeks received twice-daily intraperitoneal injections of TA at 25 nmol/kg bw or saline vehicle (0.9% (w/v) NaCl) for 21 days. Metabolic and reproductive parameters were regularly monitored. Terminal samples were collected for hormone measurement and analysis.
Results
TA significantly decreased body weight ($P < 0.05$) and blood glucose ($P < 0.01$) compared to HFD mice. Cumulative energy intake reduced ($P < 0.01$ to $P < 0.001$) on days 7 and 14 in the TA group compared to HFD mice. Only 16% of TA mice had abnormally prolonged estrus phase compared to 25% HFD mice. While proestrus frequency decreased ($P < 0.01$) with HFD, TA increased ($P < 0.05$ and $P < 0.001$) proestrus frequency compared to ND and HFD mice. TA also reduced metestrus ($P < 0.01$) and diestrus ($P < 0.05$) frequencies compared to HFD and ND controls respectively. There was a significant ($P < 0.05$) increase in plasma LH in the HFD group but no changes in LH, FSH, progesterone or corticosterone after TA administration. GIP and PYY were unaltered in plasma by TA but a decrease ($P < 0.01$) in GLP-1 was observed compared to ND and HFD mice. In the ovary, there was an increase ($P < 0.05$) in secondary follicles and corpus luteum numbers in the TA group. However, atretic follicles remained significantly ($P < 0.05$) higher in the TA and HFD groups compared to ND controls.
Conclusion
The above data highlight the importance of the reproductive effects of key gut hormones. Further understanding of these mechanisms will provide better options for the prevention of energy-related reproductive disorders.

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P195

Mapping the anatomical and transcriptional landscape of early human fetal ovary development

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Context
The complex genetic mechanisms underlying human ovary development can give rise to clinical phenotypes if disrupted, such as Primary Ovarian Insufficiency and Differences of Sex Development. In recent years, RNA sequencing (RNAseq) approaches have characterised ovary development in previously unparalleled detail; however, a challenge is synthesising and using these data to advance our understanding of clinical disease.
Methods
We combine single-nuclei RNA sequencing, bulk RNA sequencing, and micro-focus computed tomography to elucidate the anatomy and transcriptional landscape of the human fetal ovary across key developmental timepoints (Carnegie Stage 22 until 20 weeks post conception; *bulk RNA-seq*: $n = 47$ samples (19 ovaries, 20 testes, 8 control tissues); *single nuclei RNA sequencing* (snRNAseq): $n = 2$ samples, 12wpc (10,291 cells, 10X Genomics); *micro-focus computed tomography* (microCT): $n = 6$ samples; *macroscopic specimen examination*: $n = 27$ samples). Data are contextualised through a clinically-focused lens.
Results
We show the marked growth and distinct morphological changes within the fetal ovary at the critical timepoint of germ cell expansion and demonstrate that the fetal ovary becomes more transcriptomically distinct from the testis with age. We describe novel ovary developmental pathways, relating to neuroendocrine signalling, energy homeostasis, mitochondrial networks, piRNA processes, and inflammasome regulation. We define transcriptional regulators and candidate genes for meiosis within the developing ovary.
Conclusion
Together, this work advances our fundamental understanding of human ovary development and clinical ovarian insufficiency phenotypes.

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P196

Single-nucleus rna-sequencing reveals novel potential mechanisms of ovarian insufficiency in 45,x turner syndrome

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Background
Turner syndrome (TS) is the most common genetic cause of Primary Ovarian Insufficiency (POI). Morphological analyses of human fetal 45,X ovaries have demonstrated germ cell apoptosis by 15-20 weeks post conception (wpc). However, we do not know why POI develops mechanistically. Here, we use single-nuclei RNA sequencing (snRNA-seq) and bulk RNA sequencing to identify novel potential mechanisms of ovarian insufficiency in TS and to characterise X chromosome gene expression in 45,X ovaries.
Methods
We performed snRNA-seq of peri-meiotic 46,XX ($n = 2$) and 45,X ($n = 2$) fetal ovaries at 12-13 wpc; and 2) a bulk RNA sequencing time-series analysis of fetal ovary, testis, and control samples across four developmental timepoints ($n = 47$; Carnegie Stage 22-16wpc).
Results
Germ and somatic cell subpopulations were mostly shared across 46,XX and 45,X ovaries, aside from a 46XX-specific/45,X-depleted cluster of oogonia ("synaptic oogonia") containing genes related to sex chromosome synapsis; histone modification; intracellular protein regulation and chaperone systems. snRNA-seq enabled accurate cell counting within individual cell clusters; the 45,X ovary has fewer germ cells than the 46,XX ovary in every germ cell subpopulation, confirmed histopathologically. Normal X-chromosome inactivation/reactivation is disrupted in 45,X ovaries; *XIST* was not expressed in 45,X somatic cells but was present in germ cell clusters, albeit with lower expression than in 46,XX clusters. The 45,X ovary has a globally abnormal transcriptome, with low expression of genes related to proteostasis (*RSP4X*); cell cycle progression (*BUB1B*); and OXPHOS mitochondrial energy production (*COX6C, ATP11C*). Genes with higher expression in 45,X cell populations were enriched for apoptotic functions (e.g., *NR4A1*).
Discussion
We characterise the human fetal peri-meiotic 45,X ovary at single-cell resolution and offer insights into potential novel pathogenic mechanisms underlying ovarian insufficiency in TS beyond X-chromosome haploinsufficiency. We suggest ovarian insufficiency in TS may be a combinatorial process characterised by periods of vulnerability throughout early germ cell development.

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P197

Tertiary centre experience of testosterone prescribing in menopause clinic

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Objective
To determine tertiary care practice of prescribing testosterone to women attending menopause clinic and to assess its tolerability and side effects.

Methods
Retrospective electronic notes review of patients attending the University College London Hospital (UCLH) menopause clinic between 2019-2023 and Whipps Cross Hospital (WCH) menopause clinic between Jan 2021-July 2023. Patients prescribed testosterone were identified and included.
Results
Between 2019-2023, 1099 women attended the menopause clinic at UCLH. Of these, 179 women were started on testosterone. There was an average length of 5.7 years between their last menstrual period and receiving testosterone. The majority (64.8%) were started on testosterone at their first appointment with the most common indication being sexual dysfunction (50.3%), other indications included fatigue and brain fog. Testogel was the most frequently prescribed preparation (67.6%). At the time of starting testosterone, 83.8% were on oestrogen replacement therapy, with 16.2% not on oestrogen replacement due to contraindications. Within the study period, 107 (59.8%) of the women started on testosterone treatment attended follow-up; 13.1% reported side effects (including heavy legs and breast tenderness) whilst 29.9% reported benefits (most frequently being generalised improvement in symptoms and increased libido). Comparing UCLH prescribing practise to WCH, over a 2.5 year period, 28 women were initiated on testosterone. Of these, 46.4% were started on testosterone at their first appointment. Similarly to UCLH, 17.9% discontinued treatment and 7.1% discontinued due to reported side effects.
Conclusion
This data provides useful real-world experience regarding testosterone prescribing. Across two menopause clinics, 16.3% and 7.7% of all women were prescribed testosterone therapy. Testosterone is generally well tolerated with less than 10% discontinuing treatment due to side effects. Interestingly, women reported improvements beyond improved libido, despite this being the only licensed indication. Further prospective data is required to determine clinical utility of testosterone in women experiencing the menopause.

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P198

Evaluation of the myo-inositol effect in treating infertility among patients with polycystic ovary syndrome

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Polycystic ovary syndrome (PCOS) is a hormonal imbalance caused by ovarian dysfunction representing one of the most common endocrine metabolic disorder in reproductive aged women. PCOS is highly correlated with resistance to insulin and abnormal increase of androgen levels. Myo-inositol (MI) supplementation in women with PCOS has been evaluated over the last years. Many hormonal and reproductive dysfunctions associated with this disorder have been proven to be relieved by the supplement. Specifically, it was noted to increase the insulin sensitivity, reduce androgen levels and normalize the menstrual cycle. The meta-analysis was done using the systematic search performed in MEDLINE, EMBASE, PubMed and Research Gate from the inception until October 20th, 2021. Randomized controlled trials (RCTs) included women with PCOS and groups having inositols, metformin and placebo. The primary outcome was the beneficial effect of the drug on menstrual cycle whereas secondary outcomes were body mass index (BMI), parameters of carbohydrate metabolism, clinical and laboratory hyperandrogenism. Results are reported as risk ratios or mean differences (MDs) with 95% confidence intervals (CIs). In women with PCOS, treatment with metformin (MET) ameliorated the insulin sensitivity and decreased the androgens levels, but the limitations to MET use are its gastrointestinal side effects. In this case of PCOS, the role of myo-inositol was evaluated. Polycystic ovary syndrome is a complex polygenic and multifactorial disorder. Pathophysiological abnormalities in gonadotropin secretion, disruptions of ovarian folliculogenesis, impaired steroidogenesis, impaired insulin action and secretion are prominent symptoms of this condition. Studies show that MI leads to a decrease in LH and androgen levels, as well as a decrease in insulin resistance. Thus, MI is believed to be able to re-establish ovulatory menstrual cycles (especially in obese women with PCOS). Insulin resistance, elevated androgen levels disturb normal menstrual cycle and lead to anovulation further causing infertility. Myo-inositol (MI) improves the menstrual cycle, insulin sensitivity and other symptoms leading to successful pregnancies.

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P199

The GNRHR mutation: from delayed puberty to normosmic hypogonadotropic hypogonadism

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A gentleman in his 20s, was referred to the endocrinology clinic due to delayed puberty with absent secondary sexual characteristics and low total testosterone level 1.7 nmol/l (8.64-29), and free testosterone 38 pmol/l (198-619). He had no past medical history or drug history. He reported no anosmia and no family history of delayed puberty. However, he had an 11 year-old brother who remained pre-pubertal. On further questioning, he had no secondary sexual characteristics such as hair growth, deepening of the voice or increase in size of testicles. Initial investigations showed LH 1.1 iu/l (1.7 – 8.6), FSH 1.9 iu/l (1.5-12.4), SHBG 21 nmol/l (16.5 – 55.9), TSH 1.02 mu/l (0.27 – 4.2), free T4 15.8 pmol/l (11.1-22), prolactin 158 miu/l (86-324) and IGF-1 17.0 nmol/l (17.7-43). MRI of pituitary with contrast showed no pituitary adenoma and normal posterior pituitary with no ectopic tissue. DEXA scan revealed osteopenia in the spine with normal bone density elsewhere. He underwent genetic testing which showed two heterozygous mis-sense mutations in the Gonadotropin-releasing hormone receptor (GNRHR) gene at Chr4:g.67740661g>A and Chr4:g.67754019T>G. Genetic testing was recommended for his parents to determine their carrier status and confirm genetic diagnosis of their child. He was initiated on Testogel, calcium and Vitamin D3 replacement. His latest testosterone was 12.9 mmol/l with improved secondary sexual characteristics. He remained under endocrinology follow up. Congenital idiopathic hypogonadotropic hypogonadism (IHH) is a rare genetic type of hypogonadism, characterised by absence or delayed pubertal development and infertility, resulting from inadequate production, secretion or action of GnRH. GNRHR mutations account for approximately 3.5%-16% of sporadic cases of normosmic IHH. Diagnosis can be challenging, particularly in early adolescence, as clinical presentation often mimics constitutional delay of growth and puberty. Early awareness by clinicians is crucial.
References
1 https://ec.bioscientifica.com/view/journals/ec/6/6/360.xml

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Thyroid

P200

Genetic proxied IL-12 p40 inhibition and risk of Grave's ophthalmopathy: a mendelian randomization study

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Objectives
Graves' ophthalmopathy is an immunological manifestation of the orbit associated with autoimmune thyroid disease. The immunopathology, although not completely understood, is driven by B lymphocytes and plasma cells with the production of autoantibodies that have a high affinity for the thyroid stimulating hormone receptor. Understanding the pathogenic architecture of Grave's ophthalmopathy is important, particularly the role of T-lymphocytes. Two case reports demonstrated an association between Ustekinumab, a monoclonal antibody inhibiting IL-12 p40 subunit and IL-23 pathways (related to T helper 2 cell functioning and interferon pathways), and the development of thyrotoxicosis[1] . Herein we investigated the associations between circulating IL-12p40 on Grave's ophthalmopathy using two-sample mendelian randomization.
Methods
We selected SNPs from protein quantitative trait loci of *IL12B*, the gene associated with encoding protein IL12-B, also referred to as IL-12 p40 to examine the association between alterations the levels of this protein and risk of incident Grave's ophthalmopathy. Genetic association data for proteins were taken from 3,301 healthy participants and from 643 cases of Grave's ophthalmopathy from the FinnGen studies. The Wald ratio or inverse variance weighted methods used to estimate causal effects. We applied colocalization and pleiotropy-robust methods as sensitivity analyses for confounding.
Results
There was a negative association between genetically predicted IL-12 p40 and Grave's ophthalmopathy (odds ratio [OR] 2.65, 95% Confidence Interval [CI] 1.50 to 4.69), with conditional probability of 96% suggesting no genetic confounding.
Conclusion
This study provides genetic evidence that IL-12p40 has a causal role in Grave's ophthalmopathy pathogenesis. Our data suggest that decreasing levels of IL-

12p40 may be deleterious. We would not suggest selecting this drug target as a therapeutic option.
1 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7450299/

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P201

Profile and management of thyroid disease in children and young people (CYP) attending type 1 diabetes (T1D) clinics in southern health and social care trust (SHSCT)

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Introduction
Acquired primary hypothyroidism is the most common autoimmune endocrine disorder associated with Type 1 Diabetes (T1D). It is associated with presence of antibodies called Thyroid peroxidase (TPO) and requires lifelong supplementation with Levothyroxine. NICE guidelines (NG145) [1] recommends regular surveillance of thyroid levels for primary hypothyroidism every 4-6 months until puberty and then annually. Children and young people (CYP) with diabetes and hypothyroidism may not have the latter problem adequately assessed at clinics due to the complex nature of diabetes management.
Aims
To audit our practice of managing CYP with primary hypothyroidism at the T1D clinics across the Southern Health and Social Care Trust (SHSCT). This comprised both quantitative and qualitative aspects of care.
Methods
This was a retrospective chart review of CYP with T1D and thyroid disease. The management of thyroid disease in the T1D clinic was recorded and compared against national guidelines. Families were asked about their experience of thyroid management at clinics.
Results
The prevalence of hypothyroidism among children with T1D aged 0-16yrs was 3.3% with a female to male ratio of 4.1. Three out of six relevant NICE recommendations were fully met while 3 were only partially met. TFTs were checked in all CYP with T1D, FT3 was appropriately checked and all diagnosed with primary hypothyroidism and treated with levothyroxine. Criteria not fully met included TPO antibody measurements as recommended, 4-6 monthly TFT checks for prepubertal and annual checks for pubertal CYP and 6-12 weekly check post dose adjustments. Families were satisfied with information regarding medication but would like more information on risks of over or under treatment.
Conclusion
We are only partially compliant with NICE recommendation for monitoring of TFTs in CYP with hypothyroidism at T1D clinics. Valuable recommendations regarding frequency of monitoring and offering parental information as above have been made.

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P202

SVUH complex thyroid clinic 3 years on; enabling early diagnosis and management of rare forms of thyroid disease

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Background
Some forms of thyroid disease (TD) pose significant diagnostic difficulties. The quarterly complex thyroid clinic (CTC) at SVUH facilitates diagnosis and management of less common forms of TD.
Methodology
We reviewed the clinical notes of patients attending the CTC from January 2021 to March 2024.
Results
59 patients attended the clinic. The average age was 41.7 years, the majority were female (73%). Referrals were from GPs (70%), adult endocrinology (20%), paediatric endocrinology (5%) and other sources (5%). Most were from Dublin (49%), Wicklow (24%) and Wexford (8%), however patients from eight other counties attended the service. 78% (46) of patients were referred with discordant TFTs, 7% (n4) with abnormal TFTs post definite treatment of hyperthyroidism, 7% (n4) with complicated primary hypothyroidism, 5% (n3) with congenital hypothyroidism and 2% (n2) with fluctuating TFTs. Patients attended the CTC on average for 4.5 visits and received a diagnosis within 3 visits. 72% (n42) of patients had lab samples tested on Biominis assay. 52% (n31) of patients had detailed biochemical interference testing through the UK SAS laboratory and genetic testing was performed on 49 patients. A diagnosis was established in 74% (n44) of patients, investigations are ongoing in 25% (n14) and in 1% (n1) the diagnosis remains unknown. Complicated hypothyroidism 19% (n11) and complicated Graves' disease (15%) were the two most common diagnosis. However, a diagnosis of RTH Beta 7% (n4), Assay interference 7% (n4), FDH 3% (2), TTR mutation 3% (n2), TSHoma, reset HPT axis, thyroxine malabsorption, non-thyroidal illness, amiodarone induced TD and non-thyroidal illness were also made in one patient each, respectively.
Conclusion
The spectrum of TD diagnosed and managed at the CTC is highly variable. Access to a specialist clinic that is linked with international centres facilitates the timely diagnosis and appropriate management of complex and rare TD.

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P203

Liothyronine prescribing at university hospitals of leicester NHS trust – audit (2nd cycle)

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Despite that the standard treatment for hypothyroidism is Levothyroxine, it is now recognised that a certain group of patients would benefit from treatment with Liothyronine either alone or in combination with Levothyroxine. Compared to Levothyroxine, Liothyronine has shorter-half life and can be associated with less predictable biochemical outcomes. In 2021, we published the outcome of the 1 st cycle of audit of use of Liothyronine at the University Hospital of Leicester (UHL) NHS Trust. Accordingly, we implemented changes to our practice. In this 2 nd cycle, we reassessed our prescribing practice against the regional and national guidelines and compared the outcomes of both cycles to produce further recommendations.
Methods
Retrospective database search of patients who were taking Liothyronine between September 2022-September 2023. We combined endocrine electronic database search with manual list of patients who picked up Liothyronine from UHL pharmacy.
Results
see Table (1)

Table 1: Patients Characteristics and Results

• Demographics	
Total number	*n* = 60
Gender	*Female=50, male=10*
• LT3 treatment	
Sole LT3	
Combined LT4/lT3	*11*
	49
LT3 dose	*5–70 mg (average=23.8 mg)*
• Biochemical control (defined by TSH=0.55 – 4.78 mU/l)	
Yes	19
No	41
• QOL assessment	
	29
No	*31*
Yes	*SF-36 n* = 13
	Direct question n = 18
• Screening for complications	
DEXA (in the last 12 months)	
No	*36*
Yes	*24*
	Osteoporosis n = 4
	Osteopenia n = 11
	Normal bone density n = 9
ECG	
No	*49*
Yes	*11*

Discussion & Conclusion
Compared to the previous cycle in 2021;
• There has been a slight improvement in achieving biochemical control in the 2 nd cycle compared to the 1 st (normal TSH in 31.7% vs 23.8%).
• There has been an improved practice in screening for complications including DEXA (40% vs 14%) and ECG (18.3% vs. 0%) and documenting QOL questionnaire (51.7% vs. 10%).
Despite the above, we should still aim to achieve 100% target in screening for complications and assessment of QOL.

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P204

Simultaneous onset of addison's disease and hyperthyroidism

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Introduction
Polyglandular autoimmune syndrome-type 2 is defined by the presence of autoimmune primary adrenal insufficiency, autoimmune thyroid disease and/or type 1 diabetes.
Case report
A 35 year old female was referred to our endocrinology department with lethargy, poor sleep, palpitations, dyspnoea and 1 stone weight loss, menses were regular. Past medical history included iron deficiency anaemia, irritable bowel syndrome, and gastro-oesophageal reflux. Her thyroid examination was essentially normal with no goitre or dysthyroid eye disease. There was no palmar or buccal pigmentation, blood pressure was normal with no postural drop. Thyroid function testing revealed hyperthyroidism ft4 33 pmol/l (RR 12-2) TSH $<$ 0.01 (0.27-4.2 miu/l), TPO ab 118 (RR $<$ 34 iu/ml), TSH AB 2.7, thyroid ultrasound demonstrated thyroiditis. In addition a low random cortisol level of 20 nmol/l was noted with a subsequent abnormal short synacthen test with a 30-minute cortisol of 22 nmol/l (RR $>$ 450 nmol/l), a markedly elevated ACTH of 2000 ng/l (RR $<$ 63), along with positive anti-adrenal antibodies, aldosterone was low at 34 pmol/l, supporting the diagnosis of Addison's disease. T1dm and coeliac antibodies were normal. The patient was initiated on hydrocortisone therapy (15 mg in the morning and 5 mg in the evening), informed of the steroid sick day rules, and provided with a medical alert bracelet, in addition to fludrocortisone 50-100 mg od. She was also commenced on carbimazole 20 mg od with normalisation of thyroid function 4 months later with subsequent downtitration to 5 mg od.
Discussion
The coexistence of Addison's disease and hyperthyroidism was considered unusual. This case emphasizes the importance of a comprehensive endocrine assessment and investigations in patients presenting with multifaceted symptoms. The onset of these conditions is usually separated by years however the simultaneous onset of Addison's disease and hyperthyroidism in this context is relatively rare.

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P205

Selenium prescribing for thyroid eye disease in NI – the exponential rise

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Selenium (Se) supplementation is recommended by the European Group (EUGOGO) for mildly active TED (200 mg/day for six-months) based on a seminal RCT which reported slowing of disease progression vs placebo. Treatment in Se deficient geographical areas may be particularly important. We recently reported Se deficiency in a cohort of 240 pregnant women in NI. The TEAMeD-NI group was set up in 2019 as part of the UK-wide quality improvement program to take a proactive approach to TED and it is the first QI of its kind in Europe. The BNF currently recommends Se use for deficiency states (eg inborn-errors) but does not mention TED. In NI, prescriptions from secondary care to GP are advisory only and the Business Services Organisation has collected GP script data since 2010. There were no GP Se scripts from 2010 to 2016. Since then, 244 patients have been prescribed Se with year on year increases (eight-fold higher in 2023 vs 2017). Anti-thyroid drugs were dispensed in at least 72% at some point (records since 2010). In 2023, 129 patients received Se scripts (78% female, modal age 45-54 years and 63% with anti-thyroid medication scripts in same year). Given the BNF status, OTC Se was initially recommended. However in 2017 GP scripts began in the West and Southern Trusts and all other Trusts quickly followed. The majority of scripts are for patients in the most socially deprived quintiles. Given the rare alternative indications for Se (zero scripts up to 2016), GP scripts may be a useful surrogate marker of our increasingly proactive management of TED in NI. The data also demonstrates the positive relationships that exist between secondary care and our GP colleagues in NI. This has likely improved Se accessibility for patients in the most socially deprived areas who can least afford OTC supplements.

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P206

Thyroid function and antibody testing in patients receiving pegylated-interferon therapy

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Ropeginterferon alfa-2b is a mono-pegylated type I interferon (P-I) used in myeloproliferative neoplasm (MPN). Thyroid dysfunction (TD) is a well recognised side-effect of P-I (1). We conducted a review determining TD prevalence and current practice on thyroid function (TF)/antibody (TAB) monitoring during P-I treatment. Retrospective data was collected, from electronic and physical medical records from July 2019-March 2024, on 37 adult MPN patients in the South-West of Ireland. Exclusion criteria; TD, thyroid hormone replacement, radioactive-iodine or thyroid surgery prior to P-I therapy. TAB were detected using an Alllinaseed assay (Abbott Laboratories). Normal thyroid-stimulating-hormone (TSH) defined as 0.35-4.0 mIU/l, normal T4 9-19 pmol/l. Negative results defined as: thyroglobulin antibody $<$ 115 IU/mL; thyroid peroxidase antibody $<$ 34 IU/mL; and thyrotropin receptor antibody $<$ 1.75 IU/mL. The average pre-treatment TSH was 1.81mIU/l and T4 was 12.98mIU/l, although 21 patients (59%) did not have a baseline T4 analysed. Baseline TAB were checked in only 2 patients (5%). The average 2 year TSH was 6.9mIU/l and T4 was 11.11mIU/l, only 12 patients (33%) had T4 checked at regular intervals. 5 patients (14%) developed overt hypothyroidism. 3 of which (8%) were anti-TPO positive, TAB not analysed in remainder. Time to positivity was assumed to be 4 years. The average TF monitoring frequency was once per 5.53 months. 12 patients (32%) were monitored 3 monthly in accordance with guidelines. All hypothyroid patients were managed with Eltroxin 50 mg adequately and remain hypothyroid on P-I. The findings are consistent with the current body of literature surrounding P-I—induced TD. TF monitoring is not in accordance with standard guidelines for P-I treated patients. Local guidelines have been curated to guide the monitoring and management of TD in these patients. i.e. TSH, free T3 and TAB prior to treatment and 3 monthly TSH and free T4.

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P207

Identifying risk factors for relapse in graves' disease: a retrospective study

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Graves' disease (GD) poses significant challenges in management, particularly due to its higher prevalence in women and the diverse treatment modalities available. Antithyroid drugs (ATD), radioactive iodine (RAI) therapy, and thyroidectomy each offer distinct advantages and risks. While ATD is initially favoured for its safety profile, it carries a notable relapse rate and considerable costs. In contrast, RAI boasts a lower relapse rate but elevates the risk of hypothyroidism and ophthalmopathy. Thyroidectomy, although effective, remains a tertiary option due to its invasiveness and associated risks. Current NICE guidelines recommend RAI as a primary treatment for GD, reflecting its efficacy and cost-effectiveness. However, concerns persist regarding its complications, primarily hypothyroidism and ophthalmopathy. This retrospective study, conducted over two decades at a tertiary centre in the United Kingdom, aims to identify predictive factors for relapse in GD patients, thereby optimising treatment selection. Among 1236 patients initially treated with ATD, only 350 eventually received RAI. Statistical analyses revealed that age, thyrotropin receptor antibody (TRAb) levels at diagnosis, and peak free thyroxine (fT4) levels

were significantly associated with relapse. Notably, higher TRAb and fT4 levels correlated with increased relapse risk. These findings align with existing literature, emphasizing the importance of TRAb and fT4 in predicting relapse. While ATD remains preferable for its short-term benefits, the study underscores the need to identify high-risk patients early for prompt RAI initiation. Developing a predictive scoring system based on prospective studies could aid clinicians in personalised treatment decisions, minimising unnecessary ATD courses and subsequent relapses. Such an approach not only reduces patient morbidity but also offers a more cost-effective strategy for healthcare systems like the National Health Service (NHS). Future efforts should focus on refining risk stratification tools to optimise GD management and improve patient outcomes.

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P208

De novo thyroid eye disease following covid vaccination several years after radioiodine therapy

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We report the development of de novo thyroid eye disease (TED) following COVID-19 vaccination, that occurred several years after administration of radioiodine (RAI) therapy for Grave's disease, rendering the patient hypothyroid and requiring levothyroxine replacement therapy. A 52-year-old lady, who had previously been treated with RAI for an overactive thyroid gland, presented 5 years later with symptoms of dryness and protrusion of her left eye, that was initially noticed within a few weeks after receiving the first dose of AstraZeneca COVID mRNA vaccine. She was a smoker with a 40-pack year history. Clinical examination revealed exophthalmos, lid lag, and chemosis in the left eye. Of note, her euthyroid status was maintained clinically and biochemically on a consistently stable dose of Levothyroxine 75/100 micrograms on alternate days throughout the 5 years following radioactive iodine therapy and even at the time of development of TED, with no significant alterations to the dosage being required in between or subsequently. Thyroid receptor antibodies (TRAb) levels significantly worsened from 2.5IU/l (0.1- 0.9) before radioactive iodine therapy to 45IU/l (0.1-0.9) at the time of development of TED and continued to rise thereafter as well. Several reports suggest the role of adjuvants in COVID vaccines as the possible trigger for the autoimmune inflammatory response causing an immune dysregulation, much like the virus per se. Molecular mimicry and genetic predisposition of human leukocyte antigen are other suggested pathophysiological mechanisms, including the possibility of immune reactivation of residual thyroid gland remnants by TRAb. This case highlights the need for clinicians to be vigilant of such clinical situations and to closely monitor patients with prior thyroid disease receiving COVID vaccinations. It is imperative to collaborate with Ophthalmologists in the joint thyroid eye clinic as it becomes even more pertinent in these well recognised circumstances but less commonly perceived scenarios.

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P209

Incidental papillary thyroid microcarcinoma: implications of recurrence and survival on management recommendations

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Introduction
Papillary thyroid microcarcinomas (PTMC) are defined as thyroid cancers with a maximum tumour diameter of 10 mm. These neoplasms have become a topic of significant interest, particularly concerning their active surveillance and conservative management. Incidental papillary microcarcinomas (I-PTMCs) discovered post-operatively on histology are less studied compared to lesions identified pre-operatively via FNA, especially regarding demographics, histopathological features, and long-term outcomes. We aimed to perform one of the first large, 10-year retrospective studies assessing differences in outcomes between these subgroups, to delineate the clinical recommendations for follow-up of these individuals.
Methods
This single-centre retrospective cohort study assessed St. James University Hospital Head and Neck MDT data records from 2013-2023, identifying 2,015 patients diagnosed with thyroid neoplasms during this period. 59 incidental, and 57 non-incidental papillary microcarcinomas were included in the final analysis. Information on demographic, histopathological and treatment methods were collected. Recurrence-free and overall survival outcomes were analysed with Kaplan-Meier curves and compared by log-rank testing.
Results
Among demographic and histopathological factors, statistically significant differences were found between non-incidental and incidental subgroups related to neck dissections performed (26.32% v. 1.69%, $P < 0.001$), positive nodal metastases (19.30% v. 1.69%, $P = 0.002$), size of largest foci (7.37 mm v. 3.89 mm $P < 0.001$) and aggressive subtype variants present (19.30% v. 1.69% $P = 0.036$). However, recurrence-free survival ($P = 0.156$) did not differ significantly between the two groups.
Conclusion
There is a paucity of solid evidence and definitive guidelines on the management of incidental papillary microcarcinomas. Despite evidence of a less aggressive presentation, no differences in recurrence-free survival were observed, suggesting similar, or less careful monitoring compared to microcarcinomas discovered pre-operatively.

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P210

The new anthropometric indices and atherogenic indices are correlated with lipid status after radioactive iodine treatment of graves disease

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Introduction
Radioactive iodine treatment (RAI) of thyroid pathologies contributes to endocrine and metabolic complications. Cardiovascular disease (CVD) is a leading cause of mortality and morbidity worldwide. Identification of the subpopulations with a higher risk of developing CVD and lipid metabolic disorders is crucial, particularly in Graves patients.
Aim
This study aimed to investigate the usefulness of new anthropometric indices such as BAI, VAI, LAP, BRI, ABSI and new atherogenic indices such as TyG index, TyG-BMI index, TyG-WC index in the evaluation of lipid parameters in patients with Graves disease.
Material and methods
The study enrolled 49 women and men aged 20-49. Criteria for selecting the subjects were as follows: diagnosed Graves disease after TRAB positive. Blood samples were taken from patients after 6 months of RAI. Biochemical parameters (total cholesterol, HDL, LDL, TG) were determined and used for the calculation of atherogenic indices. Anthropometric parameters were measured with the use of standard methods in the morning. These measurements included body weight, height, waist circumference, and hip circumference. After this step, anthropometric indices such as BAI (Body Adiposity Index), VAI (Visceral Adiposity Index), LAP (Lipid Accumulation Product), BRI (Body Roundness Index), ABSI (Body Shape Index), AIP (Atherogenic risk of plasma) were calculated. The study was reviewed by the local bioethics committee.
Results
There was observed a significant positive relationship between BAI, VAI, LAP, BRI, ABSI, TyG index, TyG-BMI index, TyG-WC index and LDL cholesterol and triglycerides ($P < 0.005$).
Conclusion
Analyzed new anthropometric indices and new atherogenic indices have demonstrated a significant relationship with lipid profile in graves disease patients. These indices may be useful tools in predicting metabolic disorders in patients after radioactive iodine treatment.

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P211

A clinical audit of thyroid nodule management at galway university hospital

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With widespread use of sensitive imaging techniques, an increasing number of thyroid nodules are being detected. Thyroid nodules are common and reported to occur in 60% of adults. Most are benign, asymptomatic and do not warrant further intervention. Once detected, however, most patients are referred to endocrinology and/or otorhinolaryngology services for further assessment, adding to the already lengthy waiting lists and contributing to patient stress. An audit was undertaken to assess the management of patients presenting to Galway University Hospital between July 2021 and July 2022 who underwent a fine-needle aspiration (FNA). A sub-set of 50 patients from this group were assessed. 94% had an ultrasound prior to FNA. 29.8% of ultrasound reports documented a formal EU-TIRADS score. 8.5% of ultrasounds were discussed at a multidisciplinary meeting (MDM) prior to FNA with a mean waiting time for discussion of 2.75 months. 6% of nodules were Thy 1, 32% were Thy 2, 48% were Thy 3, 8% were Thy 4 and 6% were Thy 5. 74% were discussed at an MDM following FNA. The mean waiting time for discussion post-FNA was 2.7 months. 66% were advised to have surgery. The mean waiting time for surgery was 1.6 months for Thy 5 nodules, 4.7 months for Thy 4 nodules, 7.4 months for Thy 3 nodules and 6.8 months for Thy 2 nodules. 26% of patients with a Thy 3 nodule who were advised to have surgery remain on the waiting list. These results highlight a deficiency in risk stratification of thyroid nodules. If all ultrasound reports had an EU-TIRADS score, it may reduce the number of unnecessary FNAs and thus unnecessary interventions. If an EU-TIRADS score is not included in the report, discussion at MDM or review by a radiologist with expertise in thyroid pathology prior to FNA is strongly advised.

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P212

Patients with graves' disease have more severe biochemical thyrotoxicosis and develop higher rates of post radioiodine hypothyroidism than those with nodular disease

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Introduction
We aimed to characterise clinical and biochemical features, management and outcome in subjects with thyrotoxicosis who presented for definitive treatment with radioactive iodine (RAI) therapy to our unit.
Methods
This retrospective analysis examined patients with Graves' disease (GD) and nodular thyroid disease (NTD) who were treated with RAI as definitive treatment for thyrotoxicosis between 2008 – 2012. A standard activity of RAI (555 MBq) was used for all subjects. We examined previous electronic records and databases for clinical and biochemical data at presentation, details of medical management before and after RAI, and the rate of occurrence of post RAI hypothyroidism in the two groups.
Results
There were 241 GD subjects (goitre recorded in 56%, and orbitopathy in 19.6%) and 156 NTD subjects who had RAI for thyrotoxicosis during this period. GD subjects (a) were younger – median age 51 vs. 67 years, $P < 0.001$; (b) had higher median free T3 (11.95 vs. 7 pmol/l) and free T4 (30.1 vs. 19.7 pmol/l) concentrations at presentation ($P < 0.001$); (c) a longer duration of treatment with a thionamide before RAI (12 vs. 7 months, $P < 0.001$); and (d) a higher incidence of post RAI hypothyroidism (88.5% vs. 31%, $P < 0.001$) compared to NTD subjects. Most GD subjects received RAI for relapse (62.3% vs.15.6%) while the majority of NTD subjects received RAI as first choice treatment (39% vs.4.2%). The median time to post RAI hypothyroidism was 3-3.5 months in both groups.
Conclusions
Our study indicates that subjects with GD presenting for RAI mainly for relapsed disease, (a) were younger, (b) had more severe biochemical thyrotoxicosis compared to those with NDT and (c) a higher percentage of them developed hypothyroidism post RAI although both groups received a standard activity of 555 MBq.

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If at first you don't succeed, thy and thy again?

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University Hospital Limerick (UHL) is a large model 4 hospital in Ireland's Midwest serving a population of ~413,000 people. The radiology department performs an average of 220 thyroid fine needle aspiration biopsies (FNABs) per year. The aim of this study was to determine how many non-diagnostic or unsatisfactory results are returned, necessitating repeat FNAB. Data was collected on the previous 502 thyroid FNAB results using the hospital laboratory information system. Of the 502 thyroid FNAB results, 7 were excluded as inappropriately coded results and 495 results were included and classified according to their Royal College of Pathologists Thy Staging System category. Of these, Thy1/Thy1c $n = 124$ (25%), Thy2/Thy2c $n = 240$ (48%), Thy 3a $n = 98$ (20%), Thy3f $n = 17$ (2%), Thy4 $n = 10$ (2%) and Thy5 $n = 6$ (1%). One quarter of thyroid FNABs acquired are non-diagnostic or unsatisfactory, necessitating repeat procedures. Thy1c ($n = 25$, 5%) results are not thought to be operator dependent. Excluding these, there remains one fifth of thyroid FNABs reported as non-diagnostic or unsatisfactory. This figure is higher than the figure recommended by the Royal College of Pathologists. The frequency of non-diagnostic results may be affected by the lesion characteristics, accuracy of localisation, number of aspirations, needle gauge and aspiration technique. Nonetheless it is important to minimise non-diagnostic results which carry with them financial and time burden along with impacts on patient satisfaction and potential delay in diagnosis. Our institution does not have a cytopathology service with thyroid FNABs processed and reported externally. The provision of rapid onsite evaluation of acquired specimen adequacy by a skilled cytopathologist is an evidence based approach to reduce non-diagnostic results and could be considered in our institution. Further analysis of the imaging characteristics from the biopsied nodules at UHL is also needed to determine if certain characteristics are associated with a non-diagnostic biopsy.

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P214

The occurrence of rheumatoid arthritis in young females with thyroid dysfunction condition in iodine deficient region

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Introduction
The connection between rheumatoid arthritis (RA) and thyroid disorders (TD) is primarily driven by overlapping immunological mechanisms, shared genetic factors, and similar inflammatory processes. We aimed to discuss some possible causes and triggers that interplay in both conditions based on data from the literature.
Material and methods
Data analysis was done using the systematic search performed in PubMed, MEDLINE, Scopus, Web of Science database of the articles published during the past 5 years related to RA and thyroid disorders. Main factors to consider were age, gender, cortisol, TSH, T4, T3, anti-TPO.
Results
A study of 250 RA patients revealed that 33.9% had thyroid dysfunction, with 24.2% having a prior history of thyroid diseases. Anti-TPO were positive in 32.0% of cases, while AITD was present in 21.5%. Specifically, Hashimoto's thyroiditis was 2.77 times more common in RA patients compared to those without RA. The prevalence of TD in RA patients was found to be 34%, with Hashimoto's thyroiditis in 13.5% of cases. Notably, 75% of the RA patients were women aged 20-39 years, with the incidence of hypothyroidism in this group being 3.6 times higher than in men. The inflammatory cytokines TNF-α and IL-6 involved in RA can exacerbate dyslipidemia in hypothyroidism, leading to deteriorated lipid profiles and low HDL levels. Additionally, antithyroglobulin antibodies were found in the synovial fluid of 34 out of 54 RA patients. Steroid therapy, often used in RA management, can induce a hypothyroid state by increasing TSH levels and inhibiting the conversion of T4 to T3.
Conclusion
Endocrine changes during puberty, pregnancy, childbirth, abortion, and iodine deficiency state are considered as risk factors for RA and TD. Screening RA patients for TD is important in prevention of complications. Understanding the intricate relationship between RA and thyroid dysfunctions is crucial for improving patient outcomes through integrated healthcare strategies.

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P215

Thyroid dysfunction and large goitre in an adolescent with severe iodine deficiency due to dietary restrictions

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A 15 year old male presented to paediatric endocrinology with a large goitre and a thyroid function test confirming fT4 4.4 pmol/l and TSH 3.0 mU/l. Previous medical history included lifelong atopic eczema and multiple food allergies which had led to the exclusion of nuts, dairy products, eggs and fish from his diet. Autism spectrum disorder had been diagnosed at 4½ years of age. Two subsequent thyroid function tests were unchanged and thyroid auto-antibodies were negative. Secondary hypothyroidism due to isolated TSH deficiency was considered as basal pituitary function was otherwise normal as was MRI of pituitary. Treatment with levothyroxine 50 µg od normalised thyroid function. Thyroidectomy was advised but the patient had declined. At transition to adult endocrinology care at 17 years of age a diagnosis of iodine deficiency was considered on the basis of a large goitre and initial thyroid function tests. Further investigations confirmed normal basal pituitary function and severe iodine deficiency (urinary iodine concentration 150.70 nmol/l and iodine:creatinine ratio 8.41 nmol/mmol). CT imaging confirmed a large goitre (right lobe 4.3 x 2.7 x 7.0 cm and left lobe 3.8 x 2.9 x 7.2 cm) with a total volume of 160.6 ml. Following counselling on the possibility of hyperthyroidism levothyroxine was stopped and treatment with iodine 150 µg od commenced which resulted in maintenance of normal thyroid function with rapid decrease in goitre size. There are only eight previous cases in the world literature of similar dietary restriction resulting in goitre and impaired thyroid function in paediatric age group patients. Diagnosis of autism was made in three of the cases indicating a possible role for iodine deficiency in this condition. This case reinforces the suggestion made by previous authors that children with such dietary restriction should be monitored for iodine deficiency.

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P216

Thyroid orbitopathy associated with primary hypothyroidism and anti-TSH receptor antibodies; clues from a functional TSH receptor bioassay

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Thyroid Orbitopathy is rarely associated with *de novo* Primary Hypothyroidism; this phenomenon is incompletely understood. Here we present the case of a 51-year-old female presenting with Primary Hypothyroidism, Thyroid Orbitopathy, and high titres of Anti-TSH Receptor Antibodies (TRAb), and discuss the potential underlying pathogenesis. Our patient first presented to Regional Hospital Mullingar with an unrelated, and ultimately self-limiting, complaint. The Endocrinology service consulted for abnormal Thyroid Function Tests (TFTs); TSH - 42.46 mIU/l (0.33 – 4.8), Free T4 - 9.1 pmol/l (9.8 – 20). Thyroid Orbitopathy, with proptosis and mild periorbital oedema, was noted on examination. Levothyroxine was commenced and TFTs normalised within 12 weeks of presentation; TSH - 1.3mIU/l, Free T4 - 15.9 pmol/l. TRAb was grossly elevated at 68.4IU/l (<1.8). CT and MRI of the Orbits demonstrated bilateral proptosis, prominence of the inferior medial and superior rectus muscles, and increased retro-ocular fat sparing the anterior tendon, consistent with Thyroid Orbitopathy. A functional bioassay using a Chinese Hamster Ovary (CHO) cell line, expressing a TSH holoreceptor and utilising a luciferase-based homogenous cAMP biosensor demonstrated both TSH Receptor stimulating activity (+632%, ref < 140%) and TSH Receptor blocking activity (-62%, ref > -34%) of the patients serum. The patient remained biochemically euthyroid (TSH - 3.22mIU/l) but Thyroid Orbitopathy progressed; Clinical Activity Score (CAS) increased necessitating high dose, pulsed intravenous glucocorticoid therapy (Methylprednisolone) to ameliorate worsening Thyroid Orbitopathy. It seems unlikely, given the well maintained TSH levels, that endogenous TSH contributed to the progression of Thyroid Orbitopathy. We therefore hypothesise that this patient is producing TRAb that has both TSH Receptor stimulating activity and TSH Receptor blocking activity, and that these antibodies are antagonising TSH at the Thyroidal TSH receptor, but providing a stimulus to orbital fibroblasts. Functional TSH Receptor bioassay analysis of similar patients may help to better characterise this rare phenomenon.

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P217

Case report: a unique presentation of multiple cases of autoimmunity and follicular thyroid cancer

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We present the case of a patient with a diagnosis of thyroid cancer who has developed multiple, sequential autoimmune conditions. Our patient, a now 41 year-old female, was initially diagnosed with Follicular Thyroid Cancer in the context of pre-existing autoimmune hypothyroidism evidenced by serum Anti-Thyroid Microsomal antibodies as well as lymphocytic thyroiditis on post-operative histopathology. The association between autoimmune thyroid disease and Thyroid Cancer has been previously described. Following total thyroidectomy, she underwent radioactive iodine ablation at our centre and in the years post-treatment, she has maintained a sustained response to therapy although she has developed new Thyroglobulin Antibody positivity. 3 years post initial presentation, she developed Parietal-cell Antibody-positive pernicious anaemia, requiring parenteral B12 replacement. 9 years post-treatment, she developed seizures and memory loss prompting neurological assessment and diagnosis with Autoimmune Temporal Lobe Epilepsy secondary to Glutamic Acid Decarboxylase (GAD) Antibody-positivity. She demonstrated a high tire GAD >2000 (Reference range: 0.00-9.99). GAD autoimmunity has been linked to a number of conditions which include but are not limited to: Stiff-Man-Syndrome and Type 1 Diabetes Mellitus (T1DM), autoimmune hypothyroidism and pernicious anaemia. Given her initial endocrinopathy, we have opportunistically screened this patient for the emergence of T1DM with Islet Cell Autoantibodies which have been positive but HbA1c and C-peptide levels have consistently been normal. This case illustrates a unique sequence of clinical manifestations of multiple autoimmune conditions in a predisposed individual. While the autoimmune linkages are well recognised, this clinical pattern has not been previously described.

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P218

The role of endocrine specialist nurses in the current NHS era

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The NHS is an evolving organisation facing huge challenges (bed pressures, lack of workforce/specialists, outpatient waiting lists etc.) while still striving to provide best possible patient care. Our Endocrine Specialist Nurses (ESNs) are an integral part of endocrine services in creating an individualised, smooth patient pathway. They are a link between endocrinologist, patients and community services to ensure high quality care for all. A dedicated ESN clinic with direct access to endocrinologist was set up to provide ongoing care for patients with thyrotoxicosis after their initial endocrine consultant appointment. The aim was to ensure blood tests, medication titration and patient education were provided in a timely manner. We reviewed the clinical journey of 8 patients diagnosed with thyrotoxicosis. Initial free T4 ranged from 25 to 100 pmol/l (normal 11.9 to 21.6 pmol/l) and all TSH levels were <0.01 mU/l (normal 0.27 to 4.2 mU/l). All patients were commenced on oral Carbimazole with daily doses ranging from 5 mg to 60 mg. Patients were seen between 2 to 4 times by ESNs. It took 6 to 14 weeks (mean of 8.75 weeks) to achieve an acceptable thyroid results. 3 patients had a near normal free T4 of 8.5 to 9.35 pmol/l. 5 patients achieved a normal free T4 between 15.8 to 20.8 pmol/l. (with a mean free T4 of 14.8 pmol/l). The ESN endocrine clinic has enabled us to:

- increase outpatient consultant appointment capacity by reducing the number of endocrine clinic follow up visits.
- provide greater patient satisfaction due to direct access to ESNs.
- reduced the burden on hospital, community phlebotomy services.

• improved patient care by providing relevant blood tests, education and ensuring medication compliance.

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P219

Thyroid malignancy rate in U3 thyroid nodules

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Background
Thyroid nodules incidentally picked up on imaging studies are extremely common with a prevalence of around 50% in the general population. Ultrasound characterization using the British Thyroid Association (BTA) U classification system is commonly employed in the United Kingdom and Ireland. Most reported nodules are classified as U3 which indicates an indeterminate suspicion of malignancy. There are limited data on the malignancy rates in U3 nodules.
Methods
We examined the malignancy rate among U3 thyroid nodules that underwent fine needle aspiration cytology (FNAc) in our unit. FNAc was reported using the Royal College of Pathologists Thy classification (Thy1-Thy5).
Results
Eighty three U3 nodules underwent FNAc. The median size was 2.8cm in the largest diameter (range 0.8-8.6cm). Thirteen nodules were initially reported as Thy1 (inadequate sample). Repeat aspirates or follow up surveillance scans diagnosed 1 cancer. Fifty-three were initially reported as Thy 2 (benign). One of those was later diagnosed as papillary thyroid cancer following repeat aspirate and surgery. Sixteen were reported as Thy3 (indeterminate) with 1 malignancy diagnosed subsequently. One nodule was reported as Thy5 (malignant). Overall, 3/83 nodules were malignant (3.6%).
Conclusion
Malignancy rate among U3 thyroid nodules is low and similar to that reported with indeterminate nodules using other Ultrasound classification systems.

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P220

A case of uncontrolled graves' disease causing cerebral venous sinus thrombosis

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Cerebral venous sinus thrombosis (CVST) represents approximately 0.5-1% of all patients with strokes. It is associated with conditions resulting in a hypercoagulable state, typically occurring in young women during pregnancy and taking the combined oral contraceptive pill (COCP). Thyrotoxicosis is a predisposing factor in 1.7% of patients with CVST. A 26-year-old female presented with acalculus cholecystitis. Doppler ultrasound of liver demonstrated turbulent flow through hepatic veins suggestive of right heart dysfunction. Echocardiogram showed an estimated ejection fraction of 40%. She was thyrotoxic; TSH <0.01 (0.4-4.2IU/l) and Free T4 (FT4) 35.2 (12-22 pmol/l). Her TRAb was positive 19.8 (<0.8IU/l) confirming Graves' disease. She commenced anti-thyroid drugs and failed to attend a series of appointments. She returned a number of months later thyrotoxic; TSH $<$ 0.01 (0.4-4.2IU/l) and FT4 46.0 (12-22 pmol/l) and pregnant (G ^{4}P $^{1+2}$). She was managed with antithyroid drugs throughout her pregnancy and delivered a baby at 30 weeks gestation that required a period in neonatal ICU. She had no history of venous thromboembolic disease in prior pregnancies or postpartum period. Over 3 months postpartum, she returned profoundly thyrotoxic; TSH <0.01(0.4-4.2IU/l) and FT4 84.6(12-22 pmol/l). Her dose of antithyroid drug was increased. She represented a number of days later complaining of headache, vomiting and blurred vision. CT brain demonstrated a 14mm hyperdense segment in the region of the right transverse sinus. An MRV confirmed loss of flow void in the right transverse sinus, consistent with right transverse sinus thrombosis. She was commenced on a Dabigatran. Antiphospholipid screen, serum ANCA and *JAK* mutation were negative. Thyrotoxicosis is associated with hypercoagulable state and possibly endothelial dysfunction mediated via increased levels of fibrinogen, factor VIII, factor IX and VonWillebrand factor. It was felt the patient's Graves' disease most likely was a provoking factor in the development of a CVST, which is a rare but known association.

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