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47th Annual Meeting of the British Society for Paediatric Endocrinology and Diabetes 2019

27–29 November 2019
Cardiff, United Kingdom

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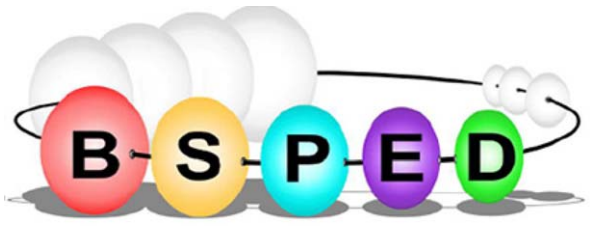

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CONTENTS

CME Training Day Sessions

Session 1

CME1.1

Abstract unavailable

CME1.2

Talking to children about sex development

Julie Alderson
University Hospitals Bristol NHSFT, Bristol, UK

Talking to children about sex development has never been easy and for professionals or for parents. The spectre of the Optimal Sex of Rearing theory from the 50s and 60's an awareness of gender fluidity with the range of possible futures for each child we see can silence us. If we don't let a child know about the surprises their body has in store for them what difficulties do we store up for them? Standard advice for talking to children is to communicate in a developmentally appropriate way. How can we reduce our professional anxiety and tread a delicate path that enables us to keep our patient with different sex development at the center of their care? How can we know what they want and how can we help them tell us how they feel or what they think? Parents need help to do their part in talking to children about Sex Development and we need their support to keep their child engaged with care. How do we share responsibility with parents for enabling children to understand what and why and how? This session introduces available materials to scaffold conversations and information exchange. We will discuss language and the way it frames patient knowledge. We will consider assumptions that might shut down children and young people and will encourage you to find some language and skills you can be happy with….for now. Communicating is subject to revision and reiteration.

DOI: 10.1530/endoabs.66.CME1.2

Session 2

CME2.1

Recognition and assessment of pituitary tumours: what the clinician needs to know

Assunta Albanese
St George's University Hospitals NHS Foundation Trust, London, UK

Craniopharyngiomas and pituitary adenomas are the most common benign tumours occupying the pituitary fossa. Neoplastic or infiltrative processes of the pituitary area, such as gliomas arising from the optic chiasm and surrounding region, germ cell tumors from the pituitary stalk, and granulomatous diseases, are less common. Pituitary adenomas are classified according to size, functional status, primary cell origin, and hormone secretion (Prolactin, GH, ACTH, TSH and gonadotropins) Prolactinomas are the most common pituitary adenomas in adults and children, and 53% of pediatric pituitary adenomas are found to be prolactinomas. Most pituitary tumours grow very slowly and those discovered by chance 'incidentalomas' may not need any active treatment. Large tumours may produce pressure effect on surrounding tissues leading to visual defects, cranial nerve impairment, headaches, rhinorrhea or symptoms of hypopituitarism due to destruction of the pituitary tissue. Hypopituitarism usually has an insidious presentation with generalized malaise, tiredness, loss of appetite, weight loss or gain, decreased mental function, dizziness, poor linear growth, delayed/arrested puberty, primary/secondary amenorrhea and loss of libido. Polyuria and polydipsia can be the presenting symptoms of diabetes insipidus. Hypopituitarism may present acutely following infarction within the pituitary adenomas (pituitary apoplexy) and require immediate medical and neurosurgical attention. Signs and symptoms of hormonal hypersecretion can lead to the diagnosis of functioning micro or macroadenomas. The lecture will focus on the clinical presentation of pituitary tumours and initial endocrine approach. It will highlight some of the more relevant pitfalls encountered while interpreting biochemical results.

DOI: 10.1530/endoabs.66.CME2.1

CME2.2

Paediatric vulval disorders

Helen Lotery
University Hospital Southampton NHS Foundation Trust, Southampton, UK

Practical points regarding the diagnosis and management of conditions affecting the vulva in childhood and adolescence. This includes history-taking, examination, investigation, clinical diagnosis and treatment.

DOI: 10.1530/endoabs.66.CME2.2

Session 3

CME3.1

Challenges in the management of the SGA child

Phil Murray
Department of Paediatric Endocrinology, Royal Manchester Children's Hospital, Manchester, UK

Approximately 650 000 children born in the UK each year, using a definition of a birth weight less than 2 s.d. 14 950 children are born SGA. 90% of these children will experience catch up growth by the age of 4 years leaving around 1500 children eligible for treatment with recombinant human growth hormone. Data from the BSPED audit in 2016 recorded 177 children started on GH at a mean age of 6.2 years – all of these children will have been short at 4 years of age so we are starting GH late in the small minority of SGA children whom we are treating! Frequently SGA children are referred to endocrinologists as possible cases of Silver–Russell Syndrome, the use of clinical scoring systems to identify children with SRS will be discussed as will starting GH from the age of two years in this group. Most endocrinologists currently treat children with GH using dose-titration based upon serum IGF-I concentrations but in SGA children this approach appears to be less effective compared to fixed dosing. The role of GnRH analog therapy or aromatase inhibitors combined with GH will also be discussed. Finally the definition and frequency of poor response to GH treatment will be discussed.

DOI: 10.1530/endoabs.66.CME3.1

CME3.2

The pituitary – growth hormone deficiency and beyond

Evelien Gevers[1,2]
[1]Queen Mary University London, William Harvey Research Institute, London, UK; [2]Barts Health NHS Trust – Royal London Hospital, London, UK

The pituitary gland is the master gland controlling many other hormone secreting organs.The gland lies within the sella turcica at the base of the brain to which it is attached by the pituitary stalk or infundibulum. Lactotrophs, somatotrophs, thyrotrophs, corticotrophs and gonadotrophs in the anterior pituitary gland secrete the polypeptide hormones prolactin (PRL), growth hormone (GH), thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and luteinizing (LH) and follicle stimulating (FSH) hormones, respectively, and magnocellular neurosecretory neurons in the posterior gland extending from the Paraventricular nucleus and Supraoptic nucleus in the hypothalamus, secrete Vasopressin and Oxytocin. The pituitary gland is derived from two ectodermal structures, the neural ectoderm, which gives rise to the posterior lobe, and the surface ectoderm, which produces Rathke's pouch, the precursor to the anterior

and intermediate lobes. Specific transcription factors are important for cell specification and lineage determination. Knowledge of pituitary development and transcription factors helps to determine the cause of congenital pituitary hormone deficiency disorders, either isolated hormone deficiency or multiple hormone deficiency, either as an isolated hormone condition or in the context of a syndrome, for example sept-optic dysplasia, holoprosencephaly, Kalmann syndrome, CHARGE syndrome, Coffin Siris syndrome. Pituitary hormone secretion is mostly pulsatile and regulated by neuroendocrine factors produced in neuroendocrine cells in the hypothalamic nuclei and secreted in the portal circulation to act on surface receptors of anterior pituitary cells. We will discuss the regulation of GH secretion in the hypothalamic–pituitary axis in more detail and relate it to different types of isolated GH deficiency and touch on the effects of GH resistance on GH secretion. The pulsatile nature of pituitary hormone secretion is a challenge for the investigation of pituitary hormone deficiencies, reason to resort to pituitary stimulation tests which however require cautious interpretation in conjunction with other investigations and the clinical phenotype of the patient in order to prevent incorrect diagnosis of pituitary hormone deficiency. Lastly, we will touch on acquired causes of pituitary hormone deficiencies, such as craniopharyngioma.

DOI: 10.1530/endoabs.66.CME3.2

Session 4

CME4.1

Diabetes technology update (CME lecture)

Sze May Ng

Southport and Ormskirk Hospital NHS Trust, Southport, UK

Self-monitoring of blood glucose (SMBG) is an important part of diabetes management but only provides a snapshot view of the blood sugar at that point in time. Technology such as Freestyle *Libre* and Continuous Glucose Monitoring (CGM) provides blood glucose readings and trends whilst omitting the more traditional method of multiple daily blood testing, and they have been reported in clinical trials to reduce hypoglycaemia, and improve blood sugar management day to day. This is a life changing technology to improve their quality of life and improve management of their blood sugar levels. The advantage of technology is the availability of information about glucose levels which helps to predict hyper and hypoglycaemia and to adjust the insulin doses accordingly. NICE guidelines NG18 recommend that children and young people with T1DM and persistent problems with hypoglycaemia unawareness or repeated hyper or hypoglycaemia should be offered CGM. A Cochrane meta-analysis showed that CGM technology can reduce HbA1C level without increase in the risk of hypoglycaemia. Aspects of CGM/Libre technology may impact upon its accuracy such as MARD (Mean Absolute Relative Difference), accuracy of glucose trend, sensitivity & specificity, measuring stability, calibration and the lag time. Barriers of usage should be addressed and education is vital. This presentation will focus on the following:

- Understanding use of CGM/Libre and its limitations.
- Effects of CGM on metabolic control, fear and frequency of hypoglycaemic episodes.
- Use a systematic approach to interpretation of analyses.

DOI: 10.1530/endoabs.66.CME4.1

CME4.2

Abstract unavailable

Main Symposia

Endocrine Track 1: Symposium 1

S1.1

Long-term outcomes for young women with PCOS

Aled Rees
Cardiff University, Cardiff, UK

Polycystic Ovary Syndrome (PCOS) is the commonest endocrine disorder in young women, affecting up to 10% of the premenopausal population. In addition to its reproductive sequelae, PCOS is now established as a metabolic disorder, characterised by defects in insulin secretion and action. These disturbances, along with comorbidities such as obesity and dyslipidaemia, may predispose to an increased risk of cardiometabolic disease in later life. Our studies confirm a higher prevalence of surrogate risk measures for cardiovascular disease, including antioxidant capacity, complement concentration and sympathoexcitation, in women with PCOS compared to matched controls. Nevertheless, differences between groups in arterial stiffness, myocardial function and carotid intima media thickness are not apparent after adjustment for obesity. Large-scale epidemiological data confirm an increased long-term risk of type 2 diabetes and fatty liver disease but not of all-cause mortality, cancer and cardiovascular events, albeit that studies were conducted in a young population (with a low event-rate) hence longer-term data are required. These risks extend into pregnancy and include an increased risk of gestational diabetes, pre-eclampsia, prematurity and miscarriage. However, age-standardised fertility ratios are not different compared to unaffected controls, providing some reassurance to patients that fertility may be restored with appropriate treatment. More recently, data show an increased incidence of depression, anxiety, bipolar disorder and eating disorder in women with PCOS, accompanied by alterations in white matter microstructure. Furthermore, linkage analysis also found an increased risk of a recorded diagnosis of autism spectrum disorder and attention-deficit hyperactivity disorder in children born to mothers with PCOS, raising the possibility that increased exposure to androgens *in utero* might affect neonatal brain development. Treatments to reduce these long-term risks are thus needed urgently. In this regard, data from randomised, placebo-controlled trials of metformin on vascular function show promise, whereas lifestyle trials comparing different exercise modalities are ongoing.

DOI: 10.1530/endoabs.66.S1.1

S1.2

Abstract unavailable

S1.3

Maternal thyroid function in pregnancy and childhood outcomes

Marian Ludgate
School of Medicine, Cardiff University, Cardiff, UK

The foetus relies on placental transfer of maternal thyroid hormones, until the thyroid matures fully, at ~36 weeks gestation. Studies in animals, and the cognitive impairment experienced by children born in areas of iodine deficiency or to mothers with hypothyroidism, highlight the importance of thyroid hormone in brain development. The impact of less severe thyroid dysfunction remained controversial until two large-scale trials investigated the effect on child IQ of thyroxine supplementation in mothers with suboptimal gestational thyroid function (SGTF). In the controlled antenatal thyroid screening (CATS) study, women whose FT4 was $<$2.5th percentile and/or TSH >97.5th percentile were treated with 150 µg thyroxine from ~13 weeks gestation. No differences were found in child IQ aged 3 from treated/untreated mothers. Similar results were obtained in a later trial which analysed subclinical hypothyroidism and hypothyroxinemia separately; no benefit was observed, from maternal treatment started at ~17 weeks gestation, on children's IQ at age 5. The results prompted questions as to whether the children were tested too young, the mothers were treated too late and/or supplementation dose was too high – following the reported bi-phasic effect of FT4 on cognition. Repeated cognitive assessments in the CATS children at age 9.5 years confirmed the original findings, found that IQ at ages 3 and 9 were strongly correlated and that the lack of treatment effect may be due to the similar proportion of IQ $<$ 85 in children of women with normal-GTF and SGTF. Behaviour problems were also measured in the CATS children using 3 questionnaires. We found no association between SGTF and offspring attention deficit hyperactivity disorder (ADHD), autism spectrum disorder or behaviour questionnaire scores. However, children of 'over-treated' mothers (FT4>97.5th percentile) displayed significantly more ADHD symptoms and behavioural difficulties than normal-GTF. Thus thyroxine supplementation during pregnancy requires careful monitoring to avoid over-treatment.

DOI: 10.1530/endoabs.66.S1.3

Endocrine Track 1: Symposium 2

S2.1

Abstract unavailable

Diabetes Track 1: Symposium 3

S3.1

Abstract unavailable

S3.2

Role of the enviroment in the pathogenesis of type 1 diabetes

F Susan Wong
Cardiff University, Cardiff, UK

Both genetic and environmental factors determine whether individuals who have a predisposition to the development of type 1 diabetes actually develop the disease. Although we now know a considerable amount about the genetics through genome wide scans, and diabetes risk scores have been developed, the actual environmental triggers or perpetuating factors are not clearly defined. There has been considerable interest in recent years in investigation of these possible environmental factors in birth cohort studies. These studies have included documenting environmental contributors in individuals who are genetically at high risk. The studies have focused on diet, various infections, the gut microbiome and other possible factors. Recent advances will be discussed in this presentation.

DOI: 10.1530/endoabs.66.S3.2

S3.3

Newer treatments for type 2 diabetes in children

Timothy Barrett

It is over 17 years since the randomised controlled trial of metformin showed efficacy in childhood type 2 diabetes. Since that time, despite much investment in paediatric investigation plans, very few interventional clinical trials have reported. This presentation reviews the evidence for childhood type 2 diabetes being different to adult type 2 diabetes. Childhood type 2 diabetes is a more aggressive disease; children have lower insulin sensitivity than adults; and complications occur earlier in the disease process. This presentation then reviews the results from the TODAY study, and the newly published results from the randomised controlled trial of GLP1-receptor agonist. While the natural history of the disease is that almost 50% of children will progress to HbA1c more than 8.5% on metformin, rosiglitazone, or lifestyle treatment, the recent study of Liraglutide (GLP-1 receptor agonist) in combination with metformin shows an improvement of over 1% in HbA1c compared with metformin alone. The presentation then reviews ongoing randomised controlled trials in childhood type 2 and the prospects for new classes of treatments becoming available.

DOI: 10.1530/endoabs.66.S3.3

Diabetes Track 1: Symposium 4

S4.1

Abstract unavailable

S4.2

QI in action – the Sheffield Children's Hospital experience

Carrie MacKenzie & Sheffield Children's Diabetes Team

Sheffield Children's Hospital NHS FT, Sheffield, UK

The Sheffield Children's Diabetes Team [SCDT] look after approximately 240 patients with Type 1 Diabetes aged 0–17 years. We have approximately 35 newly diagnosed patients each year and the level of social deprivation amongst our clinic population is high. Historically the team has always performed well in terms of measured outcomes and in the 2014–2015 National Paediatric Diabetes Audit [NPDA] data we ranked amongst the top five units in the country with a mean clinic HBA1c of 62.8 mmol/mol and 38.4% of patients having an HBA1c of $<$58 mmol/mol. In subsequent years our ranking fell with an increase in mean HBA1c [64.3 mmol/mol in 2016–2017] and only 28.6% of patients achieving an HBA1c $<$ 58 mmol/mol. The invitation to participate in the Royal College of Paediatrics and Child Health [RCPCH] Diabetes Quality Improvement [QI] pilot project afforded us the opportunity to address our relatively poor outcomes using QI methodology. We recognised a particular problem in our clinic population with control in the first year after diagnosis with Type 1 Diabetes and identified the need for change to enable and empower our patients to achieve improved outcomes by providing patients and families with individualised, bespoke education. Our QI aim is to enable and support service users to achieve an HBA1c of 48 mmol/mol at 3 and 12 months post diagnosis. Our interventions so far include: carbohydrate counting from diagnosis whilst an in-patient; micro-teaching in the clinic waiting area; revised team aims and Diasend downloading at home from diagnosis. The ongoing collection and analysis of metrics has been fundamental to the modification of our interventions and early data has been encouraging. Our data [including average blood glucose and HBA1c results] will be presented.

DOI: 10.1530/endoabs.66.S4.2

S4.3

Improving diabetes care: lessons from registries

John Gregory

Cardiff University, Cardiff, UK

The Brecon Group (Welsh Paediatric Diabetes Interest Group) was established in 1995 given the need to advise Welsh Government regarding commissioning of paediatric diabetes services. A diagnostic register was created using a minimal data-set to identify the numbers of young people aged $<$15 years with diabetes in Wales and to establish national audit. This allowed us to show the benefits of appointment of paediatric diabetes specialist nurses but also the lack of impact of a poster campaign to promote awareness of diabetes, facilitate an earlier diagnosis and reduce the risk of presentation in ketoacidosis. We have now integrated an anonymised version of this data-set within the Secure Anonymised Information Linkage Databank (SAIL) allowing linkage of anonymised individual's data across data-sets. Analyses of linked data-sets show a 5 to 6-fold increased risk of all cause hospital admissions for young people with diabetes, disproportionately so in the very young, those from more deprived backgrounds and those cared for in smaller units around Wales. The National Children and Young People's Diabetes Network in Wales is therefore initiating a national 'out of hours' on-call system, to provide young people and their families with clinical advice, regardless of where their diabetes is treated. Further analyses have shown a near 3-fold increased mortality in our young cohort. We have also evaluated the nature of increased contact with primary care that children developing diabetes experience in the year before diagnosis. This latter work provides the basis for developing an early warning tool to assist GPs in the recognition of a child developing diabetes, promoting an earlier diagnosis and reducing the risk of ketoacidosis. This registry has therefore provided a powerful tool through pseudo-anonymised linkage, to investigate a range of further outcomes (e.g. pregnancy, alcohol-related admissions, diabetes-specific complications and educational achievement) to inform the management of diabetes in childhood and young adult life.

DOI: 10.1530/endoabs.66.S4.3

Nurses' Day for Endocrine Professionals: Symposium 5

S5.1

Abstract unavailable

S5.2

Congenital TSH deficiency

Nadia Schoenmakers

University of Cambridge Institute of Metabolic Science, Cambridge, UK

Congenital thyroid stimulating hormone (TSH) deficiency occurs due to hypothalamic or pituitary pathology, with consequent impaired stimulation of the thyroid gland by TSH resulting in central congenital hypothyroidism (CCH). Although assumed to be rare, CCH may be more common than previously appreciated with an incidence of up to 1:21 000 reported in the Netherlands. TSH deficiency is most frequently associated with additional pituitary hormone deficits but may also occur in isolation with an estimated incidence of around 1:65 000, often as a result of defects in genes controlling the TSH biosynthetic pathway. Genetic ascertainment in isolated TSH deficiency has advanced over the last three

decades, with causative monogenic mutations reported in five different genes: *IGSF1*, *TRHR*, *TSHB*, *TBL1X* and *IRS4*. CCH is characterized biochemically by failure of appropriate TSH elevation despite subnormal circulating thyroid hormone levels. Therefore, the primary, TSH-based congenital hypothyroidism screening programmes which operate in the UK will not detect CCH since TSH is not raised. Severe central hypothyroidism may therefore evade diagnosis until the patient presents with clinical sequelae. Adequate circulating thyroid hormone levels are essential for normal childhood growth and neurodevelopment, therefore delayed diagnosis and treatment of CCH may result in profound neurodevelopmental delay. This presentation will focus on the diagnostic pitfalls of CCH, the genetic causes of isolated TSH deficiency, and their associated clinical, biochemical and molecular features.

DOI: 10.1530/endoabs.66.S5.2

S5.3

Abstract unavailable

Debate: Speaker Biographies

D1.1

Rachel Besser[1,2]

[1] Consultant in Paediatric Endocrinology, and Research Lead in Paediatric Diabetes, Oxford Children's Hospital, The John Radcliffe; [2]Honorary Senior Clinical Lecturer, University of Oxford

Dr Rachel Besser BSc MBBS (Hons) MRCPCH PhD, is a consultant in paediatric endocrinology at Oxford Children's Hospital, and Honorary senior clinical lecturer at the University of Oxford, working with both the NIHR Oxford Biomedical Research Centre and the Wellcome Centre for Human Genetics. She came to Oxford in 2016 and was Clinical Lead between 2016–2018, and is now Research and Audit lead for the department. Rachel splits her job between clinical diabetes and diabetes research. She runs clinics for children with type 1 diabetes aged under 5 years, and Transition (17–19y) in Oxford, and sees paediatric patients of all ages in between. Rachel has published 3 books on paediatric diabetes; *Diabetes Through the Looking Glass*, published in 2009, and still in print, is endorsed by JDRF and Diabetes UK, and won the Best New Health Care book for the General Reader by the Society of Authors. In it, Rachel shares narratives from over 100 children and adults with type 1 diabetes, and their parents, using their testimonials to explain to the reader what it feels like to live with type 1 diabetes from the child's perspective, navigating life's journey, including the healthcare system. As such, Rachel is an expert in understanding diabetes from both the patient and health care professional's perspective. Rachel oversees 10 collaborative and original paediatric research studies in Oxford.

DOI: 10.1530/endoabs.66.D1.1

D1.2

Anuja Natarajan[1,2,3]

[1]Consultant Paed Endocrinologist; [2]CYPD Network Chair, Yorkshire and Humber; [3]Clinical Director Paediatrics, Doncaster and Bassetlaw Teaching Hospitals

Anuja Natarajan completed her training in Paediatric endocrinology in 2004 and joined the Doncaster & Bassetlaw Hospitals NHS Foundation Trust (now a teaching hospital since 2018) in 2014 as a Consultant paediatrician with CCST in Endocrinology . She took up the post of lead for Paediatric diabetes and Paediatric Research in 2005 and since then has been in post for these two areas. Within the scope of her role as research lead Anuja has been successful in getting funding for appointment of a paediatric research nurse since 2010 as a result of active participation in diabetes and endocrine related research studies nationally and regionally. This was the first paediatric specific research post within her trust. She has led the paediatric research team successfully over the last 14 years and expanded the team to include general paediatric colleagues and diabetes and endocrine nurses. In 2015, 6 months after appointment to the consultant post she was able to set up a tertiary endocrine service at DRI, including getting a nurse trained formally in Auxology and endocrinology to cover the specialist clinics as well do all the dynamic testing . The service has since then grown to employ a full time endocrine nurse specialist, 2 HCA for clinics and increased number of clinics covering Doncaster, Mexborough and Bassetlaw. Anuja was appointed Chair of the Diabetes Yorkshire and Humber Network in March 2016 and her 4 year tenure (3 years with 1 year extension) will end in March 2020. Her main achievements have included the successful implementation of detailed bi-annual analysis of HbA1c outcomes from all teams across the region, initially met with some reluctance; the benefit of closely analysing outcomes at programme board level has been accepted and now embraced by the network members. Anuja was appointed as the Assistant Care Group Director (ACGD) for Paediatrics in March 2017 and subsequently to Clinical Director Paediatrics from March 2018.

DOI: 10.1530/endoabs.66.D1.2

Inquisitor Session: Speaker Biographies

IN1.1

Tim Cheetham[1,2]

[1]Newcastle University and Department of Paediatric Endocrinology; [2]Royal Victoria Infirmary, Newcastle upon Tyne

Tim Cheetham is a University Reader and Honorary Consultant Paediatrician based in Newcastle-upon-Tyne, England, UK. He was appointed in 1996 following paediatric / endocrine / diabetes training in Oxford and Cambridge – and following 6 months as a neonatal consultant at Addenbrooke's. He has a broad range of interests and has a key role in a number of clinical trials and studies in the field of clinical endocrinology including Graves' disease, longer term outcomes following preterm delivery and Duchenne Muscular Dystrophy.

DOI: 10.1530/endoabs.66.IN1.1

IN1.2

Mehul Dattani[1,2]

[1]Professor of Paediatric Endocrinology, Genetics and Genomic Medicine Research and Teaching Department, UCL Great Ormond Street Institute of Child Health; [2]Honorary Consultant and Co-Speciality Lead at Great Ormond Street Hospital for Children

Mehul Dattani is Professor of Paediatric Endocrinology based at the University College London (UCL) Great Ormond Street Institute of Child Health, and Specialty Lead in Endocrinology at Great Ormond Street Hospital for Children (GOSH). He has an active clinical practice in paediatric and adolescent Endocrinology at GOSH and University College London Hospitals (UCLH). He completed a 3-year term as Chair of the British Society for Paediatric Endocrinology and Diabetes, followed by a 7 year term as Chair of the Programme Organizing Committee and member of the Council of the European Society for Paediatric Endocrinology (ESPE). He is the currently the President of the European Society for Paediatric Endocrinology for 2020. He has also been appointed co-Chair of the Pituitary Main Thematic Group of the ENDO-ERN initiative. Professor Dattani has established a laboratory group investigating the molecular basis of hypothalamo-pituitary disease at UCL. He has identified novel genes implicated in hypothalamo-pituitary development in patients with congenital hypopituitarism, and more recently has worked on understanding the molecular basis of a paediatric brain tumour called adamantinomatous craniopharyngioma. He has more than 250 publications including original articles and scholarly reviews in a number of high impact journals, as well as book chapters. He sits on numerous advisory boards and editorial boards of journals. He has previously received the ESPE Henning Andersen and RCPCH Donald Paterson awards for his scientific work. He has co-authored 3 textbooks and is currently working on a further 3 books.

DOI: 10.1530/endoabs.66.IN1.2

PENS Presentation

PENS1.1

The evolving role of the children's endocrine nurse specialist

Jenny Walker

Leeds Children's Hospital, Leeds, UK

This is a brief reflection on how the role of the children's endocrine nurse specialist has evolved over the past 24 years and discussion around what the next 24 years may look like. What have we achieved; what is there still to do and what are the major challenges for the future? When days are filled with phone calls, clinics, paper/ computer work, supporting colleagues and caring for patients- we often forget what we have actually achieved and how much our roles have developed over the last 20 years. This will be an opportunity to celebrate what we have already achieved and to consider future aspirations and how these may be reached.

DOI: 10.1530/endoabs.66.PENS1.1

PENS1.2

Abstract unavailable

PENS1.3

Patients living with CAH

Sue Elford

CAH Support Group, Bedford, UK

Since my son was born (32 years ago) the monitoring and treatment for patients with CAH has improved considerable, with multidisciplinary teams providing excellent care from birth. It is still pretty scary for parents when they are given the diagnosis but they are able to access information on the condition, not just from their hospital team but also via support groups and the internet. Social media has enabled them to chat to other families online which can help them feel less isolated (although on occasion can cause more worries too, as not all information online is helpful or accurate). On the whole though, families are better informed and children born with CAH today have every chance of progressing 'normally' and due to medication being more finely tuned nowadays and new preparations available, they have less side effects to contend with. Injection kits are now also provided routinely for patients with CAH and training is given for parents/family members too, usually by helpful endocrine nurses at regular intervals. Although probably seldom used, an injection kit is also usually provided for schools too, When this became standard some years ago, endocrine nurses did try and visit schools and give injection training to teachers too but in recent years this has become unsustainable and is not only considered unsafe practice (as teachers leave, children change schools etc) but is also not good use of NHS resources. This has caused some upset amongst families who worry this puts their child at risk in school. However, a good care plan, advising schools of what to look out for and with the child listed as 'at risk of adrenal crisis' with their local ambulance service, the child should receive prompt expert attention, which should be perfectly sufficient to keep a child with CAH safe.

DOI: 10.1530/endoabs.66.PENS1.3

Diabetes Professionals' Day Sessions

Session 1

DS1.1

Nutrition, food science and cooking – what role in management of diabetes in children?

Francesca Annan

University College London Hospitals NHS Foundation Trust, London, UK

This presentation will review the role of nutrition in diabetes management, the evolution of advice from RD Lawrence's Red and Black lines through to the evidence from the current era of the need to consider meal compensation as the basis for insulin dosing with food, the importance of quality of good choices on outcomes, the impact of technology on our understanding of post prandial glucose responses and insulin delivery strategies.

DOI: 10.1530/endoabs.66.DS1.1

DS1.2

Using Carbs & Cals in everyday everyday practice

Chris Cheyette[1,2]

[1]Chello Publishing Limited, London, UK; [2]Kings College Hospital, London, UK

One of the corner stones of nutritional advice children and young people with diabetes is an awareness of how the food they choose can affect their blood glucose. Knowing; which foods contain carbohydrate, how to find this information out, how to estimate the amount of carbs and why not all carbs are the same, can help those living with diabetes, their families and careers make informed choices. Chris Cheyette is senior diabetes specialist dietitian at Kings College Hospital. He is also co-founder and author of the best selling Carbs & Cals series of books and app which have won numerous awards for their simple yet innovative pictorial approach to helping people understand the nutrients in their food choices. Carbs & Cals is widely recommended throughout the NHS for people with type 1 and 2 diabetes and has changed the way healthcare professionals teach carb counting. Chris will discuss how the resources were developed, and explore ways to use them in day-to-day practice.

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DS1.3

Practical diabetes – disordered eating and type 1 diabetes

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Introduction

The misuse or deliberate restriction of insulin for the purpose of weight loss is commonly referred to in the media and on social media as 'Diabulimia'[1], but this is not a medical definition. The relationship that young people with Type 1 Diabetes have with their weight, food and insulin is a commonly discussed, frequently studied but poorly understood issue. Mental health difficulties, especially eating disorders are common amongst adolescents[2], and particularly in those with chronic health conditions[3]. Dietary restriction alongside poor glycaemic control during this period of rapid growth and metabolic changes have protracted consequences on long term health outcomes[4,5]. Eating disorders (7% vs 2.8%) and disordered eating patterns (39.3 vs 32.5%) are not unique to persons with diabetes (PWD)[6]. However, insulin restriction provides young people with Diabetes a unique and dangerous purging tool. The consequences of eating disorders in diabetes carry the high mortality and morbidity risks of eating disorders alongside a 4-fold increased risk of diabetes related complications and 3 fold risk of death[7]. Understanding and supporting PWD those who have difficult relationships with body image, food and insulin is a challenge for many health professionals. Joint working remains the cornerstone of clinical guidance[8,9], however the practice of this is yet to be formally established in many areas.

Objectives

- To understand incidence of disordered eating in Diabetes.
- To explore mortality and morbidity data.
- To increase understanding of the presentation of eating disorders in Diabetes.
- To encourage cultural changes and body positive language.

Hopes for the future

Ongoing media and societal views around weight, shape and health are likely to continue to fuel a societal dissatisfaction with body and self. The misuse of insulin for weight loss is a topic which needs to be discussed, understood and young people supported through a journey.

- Prevention embedded into structured education.
- Seamless transition to adult services.
- Joined up working between medical and mental health services.
- Ongoing service improvement projects, language training and body positivity across all disciplines.

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Session 2

DS2.1

Abstract unavailable

DS2.2

Avoiding hypoglycaemia during sporting activity

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Regular physical activity during childhood is important for optimal physical and psychological development. For individuals living with type 1 diabetes, physical activity offers many health benefits including improved glycaemic control, cardiovascular function and psychological well-being. However, maintaining stable blood glucose levels around exercise remains a major challenge. In particular, exercise is associated with an increased risk of hypoglycaemia. The resulting fear of hypoglycaemia is often perceived by people living with type 1 diabetes as the most significant barrier to adopting a physically active lifestyle.

This presentation will provide an overview of the exercise physiology underpinning glycaemic excursions associated with exercise and will discuss evidence based strategies to reduce the risk of hypoglycaemia during and after activity, highlighting recent developments in this field. The overall aim of this talk is to provide health professionals with practical strategies to overcome common exercise related problems encountered in the clinic.

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Session 3

DS3.1

Getting the best out of social media in paediatric diabetes

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Ongoing patient engagement and education are vital in establishing successful self-management, long-term glycaemic management and a complication-free future for people with diabetes. Today's healthcare requires engaging the current generations where approximately 71% of adults go online everyday, and an additional 11% go online three to five times per week. One in three young people currently use social media in their daily lives. Social media has brought about a major change in societal communication and it offers huge potential as a versatile platform to deliver health interventions, recruitment to trials, collection of data and improving patient engagement within health care. However, key issues regarding ethical concerns -such as privacy, anonymity, informed consent and confidentiality remain an obstacle for healthcare professionals to engage in social media as a platform. Doctors now face a generation with social media and internet technology readily available, and online health care will soon become part of our clinical practice. It is therefore vital for health care professionals to be aware of the ethical guidelines on the use of social media and to work within the ethical principles within their regulatory bodies. The optimal and ethical use of innovative technologies and social media within a paediatric practice is shown to improve patient engagement and deliver effective education within the diabetes services.

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DS3.2

Type 2 diabetes, an increasing problem: lessons from national surveys

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Background

Type 2 Diabetes (T2DM), though a rare condition in children, is increasing in the paediatric population. The British Paediatric Surveillance Unit (BPSU) reporting framework is used to understand the clinical course and epidemiology of rare diseases in children.

Aim

To estimate the UK incidence of Type 2 diabetes (T2DM) in children aged <17 years and to compare with data collected a decade before. To characterize clinical features at diagnosis and assess the clinical progress 1-year on.

Methods

Clinician reported clinical data reported at presentation and 1-year follow-up of a cohort of children (<17 years) diagnosed with T2DM reported through the BPSU (April 2015–April 2016).

Results

The UK incidence of T2DM in children was 0.72/100 000 (95% CI 0.58–0.88) with children from ethnic minorities over-represented. Children of Asian ethnicity had a significantly lower BMI SDS compared with white children ($P<0.001$). There was a trend in increased incidence between 2005–2015, with a rate ratio of 1.35 (95% CI 0.99–1.84, P=0.062), however there was statistical evidence of increased incidence among girls (P=0.03) and children of South-Asian ethnicity (P=0.01). At 1-year follow up, HbA1c <48 mmol/mol was achieved in 38.8%. logHbA1c was predicted by clinician reported compliance and attendance concerns ($\beta = 0.12$, $P = <0.0001$) and change in body mass index (BMI) SDS at 1-year ($\beta = 0.13$, P=0.007). Metformin was the most frequently used treatment at baseline (77%) and follow-up (87%), though newer treatments like GLP-1 agonists were being used in children. Microalbuminuria prevalence at 1-year was 16.4% compared to 4.2% at baseline and was associated with a higher HbA1c compared to those without microalbuminuria (60 vs 49 mmol/mol, $P = 0.03$).

Conclusions

T2DM is an increasing especially among girls and those of south Asian ethnicity. Compliance to medication and BMI-reduction are key to positive outcomes.

Nurses' Day for Endocrine Professionals Sessions

Session 1

ND1.1

Abstract unavailable

ND1.2

Abstract unavailable

ND1.3

Abstract unavailable

Session 2

ND2.1

Assessing and monitoring growth in children with bone disorders

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Longitudinal growth in children is determined by endochondrial ossification at the growth plates of long bones and spinal growth. Whilst the assessment, monitoring and treatment of conditions which are responsive to growth hormone is well documented, conditions where children have an underlying bone disorder are more challenging. This paper will outline the important, common, primary bone conditions that impact growth, the assessment and effects that disordered growth has on the functional impact of the child. It will also summarise the latest drug therapies that are available and are currently in clinical trials, which impact the management of growth children with bone disorders.

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ND2.2

Abstract unavailable

Oral Communications

Oral Communications 1

OC1.1

Exploring trends in the glucocorticoid and mineralocorticoid treatment of congenital adrenal hyperplasia by analysing data from the I-CAH registry

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Introduction
There is no unified approach in clinical practice regarding the medical management of congenital adrenal hyperplasia (CAH), despite existent international guidance. We aimed to explore geographical and temporal variations in the treatment with glucocorticoids and mineralocorticoids of patients with CAH.
Methods
We collected data recorded by 33 centres from 16 countries in the I-CAH Registry. We analysed patient visits between 1982 and 2018, exploring the type, dose and timing of glucocorticoid and mineralocorticoid replacement. We used the conversion rate: 20 mg hydrocortisone = 4 mg prednisolone = 0.25 mg dexamethasone = 25 mg cortisone acetate.
Results
4934 patient visits from 601 patients with CAH (56% females) were analysed. Glucocorticoid replacement consisted primarily of hydrocortisone in children (88.8%) most frequently given in three daily doses (75%) and of prednisolone in adults (50.1%) usually given as one daily dose (67%). Glucocorticoid doses expressed as hydrocortisone-equivalent in mg/m^2 per day (median with interquartile range) were 13.5 (10.3–17.8) in the 0–1 years, 11.9 (9.9–14.4) in 1–8 years, 13.0 (10.7–15.5) in 8–12 years, 14.0 (11.6–17.5) in 12–18 years, 13.5 (11.1–19.2) in 18–30 years and 12.9 (8.9–16.8) in the over 30 year-old patient subgroup. Glucocorticoid doses were significantly reduced after 2010 in patients 0–1 years ($P<0.001$) and 1–8 years ($P<0.001$), increased in patients 18–30 years ($P=0.014$) and statistically similar in the other age subgroups. Mineralocorticoid replacement was used for 81.9% patients, relative doses varying across age groups, with a fludrocortisone dose (μg/m^2/day, median with interquartile range) of 312 (208–476) in the 0–1 years, 139 (94–205) in 1–8 years, 54 (42–91) in 8–12 years, 51 (34–76) in 12–18 years, 41 (31–74) in 18–30 years and 85 (51–107) in the over 30 year-old patients. There was wide variation among different countries and centres regarding type, dose and timing of glucocorticoid and mineralocorticoid treatment.
Conclusion
Our findings suggest international variations in hormone replacement therapy, with a tendency for higher doses in younger patients. Further evidence regarding the impact of different treatment regimens on health outcomes is needed to explore the benefits of a more uniform approach in the management of CAH.

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OC1.2

Pituitary Apoplexy in an adolescent male with Macroprolactinoma presenting as middle cerebral artery infarction

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Background
Pituitary apoplexy is uncommon in childhood and adolescence. Typical clinical features are acute confusion, headache, vomiting and visual disturbance. It is caused by haemorrhage into the pituitary gland. Its association with cerebral infarction is rare. We report an unusual case associated with a cerebral infarction secondary to internal carotid artery compression.
Case
16 year old male was referred to the 'Stroke Team' with acute onset confusion, visual disturbance, slurred speech and right-sided weakness. He was vomiting and complained of worsening headache. Examination revealed right-sided increased tone, reduced power and bi-temporal hemianopia. He was confused and unable to follow commands. Initial CT head revealed 3.5×2 cm sellar/suprasellar mass prompting urgent endocrine profile. This revealed Prolactin 87 089 mIU/l [100–410 mIU/l], Cortisol 494 nmol/l [130–580 nmol/l], TSH 1.0 mIU/l [0.3–5.5 mIU/l], T4 5.5 pmol/l [9–25 pmol/l], IGF-1 19.1 [15.6–66.9 nmol/l]. Serum Sodium 127 mmol/l and Osmolality 271 mosm/kg suggested inappropriate ADH secretion. The working diagnosis was macroprolactinoma with TSH deficiency. In view of neurological signs and symptoms, he underwent CT angiography. This revealed tumour mass effect causing luminal occlusion of both internal carotid arteries. MRI confirmed pituitary apoplexy with haemorrhagic fluid levels and ischaemic changes in left fronto-parietal region (Middle Cerebral Artery (MCA) distribution). Following treatment with intravenous Hydrocortisone and oral Cabergoline, there was significant improvement in focal neurology signs and vision. He underwent endoscopic trans-sphenoidal debulking of tumour within 48 hours. Post-operative imaging confirmed significantly debulked sellar/supra-sellar mass with a maturing left MCA infarct. Histology confirmed pituitary adenoma with strong immunopositivity for prolactin with increased proliferation, Ki-67 index 7%. Ongoing treatment includes replacement Hydrocortisone, Levothyroxine and Growth Hormone (post-op IGF-1 16 [16–67 nmol/l]). Cabergoline 500 mcg twice weekly has controlled his prolactin with level now down to 294 mIU/l. Further clinical assessment revealed delayed puberty (G3 PH2 TV5 ml) consistent with longstanding hyperprolactinaemia effect. Post-operative visual fields were normal. Neuro-rehabilitation assessments highlighted significant new cognitive difficulties. He completed a prolonged hospital stay for neuro-rehabilitation and has ongoing support in the community.
Conclusion
Cerebral infarction following pituitary apoplexy and internal carotid artery occlusion is rare. Assessment and knowledge of clinical, radiological and biochemical features of pituitary apoplexy is important in patients presenting with acute neurology.

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Oral Communications 2

OC2.1

National United Kingdom evidence- and consensus-based guidelines for the investigation, treatment and long-term follow-up of paediatric craniopharyngioma

Hoong-Wei Gan[1], Paul Morillon[2], Assunta Albanese[3], Kristian Aquilina[4], Konstantinos Barkas[5], Chris Chandler[5], Yen-Ch'ng Chang[6], Christina Daousi[7], Evangelos Drimtzias[8], Sarah Farndon[9], Tom Jacques[1], Marta Korbonits[10], Adam Kuczynski[4], Jennifer Limond[11], Louise Robinson[12], Ian Simmons[8], Nick Thomas[5], Sophie Thomas[13], Nicola Thorpe[14], Faraneh Vargha-Khadem[1], Daniel Warren[8], Bassel Zebian[5], Ashley Gamble[15], Sophie Wilne[13], Barney Harrison[16], Helen Spoudeas[4] & Conor Mallucci[17]

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Aims

Although rare, craniopharyngiomas are the commonest suprasellar tumour in childhood. Despite high overall survival, children and young people < 19 years with craniopharyngiomas are at risk of multiple relapses and long-term tumour- and treatment-related morbidity. We sought to provide, for the first time, a national standard for best practice based on currently available evidence for the assessment, treatment and follow-up of paediatric craniopharyngiomas under the auspices of the RCPCH, UK CCLG and BSPED.

Methods

Clinical questions were formulated based on a PICO (Population, Intervention, Comparison, Outcome) format by a multidisciplinary Guideline Development Group. Systematic searches were conducted via the Ovid MEDLINE (1946-February 2017) and Cochrane Library (2016, Issue 12) databases, identifying 2023 separate research articles. Publications underwent a three-tier filtering process and 300 were reviewed using the GRADE approach. Where recommendations could not be made, a two-stage international Delphi consensus process was conducted. The guideline was developed using AGREE II criteria.

Results

44 clinical questions were identified, leading to 35 recommendations largely based on low to very low quality evidence. 30 further recommendations achieved >70% agreement via the Delphi consensus process. Important highlights include the recommendation that craniopharyngiomas are managed in tertiary paediatric centres with sufficient neuro-oncology, neurosurgery, endocrinology, radiology, pathology and neuropsychology multidisciplinary experience. At diagnosis, tumours should be graded using the 'Paris' grading system (Puget *et al.*, *J Neurosurg* 2007; 106(Suppl 1):3–12) and subsequent surgical treatment tailored to avoid hypothalamic damage, with adjuvant upfront radiotherapy being offered where tumour resection is incomplete. Detailed recommendations on the neuroendocrine, ophthalmological and psychological pre-treatment assessment of patients and long-term follow-up of survivors are also made, with a review on the safety of growth hormone replacement therapy in this cohort.

Conclusions

These guidelines provide the first evidence- and consensus-based national recommendations for the management of paediatric craniopharyngioma, and highlight the need for further research in areas such as the efficacy of proton beam therapy, radiosurgery and intracystic therapies in children, and the management of late effects such as hypothalamic obesity. Through their implementation, we hope to achieve better consistency in the quality of care of such patients and improve long-term quality of survival.

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OC2.2

A rare but very important cause of growth failure

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Introduction

Bloom syndrome (BS) is a rare autosomal recessive disorder caused by mutations in the *BLM* gene. Classic dysmorphic features include a long, narrow face, micrognathism and prominent nose and ears. Other features of the disease include pre- and post-natal growth failure, skin rash following sun exposure, hyper-pigmented areas or cafe-au-lait lesions, high-pitched voice and immuno-deficiency. The most serious complication of BS is the significant increase in risk of malignancy due to genomic instability.

Case report

A 5-year-old girl presented to her local endocrinology clinic due to short stature. The patient was born at term (39/40 weeks) with a birth weight and length of 1580 g (SDS −4.7) and 44 cm (SDS −2.89), respectively (small for gestational age, SGA). From birth, she suffered recurrent infections of upper and lower respiratory tract, frequently requiring antibiotic treatment. She also developed hypothyroidism. Physical examination revealed significant short stature (height SDS −5.3) and low BMI (SDS −1.8). She had a long narrow face with micrognathia and café-au-lait spots were noted on her abdomen and right popliteal fossa. Baseline blood tests were unremarkable and both growth hormone (GH) stimulation and IGF-1 levels were within the normal range. As the patient was born SGA with no catch-up growth, she commenced GH therapy. Her growth velocity on hGH over a 9-month treatment period was 5.4 cm/year (5.8 cm/year prior to treatment). Given her growth failure and dysmorphic features, the patient was also referred for genetic testing. Whole exome sequencing identified a homozygous mutation in the *BLM* gene (91306246C>T, c.1933C>T, p.Q645*) which is recognised to cause Bloom syndrome. Due the increased risk of cancer development in Bloom syndrome, the decision was made to stop GH therapy.

Conclusions

Genetic diagnosis in children with short stature and concomitant dysmorphic features is important and in some rare syndromes GH therapy is contraindicated. Bloom syndrome causes pre- and post-natal growth failure and as such, may be referred to paediatric endocrinology. This case highlights the importance of detailed phenotypic assessment and referral for genetic testing in cases of undiagnosed syndromic short stature, particularly when considering GH therapy.

DOI: 10.1530/endoabs.66.OC2.2

Oral Communications 3

OC3.1

Using quality improvement methods to enhance HbA1c outcomes for newly diagnosed children and young people with diabetes

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Introduction

There is increasing emphasis on stringent glycaemic control (HbA1c <48 mmol/mol) within the first year of diagnosis for all types of diabetes, to preserve metabolic memory and reduce future risk of sub-optimal diabetes outcomes. Retrospective data collected on two previous annual cohorts of children and young people (CYP) with diabetes revealed only 9% achieved the HbA1c < 48 mmol/mol target at 12 months post diagnosis despite initial HbA1c improvement until 6 months.

Aim

To achieve HbA1c < 48 mmol/mol in 25% of patients and HbA1c <58 mmol/mol in 75% of patients at 12 months post diagnosis.

Method

A small staff representation from the wider multi-disciplinary team employed Quality Improvement processes focusing on improving HbA1c and self-management skills during the first year of diabetes care. Consensus from this group enabled intervention adoption by the wider CYP Diabetes Team. Interventions included a focused timeline from diagnosis, more frequent team contacts and clinic appointments, psychology led age specific new patient groups, earlier home downloading and data interpretation support and use of a digital education resource (DigiBete). Real time data collection highlighted those patients not achieving HbA1c targets and facilitated more intensive team support.

Results

HbA1c data from 34 new patients, aged 1–18 years, was compared with two previous patient cohorts (2015/2016 and 2016/2017). Significant improvement was demonstrated across all data collection points. At 12 months post diagnosis, the percentage of patients achieving HbA1c < 48 mmol/mol increased from 9%

to 31% whereas those achieving HbA1c < 58 mmol/mol increased from 46% to 69%.
Conclusion
Project success has resulted from a dedicated multi-disciplinary team with frequent and focused time-limited QI meetings, adoption of a 'fail fast' approach and regular review of real time data. The appointment of a QI champion was essential. More intensive early family support and increasing consistency using the timeline have contributed to improved outcomes in the new patient cohort. This is now being embedded as 'routine practice' within the wider team. Resources to support and empower families to interpret their own data and confidently make insulin adjustments between clinic visits will continue to be developed.

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OC3.2

2 year experience of 'Do-It-Yourself' Hybrid Closed Loop in an adolescent with Type 1 Diabetes

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Introduction
The use of Closed Loop (CL) system has slowly progressed from using a short time overnight to prolonged periods under everyday living conditions. In the last few years, Do-It-Yourself Closed Loop (DIY-CL) technology has become openly available as part of 'patient-led' global initiative (#Wearenotwaiting) outside the conventional regulatory pathways, raising many medico-legal and ethical dilemmas.
Methods
Majority of the DIY-CL users are adults; we describe using this new technology as a 'parent-led' initiative for 2 years in an adolescent. Type 1 diabetes (T1D) was diagnosed at 3.5 years in 2008; Islet Cell antibodies were positive at diagnosis; and patient's father was known to have T1D too.
Results

Time Period	Age (Years)	Insulin Regimen*	Average Insulin dose (units/kg per day)	Mean HbA1c (mmol/mol) (%)
2009–2010	4–5	BD	0.78	66 (8.2%)
2011–16	6–11	CSII	0.82	54 (7.1%)
2017	12	CSII + CGM	0.79	55 (7.2%)
2018–2019	13–14	DIY-CL	1.03	41 (5.9%)

*BD – Twice daily insulin injections; CSII – Continuous Subcutaneous Insulin Infusion; CGM – Continuous Glucose Monitoring
CGM sensor data capture over 90 days in Apr–Jun 2019 was 97.2%; lost readings were mainly due to sensor warm up.

Description	Glucose Value (mmol/l)	Number of readings	% of time
Euglycaemia	4–10	22 819	92.4%
Level 1 Hypoglycaemia	3–3.9	683	2.8%
Level 2 Hypoglycaemia	<2.9	142	0.6%
Level 1 Hyperglycaemia	10.1–13.9	1003	4.0%
Level 2 Hyperglycaemia	>13.9	59	0.2%

Parents reported numerous advantages (improved sleep & quality of life; no fear of hypoglycaemia; decreased diabetes care burden) and broadly no disadvantages, but high costs if not funded. Adolescent reported many advantages (100% school attendance; easy to check if system not working, less obvious than pump and no huge effect on sugar levels if a bolus dose is missed!) and no disadvantages.
Conclusions
DIY–CL system appears safe and effective in reducing hypoglycaemia, minimising hyperglycaemia and achieving good HbA1c consistently over 2 years, even during adolescence. It improved quality of life for patient & family and decreased diabetes burden for them. Many ethical dilemmas, especially the non-regulated off-license use of this technology, still persist.

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Oral Communications 4

OC4.1

Mortality after childhood growth hormone treatment in the UK – the SAGhE study

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Background: Recombinant human growth hormone (r-hGH) has been used for more than 30 years and indications for r-hGH have multiplied worldwide. There has been concern that it might raise mortality, but published data are limited.
Methods
The cohort comprised of 3902 UK patients over 18 years of age in 2009, treated with childhood r-hGH at all the major UK growth centres. The total European cohort was 24 232 from eight countries (including the UK), with > 400 000 patient years of follow-up. Patients were classified a priori based on pre-treatment perceived mortality risk from their underlying disease and followed for cause-specific mortality. Person-years at risk of mortality and expected rates from general population data were used to calculate standardized mortality ratios (SMRs).
Results
In the UK, low-risk patients with isolated GH deficiency or idiopathic short stature, all-cause mortality was not increased [SMR 1.0 (95% confidence interval 0.4–2.4)] nor was it increased in children born small for gestational age [SMR 1.1 (0.5–2.3)], but in contrast, increases in mortality in this sub-category were seen in the French sub-cohort. In patients at moderate, or high risk, mortality was clearly increased [SMR 3.6 (2.8–4.7) and 16.6 (14.0–19.7), respectively] in the UK cohort, similar to the findings from all countries. Mortality was not associated with mean daily or cumulative doses of r-hGH for any of the risk groups. Cause-specific mortality from diseases of the circulatory and haematological systems was increased in all risk groups.
Conclusions
In this, the largest cohort with the longest follow-up for r-hGH treated children, all-cause mortality was strongly related to underlying diagnosis. Results from patients with isolated GH deficiency or idiopathic short stature or SGA in the UK suggest that r-hGH treatment is not associated with increased all-cause mortality. However, mortality from certain causes was increased, emphasizing the need for further long-term surveillance.

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OC4.2

Burosumab initiation in a UK XLH cohort: real-world use resonates with research evidence

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Objectives
X-linked hypophosphatemia (XLH) is a rare inherited form of osteomalacia characterised by low blood phosphate levels which lead to inadequate mineralisation of bone resulting in rickets, skeletal abnormalities, physical impairment, weakness, and pain. Burosumab is an anti-FGF23 fully human monoclonal-antibody, and the first treatment to target the underlying pathophysiology of XLH. We report relevant real-world biochemical data following the first 6 months of burosumab treatment.

Methods
An early access program (EAP) for burosumab was made available for children in the UK with XLH in 12 specialist centres. Inclusion criteria for the EAP included radiographic evidence of disease, XLH confirmed by genetic PHEX mutation or familial X-linked inheritance mutation or family history. Patients must have also had an unsatisfactory response to conventional treatment. EAP enrolment was between January and March 2018. 135 of 142 applications were approved. 132 have commenced treatment (dose in accordance with EMA marketing authorisation), of whom 31 have completed a median of 24 weeks (22–26 weeks) of treatment.
Results
Mean age enrolled was 7.2 years (range 1.6–14.7), 68% female and 32% male. Mean height and weight at week 0 was 114.9 cm (75–157.9 cm) and 27.1 kg (10.5–67.5 kg) respectively. Mean dose administered was 0.51 mg/kg (0.28–0.95 mg/kg) at week 0 and 0.89 mg/kg (0.25–2.01 mg/kg) at week 24 (22–26 weeks). Mean fasting serum phosphorus was 0.73 mmol/l (0.5–0.91 mmol/l) in week 0 rising to 1.06 mmol/l (0.77–1.48 mmol/l) at week 24 (22–26 weeks) representing a 45% increase in serum phosphate. Mean serum ALP fell from 591.5 IU/l (261–4089 IU/l) at week 0 to 353.2 IU/l (190–733 IU/l) at week 24 (22–26 weeks), representing 40% decrease in ALP. No patients discontinued treatment due to adverse events.
Conclusions
Early data from treating children and young people with XLH with burosumab in a real-world UK setting demonstrate that key biochemical responses are aligned with the clinical research program findings. Ongoing monitoring and research is required to confirm the biochemical response translates to the expected subsequent impact on skeletal and non-skeletal outcomes, including linear growth and deformities.

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OC4.3

Defects in LGR4 Wnt-β-catenin signalling impair GnRH network development, leading to delayed puberty

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Background
The initiation of puberty is heralded by increasing gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus. During embryonic life the GnRH neuroendocrine network develops thanks to a coordinated migration of neurons from the nasal placode to the forebrain. Our group has previously demonstrated that dysregulation in GnRH neuronal migration leads to delayed pubertal onset. Late puberty affects up to 2% of the population and is associated with adverse health outcomes. Self-limited delayed puberty (DP) most commonly segregates within families with an autosomal dominant inheritance pattern, indicating a strong genetic basis. However, the genes underlying DP remain mainly unknown.
Aims and methods
To discover novel genetic mutations in pathways regulating GnRH neuronal development in our large, accurately phenotyped cohort of patients with DP. Whole exome sequencing was performed on DNA from 160 individuals of 67 multi-generational families affected with DP. Variants returned were analysed to identify rare, potentially pathogenic variants enriched in case versus controls and with biological relevance to GnRH neuronal development pathways. The candidate gene *LGR4*, identified via this strategy, was investigated using an array of *in silico*, *in vitro* and *in vivo* techniques.
Results
We identified three rare missense variants in *LGR4* in six unrelated families (17 affected individuals) and all segregated with the DP trait with the expected autosomal dominant inheritance. These variants are highly conserved and predicted to be deleterious by the main prediction software tools. *Lgr4* was specifically expressed in mice olfactory epithelium and the vomeronasal organ at different embryonic stages. The LGR4 mutants showed impaired Wnt β-catenin signalling, due to defective protein expression and a shorter protein half-life. Moreover, we investigated the role of Lgr4 in a knock-out mouse model: $Lgr4^{+/-}$ mice had a delayed onset of puberty and fewer GnRH neurons compared to $Lgr4^{+/+}$ mice, both in early embryogenesis and at the hypothalamus, whereas $Lgr4^{-/-}$ mice failed to enter puberty and showed a significant reduction in GnRH neurons.
Conclusions
Defects in *LGR4*, acting via the Wnt signalling pathway, affect GnRH neuron development in fetal life, resulting in a phenotype of self-limited DP. Our findings contribute to the ongoing exploration of genetic factors controlling pubertal timing.

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OC4.4

A novel clinical risk score that accurately predicts recurrence of craniopharyngioma – a multicentre cohort study

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Introduction
Craniopharyngiomas (CPs) are histologically benign tumours but are clinically associated with significant morbidity and mortality. Recurrence of CPs is known to influence mortality, but apart from the extent of surgical resection, no clinical characteristics have been shown to predict recurrence. Complete resection is difficult due to their infiltrative behaviour and unacceptable morbidity. Thus, predictors of risk of recurrence are needed.
Aim
To establish a multinational cohort of patients with CP and employ their clinical parameters to design a clinical tool that can predict the risk of CP recurrence.
Methods
225 patients from 15 centres (8 countries) participated in our mixed prospective and retrospective observational cohort study. Tumour subtyping was performed

by three histopathologists. Brain MRI ($n=172$) was scored for tumour size and hypothalamic invasion by a single neuroradiologist. A broad range of clinical data was collected. Statistical analyses were performed in R (2-sided, $P<0.05$ assumed significant); the primary outcome for prediction was 'time-to-first-recurrence'.

Results

Median age at presentation was 19.7 years (IQR 10.6–47.3) and 89% were adamantinomatous. Fifty-six percent had a recurrence with a median 'time-to-first-recurrence' of 23 months (IQR 9–44). A multivariate Cox model was performed using age, gender and clinical parameters before surgery (diagnosis decade; symptom duration; tumour subtype, size, consistency and location; hypothalamic invasion; endocrinopathies) and after surgery (transsphenoidal/-craniotomy, complete/incomplete, radiotherapy) as risk predictors of time-to-recurrence. A risk-score was computed as the linear predictor of the fitted multivariate Cox model. 5th, 20th and 99th centiles of the risk-score were used to categorise the patients into low, medium or high risk respectively. Kaplan–Meier curves showed a clear separation in 'recurrence-free-survival' between the three risk groups ($P<0.0001$). A cut-off value of 0.948 was selected for a 92% sensitivity at one-year follow-up (95%CI:84–98%), and corresponding specificity of 35% (95%CI:27–42%). Kaplan–Meier curves also showed that radiotherapy resulted in significantly longer recurrence-free-survival ($P<0.006$).

Conclusion

This is the first study that uses a large clinical dataset to design a model to predict risk of CP recurrence, combining several clinical characteristics. This model will facilitate identification of other risk factors and following external validation, can be used in clinical practice to improve clinical care.

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OC4.5

Novel genetic defects in a cohort of Silver–Russell Syndrome (SRS) and SRS-like patients

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Background

Silver-Russell Syndrome (SRS) is a clinically and genetically heterogenous condition. 40% patients with 'clinical' SRS remain without a genetic diagnosis despite fulfilling the Netchine-Harbison Clinical Scoring System (NH-CSS) criteria. There is increasing recognition of the wide range of clinical phenotypes within the SRS spectrum and overlap with other short stature syndromes.

Methods

We analysed 26 undiagnosed patients with features of SRS by whole exome sequencing (WES). There were 2 patient cohorts: (1) Twelve SRS ($n=9$) and SRS-like ($n=3$) patients negative for 11p15 LOM +/− upd(7)mat, (2) Fourteen patients referred to our centre with undiagnosed short stature (SS) who fulfilled at least 2/6 NH-CSS with additional SRS features (8M, mean age 5.6 years, range 1.2–17 years, mean BW SDS −1.98, range +0.95 to −4.58, mean height SDS −3.73, range −2.21 to −7.07). Genetic variants were filtered using our 'virtual' gene panel with curated list of 85 candidate SRS genes. This included genes with important roles in growth, methylation and histone modification. 16 SRS and SRS-like patients were also assessed for copy number variation (CNV) by Array CGH with median resolution of 120 Kb for 15 patients and 1 Mb for 1 patient due to reduced DNA quality.

Results

WES identified rare, putative genetic variants in 5/26 (19%) individuals. In 1 patient we identified a homozygous frameshift ANKRD11 mutation, recognised to cause KBG syndrome, a rare genetic disorder with a SS phenotype and triangular face. Additionally, 4 rare variants in 3 SRS candidate genes were validated by Sanger sequencing. 2 were predicted damaging by $\geq$ 2/3 of SIFT, PolyPhen-2 and CADD pathogenicity scores. 1 variant was predicted to cause aberrant splicing and another is in a highly conserved region in the C-terminal catalytic domain. Functional investigation is planned to determine pathogenicity. CNVs were detected in 2/16 (13%) patients. 16q23 and 17q21 deletions in a male patient and 9q34 deletion in a female patient with learning difficulty, clinodactyly and hypoglycaemic episodes.

Conclusion

We identified 2 CNVs and 5 rare variants (30% with putative diagnosis) in 7 undiagnosed SRS and SRS-like patients. This work expands our knowledge of SRS genetic aetiology and SRS subtypes.

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OC4.6

Understanding differences of sexual differentiation (DSD) MDT services across the UK; current service provision and sharing best practice

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Background

DSD services are evolving across the UK in response to both family, professional and societal pressures but MDT provision and access to specialist DSD services varies. In November 2017, DSD Clinical Standards were published by the BSPED Clinical Committee with the aim to improve and standardise DSD patient care and these were audited in March 2019. 95% of DSD centres responded with 85% listing psychology as part of their MDT.

Aim

1. To understand in greater depth the current profile of DSD MDTs in the UK, recognise scope for service development and share best practice
2. Review current psychological service in DSD and establish key needs for provision

Method

All clinical leads of DSD MDTs across the UK were invited to participate in a semi-structured telephone interview. This interview targeted the areas of MDT structure, geography and population, referral processes and psychological provision.

Results

Initial results show a wide variety in the structure of the MDT across the UK with a 'functioning' MDT taking many forms. The current standards do not distinguish between core members of the MDT vs wider peripheral input, raising questions about whether physical attendance at MDT provides superior service for DSD patients. There is variable provision of integrated psychological care within DSD MDTs. Some tertiary centres are unable to include routine psychological assessment and intervention. Some services have a referral path for arm's length psychological consultation. Others have a psychologist present and contributing to MDT clinical reviews but with inadequate provision for direct psychological work with parents and children. Few have the resource to involve expert psychological care as part of the acute assessment and diagnostic phase. Many clinicians listed psychology as the most 'needed' improvement to their service. There has been innovative use of extended services such as genetic counsellors and patient support groups as alternative sources of psychological support but clinicians do not feel these provide the full range of formal psychological services required for patient needs. Further exploration of what constitutes minimum effective psychological care within a specialist DSD multi-professional service is needed.

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OC4.7

Novel variants in the Leucine-zipper-like transcription regulator 1 (LZTR1) gene cause Noonan syndrome phenotype by upregulation of the RAS-MAPKinase pathway

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Objectives

Noonan Syndrome (NS) is an autosomal dominant multi-system disorder characterised by short stature (SS), distinctive facial features and cardiovascular abnormalities. Mutations in multiple genes regulating the RAS-MAPK pathway have been identified in NS including 5 recently described novel *LZTR1* variants. We identified 2 novel *LZTR1* variants in patients with features of growth hormone insensitivity and NS. The molecular function of *LZTR1* is unknown and we aimed to assess the impact of the *LZTR1* variants on (1) LZTR1 protein expression and (2) RAS-MAPK pathway function.

Methods

Targeted and whole exome sequencing data were analysed by Ingenuity Variant Analysis using established bioinformatic pipelines. We identified 2 novel

heterozygous missense *LZTR1* gene variants [c.466A>G; p.K156E and c.23G>C; p.G8A] in 2 subjects and 5 previously published heterozygous inactivating missense *LZTR1* variants [c.742G>A; p.G248R, c.850C>T; p.R284C, c.740G>A; p.S247N, c.356A>G; p.Y119C, and c.859C>T; p.H287Y]. Site-Directed Mutagenesis generated the 7 *LZTR1* variants in WT-*LZTR1* vector (pcDNA-Myc-Hist-LZTR1) and constructs were verified by Sanger sequencing. HEK293 cells were transiently transfected with variant and WT *LZTR1* in 3 technical replicates. Western blot (WB) analysis was performed, using anti-c-Myc, anti-ERK and anti-pERK antibodies (anti-beta-actin/GAPDH as controls).

Results

The 7 patients had characteristic facial features of NS (downslanting palpebral fissures, hypertelorism, short nose), 6/7 had cardiac defects and 5/7 had short stature (height SDS -2.3 to -1.8). WB confirmed significantly reduced mean LZTR1 protein expression in the 7 mutants (0.064 ± 0.01, 0.046 ± 0.01, 0.053 ± 0.01, 0.042 ± 0.003, 0.046 ± 0.01, 0.039 ± 0.005 and 0.058 ± 0.003, respectively) vs WT(0.277 ± 0.02); $P \leq 0.001$ for all variants. There was significant increase in mean p-ERK:total ERK ratios in mutant (0.0067 ± 0.0008, $P = 0.0281$; 0.0049 ± 0.0003, $P = 0.0139$; 0.0099 ± 0.0006, $P = 0.0049$; 0.0058 ± 0.0003, $P = 0.0081$; 0.0057 ± 0.0003, $P = 0.0079$; 0.006 ± 0.0003, $P = 0.006$; 0.0056 ± 0.0002, $P = 0.0047$, respectively) vs WT(0.0026 ± 0.0002) suggesting enhanced ERK phosphorylation and up-regulation of RAS-MAPK pathway.

Conclusions

Novel *LZTR1* variants reduce LZTR1 protein expression. Enhanced RAS-MAPK signalling would be consistent with other NS-causing gene mutations e.g. *PTPN11*. LZTR1 may negatively regulate this critical cellular pathway and further functional work is underway.

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OC4.8

SGPL1 deficiency leads to accumulation of sphingolipid species and downregulation of key enzymes within the steroidogenic pathway

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Background

SGPL1 carries out the final degradative step of the sphingolipid pathway, irreversible cleavage of sphingosine-1-phopshate. SGPL1 deficiency is associated with a pathological accumulation of sphingolipid species and a multi-systemic condition incorporating primary adrenal insufficiency (PAI). Sphingolipid intermediates, ceramide and sphingosine are postulated to act as modulators of the steroidogenic pathway, acting as second messengers altering downstream expression of steroid responsive transcriptional elements. Ceramide, sphingomyelin and sphingosine are reported inhibitors of steroidogenesis. Pathological accumulation of these sphingolipid species in SGPL1 deficiency may therefore have negative implications for the steroidogenic cascade.

Objective and hypotheses

Investigating the impact of SGPL1 deficiency on sphingolipid profile and steroidogenesis using patient derived dermal fibroblasts and RNA-seq interrogation of the differential expression of steroidogenic genes in an *SGPL1*-KD adrenocortical cell line (H295R).

Methods

(1) Primary cultures of dermal fibroblasts were established from skin biopsies of two patients with *SGPL1* mutations (Patient1 – p.F545del; Patient 2 – p.S65Rfs*6G) and PAI. The steroidogenic capacity of fibroblasts was explored using a precursor substrate, progesterone, as a stimulator of cortisol production. Culture media from treated/untreated cells were subjected to cortisol measurement (ELISA). (2) Mass spectrometric analysis of sphingolipid intermediates in control and patient fibroblasts 2. Lentiviral shRNA mediated KD of *SGPL1* in H295R cell line with subsequent RNA-seq interrogation.

Results

Control fibroblasts showed a significant cortisol response after progesterone stimulation ($P < 0.001$). In comparison Patient 1 fibroblasts were less responsive ($P < 0.05$) and Patient 2 cells unresponsive to stimulation ($P < 0.001$). Mass spectrometry revealed significantly increased ceramide and sphingomyelin levels in both patient cell lines compared to control ($P < 0.01$). Differential gene expression data from RNA-seq in the *SGPL1*-KD H295R cell line revealed functional enrichment of genes for the metabolism of steroids (FDR 0.045) and cortisol synthesis and secretion (FDR 0.0496). Further interrogation revealed significant downregulation of steroidogenic genes, with reduced transcript levels of *STAR,* CYP21A2 and CYP11B1 in the *SGPL1*-KD H295R.

Conclusion

Our results are in keeping with a prominent role for sphingolipids in modulating the acute phase of steroidogenesis, suggesting that alterations in sphingolipid metabolism due to SGPL1 deficiency negatively impact the expression of genes responsible for steroid hormone biosynthesis.

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OC4.9

Health status of children aged 8–18 years with 21-hydroxylase deficiency in the United Kingdom: results of a multi-centre cohort study

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Introduction

There is limited knowledge on the impact of congenital adrenal hyperplasia (CAH) on the health and well-being of children and young persons (CYP). We aimed to establish the health status of CYP with CAH across the United Kingdom.

Methods

We conducted a national multi-centre prospective study recruiting 107 patients aged 8–18 with 21-hydroxylase deficiency from 14 centres and 83 matched controls. Demographic, clinical, metabolic data, as well as Strengths and Difficulties (SDQ) and Paediatric Quality of Life (PedsQL) questionnaires were collected and analysed.

Results

Most CAH patients were of White (73.8%) or Southeast Asian (18.6%) ethnicity. Glucocorticoid treatment consisted primarily of hydrocortisone (94.3%), with 76.6% patients also receiving fludrocortisone. 34.3% patients required admission for adrenal crisis after diagnosis. Delta-SDS for target height was 1.2 ± 1.4 for patients younger than 12 years and 0.3 ± 1.6 for 12- to 18-year-olds; patients under 12 years were taller ($P = 0.02$) and patients aged 12–18 years shorter ($P = 0.03$) than controls. Patient weight-SDS (0.87; 0.03–1.35) and body-mass-index-SDS (0.98; -0.04 to 1.94) were significantly higher compared to controls; 27.7% of patients were overweight and 22.8% obese. Five patients had high blood pressure. Post-glucocorticoid dose androstenedione was normal in 32%, suppressed in 7%, and elevated in 50% of patients; 17-hydroxyprogesterone was within target range in 20%, suppressed in 19%, and increased in 43% of patients. Biochemistry indicated normal sodium in all patients, low potassium in 1 patient, normal glucose in all, mildly raised creatinine in 9.8%, high lipids in 9.8% patients. Associated behavioural and mental health problems were reported for 11.3% patients aged 12–18 years, similar to the general population. SDQ questionnaires showed 'high' or 'very high' scores for 15.1% patients, most commonly related to hyperactivity and peer problems. The median with interquartile range for PedsQL scores was 81(72–88), the areas marked lowest being emotional and school functioning.

Conclusion

Our findings suggest that children with CAH have increased prevalence of growth problems and metabolic co-morbidities, as well as reduced quality of life and mental health well-being. The development of improved standardised strategies for the management and monitoring of CAH in childhood is required in order to improve long-term patient outcomes.

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Oral Communications 5

OC5.1

Project to develop BSPED UK standardised guidelines for sex hormone priming and glucagon stimulation testing (GST) in children and adolescents

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Background
The GST is commonly used in children and adolescents for the diagnosis of growth hormone (GH) deficiency. Evidence supports the use of sex steroid priming to improve diagnostic accuracy in GH provocation tests. This project, undertaken on behalf of the BSPED Clinical Committee, aims to identify current practice and develop consensus in sex hormone priming and GST protocols for the development of standardised UK protocols.
Method
(1) Audit of sex hormone priming and GST protocols among UK tertiary paediatric endocrine centres. (2) DELPHI consensus process over 8 weeks, involving all UK paediatric endocrine specialists undertaking the GST. An electronic survey, developed by a working group of 4 consultant paediatric endocrinologists and approved by the BSPED clinical committee, was distributed via the BSPED newsletter. The survey consisted of 9 statements with 4 fixed responses and free text comments covering aspects of the criteria and preparation used for sex hormone priming; the glucagon dose, hypoglycaemia risk and presence of medical personnel for the GST. Consensus was considered achieved when 70% of respondents agreed with the statements.
Results
Audit: Priming was used in 20/22 centres with variations in patient criteria (bone/chronological age or pubertal stage), drug preparation and dose. GST was performed in 20/22 centres under 13 protocols with differences in glucagon doses (0.15–0.1 mcg/kg, maximum 0.5–1 mcg), timing of samples and length of tests (150–240 min), Delphi: 39 responses from 17 tertiary and 12 secondary centres (26 tertiary paediatric endocrinologists,12 paediatricians with endocrine interest, 1 paediatric endocrine nurse). All statements reached consensus. Four statements for priming agreed (86–100%) informing a new guideline. Five statements for GST concerning glucagon dose and safety criteria agreed (89–100%) but with a range of comments. Common themes from free texts included the definition of hypoglycaemia (2.6–3.5 mmol/l), when a test can proceed or should be abandoned, and the immediate availability and skills needed for a doctor on the unit supporting the nurse performing the test.
Conclusions
Consensus was reached for the use of sex steroid priming for GH testing and safety precautions required for the GST. This information will inform the development of safe standardised BSPED national protocols.

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OC5.2

Longitudinal outcomes of well, term infants who present with persistent hyperthyrotropinaemia

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Background
Neonatal hyperthyrotropinaemia (HT) is defined by elevated thyroid stimulating hormone (TSH) and normal free-thyroxine (FT4) level. Persistent HT in the neonatal period is often a diagnostic dilemma for clinicians to either treat to prevent subclinical hypothyroidism or to wait and monitor thyroid function tests (TFTs).
Methods
As part of an audit, 1449 term infants who had TFTs undertaken as part of a prolonged jaundice screen from 2012–2017 were reviewed. Infants with HT (defined by TSH>5 mU/l) were followed up in clinic. We evaluated perinatal factors and TFTs were monitored in 2–4 weeks, then regularly 2–4 monthly until 2 years of age or until HT resolved.
Results
There were 37 term infants (27 males) with a raised TSH (>5 mU/l) and normal FT4 level over the 5-year period. This represents 2.6% of the 1449 term infants found to have HT. All infants with HT were born in good condition. Mean gestation was 38.1 weeks ($\pm$2.1 SD, range 33.1–42.0). 4 infants had Trisomy 21 and 3 infants had a maternal history of hypothyroidism. In 2 infants, we started levothyroxine treatment due to rising TSH and falling FT4 levels. 9% of infants had TSH normalised to 5 mU/l in 4 weeks without treatment, 54% normalised their TSH in 8 weeks, 83% normalised in 3–6 months, 94% normalised in 12 months and 1 patient had persistent TSH >5 mU/l which did not require treatment at 24 months.
Conclusions
In 95% of all the cases of HT in well term infants, the natural course was that the TSH resolved to normal $<$ 5 mU/l by 2 years of age. In 3% of cases, TSH remained elevated (> 5 mU/l) at 2 years but FT4 levels were normal and in the upper quartile range (>15 pmol/l) without treatment. We recommend TFTs monitoring due to the risk of decompensation although the risk of decompensation is low; and frequency of monitoring can be reduced after 2 years.

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OC5.3

Causes of central diabetes insipidus in children: a single-centre experience

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Background
Central diabetes insipidus (CDI) presents with various underlying diagnoses in children.
Objective
To determine causes of CDI and long-term outcome in children and adolescents from a Tertiary Paediatric Endocrinology unit providing Regional Paediatric Neurosurgery and head trauma services.
Methods
The clinic database was searched to identify patients with CDI managed between 1993 and 2019. Relevant clinical information was collected from electronic patient records.
Results
A total of 155 CDI patients, median age 6 years (range $<$1–18) were identified. Principal CDI aetiologies were craniopharyngioma ($n=44$, only 1 had CDI pre-surgery), midline CNS malformation ($n=20$), post-neurosurgery (non-craniopharyngioma; $n=18$), germ cell tumor (GCT; $n=15$), CNS infection ($n=14$), head trauma ($n=9$) and Langerhans cell histiocytosis ($n=6$). Miscellaneous causes included raised intracranial pressure ($n=8$), ventricular haemorrhage ($n=8$), pituitary apoplexy ($n=1$) and IgG4 hypophysitis ($n=1$). Threepatients had familial disease. Eight patients currently have idiopathic disease. Of the 15 GCT patients with CDI, six presented with CDI and GCT concurrently and five were diagnosed with GCT after median interval of 4 years (range 3–5) from CDI presentation. Four patients developed CDI after tumour debulking/biopsy. An additional seven GCT patients in our database did not develop CDI. Of the seventeen patients with head trauma-/brain haemorrhage-associated CDI, seven died before hospital discharge, four had transient CDI and 1 was lost to follow-up. Of the 20 midline CNS malformation patients, 12 had Septo-optic Dysplasia (SOD). An additional 60 SOD patients in our cohort had hypopituitarism without CDI. Of the 14 patients with CDI associated with CNS infection, two died during the initial illness, one had transient CDI and three were lost to follow up. A further seven patients from this subgroup died subsequently, one of which was due to inappropriate management of CDI and one patient has persistent CDI.
Conclusion
In our Tertiary Paediatric Endocrine setting, the most common etiologies of CDI were craniopharyngioma, other intracranial tumors and malformations. Presentation of craniopharyngioma with CDI in this series was very rare. 50% of GCTs had CDI as part of first manifestation symptomatology. CDI associated with CNS trauma, haemorrhage and infection carries very poor prognostic outcome.

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OC5.4

Tolvaptan for hyponatraemia in infants with brain tumours

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Background
Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH) is a well-recognized complication of intracranial tumours (ICT). Fluid restriction as treatment for SIADH is challenging in infants since it is coupled with calorie restriction. Moreover, it may conflict with chemotherapy-associated hyperhydration protocols. Existing evidence on the use of the type-2 vasopressin receptor antagonist (Tolvaptan) for refractory SIADH in infants and young children is limited.
Objective
To assess the efficacy and safety of Tolvaptan in managing infants with ICT associated SIADH.
Methods
Retrospective review of clinical data on patients diagnosed with ICT associated SIADH in infancy and treated with Tolvaptan at our quaternary centre (2012 and 2019).
Results
We identified 4 children (2 females; 2 males) matching the entry criteria and data on clinical presentation, management and treatment outcome of SIADH. Three patients (5, 5, 24 months) were diagnosed with suprasellar pilocytic astrocytoma of whom one receiving chemotherapy at the time of SIADH. One diagnosed antenatally with a large supra-and-infra tentorial teratoma was receiving palliative care from 10 days of life. Severe and persistent hyponatremia (range 118–130 mmol/l) occurred in all within 4–8 days of neurosurgical biopsy (2), shunt revision (1) or tumour debulking (1). All patients were euvolaemic, meeting diagnostic criteria for SIADH with normal renal, adrenal and thyroid function. Serum copeptin was elevated in 2 patients. All patients were refractory to initial fluid restriction. Salt supplementation in one patient resulted in hypertension. Tolvaptan was started 4 to 16 weeks after SIADH diagnosis, initially at 0.1 mg/kg per day and titrated up to 1 mg/kg per day according to urine output and plasma sodium (P.Na). P.Na normalised and fluid intake was liberalised without side effects in all patients. In one patient SIADH resolved after 2 weeks of Tolvaptan (maximum dose 0.2 mg/kg per day), the others being switched to Urea [1–1.5 g/kg per day, dose range 2–15 g BD] for cost-effectiveness after > 1 week.
Conclusion
Tolvaptan is a safe and effective therapeutic option in children with intracranial tumours and SIADH to optimise calorie intake and facilitate intravenous hydration during chemotherapy. Close twice daily monitoring of P.Na and urine output to inform safe dose titration during Tolvaptan therapy is imperative.

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OC5.5

Recombinant human Insulin-like growth factor-1 (rhIGF-1) therapy: a 15-year experience in a tertiary care centre

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Background
Recombinant human Insulin-like growth factor-1 (rhIGF-1) is the only treatment for short stature due to primary IGF-1 deficiency and related disorders. However, treatment needs meticulous monitoring for adverse effects, especially hypoglycemia, obstructive sleep apnoea (OSA), raised intracranial hypertension, cardiac complications and skin reactions.
Method
To determine therapeutic potential, efficacy and safety of rhIGF-1 treatment, case notes were reviewed for all patients treated in a tertiary care centre. Diagnosis, rhIGF-1 doses, height velocities (HV) and adverse effects were documented.
Results
11 patients (8 male) received rhIGF-1 over 15 years. Underlying diagnoses included: Laron syndrome ($n=3$); GH insensitivity due to signaling defects ($n=3$) or unknown aetiology ($n=3$); GH gene deletion with GH antibodies ($n=1$); syndrome with complex panhypopituitarism unresponsive to GH therapy ($n=1$). Median presentation was 2.23(1.57–13.97) years. Starting rhIGF-1 dose was 73–80 (g/kg/day at 5.14(2–22.6) years. In 10 patients, HV increased; the syndromic child with panhypopituitarism was unresponsive to rhIGF-1. Mean HV pre-treatment was 3.66(1.75–6.46)cm/year. With rhIGF-1, maximal HV occurred within 3–6 months (7.55 cm/year), followed by gradual decline to 6.30 cm/year at 1 year, 6.25 cm/year at 2 years, and 4.73 cm/year after 4 years. Hypoglycaemia ($n=7$, 63.63%) was the most frequent adverse effect, then adeno-tonsillar hypertrophy leading to OSA ($n=3$), and cardiac left ventricular dysfunction ($n=1$). Hypoglycaemia, always pre-meal or fasting, occurred in the first 3 months of treatment; the earliest after only one rhIGF-1 dose. In 5 cases, hypoglycaemia resolved by giving rhIGF-1 post meals. However, in one case, bedtime cornstarch, and in another, overnight continuous feeds were needed to manage hypoglycaemia. The 3 OSA cases were within 4–10 months of starting treatment. One patient developed left ventricular dysfunction after 2 years. There were no reports of skin reactions or raised intracranial pressure.
Conclusion
rhIGF-1 therapy is a promising treatment for children with IGF-1 deficiency, resulting in increased HV. Hypoglycaemia is the most frequent side effect but can be successfully managed with dietary interventions. Clinicians must be mindful of other potentially life-threatening complications (OSA, cardiac failure), the need for monitoring and joint decision making with families. Further follow-up should take place within international registries.

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OC5.6

Monitoring and long-term disease activity in children with X-linked hypophosphataemia on conventional therapy

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Background
Conventional treatment of X-linked hypophosphataemic rickets (XLH) involves administration of oral phosphate and vitamin D analogues. Newer therapies such as Anti Fibroblast Growth Factor 23 antibodies (burosumab) have now become available. An important treatment goal is to heal rickets; assessed by normalisation of serum alkaline phosphatase (ALP) levels and resolution of radiological signs of rickets.
Objectives
(1) Assess disease severity on wrist and knee radiographs as determined by rickets severity scores (RSS) and Thacher scores on conventional therapy. (2) Determine the usefulness of serum ALP in assessing rickets severity on radiographs
Methods
Data was collected, retrospectively from case notes and electronic database, as part of National Institute for Heath and Care Excellence review of burosumab. Patients from 3 UK tertiary centres, with a confirmed diagnosis of XLH (*PHEX* mutation in the patient or family member) and $\geq$ 3 radiographs were included. Radiographs were scored for RSS and Thacher scores by a consultant in metabolic bone disease (RP) and radiologist (RS). Due to different assays used for ALP measurements, ALP z scores were calculated using age- and sex-specific mean/standard deviation (S.D.) CALIPER reference data. Spearman's correlation was used to determine the relation between ALP z scores and Knee RSS and Thacher scores.
Results
Forty (male = 12) patients with a median age of 9.3 years (range 0.8–18.9) were identified. Median age at diagnosis was 1.17 years (range 0.2–11.7). The majority (48%, $n=19$) were diagnosed in infancy. The median follow-up duration was 7.2 years (range 0.6–18.7). The mean $\pm$ S.D. knee RSS and Thacher score at baseline were 1.9 ± 1.2 ($n=19$) and 3.3 ± 1.3 ($n=8$) respectively and at most recent follow up visit were 1.6 ± 1.0 ($n=26$) and 2.4 ± 1.6 ($n=6$). The mean $\pm$ S.D. ALP z score at diagnosis and most recent visit were 4.2 ± 2.9 ($n=36$) and 4.1 ± 2.7 ($n=34$). There was no significant correlation between ALP z score and knee RSS ($r=0.17$) or wrist RSS ($r=0.32$) or Thacher scores ($r=0.14$).
Conclusions
(1) Conventional therapy was not effective in significantly improving biochemical and radiological features of disease.
(2) Lack of association of serum ALP with RSS limits its value as the sole indicator of rickets activity.

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OC5.7

Longitudinal changes in external masculinisation scores in boys born with XY disorders of sex development

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Introduction
Although a number of studies have reported on the External Masculinisation Score (EMS) and have validated its use for numerical descriptions of the external genitalia, the methodology in these studies has not considered longitudinal changes in EMS.
Objectives
To examine longitudinal changes in EMS in boys with XY Disorders of Sex Development (DSD) and determine the causes of these changes.
Methods
All boys of confirmed or presumed karyotype 46,XY who were reviewed at the DSD clinic at the Royal Hospital for Children in Glasgow from 2010 to 2018 were included. Patients on the I-DSD Registry and those who underwent an hCG stimulation test were also included. The information required to calculate the first and latest scores was obtained from medical records. Surgical interventions (SI) – orchidopexies, orchidectomies, hypospadias repairs, and biopsies – as well as therapeutic interventions (TI) – testosterone therapy – were recorded. Total EMS was calculated at first assessment (EMS1) and at the latest assessment (EMS2). This calculation was done in duplicate by two independent authors. Any discrepancies found were discussed and resolved.
Results
In total, 143 boys were identified, with a median age of 0.93 years (range 0.00–16.93 years) and 4.58 years (range 0.45–19.05 years) at EMS1 and EMS2, respectively. Median interval time between EMS1 and EMS2 was 3.26 years (range 0.27–15.48 years). Median EMS out of 12 was calculated as 9.0 (range 1.5–12.0) and 11 (range 3–12) at first and latest assessment, respectively ($P<0.0001$). Median change in EMS was 2 (range 9–11). Of the 143 boys, 121 had solely SI, one had solely TI, five boys had both SI and TI, and 16 boys had no intervention. In boys who had SI ($n=121$), 120 showed changes in their EMS. In boys who had TI ($n=6$), two showed changes in EMS, but this could also be attributed to their SI. There was no significant change in EMS in boys who had TI and no SI.
Conclusion
EMS increases over childhood and adolescence, and the main determinant of this increase is surgical intervention. Testosterone therapy is not a cause of EMS changes, but more research needs to be undertaken in a larger patient cohort.

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OC5.8

TSH-Receptor testing in pregnancy allows stratification of risk of neonatal thyrotoxicosis and promotes earlier discharge

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Background
Local guidelines for infants born to mothers with a history of thyrotoxicosis previously recommended that infants were observed in hospital until thyroid function tests were checked on day 4, with follow up on day 10, causing inconvenience to families and unnecessary cost to services. Following a literature search, our revised local guidelines recommend low-risk infants can be discharged on day 0 without follow up, stratified using maternal TSH-receptor antibody (TRAb) levels in pregnancy and whether siblings have been affected. A re-audit was undertaken to assess the effect of the new guideline.
Method
Infants were identified from the list of mothers who had thyroid disease noted in their maternity records, excluding those who had never been hyperthyroid. Removal of routine day 4 thyroid function tests in the new guideline prevented the previous method of identification. Health records of infants and mothers were reviewed to establish maternal thyroid history, maternal TRAb levels in pregnancy, length of stay, clinic follow up, thyroid function testing and symptomatic thyrotoxicosis in the infant.
Results
Twenty-two infants were identified in a one year period (55% male, 45% female), a significant reduction compared to the original audit ($n=57$). TRAb results were available on 11/23 (48%) patients, of which six were below 1 IU/l; results did not change the stratification in three infants, increased it in four patients and decreased it in another four. The median (IQR) length of stay reduced from 4 (4–5) to 2 (1–4) days ($P<0.001$). Two patients were incorrectly treated as low risk (primip without TRAb results) and one was incorrectly treated as high risk (unaffected sibling without TRAb results). No infants were symptomatic or required treatment.
Conclusions
Awareness of the option of early discharge has reduced the median length of stay despite risk category being raised in as many patients as it was lowered. Less than half of women had TRAb levels checked, especially where impression in antenatal endocrine was of non-Graves thyrotoxicosis. The reduction in the number of infants suggests the current method of identifying patients may need revising.

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OC5.9

Rare causes of primary adrenal insufficiency (PAI) in children from Sudan

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Background
Primary adrenal insufficiency (PAI) is a rare, genetically heterogenous condition, characterised by hypocortisolaemia and high plasma ACTH levels in the presence or absence of mineralocorticoid deficiency. PAI can be life-threatening if unrecognised, misdiagnosed or under/untreated. Familial glucocorticoid deficiency (FGD) is a rare autosomal recessive form of PAI characterised by isolated glucocorticoid insufficiency. Mutations in the *MC2R*/ACTH receptor, *MRAP*, *STAR* and *CYP11A1* account for >50% of cases of FGD. No previous studies have characterised PAI in the Sudanese paediatric population.
Aims
(1) To describe the clinical presentation of PAI in a small cohort of Sudanese paediatric patients, and (2) to identify monogenic causes of PAI.
Methods
Sanger sequencing was undertaken for variants of candidate genes: *MC2R*, *MRAP*, *STAR*, *CYP11A1* and, in one patient with clinical features of autoimmune polyglandular syndrome (APS) type-1, *AIRE*. Whole exome sequencing (WES) was performed for patients who were mutation negative on candidate gene sequencing.
Results
Fourteen patients from 13 families (7M; 7F, aged 0–7.5 yrs at presentation) with PAI of unknown aetiology were studied. The most frequent presenting clinical features were generalised hyperpigmentation (100%), fatigability (50%) and infection (43%). 29% of the patients experienced recurrent hypoglycaemia. Diagnosis was established biochemically with a low serum cortisol and high plasma ACTH. A genetic diagnosis was obtained in 2/14 patients by candidate gene approach. A homozygous missense mutation in *MC2R* (c.437G>A, p.R146H) previously reported to cause FGD and a homozygous nonsense mutation in *AIRE* (c.769C>T, p.R257X) linked to APS type-1. WES in a third patient revealed a novel homozygous nonsense mutation in *NNT* (c.69T>A, p.C23X). 11/14 PAI patients remain genetically unsolved and have been sent for WES.
Conclusion
Determining the aetiology of PAI can be challenging, owing to phenotypic heterogeneity. A genetic diagnosis can help guide management as well as provide vital prognostic information. Candidate gene approaches are still helpful and here solved 2/14 PAI children. However, with reducing costs, WES may by-pass candidate gene approaches and be the first line to solving the genetic cause of PAI.

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OC5.10

Review of neonatal cortisol evaluation between 2012–2018 in a single centre: trends, outcomes and associations

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Background
Neonatal cortisol assessment is indicated in suspected adrenal insufficiency.
Aims/objectives
Review of neonatal cortisol assessment within our Trust over seven years, to analyse trends, indications, outcomes; and relationships between gestational age (GA), birth weight (BW) and cortisol assessment.
Methodology
From cortisol results on neonates ($\leq$30 days age) between 2012–2018 (inclusive) we identified random/serial ('screening cortisols') versus cortisols done as part of Synathen tests. We analysed trends for testing. Further data collection was as follows:

- screening cortisols: Indication, number of tests, outcomes.
- Synacthen tests: Indication, type of test [short Synacthen test (SST) vs low dose Synacthen test (LDST)], results, short/long term outcomes, relationship to BW/GA.

Results
There were 412 cortisol tests over the 7 years, in 172 patients. Numbers were stable between 2012 and 2014, but between 2015/2016 and 2017/2018 there was a 230% increase in cortisol; and 430% rise in Syacnthen tests. This was despite stable admission rates: 1997 patients over 2015/2016 and 1916 in 2017/2018. Further results: Table 1.

Table 1 Screening cortisol versus Synacthen tests.

	Screening cortisols	Synacthen tests
Number of patients	143 (=83%)	29 (=17%)
Split	66.4% (n=95/143): single screening cortisol test	72.4% (n=21/29) were SSTs
	33.6% (n=48/143): ^{3}2 screening cortisol tests	27.6% (n=8/29) were LDSTs
Top 3 indications:	Hypoglycaemia(35.6%), ambiguous genitalia(16%), conjugated jaundice(9%)	Hypoglycaemia(44.8%), ambiguous genitalia(6.9%) and hyponatremia(6.9%)
Outcomes:	Only ONE patient was started on treatment based on just screening results. Subsequent SST confirmed adrenal insufficiency.	38% of the initial Synacthen tests were abnormal (n=11/29). Of these only 36% (n=4/11) remained on treatment after age of 2 years: Dx=2x Hypopitutarism + 1x Hypoglycaemia, SGA and maternal pre-eclampsia +1 Preterm (repeat SST pending).

There was no significant relationship between premature versus term deliveries and abnormal Synacthen tests (P=0.32); or between BW (i.e. SGA vs AGA) and abnormal Synacthen tests (P=0.67).
Summary/conclusions
Despite an exponential increase in cortisol assessments, 91% of testing indications were appropriate. Initial pick-up of adrenal insufficiency was low (6%). Subsequent reassessment of adrenal function is imperative as 64% of these results were transient. There were no associations between BW or GA and abnormal Syancthen results.

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Oral Communications 6

OC6.1

A survey into the care of children with type 2 diabetes in England and Wales

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Background
The incidence of type 2 diabetes in childhood in the UK is increasing. It is often an aggressive disease associated with poor health outcomes. Despite this, there is little formal training and evidence based guidance.
Objectives and method
A questionnaire was sent to each paediatric diabetes unit in England and Wales, evaluating variation in practice, training and confidence in the management of type 2 diabetes.
Results

- 83 out of 173 units responded, including tertiary centers and district general hospitals and incorporating different professionals within the multidisciplinary team.
- Most centers – 62%, provided care for relatively few (between 0 and 4) patients with type 2 diabetes.
- There was a wide variation on service and care provision between centres. For example the guidelines being used, with 18% were uncertain if they were following guidelines or not. A minority were offering a structured education program. 8% offered separate clinics for Type 2 diabetes and 30% had access to healthy eating and exercise programs.
- 70% did not have formal training in managing type 2 diabetes and 76% felt under-confident in managing the condition.
- 60%, rated their service's impact on quality of life and health of patients as a small positive or none at all.
- One in five units said their team had
  – no formal training,
  – low confidence,
  – little or no support from adult services.

Respondents requested:

- Further education and training. Popular suggestions were:
- Network events, a national training program and team training events.
- Evidence based national guidelines.

Conclusions
The majority of children with type 2 diabetes are cared for in centers that have small patient numbers highlighting the need for sharing good practice, training and guidelines. There is wide variation in the services offered to children with type 2 diabetes across England and Wales with the most units having no formal training. Consequently the majority of respondents rated their confidence as low. This survey highlights the need for standardisation of care and service provision with nationally accredited guidelines training program in order to help improve outcomes.

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OC6.2

An exploration of the perceptions and lived experience of primary school aged children using insulin pump therapy

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Background
In the UK, the use of insulin pump therapy in children with Type 1 diabetes is increasing. Many studies have investigated the effectiveness of this treatment in improving biomedical outcomes and quality of life measures. However, few studies have explored the perspectives of children themselves on their use of pump therapy, particularly in the pre-adolescent age group. This study focussed on primary school aged children and aimed to explore in depth how they experienced insulin pump therapy in the context of their everyday lives.
Methods
This was a qualitative study using a hermeneutic phenomenological research design. Fifteen children were recruited from two paediatric diabetes clinics in England. Each child participated in a single semi-structured interview conducted in the home setting. Data was used analysed for themes to describe their experiences.
Results
Diverse and sometimes contradictory experiences were highlighted, demonstrating that children were both helped and hindered by their treatment. Although young, they were actively involved in the management of their own condition not only operating the technology themselves, but also in managing their identities and adjusting to their treatment. Despite the considerable effort that this involved and the negative experiences they described, all but two of the children were enthusiastic about pump therapy and viewed it favourably. Six key themes were

used to illustrate these findings: Disrupted bodies / Disrupted lives; Transformed bodies / Enhanced lives; Shaping identities – feeling different and the same; Empowering / Disempowering; 'Getting used to it' and Feeling supported / Being unsupported.

Conclusions

The findings offer clinicians the opportunity to gain a deeper understanding of what it might be like for a young child to use insulin pump therapy every day. This in turn, may help to ensure that the delivery of care and support to these children is responsive and relevant to their particular needs.

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OC6.3

Here's the POInT: a multicentre European Primary Oral Insulin Trial

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Introduction

The successful prevention of type 1 diabetes (T1D) is a major clinical goal. The pathogenesis is multifactorial, with genetic and environmental influences that lead to a break in immune tolerance toward pancreatic beta cells. Through a number of prospective cohort studies, it is now understood that the presence of two or more diabetes-associated autoantibodies is highly predictive of future T1D diagnosis. In addition to the genetic rationale (insulin gene sequence variations increasing T1D risk four fold), insulin autoantibodies, often appearing first within 9 months after birth, indicate that the loss of tolerance to insulin is an important step in the progression of T1D and therefore if prevented, T1D could be delayed or avoided.

Aim

As part of the Global Platform for the Prevention of Autoimmune Diabetes (GPPAD), the aim of POInT (Primary Oral Insulin Trial) is to conduct a T1D primary prevention, double-blind randomised controlled trial, aiming to induce tolerance towards insulin by administering oral insulin.

Design

Through the INGR1D study (Investigating Genetic Risk for T1D) babies are genetically screened for a 1:10 chance of developing multiple autoantibodies (against a background risk of 1:250). Between 4 and 7 months of age, participants with an increased risk of T1D can enrol to POInT and are subsequently randomised 1:1 to receive either daily placebo or oral insulin until their 3rd birthday. Follow-ups are mostly at 6-monthly intervals thereafter, with a maximum 7-year follow-up. There are currently seven study centres across five European countries recruiting to INGR1D and POInT, with the aim to screen 300 000 newborns over 3.5 years, leading to randomisation of 1,040 children into the trial.

Analysis

At every visit, participants are tested for the presence of autoantibodies against insulin, GAD65, IA-2 and ZnT8. The primary outcome is the development of multiple autoantibodies or diabetes. Secondary outcomes include single autoantibodies or an abnormal glucose tolerance test. The POInT accrual objective of 1040 children provides 80% power to detect a 50% reduction in the incidence of beta-cell autoantibodies by age 6 years.

Accruals to date

Between October 2017 and June 2019, over 95 000 and 290 participants have enrolled to INGR1D and POInT respectively.

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OC6.4

Exam preparedness in students with type 1 diabetes and their schools – a quality improvement study

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Introduction

Type 1 diabetes (T1D) is a lifelong condition affecting over 29 000 children in the United Kingdom, the majority of whom are in full time education. Both hypoglycaemia and hyperglycaemia have been shown to impact the young person's overall school performance and learning capacity. During exams, children and young people (CYP) with T1D have the additional stress of managing their diabetes appropriately, and therefore require special provisions. Currently, the reference for schools for special arrangements in exams is the 'Access Arrangements and Reasonable Adjustments' document. However, this 105-page document only mentions the word 'diabetes' once. The Diabetes UK leaflet, 'Type 1 Diabetes and School Exams', is a valuable resource.

Aim

To analyse how prepared schools, exam boards, and CYP with T1D are in dealing with diabetes during school exams.

Methods

We distributed anonymised questionnaires to participants in the Cardiff and Vale area, including students with T1D in school years 10, 11 and 12, their families, schools, and exams officers.

Results

Almost all parents reported that their child's diabetes affected their exam performance a moderate amount or less, whereas nearly half the students said their diabetes significantly affected them during exams. Over 90% of students said their blood glucose levels were more difficult to manage during revision and exams, whereas only 60% of parents agreed with this. Whilst 70% of parents had discussed exam arrangements with school, less than half the students were involved in these discussions. 50% of school staff had contacted the diabetes team during exam periods, whereas none of the exams officers had. 45% of the students had read the Diabetes UK leaflet, in contrast with just one of the school staff and one exams officer.

Conclusion

Our study clearly highlights that CYP with diabetes are not receiving the special provisions they require to achieve their full potential during exams. The diabetes teams, students, families, schools and exam boards need to work together to ensure that all parties involved feel more prepared. We have highlighted areas for improvement in order to create a resource for schools to help support CYP with T1D sitting exams.

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OC6.5

Factors affecting the practice of routinely downloading blood glucose data at home for families and children with type 1 diabetes

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Background

In type 1 diabetes (T1D), optimal glycaemic control requires intensive self-management to reduce the risk of complications. While routine downloading and review of blood glucose data is part of clinical practice of healthcare providers in an outpatient setting, patients and families are also educated, advised and encouraged to regularly download and review blood glucose data at home in order to make adjustments to insulin dosing for carbohydrate intake and insulin sensitivity factors. In this study, we describe the characteristics between two groups of patients with T1D who routinely download and review their blood glucose data at home compared with a cohort that do not download data at home.

Methods

Patients and their families were considered a 'routine downloaders' (RD) if their blood glucose device data was downloaded and reviewed at home at least once a month between routine clinic visits which was scheduled every three months. 'Non-downloaders' (ND) were defined by those who did not download or review data at home at least once a month, despite being educated on the use of free software and encouraged by healthcare professionals to download regularly. We evaluated demographics, age, duration of diagnosis, socioeconomic deprivation scores, quality of life scores and mean Hb1A1c between RD and ND patients.

Results
98 patients were included in the study (52 males) with a mean age at diagnosis of 7.4 years (S.D. ±3.8, range 1.1–15.0), mean diabetes duration of 5.2 years (S.D. ± 0.36). The patients' characteristics are reported with 33 in the RD group and 65 patients in the ND group. Mean HbA1c (mmol/mol) in the preceding 12 months was significantly better in the RD group (60 vs 66, $P=0.03$). The ND group had significantly poorer overall deprivations scores, poorer employment and education levels ($P<0.05$). Multivariable regression analysis examining the factors affecting families downloading found that overall deprivation was the only independent determinant ($P=0.03$).
Conclusions
This study shows that social deprivation is an important determinant towards the practice of routinely downloading data at home for families with T1D. Healthcare professionals should target deprived areas with further support, education and resources for management of T1D.

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OC7.1

Increased and younger alcohol-related hospital admissions in young people with childhood-onset type-1 diabetes: a record-linked longitudinal population study in Wales

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Background
Children and young people with type-1 diabetes (T1D) have excess all-cause hospital admissions, particularly younger children with lower socioeconomic status. Education on managing alcohol is provided to teenagers with T1D in paediatric clinics, but its effectiveness is unknown. We compared the risk of alcohol-related hospital admissions (ARHA) in young people with childhood-onset T1D with the general population for the same birth years.
Methods
We extracted data for 1 791 577 individuals born 1979–2014 with a GP registration in Wales, and record-linked these to ARHA between 1998 and June 2016 within the Secure Anonymised Information Linkage Databank (SAIL). Diabetes status was ascertained by record-linkage to a national register (Brecon Cohort), containing 3 575 children diagnosed with T1D aged <15 years since 1995. Linkage to the Welsh Demographic Service dataset provided information on age, sex and the lower super output areas (LSOAs) of residence, including moves, and linked Welsh Index of Multiple Deprivation 2008 quintiles. We censored for death or leaving Wales. We estimated hazard ratios (HRs) with 95% confidence intervals (95% CIs) for the risk of ARHA for sex, age and deprivation group using recurrent-event models, including interaction terms.
Results
There were 37 905 admissions and 19.1 million person-years of follow up. Individuals with T1D had 248 admissions (up to 4 admissions each), and overall had a 78% higher risk of ARHA (HR 1.78; 95% CI 1.60–1.98) adjusted for age group, sex and deprivation. In diabetic individuals the risk of ARHA was highest in the 14–17 year-old age-group (HR 6.01; 95% CI 4.70–7.75), 2.7 times higher than the peak in the general population aged 18–22 (HR 2.23, 95% CI 2.14–2.32), both relative to 11- to 13-year olds in the general population. Socioeconomic inequalities in ARHA were smaller for the T1D group.
Conclusions
Young people with T1D have increased risks of ARHA, highest at school age (14–17 years) and earlier than the peak at student age (18–22 years) in the general population. New effective interventions aiming to reduce alcohol-related harm in T1D are needed. These may include modification of current education and guidance for teenagers on managing alcohol consumption and reconsideration of criteria for hospital admission.

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OC7.2

Impact of continuous glucose monitoring on sleep quality in children with type 1 diabetes and their parents: a pilot study

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Introduction
Many children with Type 1 Diabetes (T1D) and their parents/carers anecdotally report poor sleep quality. This is particularly problematic in patients experiencing frequent hypoglycaemia despite intensive blood glucose monitoring (BGM). Continuous glucose monitoring (CGM) overcomes some of the burdens of BGM and can reduce overnight hypoglycaemia.
Objectives
This pilot study explored the impact of CGM on sleep quality in children and adolescents with T1D experiencing labile glycaemic control and frequent hypoglycaemia. Impact of CGM use on parental sleep quality was also investigated.
Methods
Actigraphy was used to measure sleep quality in children and adolescents aged 2–-18 with T1D ($n=10$) and their parent(s) ($n=18$). Sleep quality was measured one week prior to the patient starting CGM and during week 5 of CGM use. Additionally, all participants recorded a sleep diary during each sleep monitoring week.
Results
Sleep efficiency improved by 7.03% in children and adolescents (95% CI 3.09 to 10.99; $P = 0.003$), and 4.14% in parents (2.21 to 6.06; $P < 0.001$). This was accompanied by a significant reduction in nocturnal wakening. In children and adolescents, mean reduction in nocturnal wakening was 42.5 minutes (−66.5 to −18.4; $P = 0.003$), and in parents, 18.5 min (−28.6 to −8.4; $P < 0.001$).
Conclusions
This was the first study that objectively explored sleep quality in both children and adolescents with T1D, and their parents, before and during the use of CGM. The improvements in sleep efficiency and nocturnal wakening may be clinically significant for both patients and parents with regards to functioning, quality of life and neurocognition. Reasons for improved sleep quality may include reduced overnight disturbance from BGM, reduced hypoglycaemia and reduced anxiety related to hypoglycaemia. These factors may directly and indirectly impact upon an individual's T1D self-management and consequently, may affect a patient's glycaemic control. This area warrants further research.

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OC7.3

Improving HbA1c outcomes in young people of transition age with type 1 diabetes using quality improvement methodology

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Introduction
Effective transition care is vital to empower young people (YP) to optimally self-manage their diabetes. National data highlights the concern regarding poorer care outcomes due to lower completion of annual care processes and higher rates of DKA whilst transitioning to adult care. The Children and Young People's Diabetes Team provides care for 170 YP aged 16–19 years. In April 2017, 19% of this age group had a HbA1c <58 mmol/mol, significantly lower than the total clinic population of 29%.
Aim
To increase the percentage of 16–19 year olds achieving a HbA1c of <58 mmol/mol by 10% each year commencing in September 2017.
Method
All multi-disciplinary team members were trained in Quality Improvement (QI) as part of a Trust wide Transition Transformation Programme. Process mapping of the transition model of care for 16–19 year olds identified patient pathway improvements. The success of interventions was tested using 'Plan Do Study Act' (PDSA) cycles. Interventions included; monthly HbA1C tracking, recruitment to structured education, employment of a Youth Worker, signposting to online resources, parent support sessions and development of an age-adjusted annual review proforma in conjunction with the Ready, Steady, Go programme for individualised care.
Results
In April 2018, the goal of 10% improvement in one year was met by 9 months, with 29% of YP achieving a HbA1c <58 mmol/mol. This transition improvement work continued during participation in the RCPCH National Diabetes QI programme from November 2018 to June 2019, and saw a further improvement to 37% achieving the aim.
Conclusion
The success of the interventions were due to the whole team adopting and implementing changes, despite the challenge of scheduling regular meetings to

suit all team members. Review and tracking of real-time data allowed timely feedback of intervention effectiveness reinforcing the value of all team members' efforts. Support of YP from a Youth Worker improved service engagement especially with structured education. Effective transition care is vital to empower YP to optimally manage their diabetes during this critical time. Further work is planned to develop a fully integrated diabetes service for 19–25 year olds working closely with our adult diabetes colleagues.

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OC7.4

Monitoring lipid profiles in children and young people with type 1 diabetes mellitus: what should we do with these results?

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Introduction
Evidence is currently limited regarding the management of abnormal lipid profiles in children and young people (CYP) with Type 1 Diabetes Mellitus (T1DM). ISPAD recommend monitoring every five years and statin use to maintain LDL cholesterol <3.4 mmol/L[1]. Guidance is specific to LDL. NICE guidelines do no recommend routine screening for CYP with T1DM.
Methodology
We reviewed all lipid profiles (including cholesterol, triglycerides, LDL and HDL) performed in our population of CYP with T1DM over 12 months. We recorded the results and management of these lipid profiles.
Results
351 patients had their lipid profiles checked as part of their annual review process. 108 patients had an abnormal profile. 47 patients had a high LDL (>2.85 mmol/l). 30 patients had their lipid profiles repeated when fasted. The results of these are shown in Table 1.

Table 1: Table showing results of repeated fasting samples where LDL was >3.3 mmol/l.

	Number of patients
Sample not repeated	13
LDL improved to within the normal range (<2.85 mmol/l)	5
LDL improved to <3.3 mmol/l but remained >2.85 mmol/l	5
LDL remained >3.3 mmol/l	7
LDL remained >4	1

47 patients required additional dietetic and lifestyle interventions to further tighten their diabetes control. 7 patients fit the criteria for consideration for statins.
Conclusion
There is limited evidence regarding the use of statins in CYP with T1DM. 2% of our population fit the criteria for consideration of statins whilst 14% have a raised LDL requiring more intensive management of their diabetes, diet and exercise. Other parameter abnormalities, including raised triglycerides and cholesterol and reduced HDL, are common affecting 31% of our population. There is even less evidence relating to the outcomes associated with these abnormalities. NICE suggest using a cardiovascular risk assessment in adults before performing lipid profiles and treating with statins[2]. There is no guidance for CYP with T1DM. We suggest that further prospective studies are required to address these issues and further our knowledge of lipid abnormalities in CYP with T1DM.
References
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2. NICE Cardiovascular disease: risk assessment and reduction, including lipid modification (CG181) 2016.

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OC7.5

Medication adherence during adjunct therapy with statins and ACE inhibitors in adolescents with type 1 diabetes

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Background
Suboptimal adherence to insulin treatment is a main issue in adolescents with type 1 diabetes (T1D). However, to date, there are no available data on adherence to adjunct non-insulin medications in this population. The aims of this study were to assess adherence to ACE inhibitors and statins and explore potential determinants in adolescents with T1D in the context of a clinical trial.
Methods
443 adolescents (aged 10–16 years) were recruited into the Adolescent Type 1 Diabetes cardio-renal Intervention trial (AdDIT) and exposed to treatment with two oral drugs: an ACE inhibitor, a statin, combinations of both or placebo for 2–4 years. Adherence was assessed every 3 months with the Medication Event Monitoring System (MEMS) and pill count. The effect on adherence of baseline age, diabetes duration, age at diagnosis, HbA1c, method of insulin administration, country and sex were assessed.
Results
Median adherence during the trial was 80.2% (interquartile range: 63.6–91.8), based on MEMS, and 85.7% (72.4–92.9) based on pill count. Adherence dropped from 92.9% at the first visit to 76.3% at the last visit. Adherence was lower in participants with an HbA1c >85 mmol/mol (69.4 [50.8–87.1]%) vs those with an HbA1c 58–85 mmol/mol (79.5 [63.3–91.0]%) and <58 mmol/mol (88.1 [75.5–93.9]%), $P=0.001$. Adherence varied across the three countries involved in the AdDIT trial: Australia (83.4[70.1–92.9]%), UK (78.9 [61.7–91.6]%) and Canada (73.8[56.8–88.3]%), P for trend$=0.001$. There was also a trend for a decreasing adherence with age ($P=0.07$).
Conclusions
We report a good adherence rate with ACE inhibitors and statins in adolescents with T1D. Older age and higher HbA1c predicted adolescents with worse adherence, highlighting two key potential targets for strategies aiming at improving adherence. Adherence also differed by countries likely reflecting differences in practice or approaches between countries. *On behalf of the Adolescent type 1 Diabetes cardio-renal Intervention Trial (AdDIT) study group.*

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OC7.6

Improving referral pathways from primary to secondary care in newly diagnosed type 1 diabetes

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Introduction
Most children & young people (CYP) with symptoms of type 1 diabetes (T1D) tend to present to primary care. Delayed diagnosis is common and is associated with a risk of developing diabetic ketoacidosis (DKA). The prevalence of DKA at diagnosis over the last 20 years remains unchanged despite current NICE guidance and Diabetes Delivery Plans which promote prompt diagnosis of T1D. The aim of this QI initiative was to develop effective pathways to facilitate early diagnosis of T1D with the primary long-term objective of reducing the DKA incidence at diagnosis.
Methods
Key partners in primary and secondary care identified barriers faced by healthcare professionals and developed QI initiatives to improve timely diagnosis. This included a simple referral pathway, feedback tools and sustained GP training in early recognition of diabetes. Two annual audit cycles using retrospective case note analysis of all newly diagnosed CYP in Cardiff were completed. The first cycle (2017) represented pre-change with the second cycle after adopting QI changes in 2018. Key outcomes included blood glucose (BG) testing and prompt referral.
Results
Pre change: 22 CYP were newly diagnosed with T1D,19/22 presented to primary care; of the 19, 4 were in DKA, 10 had point of care(POC) BG testing and 2 had urine tests prior to referral. 3 had had fasting BG resulting in delayed referral. 3 of the 4 in DKA had delayed diagnosis. Post QI initiatives: 32 were newly diagnosed, 22/32 presented to primary care; of the 22, 6 were in DKA,17 had POC BG test, and 3 had urine tests. Of the 6 in DKA, 5 were at first presentation to

primary care, had POC testing and were promptly referred. Post QI initiatives, 91% had POC testing and prompt referral to secondary care, contrasted with 63% pre change.
Conclusion
Although there was no reduction in overall DKA rates at diagnosis of T1D, we have demonstrated a clear improvement in prompt diagnosis following QI initiatives between primary and secondary care. This QI programme is now being tested across other parts of Wales with a long-term plan to promote early diagnosis and reduce the incidence of DKA.

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OC7.7

Paediatric Type 2 diabetes in a single centre in East London in the period 2009–2018

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Background
The incidence of Paediatric type 2 diabetes is increasing, especially in areas of deprivation.
Aim
To describe the cohort of CYP with T2D in Royal London Hospital over the period 2009–2018.
Methods
Retrospective analysis of patient cohort.
Results
Number of new patients doubled from 2.6/year in 2009–2013 to 5.3/year in 2014–2018. Prevalence in our cohort is 7.5% (national average of 2.5%, NPDA 2017–2018). Fourty patients (25 female, 15 male) were diagnosed in 2009–2018, with a mean age at diagnosis of 13.9+/−1.7yrs. Males had more frequently learning difficulties compared to females (40% vs 20%). Sixty % of patients were Asian compared to 28% in our T1D cohort. BMI at presentation was 31.5 kg/m^2 (23 females) and 33.85 kg/m^2 (13 males). BMI remained stable for females for the first year after diagnosis but in males increased to 34.6 kg/m^2 ($n=10$). At diagnosis, Metformin was started in 38/40 patients although 7 patients reduced the dose and 6 stopped due to side effects. 12/36 patients started also on long-acting insulin (0.28+/−0.17 U/kg), in 6 combined with prandial insulin (0.42+/−0.20 U/kg). Seven patients started long-acting insulin at a later stage and 6 required prandial insulin too. 1 patient was treated with Sitagliptin. HbA1c at diagnosis ($n=27$) was 75.2+/−20 mmol/mol, similar for males and females. HbA1c dropped to 55.0+/−17.4 mmol/mol after 3 months, to increase again to 63.0+/−25.8 and 67+/−28 after one ($n=25$) and 2 years ($n=23$). Nineteen of 38 patients achieved a HbA1c $<$ 48 at least once, but only 9 of 35 achieved an HbA1c $<$ 48 for a year. Of these, 3 continued to be on insulin and in 1 patient insulin was stopped. Two patients relapsed. Complications were as follows: 11/21 hypertension, 6/28 sleep apnoea, 10/30 raised ALT and 9/24 fatty liver.
Conclusion
Learning difficulties in patients with T2D are frequent. Complications of obesity/T2D are common in this cohort. Current treatment does not achieve permanent reduction in BMI and HbA1c in most patients although temporary reduction of HbA1c is possible. New treatment approaches are needed to improve outcomes.

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OC7.8

Children with type 1 diabetes on intensive insulin, in deprived areas and younger onset are at risk of being overweight

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Introduction
Children with type 1 diabetes mellitus (T1DM) are at increased risk of being overweight. Being overweight could be related to insulin requirements, female gender, and duration of diabetes. The aim of this study is to examine the Body Mass Index (BMI) of children and young people with T1DM at the Children's Hospital for Wales and explore co-factors that may contribute to risk.
Methods
A retrospective review of all patients with T1DM attending the Children's hospital for Wales from May 2016 to May 2019 was undertaken. Age and gender adjusted BMI (weight[kg]/height^2[metres]) centile for the latest recorded visit was compared to HbA1c, insulin regimen, total daily insulin dose, duration of diabetes, and deprivation index.
Results
Overall BMI centile of children with T1DM in this population was high at 69 (95% CI 65–71). BMI centile was associated with daily insulin dose ($r=0.24$, $P=0.01$). On average those using pumps had a higher BMI centile and lower HbA1c respectively compared to those on MDI (74 (95% CI 68–79) vs 65 (95% CI 61–70) $P=0.043$ and 63 mmol/mol (95%CI 60–65) vs 71 mmol/mol (95% CI 68–74) $P<0.0001$). Children living in the most deprived quintile had a BMI 9 centiles higher than those living in the least deprived quintile ($P=0.035$). A multiple regression showed that a younger age at diagnosis, duration of diabetes, living in a higher level of deprivation, a higher total daily insulin dose, and usage of pumps, were all risk factors for a higher BMI ($P<0.0001$).
Conclusion
Children with T1DM have a higher BMI than the UK reference population. A higher BMI centile was associated with living in higher deprivation areas, a younger age of onset and more intensive insulin regimens. Being overweight is a risk factors for developing long-term adverse cardiovascular outcomes in T1DM and care should be taken to monitor weight carefully.

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OC7.9

Does having a first degree relative with type1 diabetes impact on a child and family's engagement and glycaemic control?

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Introduction
Although not directly inherited, genetics play a significant role in the chances of developing Type1 Diabetes (T1DM), yielding a risk of 2–40% depending on the first degree relative (FDR) affected. T1DM is a self-managed condition in which education and patient/carer engagement are key. We had noted cases of poor engagement and glycaemic control in our patients with a FDR with T1DM but found a paucity of literature examining this relationship.
Methods
We conducted a retrospective, case-controlled study in spring 2019. Our study cohort of patients with one or more FDR with T1DM were matched by age, sex, insulin regimen, duration of diabetes and age at diagnosis. We collated data on clinical presentation, HbA1c, hospitalisations, insulin regimen and clinic attendance (including education clinic). Statistical analyses used Students' *t*-test, Mann–Whitney *U* and Fisher's exact test.
Results
We identified 25 patients (11F) with a FDR with T1DM, ~12% of our patient population. Eleven had a parent, 12 at least one sibling and two both a parent and sibling affected. For the study and control cohorts: mean age at diagnosis was 8.12 (range 0.92–15.92) and 9.26 (2.17–15.67); mean duration of T1DM was 6.53 (1.27–16.80) and 5.70 (0.57–15.11) and mean deprivation decile was 3.80 and 3.71 respectively. There were no significant differences in these figures or insulin regimen between the two groups. At presentation, the study cohort had lower mean HbA1c (87.7, 110.5 mmol/mol; $P=0.02$). Although not statistically significant, fewer patients in the study cohort presented in DKA (13.6%, 31.6%; $P=0.46$) and a lower proportion had subsequent hospital admissions for DKA (25%, 37.5%; $P=0.24$). The study cohort had a higher mean HbA1c one year after diagnosis (65.2, 56.6 mmol/mol, $P=0.02$). Although not significant, the study group had poorer clinic (81.3%, 87.2%; $P=0.17$) and education clinic attendance (30.09%, 33.88%; $P=0.60$).
Discussion
Our patients with a FDR with T1DM presented earlier but had a higher HbA1c a year after diagnosis with a trend to lower levels of engagement with the diabetes team, highlighting the need for healthcare professionals to guard against complacency and ensure appropriate support and education for patients with a FDR with T1DM.

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OC8.1

Random cortisols – as useful as a chocolate teapot (but less tasty)?

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Introduction
Unstimulated cortisol is commonly used as a screening test for adrenal insufficiency. In the UK over the last decade there has been a large increase in the numbers of requests for cortisol being made in both primary and secondary care. To increase the specificity of an unstimulated cortisol, and thus reduce unnecessary referrals and Short Synacthen Tests, the recommendation is that an early morning cortisol (EMC) is performed between 08:00 and 09:00 h. There is evidence that an EMC below <160 nmol/l is highly predictive of failing the SST and the corollary is seen with an EMC above >340 nmol/l. We analysed our cortisol data over a six-month period to evaluate the proportion of samples taken outside the recommended time period and evaluate the effect of timing on the cortisol result.
Methods
A retrospective analysis was performed of all serum cortisol samples processed in our Trust between November 2017 and April 2018. Cortisol samples taken as part of a hypoglycaemia screen or SST were excluded. Cortisol quantification was performed on the Abbott Architect i1000 chemiluminescent immunoassay (CVs <5%). Based on published data the results were grouped into <160 nmol/l, 160–339 nmol/l or >339 nmol/l and the time each sample was taken collected. Before 09:15 h (to allow some leeway) was considered 'early morning cortisol' and after 09:15 h 'random cortisol' (RC).
Results
Overall 226 serum cortisol samples were analysed, 50% (114) were EMC and 50% (112) RC. The EMC group resulted in 36% of samples <160 nmol/l compared to 64% of the RC group. The reverse was seen in results >340 nmol/l, with 67% from the EMC group and 33% from the RC group. Of samples collected before 0915 h 46% (52/114) were >340 nmol/l, thereby confidently excluding adrenal insufficiency, compared to 23% (26/112) of those samples taken after 09:15 h.
Conclusions
Taking cortisol samples before 09:00 h significantly increases the specificity of the screening for adrenal insufficiency and avoids unnecessary referrals to endocrinology and SSTs. As a result of our study we have introduced a new autocomment issued on all cortisol samples with interpretative comments ONLY provided for those timed before 09:00 h.

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OC8.2

Adrenal Insufficiency: hydrocortisone prescribing and sick day rules

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Introduction
Exposure to deficient/excess glucocorticoids can lead to long-term health problems in patients with adrenal insufficiency. Historically and age-appropriate hydrocortisone formulation has not been available. Adrenal crisis is associated with significant morbidity and mortality.
Aims
To assess prescribing practice for oral hydrocortisone and sick day advise across the UK.
Methods
Paediatric endocrinologists and parents[HC(UC1] of children with adrenal insufficiency from across the UK completed a survey assessing hydrocortisone dosing and sick day advise in children taking oral hydrocortisone.
Results
32 consultant paediatric endocrinologists and 134 parents from across the UK completed the questionnaire. To achieve doses of <10 mg in children aged <6 years; 31% physicians recommend a pharmacy suspension, 28% buccal hydrocortisone and the remainder a dispersion prepared by cutting or crushing the tablet. Overall 47% of respondents are comfortable prescribing multiples of 2.5 mg sublingual hydrocortisone and 28% are comfortable prescribing half a sublingual tablet. 34% prescribe hydrocortisone solution. 30/32 consultants responded to the question on sick day advice. The following regimens were advised; double standard dose ($n=8$), double or triple standard dose dependent on illness severity ($n=5$), double the dose with an additional dose overnight ($n=7$), double or triple dose dependent on illness severity with an additional overnight dose ($n=6$), 30 mg/m^2 every 6 hrs ($n=4$). Data on timings of hydrocortisone dosing was available from 134 parents. The average gap between overnight doses was 10.2 h (range 5–16 h) with the last dose being administered at 2045 h (range 1500–2400 h) and the first dose at 0630 h (range 0100–0800 h). In the last 12 months 55 out of 134 respondents (41%) reported needing to use their emergency injection.
Conclusion
There is a wide variation in hydrocortisone prescribing practice in the UK. Parents of patients who participated in this survey report a high rate of requiring emergency hydrocortisone management. Further studies should focus on the timing of reported adrenal crisis and whether this relates to the length of time between hydrocortisone doses.

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OC8.3

Specially identified patients (SIPs) – how do they work?

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Introduction
Children with adrenal insufficiency require emergency hydrocortisone for serious illness in addition to any regular requirements. Individualised emergency plans for patients during sick days, detailing their oral and intramuscular hydrocortisone requirements, should be maintained, alongside appropriate alerts on hospital and pre-hospital systems to ensure health professionals are aware of their requirements promptly if they present acutely unwell. Following a child death review, we audited whether patients had appropriate plans and corresponding alerts in place.
Methods
Data was collected from two local paediatric endocrinology databases. Patients on these databases who were seen in outreach, had transitioned to adults, died or whose adrenal deficiency had resolved, were excluded. The digital health records and local alert systems were reviewed to identify the presence of a steroid plan, the presence of a steroid deficiency alert and whether the steroid plan was current (defined as <12 months old or with appropriate emergency doses based on auxology from the last clinic attendance).
Results
79 patients were identified. Reasons for steroid deficiency included: multiple pituitary hormone deficiency (46%), congenital adrenal hyperplasia (35%), congenital adrenal hypoplasia (1%), Addison's disease/APECED (5%) and exogenous steroid use (13%). 68 patients (86%) had an alert and plan. Of the 11 patients without an alert, 4 also did not have a steroid plan (omission: $n=3$; lost to follow-up: $n=1$). Of 7 patients with a plan but no alert, 2 were outreach patients (and may have had alerts at their local hospitals) with oncology follow-up at our hospital, and 5 were omissions. The plan was up to date in 66/75 patients (88%): 9 recommended a suboptimal intramuscular hydrocortisone dose and 4 recommended a suboptimal oral hydrocortisone stress dose.
Conclusion
The majority of patients have both a steroid plan and alert. However an important minority are missing either an alert or both. In addition, there is a possibility that the databases are incomplete. Imminent implementation of SNOMED CT should reduce this risk in the future. At times of serious illness, alerts and steroid plans can be lifesaving. The omissions identified have been rectified. Annual re-audit will allow omissions to be promptly identified.

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OC8.4

Optimising transition care in endocrinology: an example of patient-focused quality improvement

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Introduction
The importance of good transition care has been highlighted by NICE and NHSI. Over the last 5 year we have focused on transforming our endocrine transition service.
Background
Our centre took part in the BSPED/BES-led 2014 National Adolescent Care and Transition Audit of Young people with Hormone Conditions. From this we identified key areas for service improvement including: families wanted to establish a better relationship with and have more confidence in staff looking after their children; wanting more information/support around transition processes and about their condition, allowing them to feel more empowered.
Methods
We worked on the following:
- Named Paediatric, and Adult Consultant; named Adult Endocrine Nurse for the transition Clinic.
- Engaged managers from adult/paediatric service teams; members of the Children's Network Transition Working Group, to facilitate changes in job plans, IT processes, and implementation of the Ready Steady Go (RSG) programme.
- Worked closely with a pharmaceutical company which was piloting a Structured Endocrine Transition project, providing facilitation support to align our service with the NICE guidance on transition care.
- Involved parents/patients in drafting a standard operating procedure (SOP).
- Follow-on service evaluation 5 years after the initial BSPED/BES audit.

Outcomes
- A SOP has been agreed with critical input from families.
- From January 2016 we transformed the transition clinic from a single handover appointment to a longitudinal clinic, seeing patients 2–3 times in a joint adult-paediatric consultation; with marked improvement in care outcomes:

	May 2013-December 2015 (2.5 years): One handover clinic	January 2016–June 2018 (2.5 years): Longitudinal clinic
Clinics/year	4	6
Total clinics	10	15
Total number patients seen	41	69
Lost to adult follow-up	10%	3%
Referrals to adults seen ≤6 months	42%	81%

- All patients now complete a RSG questionnaire which is discussed during clinic; appropriate condition-specific patient information leaflets and sign-posting information are provided.
- Patient and family satisfaction ($n=21$):
  - 'happy with the care I receive from the transition service' = 95%
  - 'treated well by the people who see me' = 90%

Conclusions
Through extended collaborative working we transformed our endocrine transition service into a results driven, patient-centred service, with excellent outcomes.

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OC8.5

The impact of Prader–Willi syndrome multidisciplinary clinic on growth parameters

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Introduction
Prader–Willi Syndrome (PWS) is a rare genetic disorder due to loss of paternally inherited genes on chromosome 15q11-13. It is characterised by neonatal hypotonia, childhood hyperphagia and obesity, hypogonadism, cognitive and behavioural disabilities, and development of scoliosis. PWS multidisciplinary (MDT) clinics were introduced from 2004 at Birmingham Children's Hospital, a tertiary paediatric centre. This enabled centralised coordination of growth hormone (GH) and scoliosis management, with orthopaedic support. Our objective was to review the impact of PWS MDT clinics on growth parameters, in particular in children with scoliosis.
Methods/design
Retrospective observational study of sixty-eight children with genetically confirmed PWS, seen in a tertiary paediatric centre, from 2001 to 2019. Duration of follow-up was 1 year (reviewed in the last 12 months) to 14 years. Data were collected on growth hormone dose, scoliosis and treatment, height, weight and BMI SDS. We compared children with ($n=34$) and without ($n=32$) scoliosis defined by a Cobb angle greater than 10 degrees.
Results
Median height SDS at 14–16 years was −2.9 in patients born before 2004 ($n=21$), compared to −1.47 in patients born after 2004 ($n=5$), ($P=0.01$). The prevalence of scoliosis in patients born before 2004 was 76.9% (20/26), compared to 35.0% in patients born after 2004 (14/40) ($P<0.001$). 52.2% (12/23) of patients born before 2004 were on GH, compared to 85.4% (36/41) in patients born after 2004 ($P<0.001$). When all children with scoliosis were reviewed, aged 1 to 20 years, the last known median height SDS was −1.25, compared to −1.69 in the non-scoliosis group ($P=0.01$). However, this difference was not apparent when comparing each groups' height SDS at 14–16 years, −2.74 vs −2.62 ($P=0.82$). There was no significant difference when comparing height SDS before and 1 year after scoliosis treatment, and neither in the GH doses between scoliosis and no scoliosis groups.
Conclusions
Introduction of a PWS MDT clinic has resulted in: more children treated with GH; decrease in scoliosis prevalence; relatively taller children; continuing GH treatment in children with scoliosis and comparable final height SDS between children with and without scoliosis.

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Poster Presentations

Adrenal, Gonadal, DSD and Reproduction, and Basic Science

P1

Learning from clearance studies, 24 h profiling and pump therapy – PUTTING the onus on cortisol replacement rather than 17OHP and androstenedione

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Convention places 17OHP measures as the way to monitor replacement therapy in congenital adrenal hyperplasia due to P_{450}c21 deficiency. One case several years ago led to questioning of this approach as the 17OHP measures suggested inadequate replacement with hydrocortisone using a general dosing regimen of 12 mg/m^2/day and questions about compliance. 24 h cortisol profiles showed high 17OHP concentrations with low cortisol concentrations. Careful studies revealed rapid clearance of hydrocortisone (half-life 40 min), reduced bioavailability of 80% with increased conversion of cortisol to cortisone via the cortisol 'shuttle.' Subcutaneous hydrocortisone delivered by a pump system corrected the cortisol deficiency, mimicked the circadian rhythm and normalised 17OHP and androstenedione. Personalised treatment needs an understanding of pharmacology. Studies in 72 individuals has revealed half-life values ranging from 40 to 223 min (average 80 min) and absorption maximum concentrations at 60 min (range 20−120 min) after a dose with a $T_{max}$of 60 min in the morning and 100 min at night ($P=0.01$). Hydrocortisone replacement is an open loop system but it is cortisol that regulates the hypothalamo-pituitary axis not the normal hypothalamus and ACTH. 24 h profile data show a complex relationship between cortisol and the often used biomarker of control – 17OHP. There is a feedback lag in the system of 2 h between the cortisol peak and the resulting effect on 17OHP. With a 24h mean plasma cortisol concentration of 150 nmol/l, plasma 17OHP and A4 are undetectable. This mean plasma cortisol concentration is lower than the range encountered in individuals without adrenal problems. What may appear as 'over-treatment' based on 17OHP and androstenedione may be under-treatment from the cortisol rhythm standpoint. Attaining the target of 17OHP and/or A4 suppression does not mean that ambient cortisol concentrations are adequate. 17OHP is also influenced by stress, pain, polycystic ovaries and the presence of rests. Finally, assessing the relationship between cortisol and 17OHP has demonstrated that the IC_{50} for 17OHP is 50 nmol/l which indicates the need to ensure cortisol delivery, whether by oral therapy or pumps, with plasma cortisol concentrations maintained as much as possible above 50 nmol/l.

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P2

Variations in 17α-hydroxyprogesterone response to hydrocortisone treatment for congenital adrenal hyperplasia in children

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Introduction

Hydrocortisone is the main treatment for congenital adrenal hyperplasia (CAH) in children. The optimal biochemical monitoring and replacement regimen of these children continues to be debated. We explored variations in blood spot 17α-hydroxyprogesterone (17-OHP) levels.

Methods

Single centre retrospective cross-sectional study of children with 21-hydroxylase deficiency aged <18 years. Patients treated with hydrocortisone who had dried blood spot 17-OHP levels measured between October 2014 and April 2018 were included. On sampling days, patients collect four blood spots on filter paper cards; one before each hydrocortisone dose and one at midnight. Most patients had multiple samples; the first sample in prepubertal patients and the last sample in postpubertal patients was selected. Clinical data at the time of sampling was recorded.

Results

Twenty children were included in the study; baseline characteristics and treatment specifics are shown in Tables 1 and 2.

In a linear regression model (independent variables: gender, puberty, BMI SDS and glucocorticoid dose), mean daily 17-OHP levels were negatively associated with total daily hydrocortisone dose (B = −18.4; $P=0.036$), positively associated with being postpubertal (B = 147.3; $P=0.013$) and borderline negatively associated with BMI SDS (B = −31.0; $P=0.087$). However, morning 17-OHP levels were not associated with evening hydrocortisone dose nor with total hydrocortisone dose. Evening 17-OHP levels were borderline negatively associated with afternoon hydrocortisone dose (B = −47.3; $P=0.086$). Gender, age, height or phenotype were not associated with 17-OHP levels.

Table 1

Baseline	*N*=20
Gender (male/female)	10/10
Age at visit (years)*	11.4 (3.6)
Puberty stage (pre/postpubertal)	13/7
CAH phenotype (salt losing/late onset)	16/4
Total glucocorticoid dose (mg/m^2)*	13.6 (3.2)

Table 2

Treatment	Morning	Afternoon	Evening	Night
Glucocorticoid dose (mg/m^2)*	4.9 (1.3)	2.9 (1.1)	5.7 (2.4)	
17-OHP level (nmol/l)†	239 (307)	37.0 (167)	7.9 (79.0)	7.9 (3.0)

Values expressed as *mean (S.D.) or †median (IQR).

Conclusion

17-OHP levels were negatively associated with total daily hydrocortisone dose and therapy could be titrated based on blood spot 17-OHP levels. Morning 17-OHP levels, however, are not associated with evening hydrocortisone dose. Therefore, our results do not support reverse circadian rhythm hydrocortisone therapy in children with CAH.

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P3

Non classical congenital adrenal hyperplasia presenting with a severe salt losing crisis

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Introduction

Non-classical congenital adrenal hyperplasia (NCCAH) is a common autosomal recessive disorder characterized by androgen excess. It classically presents in later life with symptoms of acne, hirsutism, and premature adrenarche. This case illustrates a rare case presentation of NCCAH in early infancy.

Clinical case

An 18 day old term male infant was brought to the A&E for 9% weight loss. On review he was mottled, but otherwise examination was unremarkable; he had normal male external genitalia with bilaterally descended testes. Initial investigations revealed a severe salt losing crisis (sodium 121 nmol/l, potassium 8 mmol/l) and a mild metabolic acidosis. He was initially treated with IV fluids and antibiotics for suspected urosepsis. Following investigations intravenous hydrocortisone, sodium chloride supplements and fludrocortisone were commenced in view of suspected CAH. Initial random baseline cortisol and androgen profile was normal, with markedly raised aldosterone (18 900 pmol/l) and Renin (307.8 nmol/l per hour) concentration but a normal urine steroid profile (USP). A standard synacthen test (SST) showed baseline cortisol 707 nmol/l and stimulated 1046 nmol/l with normal androgens. Hydrocortisone, fludrocortisone and salt supplements were therefore stopped with a provisional diagnosis of pseudohypoaldosteronism. Surprisingly, 17-OHP results from the SST subsequently demonstrated a significant rise from a baseline of 15.1 to 203.0 nmol/l at 60 min. A repeat SST at age 1 month off all medications again confirmed an adequate cortisol response to 538 nmol/l but with abnormally raised 17-OHP. Pre- and post-synacthen USP were initially reported as normal. CYP21A2 Sanger sequencing subsequently revealed a compound heterozygous mutation for c.841G>T (p.V281L) and C.1357C>t (p.P453S), both known to be associated with NCCAH. Serial U&Es remained stable off treatment but ACTH concentrations were intermittently raised up to 314 ng/l, now normalized to

37 ng/l. Aldosterone levels have normalized (2740 pmol/l) but Renin remained raised (23.5 pmol/l per hour). Retrospective analysis of previous urine steroid profiles showed very mildly raised 11-oxopregnanetriol concentrations in keeping with the diagnosis.
Discussion
To our knowledge, this is the earliest reported presentation of salt-losing crisis in a patient with genetically proven non-classical CAH, most likely reflecting an additional diagnosis of transient pseudohypoaldosteronism

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P4

A regional service for children and young people with familial hypercholesterolaemia: lessons learnt

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Introduction
Familial Hypercholesterolaemia (FH) is an autosomal dominant inherited disorder of lipid metabolism. Affected children have elevated cholesterol from birth with accelerated atherosclerosis and significant cardiovascular disease (CVD) from the third decade. 1 in 250 people are affected and early treatment can eliminate the risk of premature CVD. Genetic testing guidance was published in August 2008 and a CVD outcomes strategy was produced in 2013. From 2014 the British Heart Foundation began to fund specialist FH nurses.
Service report
A formal regional paediatric service was established at University Hospital Southampton in 2014, encompassing a consultant, dietician and specialist nurse. 118 children and young people have been identified with FH since then, with increasing numbers year by year. Average age at referral is 9.3 years (4 months to 16 years); almost all are referred by nurse specialists via the cascade screening program. In our cohort average LDL-cholesterol at diagnosis was 4.9 mmol/l (1.6–9). LDLR variants were identified in 70%, APoB variants were identified in 20% and PCSK9 variants in 3% (remainder polygenic or unknown). All children were offered diet and lifestyle advice with face to face input from a specialist dietician. At the time of this review, 57 children are on statin therapy, this was initiated in 14 children before 10 years of age. Statin treatment led to a LDL-cholesterol fall of 46% (6.15–3.31 mmol/l) for children under 10 years and for those older than 10 years: 40% (5.52–3.34 mmol/l). 86% of young people on treatment are on atorvastatin monotherapy; the majority are on 10 mg. Only one child changed medication due to side-effects.
Conclusions
In our experience, effective control of cholesterol levels can usually be achieved on low doses of statin with good tolerance. The creation of a formal sub-speciality paediatric service has aided diagnosis and started to standardise care, optimising long-term health outcomes. However, detection rates remain low with approximately only 10–15% of local cases diagnosed so far. In light of the significant health impact of this condition, we believe population screening needs to be considered to improve identification and early treatment.

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P5

Optimisation of transfection methods using various formats of gRNA delivery for CRISPR Cas9 mediated gene knock out in Beta-TC-6 cells

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Background
The CRISPR/Cas9 genome-editing platform is a powerful technology to create genetically engineered cells and organisms. However, the success of CRISPR genome editing experiments is limited by the intracellular delivery and expression of Cas9 endonuclease protein and guide RNA (gRNA). Beta-tumour cells (βTC-6), derived from transgenic mice, exhibit glucose stimulated insulin secretion which makes them a valuable tool in understanding the mechanisms that regulate insulin secretion.
Aims
The aim was to identify the optimal transfection conditions for the intracellular delivery of Cas9 protein and gRNA in βTC-6 cells so as to create a KO mouse cell model of Congenital Hyperinsulinism (CHI). Such cellular models would play a key role in the elucidation of the molecular mechanisms underlying CHI.
Methods
gRNAs were designed to target two genes of interest- *Abcc8* and *Hadh*. Optimisation of the delivery of CRISPR/Cas9 system included the evaluation of different formats such as plasmid DNA, mRNA and RNP complex using a reporter gene. Transfections were performed using different combinations of molecules including: plasmid DNA, Cas9 protein and gRNA in an RNP format to maximize targeting of the *Abcc8* and *Hadh* gene in βTC-6 cells. A reporter (GFP) was initially used to evaluate the transfection efficiency of the plasmid DNA and mRNA with flow cytometry and fluorescent microscopy being used to detect the GFP signal. To obtain the highest transfection efficiency, conditions were optimised by varying cell density and amount of transfection reagent. For the delivery of Cas9/gRNA as an RNP format, different non-viral vectors including Lipofectamine 2000 and nanocomplexes were used. At the molecular level, the disruption of the gene was confirmed by Sanger sequencing and T7 ENDO assay.
Results
Progress so far has addressed the optimisation of transfection conditions to deliver CRISPR/Cas9 in βTC-6 cells. Determination of editing efficiency using the ICE tool by Synthego revealed a low KO score.
Future work
Transfection by electroporation using synthetic sgRNA pre-complexed to the Cas protein in the ribonucleoprotein (RNP) format may improve editing efficiencies.

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P6

Improving midwives' recognition of atypical genitalia and differences of sexual development (DSD) through the use of an e-learning module

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Background
Confident recognition of atypical genitalia of the newborn and early referral to specialist centres allows for the smooth and successful management of DSD patients. Midwives conduct the majority of newborn infant physical exam (NIPE) yet may not be confident in recognising DSD and talking to families affected.
Aim
To develop an e-learning module for examining newborn genitalia, recognising the significance of differences in genital appearance and how to communicate and support a family with DSD.
Methods
A questionnaire was completed by midwives to assess the need for education around DSD. This revealed confidence in DSD recognition is poor and that there is concern around how to communicate and support families with DSD. The Royal College of Midwives (RCM) was approached with this data and a decision was made to develop an interactive e-learning module to be hosted on the RCM e-learning environment; accessible by all midwives who are registered with the college.
Results
An online and interactive module was co-produced with endocrinologists, a clinical psychologist and midwives and covers the following areas;
- DSD background
- Examination of newborn genitalia
- Recognising the variations of normal genitalia
- Recognising atypical genitalia
- Discussing concerns with parents
- Referring to paediatrics
- Supporting families at times of uncertainty
- Sources of information and support
- DSD quiz

We plan to review the impact of this training module in future through reviewing the results of the end of module quiz and through feedback from participants. It is hoped this module will improve midwives confidence in examining newborn genitalia and give them the practical tools to communicate with and support families affected by DSD.

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Bone

P7

Burosumab experience in UK XLH children under five years old

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Objectives

X-linked hypophosphatemia (XLH) is a rare inherited form of osteomalacia characterised by low blood phosphate levels which lead to inadequate mineralization of bone and rickets. Burosumab is an anti-FGF23 fully human monoclonal-antibody, and the first treatment to target the underlying pathophysiology of XLH. We report relevant real-world biochemical data on children under five years old for the first 6 months of treatment.

Methods

An early access program (EAP) for burosumab was made available for children in the United Kingdom with XLH in 12 specialist centres. Inclusion criteria for the EAP included radiographic evidence of disease, XLH confirmed by genetic PHEX mutation or familial X-linked inheritance mutation or family history. Patients must have also had an unsatisfactory response to best available care and treatment. EAP enrolment was between January and March 2018. A total of 142 applications were received of which 135 were approved with 132 receiving treatment (dose in accordance with EMA marketing authorisation).

Results

Data are available on 10 children under five years (mean age 2.8 years; 1.6–4 years) who have completed a median of 6 months (20–26 weeks) of burosumab treatment. Mean height and weight at week 0 was 85.5 cm (75–97.3 cm) and 12.8 kg (9.9–18.2 kg) respectively. Mean dose administered was 0.81 mg/kg (0.55–1.01 mg/kg) at week 0 and 1.09 mg/kg (0.57–2.01 mg/kg) at the end of the 20–26 week period. Mean fasting serum phosphorus was 0.73 mmol/l (0.6–0.83 mmol/l) in week 0 rising to 1.02 mmol/l (0.82–1.3 mmol/l) at week 20–26 representing a 40% increase in serum phosphate levels. Mean serum ALP fell from 808.2 IU/l (297–2124 IU/l) at week 0 to 612 IU/l (291–1459 IU/l) at week 20–26, representing a 24% decrease in ALP. No patients discontinued treatment due to adverse events.

Conclusions

Early data from treating young children with XLH with burosumab in a real-world UK setting demonstrate that key biochemical responses are aligned with findings from the clinical study program. This provides reassurance that the improvement in key biochemical parameters is consistent across all ages within its licensed indication.

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P8

Clinical, functional and quality of life outcomes of Burosumab therapy in children with X-linked hypophosphoataemia: a real world, London experience

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Burosumab, monoclonal antibody targeting fibroblast growth factor 23, is now available for clinical use in children with X-linked hypophosphatemia (XLH). We explored the effects of this treatment in a clinical setting, considering biochemistry, growth, deformity, functionality, quality of life, pain and fatigue.

Methods

Clinical, biochemical, radiological and questionnaire data were reviewed at 6 and 12 months(m) for 8 children with XLH starting burosumab as well as 6-minute walk test (6MWT) and Timed Up and GO (TUG). Questionnaires included: Core Paediatric Quality of Life Inventory (PedsQL-Core), PedsQL multidimensional fatigue scale (PedsQL-Fatigue), and Brief Pain Index Pain Severity Score (PSS).

Results

Median age was 5.5 years(y) (range = 19m–11y). Table below shows clinical and functional improvements over 12m.

Test	Baseline Mean ± s.d.	12m Mean ± s.d.	*P* value
Phosphate (1.0–1.9 mmol/l)	0.7 ± 0.1	1.1 ± 0.1	$P<0.001$
ALP* (139–347 IU/l)	415 ± 73	322 ± 70	$P<0.001$
PTH** (10–65 ng/l)	31 ± 14	42 ± 16	$P<0.05$
Ur Ca:Creatinine (0.05–0.60)	0.44 ± 0.21	0.37 ± 0.23	Not significant, $P=0.51$
TmP/GFR[1] *** (1.15–2.44)	0.56 ± 0.11	1.19 ± 0.18	$P<0.001$
Height Z-scores	−2.600 ± 0.813	−2.435 ± 0.787	$P<0.05$
Thatcher Scores (out of 10)	2.0 ± 1.5	0.4 ± 0.3	$P<0.05$
TUG ($N=5$,seconds)	5.7 ± 0.5	4.8 ± 0.6	$P<0.05$
6MWT ($N=4$, metres)	258 ± 75	447 ± 53****	$P=0.05$

**Alkaline Phosphatase, **Parathyroid hormone, ***Ratio of renal tubular maximum phosphate reabsorption.*

Deformity

Six children had lower limb deformity; varus($N=3$), valgus($N=2$), windswept($N=1$). All but one noticed improvement at 12m with reduced intercondylar/intermalleolar distances.

Pain/fatigue

One child reported no pain. 12m PSS scores decreased for 6 patients and increased for 1. 3 recorded higher PSS at 6m, improving by 12m. PSS Mean ± s.d. was 2.3 ± 1.3 at baseline and 1.0 ± 1.2 at 12m (maximum score 10). Mean ± s.d. PEDsQL-Fatigue scores were 64 ± 19 at baseline and 76 ± 17 at 12m (maximum score 100, $P=0.2$).

Quality of Life

Mean ± s.d. PEDsQL-Core score improved from 69 ± 17 at baseline to 81 ± 15 at 9m, however decreased to 67 ± 17 by 12m ($N=7$,maximum score 100). This is despite verbal reports of improvements and may reflect a shift in expectation.

Conclusion

In a real-world setting, burosumab can improve biochemistry, growth, deformity, pain and function in children with XLH.

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P9

Evidence for association of PTEN-harmatoma-tumor syndrome with osteosarcoma

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Introduction

PTEN-harmatoma-tumor syndrome is an umbrella term that describes a group of genetic disorders linked to germline mutations of PTEN (Phosphatase and tensin homolog), a tumor suppressor gene that inhibits the PI3/Akt signalling pathway thereby inhibiting proliferation, cell survival and angiogenesis. PTEN-harmatoma-tumor syndrome encompasses Cowden's Syndrome, Bannayan–Riley–Ruvalcaba syndrome, and autism spectrum disorder (ASD) associated with macrocephaly. It is associated with increased tumor risk mostly breast, endometrial, thyroid, colon and renal malignancies and with benign growths such as gastrointestinal polyps, brain and skin lesions. It has not been related to osteosarcoma. Here we describe an osteosarcoma in a patient with a familial PTEN mutation.

Clinical case

A 10 year old girl with, ASD, macrocephaly, global developmental delay (GDD), obesity and epilepsy, was found to have inherited a PTEN mutation form her mother, when the mother was diagnosed with Cowden syndrome due to thyroid cancer and mild learning difficulties. The girl was regularly monitored for thyroid malignancy. She presented with a 1 week history of a limp. Imaging revealed periosteal reaction and findings suggestive of osteosarcoma of the distal left femur. Histological analysis of a biopsy confirmed high grade chondroblastic osteosarcoma. Staging was T2,N0,M0,G3, Overall America Joint Committee on

Cancer Stage: IIB. She underwent primary surgical resection and insertion of endoprosthesis as behavioural difficulties precluded safe administration of chemotherapy. She developed pulmonary and bone metastases 9 months later, had palliative radiotherapy, but passed away 5 months later. Her younger brother with the same mutation has ASD, GDD, tall stature, obesity and macrocephaly. He developed a thyroid nodule, aged 10. A biopsy was in line with Th2 classification and he is under close surveillance. He had several episodes of leg pain without clear etiology.

Conclusion

This case report suggests the association between PTEN and osteosarcoma confirming two recent case reports. PTEN is expressed in osteoprogenitors and targeted deletion in mice results in increased osteoblast number due to autonomous differentiation from growth plate chondrocytes. Thus, osteosarcoma should be considered in patients with PTEN-harmatoma-tumor syndrome and bone pain. Further research is required to establish incidence and requirement for surveillance.

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P10

Vitamin D levels of mothers with and without vitamin D supplementation in pregnancy and their newborns

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Introduction

Vitamin D regulates calcium and phosphorus metabolism. Although Turkey is a sunny country, vitamin D deficiency is a major problem in pregnant mother and their infants. The purpose of this study was to evaluate vitamin D levels in mothers with or without vitamin D supplementation and their newborns' cord bloods.

Methods

Healthy pregnant women and their healthy term babies were enrolled in the study. Levels of vitamin D, parathyroid hormone, calcium, phosphorus, magnesium and alkaline phosphatase were measured in maternal venous blood and cord blood specimens during birth. Mothers were divided into two groups receiving and no receiving vitamin D.

Results

46 mothers and healthy babies were enrolled. Twenty-nine mothers (63%) had used vitamin D during pregnancy, while 17 (37%) did not use it. The mean vitamin D level of mothers were 8.9 ± 4.8 mg /dl, and 5.4 ± 2.8 mg/dl, respectively. The difference between the two groups was statistically significant ($P=0.015$). Significant correlation was found between the vitamin D levels of mothers' venous blood and cord blood samples ($r=0.410$, $P<0.001$). When mothers were grouped depending on vitamin D supplementation, cord blood vitamin D levels of babies of mothers receiving vitamin D were significantly high ($P=0.004$). Vitamin D levels in cord blood were deficient in 17.4% ($n=8$), insufficient in 28.3% ($n=15$) and sufficient in 54.3% ($n=25$). Following neonatal vitamin D supplementation, it was determined deficiency in 2.2% ($n=1$), insufficiency in 10.9% ($n=5$) and sufficiency in 87% ($n=40$). Vitamin D levels do not affect growth in the neonatal period.

Conclusion

Vitamin D supplementation in pregnancy affects cord blood vitamin D levels. After birth 400 U/day prophylactic vitamin D is sufficient to prevent vitamin D deficiency even in those newborns of vitamin D deficient mothers.

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P11

Hypercalcaemia as a presenting feature of sarcoidosis: the need for an open mind

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Sarcoidosis is a rare multisystem granulomatous disease that most commonly affects the lungs and skin, and can also affect eyes and lymph glands. We describe an unusual case of sarcoidosis presenting with hypercalcemia, causing diagnostic challenges. A 5year old boy was incidentally found to have asymptomatic hypercalcaemia during a routine clinic review for failure to thrive. Apart from a recent Influenza A infection, when he was found to have normal calcium levels and severe vitamin D deficiency (10.2 nmol/l), he was well. He was started on vitamin D treatment (6000 units daily). Blood tests 3 months later showed hypercalcaemia (3.52 mmol/l), with renal impairment (creatinine 65 micromol/l), low-normal PTH (1.6 pmol/l), normal vitamin D (152 nmol/l), phosphate (1.03 mmol/l) and magnesium (0.84 mmol/l). He had resistant hypercalcaemia despite hyperhydration and furosemide, and required three doses of calcitonin, and two doses of pamidronate, to normalise his calcium levels. Parathyroid USS showed bilateral hypoechoic lesions. A whole-body nuclear medicine scan showed no parathyroid or bony foci. A renal USS showed bilateral echogenic kidneys with no hydronephrosis or nephrocalcinosis. Tuberculosis and syphilis screens were negative. In view of persistent conjunctivitis, he was referred to ophthalmology. They found pan-uveitis with choroid scars, which together with high-normal serum angiotensin converting enzyme (ACE 108 U/l; range 29–112 U/l) was suspicious of sarcoidosis. Further blood tests showed his 1,25-dihydroxyvitamin D level was raised (154 pmol/l; range 55–139 pmol/l), with normal 25-hydroxyvitamin D (93.5 nmol/l). He was given a clinical diagnosis of sarcoidosis in view of pan-uveitis, choroidal scars and raised ACE (185 U/l), with hypercalcemia likely secondary to raised 1,25-dihydroxyvitamin D. At 1 year, the sarcoidal changes in his eyes have improved. He remains well, with no musculoskeletal or respiratory symptoms, headache, hair loss, or mouth ulcers. His calcium and renal function remain normal. It is unclear if his initial renal impairment was secondary to hypercalcaemia or sarcoidosis. There are numerous case reports of children with sarcoidosis presenting with hypercalcaemia, secondary to increased 1-alpha-hydroxylase activity in granulomas, leading to increased 1,25-dihydroxyvitamin D, requiring treatment with steroids/bisphosphonates. Sarcoidosis should therefore remain in the differential of unexplained hypercalcaemia, especially if associated with additional skin, eye, renal or respiratory features.

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P12

Vitamin D dependent rickets

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Introduction

Most common cause of rickets is vitamin D deficiency. Genetic mutations in the metabolism and function of Vitamin D is a rarer cause of rickets.

Case report

A16 month old male presented with bilateral clavicular swelling, constipation, generalised weakness and poor growth. He also had delay in motor milestones and was only able to sit with support. He was born in the UK to consanguineous parents of Asian origin.

Examination

Weight and height were on 2nd centile. He had frontal bossing, rachitic rosary, widened wrists and ankles, limited dentition. Investigations: Adjusted Calcium : 1.17 (2.2–2.6 mmol/l), Phosphate 1.3 (0.9–1.8 mmol/l), ALP 2027 (60–425 U/l) and PTH 44.5 (1.95–8.49 pmol/l). Vitamin D – 62.4 (50–150 nmol/l). X-ray showed severe rickets. Subsequent investigation results: 1,25-dihydroxyvitamin D undetectable – result consistent with 1a-hydroxylase deficiency. Genetic investigation showed mutation in the CYP27B1 confirming the diagnosis.

Management

Initially treated with calcium supplement and Alfacalcidol. Calcium was gradually weaned off. He remains on Alfacalcidol. Follow up after 9 months: Rickets has healed on X-ray. Calcium and PTH levels have normalised to 2.49 mmol/l and 5 pmol/l respectively.

Discussion

Vitamin D dependent rickets type 1, is an autosomal recessive disorder characterised by lack of 1-alpha hydroxylase enzyme. As a result, 25(OH)D cannot be converted to active form 1,25(OH)2D. It occurs as a result of mutations in the CYP27B1. Treatment is correction of initial hypocalcemia with Ca supplements and active form of Vitamin D e.g. Alfacalcidol.

Summary

Vitamin D dependent rickets presents similarly to nutritional rickets.

- In nutritional rickets the measured vitamin D level is 25(OH) D is low, but in VDDR1 it is normal or high as the genetic defects affects the 2nd hydroxylation of vitamin D to active 1,25(OH)D.
- Routinely laboratories measure the inactive form, 25(OH)D.
- When there is a clinical picture of rickets, but the initial vitamin D result is normal, that is above 50 nmol/l, this excludes nutritional Rickets.

- In this case, it was key to liaise with Biochemistry laboratory to analyse 1,25 (OH)D level. This then allowed clinicians to initiate appropriate treatment and initiate genetic investigation.

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P13

Dental manifestations of vitamin D deficiency in adolescents

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Background
Bone metabolism and development of teeth are under the influence of systemic factors. Recent studies confirmed the close relationship between the oral tissues with the most prevalent systemic bone disorders in adolescents.
Objective and methods
This study employed a simple method to be easily reproducible: oral clinical exam and radiographic evaluation. Eight patients were studied, 4 males, median age of 15 years (12 to 17).
Results
Occlusion defects (62.5%), enamel hypoplasia (12.5 %) tooth rotations (37.5%), diastemate due to frenulas (37.5%), congenitally missing teeth (12.5 %) and enlarged pulp chambers in 37.5 % of the patients. We could not detect a significant correlation between dental abnormalities and delayed treatment (P>0.05). DMFT index for 12 to 17 years patients ($n = 8$) showed that the oral health is unsatisfactory (mean DMFT = 5).
Conclusions
This study will help practitioners to integrate the oral health into the systemic health and improve the multidisciplinary approach of pediatric patients between medicine and dentistry.

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P14

A novel case report of severe hypercalcaemia occurring after four years on the ketogenic diet

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Hypercalcaemia has been previously described in association with ketogenic diet (KD), occurring within 12 months of starting KD. We present a case where severe hypercalcaemia occured after four years on KD.

Table 1 Investigations on presentation.

Investigation	Result	Reference Range
Corrected calcium	4.07 (High)	2.19–2.69 mmol/l
Phosphate	1.7	1.0–1.9 mmol/l
Alkaline phosphatase (ALP)	99 (Low)	139–347 IU/l
Parathyroid hormone (PTH)	6 (Low)	10–65 ng/l
Magnesium	0.9	0.65–1.05 mmol/l
Creatinine	73 (High)	24–45 umol/l
Vitamin D	84	>50 nmol/l
PTH-related protein	<1.40	<1.40 pmol/l
Urine Calcium:Creatinine Ratio	1.3 (High)	0.05–0.60
Vitamin B6	70.1	35.2–110.1 nmol/l
1,25 Vitamin D	24	48–192 pmol/l
Chest/hand/wrist Xrays	Low bone mineral density, otherwise normal	
Renal Ultrasound	Nephrocalcinosis	
Full Blood Count	Normal	
Thyroid Function Tests		
Electrolytes		
DEXA scan		

Case
A 5.5-year-old boy referred for hypercalcaemia in context of early sepsis and background of Dynamin-1 gene mutation causing infantile epileptic encephalopathy. He had been commenced on KD at 18 months of age for drug-resistant seizures. A Deep Brain Stimulator (DBS) was inserted at 3 years for refractory hyperkinetic movements. He has since had intermittent antibiotics for recurrent DBS infections without systemic symptoms. There were no recent changes to medications: sodium valproate, gabapentin, clobazam, clonidine, intravenous flucloxacillin and azithromycin (Table 1).
Calcium was normal 6 months prior to presentation (2.57 mmol/l). Intermittent mild hypercalcaemia was noted over the last 12 months (highest 2.83 mmol/l). ALP had been low for 3 years. Patient became unstable due to DBS infection, managed surgically and with antibiotics. Hypercalcaemia persisted despite hyperhydration and 2 pamindronate infusions. While serum calcium eventually normalised after two weeks, hypercalcaemia recurred with hyperhydration cessation. KD was gradually weaned and replaced with low calcium milk. Once KD was ceased, serum calcium normalized and remained normal after hyperhydration was discontinued. PTH increased after one week to 73 ng/l. Calcium was gradually re-introduced into his diet to 550 mg/day with no recurrence of hypercalcaemia and normalization of PTH.
Conclusion
This case suggests hypercalcaemia may occur years after KD commencement and can be refractory to standard management. In this case, hypercalcaemia may have been caused by the combination of long-term KD and sepsis with acute kidney injury. Despite clinical improvement, hypercalcaemia only resolved with cessation of KD.

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P15

Not your typical rickets case

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Introduction
Rickets was once considered to be a disease of the Victorian Era but it has become increasingly common in recent years. The most common cause is Vitamin D deficiency; however it is important to investigate for rarer causes if Vitamin D deficiency has been excluded.
Case report
A healthy, Caucasian 3 year old girl was referred due to bowing of her femora, apparent since she started walking at 13 months. She was reported to be clumsy and tire easily. There was no history of fractures or leg pain. Her height had dropped from the 75th centile to between the 25th and 50th centiles. Investigations showed mildly low corrected calcium and phosphate, slightly raised alkaline phosphatase and a sufficient vitamin D level of 50 nmol/l. After 6 months of Vitamin D treatment, bowing had progressed and height had fallen further so further investigations were performed including: urinary calcium: creatinine ratio (normal at 0.07) and urinary phosphate: creatinine ratio (elevated at 4.36). Tubular reabsorption of phosphate was reduced in keeping with a diagnosis of hypophosphataemic rickets. This was confirmed by detection of a mutation in the PHEX gene. Skeletal survey showed lower limb abnormalities and renal ultrasound excluded nephrocalcinosis. She was treated with oral phosphate supplements and alfacalcidol, resulting in improved growth and was subsequently diagnosed with moderate sensorineural hearing loss, another feature of hypophosphataemic rickets.
Conclusion
Rickets is a disorder of the growth plate, due to inadequate supply of phosphate to growing bones. Mutations in the PHEX gene cause increased levels of fibroblast growth factor 23 (FGF23), resulting in reduced absorption of phosphate in the proximal renal tubule. It is the most common form of hereditary rickets, and usually presents before 2 years. The key feature is significant phosphaturia (calculated by TmP/GFR). Patients are at increased risk of dental complications, enthesopathy, lumbar lordosis and hearing impairment. Phosphate supplements replace renal losses and calcitriol increases phosphate absorption from the gut and reduces PTH, preventing nephrocalcinosis. A new treatment, Burosumab® is a monoclonal IgG1 antibody that binds excess FGF23.

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Diabetes 1

P16

Improving the rate of completion of 7 care processes at a busy district general hospital by using quality improvement methodology

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Background
The NPDA has been providing annual audit reports to paediatric units in UK from 2003 and a compliance report for 7 care processes since 2016–2017. Over the years the focus on the type of data and implications of data has changed and become more focused especially after introduction of BPT and PEER review. The paediatric diabetes services at Basildon and Thurrock University Hospitals (BTUH) were identified as negative outliers in 2016–2017 NPDA report. A QI programme was undertaken to improve care of diabetes patients 0–19 years at BTUH from November 2017 till April 2019. The paediatric diabetes team at BTUH is caring for around 220 patients with type 1 diabetes.
Methodology
The team started a QI project in November 2017 spanning over 18 months. After BTUH paediatric diabetic team received outlier status, the team took part in the RCPCH QI pilot initiative. We used learned QI techniques including pathway mapping exercise, driver diagram and PDSA cycles to implement several small changes. The clinic proforma was tailored to capture NPDA requirements and practical training sessions were organised for admin staff for accurate input of seven care processes data onto Twinkle. The default reminder letters were designed for patients who did not have their annual review bloods and other investigations performed. The live NPDA data was shared with team in MDT meetings and adjustments were made wherever necessary to improve data capture and recording.
Results
The changes implemented have shown significant improvements in seven care process completion rates. The Retinal screening improved from 55 to 82%, the albumin creatinine ratio increased from 24 to 72%, the foot examination increased from 65 to 80% and the TSH increased from 66 to 74%. The overall median HbA1c improved from 66 to 60 mmol/mol. The percentage of children who received all the seven care elements increased from 15% in 2016–2017 to 56% in 2018–2019.
Conclusion
The implementation of skills learned at RCPCH QI pilot have shown improvements in completion of 7 care processes. The key to success was to work together as cohesive team and to have ability to review our progress with regular 'live' data.

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P17

The hospital school as a resource for supporting children with type 1 diabetes during planned admissions

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Introduction
Hospital schools can provide structure and learning for young people throughout a planned admission. With guidance, teachers can be a vital resource for assessing the numeracy and literacy skills essential in the management of diabetes. They can also provide a source of valuable pastoral and organisational expertise useful to the diabetes multidisciplinary team (MDT).
Method
School teaching, pastoral and planning skills can be used to help with the following:

- Co-produce an MDT timetable of appointments before the admission.
- Dyslexia and Dyscalculia screening to gauge whether young people have the necessary skills to understand carb counting, insulin ratios and correction doses.
- Send work requests to home schools and share information to ensure no child falls behind or is forgotten.
- Complete before and after questionnaires regarding diabetes knowledge to assess learning.
- Complete 'All About Me' forms gathering personal information such as family support, likes and dislikes, social and educational needs and dietary requirements that can be shared with the ward housekeeper.
- Help download useful technology such as Diasend and Freestyle libre, encouraging this regularly.
- Share observations from parents and young people with the MDT.
- Advise on Diabetes charities/on-line resources and provide guidance on applying for disability living allowances.
- Fund a mini library of useful Diabetes textbooks
- Provide information regarding social, education and information days local and wider
- Complete before/after and patient experience questionnaires.
- Explain Access Arrangements and Special Consideration for SATS, GCSES and A 'level examinations.

Results
We have an abundance of quotes and very positive graphical/pictorial data from clinical staff, young people and parents.
Conclusion
Every parent, young person and member of the MDT interviewed, deemed the hospital school a vital resource in providing structure, information and guidance during planned admissions. Their teaching expertise helps immensely in both the teaching and the assessment of learning. Hospital Schools can make admissions seem more planned, timetabling the week. They also introduce additional watchers, leading to more effective overall care, which can lead to shorter stays, reductions in emergency admissions and subsequent savings of hospital funds.

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P18

Botswana children and young people with diabetes partnership project

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Introduction
In April 2019 a team of healthcare professionals took a group of young people with type 1 Diabetes to Botswana for a healthcare partnership project with Diabetes Botswana. The trip included a joint diabetes youth camp and the delivery of Botswana's first ever Diabetes Educational Symposium.
Objectives
The primary aim of the project was to provide a reciprocal learning experience for the management of type 1 diabetes for healthcare professionals across Botswana. The secondary aim was to develop a partnership between British and Batswana health care professionals and young people leading to shared knowledge, peer mentorship and an ongoing healthcare relationship.
Description
A team of young people and staff were selected through an application process. The team consisted of 12 young people from 15 to 19 years old with type 1 diabetes. The staff team was made up of the diabetes network manager, 9 healthcare professionals, 1 parent and 1 volunteer. The team attended a camp run by Diabetes Botswana, this provided the opportunity to spend time with Batswana young people with type 1 diabetes. The camp included education sessions and a time of reflection and discussion. The young people found this an enriching experience and enjoyed meeting people from a different culture who had a shared understanding of living as a young person with type 1 diabetes. The Diabetes Educational Symposium was a 3 day educational meeting. The opening ceremony was attended by the British High Commissioner and the Minister of Health and Wellness for Botswana. The Batswana and British young people spoke about life with type 1 diabetes. The symposium consisted of plenary sessions and small group teaching. Each British healthcare professional was joined by a Batswana healthcare professional to assist with group facilitation and application to local practice. The symposium was attended by over 150 healthcare professionals from all over Botswana.
Conclusion
The partnership project met its aims and objectives and has paved the way for a longterm relationship and future educational events between our regional diabetes network and Diabetes Botswana.

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P19

Diasend download data and relation to diabetes control in a tertiary clinic cohort

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Our large tertiary hospital-based diabetes service high HbA1c policy selects Children and Young People (CYP) with HbA1c above 64 mmol/mol for additional support. Two-week average blood glucose (ABG) is utilised in the high HbA1c clinic as a proxy for HbA1c and CYP are encouraged to reduce their 2 week ABG as a primary goal.

Aims

To determine the relationship between HbA1c, 2 week and 3 month ABG and standard deviation (S.D.) in CYP with Type 1 Diabetes (T1DM) in our cohort and to identify related factors with the potential to improve control.

Method

Diasend downloads between 1/11/17 to 31/8/18 related to clinic visits were analysed for 1 in 3 randomly selected patients with T1DM greater than 12 months duration, aged 1–18 years, for correlation of 2 week and 3-month ABG, S.D., test frequency and bolus advisor use with clinic visit HbA1c and therapy.

Results

95 randomly selected downloads of 349 CYP with T1DM were analysed. Bolus calculators were used by 85 (89%) with 53/85 (62%) entering at least 3 carbohydrate containing meals or snacks per day and 31/95 (33%) using CSII. Correlation with HbA1c was greater for 3 month ABG vs 2 week ABG ($R=0.58$ vs 0.44) and for patients performing 5 or more tests per day ($R=0.78$ vs 0.46). Blood glucose S.D. $<$ 4 mmol, achieved by 22/95 (23%), was significantly associated with both improved HbA1c 51.9 vs 68.3 mmol/mol ($P<0.00001$) and lower 3 month average BG.

Discussion

Our unit will continue to specify that reviewing and reducing the 2 week ABG is the short term interval goal to facilitate improved control. However, CYP will be informed the 3 month ABG is more representative of the HbA1c to be expected in clinic, to avoid disappointment, and predictive accuracy of ABG is improved when at least 5 BG tests are taken each day. The team will focus on strategies to educate and support CYP to understand and reduce the blood glucose S.D. to below 4 mmol/l as a means to further improve control and outcomes.

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P20

Identifying barriers and solutions to the optimal management of a patient with T1DM and a severe life limiting dermatological condition

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Background

We present a case of a 10 year old female with T1DM, referred to our tertiary centre for complex diabetes care due to her other severe chronic dermatological condition. We discuss the difficulties with optimizing diabetes control in such a chronic debilitating condition which has a pervasive effect on T1DM treatment.

Case

To our knowledge this is only the second reported case of a child with T1DM and Epidermolysis Bullosa. Severe Recessive Dystrophic Epidermolysis Bullosa (RDEB) is characterized by a lack of adhesion under the basement membrane of the skin, leading to blisters which heal with scarring, contraction of the joints, fusion of the fingers and toes, contraction of the mouth membranes and narrowing of the oesophagus. Additionally, RDEB patients have a high chance of developing squamous cell carcinoma. The particular issues that have arisen in relation to T1DM care include:

1) Poor skin integrity affecting insulin administration and glucose monitoring (including both continuous and sporadic testing).
2) Pain for multiple reasons; In particular, pain on swallowing due to oesophageal strictures which in turn lead to variation in oral intake and reliance on gastrostomy feeds. This impacts on carbohydrate counting, carbohydrate ratios and overall effectiveness of insulin requirements/absorption.
3) Limitations of physical ability, particularly reduced hand dexterity, effecting ability to provide her own diabetes care and resulting in reliance on others. This lack of autonomy had led to emotional difficulties especially around school.
4) Language barriers due to relocation for care of her RDEB, which has made relationships between healthcare centres and recognition of the patient and her family's diabetes knowledge more complex. This has impacted on the treating diabetes team deciding the best course of treatment in her condition.

In addition, there are deep psycho-social implications of this life limiting condition combined with the new diagnosis of T1DM.

Discussion

This particular case highlights the complexities of management of a patient with T1DM and a severe dermatological condition. Discussion around this case helps to highlight those aspects of care that can best support patients, families and healthcare professions in caring for these patients.

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P21

Will informing patients with diabetes about their care processes results help improve care processes completion rates? An innovative project

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Evidence suggests that empowering patients of chronic illness with self-management skills improves the outcomes. European countries with high emphasis on diabetes self-management education report significantly better clinical outcomes. In PREM survey, few service users expressed the desire to know the results of their annual review blood results. We used this as a trigger for a project to inform service users about their annual care processes completion status. We describe the project and its progress below.

Materials and methods

We designed a standard format for an Annual Review Letter. The letter contained three pages. The opening page listed all annual care processes with explanation of each care process and its importance. The second page listed all HbA1c values of individual patient for that year with a custom colour coded HbA1c chart. This page also listed completion status/results of other care processes with individualised comments entered by a clinician. Third page suggested goals for that patient to work on in the next year of care. The content and design of the letter was reviewed by service users through Patients Relations Team and their suggestions were incorporated in final design. Generating these letters manually for all patients was felt to be time consuming and difficult considering wide variation in IT skills in our team. Therefore, a semi-automated process was developed. Data was downloaded from diabetes database in the form of three MS Excel sheets and fed into a custom developed Microsoft Excel workbook with advanced formulas to generate the letter including the graph and get it ready for comments input by clinician. This workbook can be re-used by pasting new data next year. The letters were printed in colour and sent to all patients by post. We used Microsoft Teams and Planner to coordinate and monitor the project.

Result and conclusion

The project was completed by sending out annual review letters to all patients in the service ($n=143$). We shall launch a survey after 2 months to seek formal feedback from patients/parents on this project. We shall evaluate impact of this project on care process completion rates in next NPDA cycle.

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P22

Group outpatient clinics for children and young people with type 2 diabetes: a service evaluation

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Introduction
Youth-onset type 2 diabetes is an emerging public health crisis with a more aggressive phenotype than both adult-onset type 2 and child-onset type 1 diabetes. Family-focused, lifestyle intervention provided by a multidisciplinary team is central to effective management. Group clinics were introduced for all paediatric patients with type 2 diabetes. A service evaluation assessed the clinical impact and effectiveness of this innovative approach.
Methods
All patients, aged 11–17 years, with type 2 diabetes were offered four group clinics instead of individual appointments, over a 1-year period. There were 12 participants and all immediate family were encouraged to attend. Clinic consisted of routine biomedical measurements, a 1-h group education session and a 10-min individual review. HbA1c, waist circumference and age-gender related BMI centile were measured at each appointment. Patient and parent satisfaction was assessed using mixed-methods questionnaires and attendance rates analysed.
Results
Complete HbA1c data ($n = 11$) demonstrated a statistically insignificant rise ($P = 0.53$). Median HbA1c increased from 44 mmol/mol to 48 mmol/mol over the 1-year. Age-gender related BMI remained static on the 99th centile. Waist circumference data ($n = 8$) showed a statistically insignificant rise ($P = 0.09$). Combined patient/parent Likert-scale feedback was positive on all aspects of group clinic: structure, experience, content and lifestyle changes. 92% of respondents would recommend group clinic, however 54% would prefer an individual appointment. Attendance rates were 59.6%, compared to 78.7% for the previous year of individual appointments ($P = 0.127$). No patient attended all four appointments and an inverse correlation was identified between length of diagnosis and attendance rates.
Conclusions
There was no statistically significant rise is HbA1c or waist circumference. Extrinsic factors such as increased insulin resistance and other challenges of adolescence rather than clinic approach may have prevented improvement. Poor attendance may also have limited the impact of the group clinic. Questionnaire responses were predominantly positive towards the group clinic and participants reported learning more nonetheless, most would prefer individual appointments. Overall, the group clinic delivered increased multidisciplinary, family focussed, lifestyle intervention and peer support, without increasing workload or having a statistically significant negative impact on biomedical outcomes.

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P23

Different financial models employed by diabetes transition units within Yorkshire and South West London's Children and Young People's (CYP) networks

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Introduction
The ultimate goal of a diabetes transition service is to provide coordinated, uninterrupted and developmentally appropriate healthcare, which promotes skills in decision-making, communication, autonomy, and self-care, with an essential component required to achieve this, being adequate resourcing.
Methods
Data from Yorkshire and South West London CYP diabetes networks were collected via questionnaire. The primary focus was to ascertain which diabetes units used Best Practice Tariff (BPT) to finance their transition service, and whether this correlated with a better resourced and more efficient transition service.
Results
Responses were received from 15/16 units in Yorkshire, and 7/11 in SW London. Within Yorkshire, 2/16 units did not receive BPT for 16–19 years. 7/16 units financed their transition service using BPT (group 1), 2/16 did not use BPT and had a reciprocal (goodwill) agreement with adult services (group 2), and 6/16 did not use BPT and financed their transition service from adult resources (group 3). All units in group 1 commented that transition services ran well and were well-resourced, having at least 4 team members in clinic, compared to 10/16 in group 3, which was less well-resourced, having at least 3 team members in clinic. Group 2 were not satisfied with their transition service. Transition preparation was initiated at a younger age in group 1 (43% started transition at 11–12 years) compared to 33% in group 3. In SW London, only 1/7 diabetes units did not receive BPT for 16–19 year olds. 6/7 units used BPT to finance their transition service and 57% (4/7) thought it ran well. The diabetes units were well resourced with 71% having at least 4 team members in clinic, and 43% started transition preparation at 11–12 years. The single unit that did not finance their transition service using BPT were dissatisfied with it.
Conclusion
The diabetes units which used BPT to finance transition, were more satisfied with their service, which was better resourced, and they initiated transition preparation at a younger age. With uncertainty regarding the future of diabetes BPT, allocating funds from BPT to develop and adequately resource the transition service should be given important consideration.

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Diabetes 2

P24

Characterizing putative mutant variants of monogenic diabetes

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Diabetes mellitus is a disease with one of the greatest burdens to both the economy and the individual. Monogenic diabetes mellitus, responsible for neonatal diabetes mellitus and maturity-onset diabetes of the young (MODY), results from one mutation in a single gene. Many of these genes play a role in pancreatic development and their variants can increase risk of type 2 diabetes mellitus (T2DM). Therefore, while the monogenic form of diabetes contributes the least to the overall disease burden, its study can both bring insight into the pathogenesis of polygenic T2DM and advance ß-cell differentiation protocols by improving knowledge of pancreatic development. Previously, novel mutant variants of numerous genes have been identified in a cohort of patients with non-autoimmune puberty-onset diabetes of unknown pathogenesis (strongly suggestive of monogenic diabetes). Two of these genes, an epigenetic modulator (two mutants studied) and a zinc-finger protein (one mutant studied), have been evaluated *in silico* for the likelihood of causing a deleterious outcome *in vivo*, yet their exact phenotype remains unknown. Over-expression of human wild-type and mutant variants of these genes was achieved by electroporation of MIN6 murine insulinoma cell line with the respective plasmids. Our findings reveal dysregulation of pancreatic gene expression following mutant transfection. Specifically, both of the studied epigenetic modulator mutants showed down-regulation of *Insulin*, *MafA*, and *Isl1*. This suggests a potential mechanism of ß-cell physiology disruption in the individuals carrying these mutant variants and hence the importance of this epigenetic modulator in endocrine pancreas. Similarly, the zinc-finger mutant showed dysregulation of pancreatic gene expression, particularly it caused reduction in *Chga*, *NeuroD1*, and *Mafa*, all of which are crucial for ß-cell function. This indicates the zinc finger mutant identified in the patient cohort might be a loss-of-function mutation, leading to an impaired mature ß-cell differentiation state. Together, these experiments suggest their role as putative mutant variants leading to monogenic diabetes. Future work will aim to replicate these mutations in human induced pluripotent stem cell line and study them in small rodents to further decipher their phenotype.

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P25

Modifiable dietary factors and a case for tracking dietetic outcomes in the National Paediatric Diabetes Audit

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Children and young people (CYP) with Type 1 Diabetes who maintain a healthy BMI, diet and accurate carbohydrate-counting have lower risk of cardiovascular disease and diabetes complications. The tracking of key Diabetes health checks and outcomes via the National Paediatric Diabetes Audit (NPDA) has been successful in ensuring year-on-year improvement of national average HbA1c. Aside from BMI however, Dietetic-specific outcomes are not currently included in the NPDA. Therefore, the present audit designed and trialled 5 Dietetic outcome measures which can be used to track adherence to dietary management goals (as per 2015 NICE guidelines for Paediatric Type 1 Diabetes) year on year. These outcomes are: 1) Daily serves of fruit, 2) Daily serves of vegetables, 3) Daily serves of ultra-processed and discretionary foods, 4) meeting Calcium requirements, 5) main carbohydrate-counting method used. Baseline data for these outcomes were collected through a standard Dietitian-led questionnaire at each patient's annual Dietetic review during the last full financial year (April 2018–March 2019). Latest HbA1c and BMI centile at the time of the Dietetic review were also collected. The cohort comprised 107 patients with type 1 diabetes, aged 2–18 years who attended their Dietetic annual review at a UK-based Paediatric Diabetes unit. Gathering of baseline Dietetic outcomes for the whole patient cohort provided key insights into Dietary trends and problem areas. Only 6% of CYP meet minimum recommendations for daily vegetable intake (3 serves), whilst 46% meet daily fruit recommendations (2 serves). Ultra-processed foods appear to replace daily vegetables for the majority of CYP, with 75% of cohort significantly exceeding recommended limits (0–1 serves per day). Indeed, 50% of CYP interviewed reported 3 or more ultra-processed foods per day. Calcium requirements were met by just over half (55%) of children. Finally, CYP who reported using weighing scales regularly displayed significantly lower average HbA1c (60 mmol/mol) compared to those who relied on pictorial tools (71 mmol/mol) or guessing (78 mmol/mol). In conclusion, Dietetic outcomes are valuable monitoring tools which highlight specific problem areas in need of addressing, and inclusion in the NPDA.

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P26

Two cases of bilateral cataracts in early type 1 diabetes

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Introduction

Cataract development as a complication of diabetes is usually associated with increased age and longer duration of diabetes. However, rapidly progressive cataracts have also been described at, or soon after, diagnosis of type 1 diabetes (T1DM). We report two cases of adolescents with T1DM and bilateral cataracts, including one case in which visual loss was the presenting symptom.

Cases

A 16-year old non-obese, caucasian boy presented to his GP with acute bilateral visual loss. He described increasingly blurred vision in his left eye for three weeks and had noticed similarly blurred vision in his right eye that morning. He also reported tiredness and new-onset nocturia for approximately a month, although he denied polydipsia or weight loss. Blood glucose was 26 mmol/l and ketones were 2.6 mmol/l, leading to a diagnosis of T1DM. His HbA1c was 149 mmol/mol at diagnosis. Ophthalmologic examination demonstrated bilateral dense posterior subcapsular cataracts; the left cataract was visible with the naked eye. He underwent sequential bilateral cataract removal within two weeks of diagnosis due to severely impaired vision, with good outcome. A 13-year old non-obese, caucasian girl had a one-year history of T1DM, treated with a basal bolus insulin regimen. She saw her community optician due to visual glare and was referred to the ophthalmology clinic where she was diagnosed with bilateral early cataracts. Her symptoms progressed quickly, and within a month her vision had significantly worsened . She underwent sequential bilateral cataract removal which restored her vision to normal.

Discussion and learning points

Cataracts in early type 1 diabetes are rare, with an incidence of less than 1%. The pathogenesis of cataracts in diabetes is not fully understood; likely mechanisms include osmotic stress from sorbitol accumulation in the lens, oxidative stress, and glycation of lens proteins. Previous literature suggests that early diabetic cataracts are more common in adolescent females. Another postulated risk factor is a prolonged period of hyperglycaemia, such as prior to diagnosis in our first case. Our cases reinforce the need to conduct ocular screening from diagnosis of diabetes, and to consider diabetes in any young person presenting with cataracts.

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P27

Observational Study looking at the Impact of changing from novorapid to insulin aspart on glycaemic control in the clinic setting

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Introduction

The first multi-center randomised trial looking at the efficacy and safety of Insulin Aspart, a faster acting insulin which aims to mimic endogenous prandial insulin action, was published in May 2019. We report our experience of using Insulin Aspart in the Norfolk and Norwich University Hospital children's diabetes clinic.

Methods

Children and young people with type 1 diabetes seen the Norfolk and Norwich paediatric diabetes service (total patient population aged 0–19 years 289 individuals) were invited to change from Novorapid to Insulin Aspart between May and September 2017. Consent was taken from patients and their families for the unlicensed use of Insulin Aspart. Data including point of care HbA1C mmol/mol, percentage time in target (4–9 mmol/l) and percentage time below target ($<$4 mmol/l) was collected as part of routine clinic follow up.

Results

Forty-eight children and adolescents (25 male) with type 1 diabetes aged a median of 11.3 years (standard deviation 3.8 years) elected to change to Insulin Aspart. Median time since diagnosis was 3.9 years (range 1–14 years). To make decisions regarding insulin therapy twelve children used DEXCOM CGMS, twenty Libre FGM and sixteen blood glucose testing strips. HbA1C was 58.4 mmol/mol at baseline (s.d. 9.5), and 58.9 mmol/mol (s.d. 11.4) at 9 months ($P=0.8$). In patients using DEXCOM/CGMS, time in target was 51.5% at baseline and 47% ($P=0.8$) at 9 months and time below target was 6% at baseline and 5% ($P=0.8$) at 9 months. Anecdotally patients reported that contrary to expectations Insulin Aspart needed to be administered 15–20 min prior to food to manage the post prandial rise. Six children stopped Insulin Aspart during the 1.5 year follow up period. One individual stopped insulin Aspart due to the development of severe lipodystrophy after 18 months of treatment, one developed a localised allergic rash and one reported frequent cannula blockages.

Conclusion

Overall Insulin Aspart was well tolerated. We saw no significant difference in HbA1C in the patients on Aspart with no significant improvement in time in/below target. Further data should be collected with regard to the optimal timing of Insulin Aspart in relation to meal times.

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P28

Using quality improvement (QI) to improve the care pathway and outcomes for children newly diagnosed with type I diabetes mellitus

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Background

Early glycaemic control improves long-term outcomes in children with Type I diabetes. The NICE target for children with T1DM is HbA1c $\leq$ 48 mmol/mol. 2018 data from our newly diagnosed patients (pre-QI) demonstrated mean HbA1c 50 mmol/mol at 3 months and 62 mmol/mol at 12 months.

Aims and methods
Our aim is to improve average blood glucose levels at day 28 post diagnosis and achieve a median HbA1c of <48 mmol/mol at 3 and 12 months post diagnosis in 75% of our newly diagnosed patients by November 2020.
Drivers for improvement included:
1) Implementing Carbohydrate Counting and Expert meters at diagnosis of Type I diabetes.
2) Intensive inpatient management with multiple insulin correction doses and overnight corrections.
3) Achieving blood glucose levels in target prior to discharge to emphasise the importance of this to our families.
4) Additional MDT clinic 6 weeks post diagnosis.
5) Setting up home downloading and Diasend accounts prior to discharge for new patients.

We used Fishbone analysis to undertake a needs assessment for implementing carbohydrate counting and Expert meters at diagnosis. The main barriers were ward staff training and communicating key changes to the wider paediatric team. 'Tea Trolley' training and 'Newly Diagnosed Packs' helped facilitate change. Outcome data on average blood levels, HbA1c, days to carbohydrate counting and balancing measures including length of stay were collected.
Results
10 new patients have been managed along the new care pathway. Mean average blood glucose at D28 post diagnosis has improved from 8.0 mmol to 5.9 mmol. Mean HbA1c at 3 months post QI is now 45.9 mmol/mol ($n=7$). Average length of initial hospital stay increased from 3.2 to 4.3 days. All patients had the facility to home download at discharge.
Lessons learnt
Weekly QI meetings and maintaining run charts of average blood glucose and HbA1c for new patients has been a powerful team motivator. Working with other teams in the National QI Collaborative has made us braver to implement change and initial project results are encouraging. We are now using QI methodology to improve clinic experience and education around download interpretation.

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P29

Bridging the gap: a young person-centred diabetes transition service

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Introduction
Within the Bristol diabetes service, we recognised that we were failing to meet the needs of young people (YP), who reported feeling unprepared for transition and intimidated by the unknown entity of the adult service and changes in their diabetes management.
Methods
We set up a multi-disciplinary steering group, including the paediatric and adult diabetes teams and a youth involvement worker, to develop an effective, multi-faceted transition strategy. To enable patient-led service improvement, we sought the opinion of YP with diabetes in a focus group ($n=5$). Utilising focus group feedback, the following changes were established:
i) Introduction of age-banded clinics
- In paediatric service – fortnightly YP's clinics for over 14 years to transition, attended by an adult consultant or diabetes nurse specialist (DSN).
- In adult service – paediatric DSNs to start attending pre-existing monthly young adult's clinic from transition to 25 years.
- Patients over 14 years given the opportunity to be seen alone at every consultation.

ii) Transition paperwork
- Introductory transition pack was developed, including an introductory letter explaining the new clinics and service changes, a leaflet about transition, and transition checklists for patients and parents to be discussed at clinic.
- Checklists covered: a) education, b) lifestyle, c) access to support and services, d) transition.
- Additional copies of clinic letters sent to patients, not just parents.

iii) Diabetes transition website
- Developed website to provide reliable, accessible information for YP covering transition, management of diabetes and various lifestyle topics such as exercise, alcohol, sex, smoking and education.

Results
1 year later, YP ($n=21$) were asked to complete an anonymous questionnaire. 70% reported that they had been spoken to about transition, 71% knew more about the adult service as a result and 85% valued having met the adult team. Patients frequently reported they wanted more opportunities to both meet the adult team and be seen alone.
Conclusion
The transition service changes, designed utilising patient voices, have been well received by YP although further work is needed. To facilitate continual improvement, we plan to incorporate further valuable patient input from additional focus groups, ongoing questionnaires and patient satisfaction surveys into service design.

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P30

Perceptions of multi-disciplinary team members and their roles: a survey of 82 carers and patients

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Background
Patients and carers encounter a range of diabetes multi-disciplinary team (MDT) members. Patients in focus groups have indicated that nurses are more approachable than doctors[1], and the presence of specialist nurses in the MDT improves glycaemic control[2]. Nurses are perceived to be the core providers of diabetes care but this has not been quantified, nor have the perceived roles of other members of the MDT been explored.
Methods
In June 2019, an online survey was sent to the primary contact of all children with diabetes in our centre. The ten-question survey examined the influence of different MDT members and the perceived roles of each member.
Results
Of 82 returned surveys, most (87%) were completed by a carer and 11% by the child with diabetes (2% unanswered). Specialist nurses were reported to be the most frequent point of contact by 95% of participants overall, but among patient participants 22% reported the doctor as the most frequent contact. When listing MDT members, nurses (98%), doctors (77%), dietitians (51%), and psychologists (34%) were most frequently named. Nurses were described as the most important source of support (85%) and help with diabetes control (73%). In the descriptive section, participants had a varied understanding of the role of administrators, dietitians, and psychologists. Specialist nurses were strongly associated with being a first point of contact, helping with day to day issues, and 'advice,' 'support' and 'help' were frequently used to describe their role. Doctors were associated with 'control,' 'targets,' and 'HbA1c' as well as oversight, maintenance, and monitoring.
Discussion
This is the first quantitative data confirming that participants perceive nurses to be of primary importance in the MDT, despite some fluidity between the roles of doctor and nurse in practice. Disappointingly, administrators, dietitians, and psychologists were less often listed as core members of the MDT and diabetes teams should work to actively promote their role. In addition, these results emphasise the continued need for medical staff to consider their patients holistically and work in partnership with them.
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P31

Continuous glucose monitoring improves A1c, time in hypoglycaemia and time spent in target range within the paediatric population

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Objective
We aim to examine the effects of continuous glucose monitoring (CGM) within our local population by means of pre- and post-CGM introduction A1C, time spent in hypoglycaemia and time spent within personalised target.
Methods
Retrospective study of the County Durham and Darlington Foundation Trust (CDDFT) patient group who use CGM was undertaken via the platform 'twinkle' and 'diasend'. Results were graphed prior to statistical evaluation. Primary outcome was change in HbA1c.
Results
The primary outcome of A1c showed improvement from pre-CGM measurements to post-CGM introduction. We also present data showing time spent in hypoglycaemia and time spent in personalised target which compares favourably to International data across adult and paediatric populations.
Conclusion
Use of continuous glucose monitoring locally has similar results to those in national adult trials. All parameters studied (A1c, time in hypoglycaemia, time within target) have improved within our local trust. Ongoing use remains recommended.

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Diabetes 3

P32

Development of a live visual HbA1c dashboard to improve engagement and clinical outcomes – a type 1 diabetes QI project

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Introduction
An HbA1c target level of 48 mmol/mol or lower in children with type 1 diabetes is recommended by the National Institute for Health and Care Excellence. Only 7.1% (national average 7.2%) of children in our unit achieved this target. In response, during a multidisciplinary diabetes away day, we explored innovative approaches to timely and efficient identification and intervention in patients with high HbA1c levels. The National Paediatric Diabetes Audit web portal, at present, does not allow a prospective dashboard function at a unit or individual patient level.
Methods
We developed a free and user-friendly spreadsheet to record and analyse HbA1c levels prospectively for every patient. 'Sort' and 'chart' functionalities were used to make the data relevant for the unit and individual patients and parents.
Results
Our bespoke database serves as a visual HbA1c dashboard, where prospectively inputted HbA1C levels are automatically 'RAG' rated, to effectively flag patients with poor control. This database is utilised at fortnightly multidisciplinary diabetes meetings to quickly identify and discuss patients (2–3 children at each meeting) with highest or worsening HbA1c levels and those who have missed their quarterly measurements. Moreover, each patient is able to see their HbA1c temporal trend in clinic, as a bar chart, facilitating engagement. Ongoing work in the second stage of this QI project include analysis of factors associated with poor HbA1c control. We aim to devise patient-specific input from the multidisciplinary team to empower patients and parents.
Conclusions
We are keen to share how we have creatively utilised a simple and already-available software on Trust computers to develop a patient-centred tool to improve clinical outcomes and patient and parent engagement. We believe that this can be replicated in other units.

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P33

C-peptide and antibody testing to aid diabetes diagnosis in children and young people

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Introduction
Recent experience of C-peptide testing in adults with longstanding diabetes has revealed misdiagnosis of monogenic diabetes as either type 1 or type 2 with important implications for quality of life and healthcare costs. Correct diagnosis earlier in life may be possible with the use of routine antibody testing at diagnosis and c-peptide measurement 3 years after initial diagnosis. Negative or low titres for all 3 antibodies suggest non-type 1 diabetes. Persistence of detectable c-peptide beyond 3 years from diagnosis raises the possibility of non-type 1 diabetes
Methods
All children and young people with type 1 diabetes known to the Royal Hospital for Sick Children diabetes team underwent testing. C-peptide levels were measured at the time of annual review with paired serum glucose, and considered positive if >50 pmol/l. Glucose >8 mmol/l required at time of testing to avoid false negative. Antibodies were measured at diagnosis, or at annual review appointment for any patients in whom antibodies had not previously been checked. Cut-off values for positive results were GAD>5, IA2 >7.5 and ZnT8 >15.
Results
214 individuals aged <18y had c-peptide levels requested. Results were available for 203 patients. Results were categorised as 1–3 years or >3 years since diagnosis. 7 patients had persistent c-peptide at >3 years, of which 1 was >200 pmol/l. 14 patients had persistent c-peptide at >3 years, of which 2 were >200 pmol/l. 230 patients aged <16y had antibody testing. 72 tested for GAD & IA2, 153 tested for GAD, IA2 & ZnT8, 5 tested for a single antibody. 45 patients were single antibody positive. 12 patients were, of whom 2 had been diagnosed less than 2 years. 1 triple antibody negative patient had undetectable c-peptide. The other triple antibody negative patient had c-peptide of 170 pmol/l at 13 months since diagnosis, raising possibility of non type 1.
Conclusion
This study has identified a number of young people with persistent c-peptide beyond 3 years from diagnosis. Negative antibody testing can guide future investigation. We recommend measuring GAD, IA2 and ZnT8 antibodies in all patients at diagnosis, and C-peptide at 3 years.

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P34

When one diagnosis just isn't enough – diabetes as a first presentation of cystic fibrosis

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Diabetes is a common presentation in children and young people. We describe a case of undiagnosed cystic fibrosis (CF), where diabetes was the presenting diagnosis. A 14 year old girl presented with a 2-month history of weight loss, abdominal pain, polyuria and polydipsia. Blood glucose was 31.4 mmol/l with ketones of 0.8 mmol/l, and a diagnosis of T1DM was made. Initial bloods showed HbA1c 150 mmol/mol, normal thyroid function, negative TTG, and negative TPO, GAD and IA2 antibodies. Her HbA1c remained well controlled for the next few years on MDI's, at 42–51 mmol/mol. Recent urine C-peptide was 3.15 nmol/l, indicating preserved pancreatic beta-cell function 4 years after diagnosis of diabetes. At 16 years she noted that large meals caused diarrhoea and she had a persistent cough. At 17 years she presented with haemoptysis, and reported 6 months of productive cough, requiring recurrent antibiotics, with a 4-month history of weight loss. Chest X-ray suggested bronchiectatic changes and a high-resolution CT confirmed widespread cylindrical and cystic bronchiectasis. She was negative for HIV and TB, with a negative vasculitis screen and normal

alpha-1-antitrypsin levels. Her lung function tests were normal, with good exercise tolerance. A genetic screen showed homozygous △F508del, confirming the diagnosis of CF. Newborn screening for CF was fully introduced across the UK in 2007 and has helped in the early identification of children with CF. Most late onset (after 16 years) diagnoses of CF occur in people with compound heterozygote mutations, the majority presenting with respiratory complications. To our knowledge there are three case reports of children with diabetes as the presenting feature of CF. We describe an unusual case of an adolescent with homozygous △F508del who presented initially with diabetes, before the respiratory manifestations of CF became apparent. In retrospect, respiratory and gastrointestinal symptoms were present previously. The lack of clear autoimmune features of T1DM should have raised the possibility of an alternative form of diabetes. It is therefore important to consider the possible diagnosis of CF in adolescents with diabetes who have associated respiratory or gastrointestinal symptoms, and who may have missed newborn screening, particularly with negative pancreatic beta-cell antibodies and high urine C-peptide.

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P35

Rare association of type 1 diabetes mellitus (T1DM) with tubulo-interstitial nephritis and uveitis (TINU) and hypercalcaemia

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Children and adolescents with Type 1 Diabetes Mellitus (T1DM) are at increased risk for developing other autoimmune diseases. We are presenting this rare association of tubulo-interstitial nephritis and uveitis (TINU) with severe hypercalcaemia and type 1 DM. 12 years old girl, with Type 1 Diabetes for 5 years presented with 4 months history of weight loss, abdominal pain, nausea, tiredness, anorexia and recurrent hypoglycaemias. Her HbA1c levels was 38 mmol/mol (5.6%). She was also noted to have normocytic anaemia and proteinuria. Further investigations showed a normal Synacthen test however urea and creatinine were elevated with significant hypercalcaemia. Subsequently, she also developed bilateral granulomatous uveitis with topical steroids. There were no chest symptoms or skin lesions. In view of hypercalcaemia, abnormal kidney functions and granulomatous uveitis she was investigated for Sarcoidosis. She had raised serum Angiotensin Converting Enzyme (ACE) levels. She had normal chest X-ray and ultrasound abdomen. Renal biopsy revealed acute tubule-interstitial nephritis with no evidence of granulomas and giant cells. Her calcium levels continued to be high despite hyperhydation regime, low calcium diet and diuretics, hence received a dose of IV Pamidronate. She was treated with oral prednisolone for 3 months and her renal function and hypercalcaemia recovered completely with no flare-ups in last 18 months. Even though our patient was diagnosed to have TINU, we could not explain raised ACE levels and significant hypercalcaemia. Our patient also had markedly raised 1,25 di-hydroxy vitamin D levels suggesting increased macrophage activation of 1-alpha hydroxylase enzyme causing conversion of 25-OH vitamin D to active hormone. So we suggest patient also had Sarcoidosis in spite of absence of granulomas in renal biopsy.

Investigation	Results	Normal range
Urea	12.8	2.5–6.5 mmo/l
Creatinine	228	38–74 micromol/l
Haemoglobin	83	115–165 g/l
Urine Protein creatinine ratio	337	0–30 mg/mmol
Calcium	3.48	2.2–2.6 mmol/l
Phosphate	1.8	0.9–1 mmol/l
Alkaline Phosphatase	130	60–425 iu/l
PTH	<0.3	1.6–7.53 pmol/l
25 OH vitamin D	98	>50 nmol/l
1,25 di-OH vitamin D	>440	20–120 pmol/l
Urine calcium creatinine ratio	1.77	0–0.59 mmol/mmol
ACE	103	8–52 U/l

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P36

Using NPDA data for quality improvement: dedicated annual review clinics are effective in increasing completion rates of health care processes

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Introduction
NICE recommends specific annual health checks for children and young people (CYP) with diabetes aged 12 years and over to check for health of feet, kidneys, thyroid and eyes in addition to BP, BMI and HbA1c. Historically, we included annual review care processes into regular diabetes multi-disciplinary clinics. In 2017, our service was identified as negative outlier in the National Paediatric Diabetes Audit for completion of health care processes. In particular, completion rates for blood tests, urine analysis and foot examination were unsatisfactory. As part of a wider quality improvement project, dedicated Annual Review Clinics (ARC) were developed and started in September 2018. ARC consist of three separate 30 min appointments with nurse, dietitian and doctor; the clinic is run in the morning and located in close proximity to phlebotomy services. Specific ARC templates for each profession were designed.
Method
Retrospective audit comparing completion rate of specific care processes (blood test, urine analysis, foot exam) before and after introduction of a dedicated ARC. A total of 55 CYP aged $^{3}12$ years attended the newly designed ARC between September 2018 and March 2019. Data on investigations (blood tests, urine analysis) and foot examination were collected from the laboratory database and diabetes management system respectively. Completion rates of specific annual review care processes for those CYP were compared with their individual completion rates for the same care processes during the previous year.
Outcomes
The rate of completion increased for all of the specific care processes. Almost 93% (51/55 CYP) had at least one of the assessments completed in the Annual Review Clinic compared to 70% (29/55) for the same group for the previous year. The same CYP had much higher completion rates for the specific care processes compared to the previous year (foot exam 87.2% vs 63.6%; blood test 87.2% vs 65.5%; urine analysis 81.8% vs 49%). More CYP had all seven recommended care processes completed.
Conclusion
A dedicated Annual Review Clinic is effective in ensuring CYP with diabetes receive recommended health care processes. Ongoing review of clinic processes is required to ensure completion rates improve further to maximise health.

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P37

Improving outcomes for young people with type 2 diabetes mellitus

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Background
Our Paediatric Diabetes service has a challenging rise in proportion of patients with Type 2 Diabetes Mellitus (T2DM); 8.5% of our current cohort; compared to 3.5% regionally and 2.5% nationally (NPDA 2017–2018).
Objectives
Establish a T2DM New Diagnosis Pathway and T2DM clinics aiming to achieve HbA1c < 48 mmol/mol for all new patients at 3 months and a year, with 10% weight loss.
Methods
Patients diagnosed with T2DM since November 2018 are admitted for education/treatment according to the new pathway. Comorbidity screening is undertaken at diagnosis with psychology and dietetic screening of well-being/eating behaviours. Patients have monthly MDT review for the first 3 months with adjustment of treatment, diet/activity prescriptions and agreed goals. Patient outcomes were compared with the preceding 6 patients.
Results
Six patients were newly diagnosed with T2DM (mean HbA1c 78 mmol/mol; previous group mean 54 mmol/mol). HbA1c significantly improved at 3 months for both current and previous patients (mean HbA1c 44 and 42.5 mmol/mol respectively), with no significant difference between groups. However, with the new pathway, a greater proportion achieved HbA1c <48 mmol/mol compared to previous (80% vs 67%). A greater proportion had comorbidity screening at diagnosis, with improved profiling of lipids and sleep assessment (100% vs 67% and 83% vs 0% respectively). In the previous group, 2/6 had evidence of fatty liver disease and dyslipidaemia. In the current group 1/ 5 screened had evidence of sleep disordered breathing. Median BMI Z score SDS was unchanged in the previous group between diagnosis and 6 months (+2.8 SDS). In the current patient group the median had improved to +2.4 SDS from +2.7. Overall however the mean BMI Z score had not changed significantly from diagnosis to 6 months in either group. Additional outcomes included coordinated comorbidity screening, reducing appointment burden. Specialised clinics have facilitated recruitment to clinical trials. Wider impact of the service includes the initiation of young people friendly local gym opening times.
Conclusion
The tailored T2DM pathway and clinics have improved the proportion of patients achieving the target HBA1c at 3 months with a more holistic and streamlined approach.

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P38

Remission rates, demographics and outcomes of paediatric patients with type 2 diabetes at a single centre: 2006–2018

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Background
Incidence of type 2 diabetes (T2DM) is increasing in children and young people under the age of 18 years. This group has a higher risk of microvascular complications and a more adverse cardiovascular risk profile than those diagnosed later. Weight loss is essential for remission, but intensive input is often required to achieve this.
Aims
1. Describe the demographics of our T2DM population
2. Look at our remission rates
Methods
Patients were identified from a local database of patients with T2DM. Their hospital records were reviewed to identify baseline characteristics, treatment, progress and whether remission was achieved ($n=34$).
Results
Patients were most commonly female (38% male, 62% female), white (53% White, 35% Asian, 12% Black) and 75% had a family history of T2DM. Co-morbidities at baseline included polycystic ovary syndrome ($n=4$) and hypertension ($n=7$). Remission was achieved in nine and maintained in five (relapsed: $n=3$; unknown: $n=1$). Weight loss at remission was 8.0±3.3% and remains below baseline (7.6±4.2%, $n=7$) compared to the non-remission group, who have gained weight (1.8±11.2%, $n=16$). Patients who achieved remission most commonly opted for healthy eating and lifestyle management. One patient followed a supervised very low-calorie diet (<800 kcal/day) for six weeks followed by introduction of regular balanced meals.

Table 1 Characteristics of patients with T2DM at baseline, remission and present.

	Remission	Non-Remission	*P*
N	9	25	
Age (years)	15.5±0.8	14.7±2.0	0.08
Baseline BMI SDS	3.29±3.9 ($n=4$)	3.37±3.8 ($n=10$)	
Baseline HbA1C	77±29	74±28	0.82
Remission BMI SDS	1.48±1.07	N/A	
Current BMI SDS	1.55±0.65	2.97±2.47	
Current HbA1c	39±5 mmol/l ($n=8$)	73±28 mmol/l ($n=20$)	

Conclusions
Remission is achieved in a minority of patients despite intensive input from hospital teams. Patients who achieved remission maintain a lower HbA1c and BMI SDS in comparison to the non-remission group, even if they have experienced a relapse. This demonstrates the importance and positive impact of weight loss, even if relapse occurs.

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P39

Paediatric diabetic ketoacidosis (dka)-management in a district general hospital

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Background
Diabetic ketoacidosis (DKA) can have significant morbidity and mortality in children and young people (CYP). Its management is very well standardised, based on National Guidance (National Institute of Clinical Excellence – NICE). In the UK, CYP DKA Guidelines have been reviewed in 2015 in order to reduce the risks of cerebral oedema. There have been concerns that the new recommended fluid management has the potential to increase the risk of acute kidney injury (AKI) or other complications due to significantly reduced fluid management volumes. In our Trust, the 16–18 year olds are managed by adult physicians but based on CYP guidelines. We wanted to review the practice in our hospital and to establish our compliance and any deviations from the guidelines and if there are any significant complications in our patients.
Methods
We looked at the notes, discharge letters and lab reports.
Results
Over 12 months (October 2017–September 2018) we had a total of 19 episodes of DKA in 0–19 year old children. 3 episodes were of severe and 16 of mild/moderate DKA. 12 patients received fluid boluses. In 15 cases the ongoing fluid prescription was correct. In all patients insulin was started at least 1 hour after the initial fluids were given. 8/19 (42%) of our DKA episodes occurred in patients with known Type 1 Diabetes Melitus. The guideline was not appropriately used in 8/9 of over 16 year old episodes and 2/11 under 16 year old episodes. 12/19 (63%) received fluid boluses. 2 patients with altered Glasgow Coma Scale (GCS-14/15) received fluid boluses. 2/18 patients were in mild AKI at presentation and 1 was unknown.
Conclusions
In our cohort the majority of patients received fluid boluses, despite this not being the recommended measure on the current guideline. DKA still occurs in patients with known diabetes. Fluid management in DKA still remains a topic of some controversy. The British Society of Paediatric Endocrinology (BSPED) is currently reviewing the fluid management recommendations. There is ongoing national interest and participation in this review. The 16- to 18-year-old patients could potentially be managed on adult protocols in the future.

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Diabetes 4

P40

Neonatal diabetes, Don't sugar coat it!

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Background
Neonatal diabetes is an exceedingly rare condition, defined by the presence of persistent hyperglycaemia in the first months of life. It is sub-categorised into transient neonatal diabetes mellitus (TNDM) which resolves early and permanent neonatal diabetes mellitus (PNDM), which requires lifelong treatment. Transient neonatal diabetes is reported to have a global incidence of between 1/95 000–1/400 000 births. At present, there are less than 100 patients diagnosed with neonatal diabetes in the UK. The infant we describe was born at 39 + 3 weeks gestation and delivered via spontaneous vaginal delivery. She had a low birth weight of 2.28 kg and was asymmetrically growth restricted. She had hypoglycaemia monitoring which was normal and was discharged home on day 3 of life. She was reviewed in the community by the midwife on day 5 with a 16.6% weight loss and was found to be emaciated on examination. Her blood glucose was 37.8 mmol/l and her cortisol level was 200 nmol/l. Her C-Peptide level was < 0.10. She initially received intravenous insulin (requiring doses of 0.02–0.05 iu) with frequent adjustment of insulin dose required due to challenging glycemic control. After a period of adequate weight gain she was commenced on insulin via a subcutaneous pump which subsequently allowed her to transition to general paediatric care prior to discharge home. She had an echocardiogram which demonstrated a structurally normal heart and cranial ultrasound scan which was normal. Of note, there was a finding of a hemivertebra at T3 on chest x-ray and a finding of a conjugated hyperbilirubinaemia from birth, which slowly improved, with investigations for cholestasis unremarkable, including a normal liver and biliary ultrasound. Her genetic testing revealed she was positive for the 6q24 gene locus for transient neonatal diabetes. At present it is thought that the findings of a hemivertebra and conjugated hyperbilirubinaemia may well be linked to her genetic finding, As the 6q24 locus is associated with abnormalities in other systems. This is of particular interest as hemivertebra in neonates has a recognised association with maternal diabetes but the literature regarding an association between transient neonatal diabetes and hemivertebra is not well described at present.

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P41

Young person with Prader–Willi syndrome and type 2 diabetes – management challenges

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Introduction
Prader–Willi syndrome [PWS] is a complex genetic disorder with hypothalamic pituitary dysfunction that includes obesity, diabetes and behaviour changes. Obesity in PWS is due to decrease of oxytocin neurons and leptin resistance causing hyperphagia. Prader–Willi syndrome is associated with high incidence of altered glucose metabolism. The etiology for diabetes in PWS may be related to morbid obesity and resultant insulin resistance.
Case report
We present a case report of 15 yrs old boy with Prader Willi Syndrome and type 2 diabetes who was followed up in our endocrine clinic for severe obesity (BMI 46), developmental delay and behavioural problems. The TFT, MRI brain and CGH array test were normal. In view of his behavioural problems and severe obesity, a detailed genetic test for PWS was undertaken at the age of 12 years, which confirmed the diagnosis of PWS. He was on metformin from an early age. At 15 yrs, he developed polydipsia with a high HbA1c (105 mmol/mol). He was admitted to monitor the blood glucose levels (BGL) which was high (13–16 mmol/l). Continuous glucose monitoring [CGM] was commenced for five days showed values ranging from 12 to 24 mmol/l. Diabetes related antibodies – GAD, ZnT8 and insulin antibodies – were negative. In view of poor glycaemic control, he was started on mixed Insulin regimen along with Metformin to tackle adherence. Maintenance of optimal glycaemic control remains a significant challenge. Treatment options for youth-onset type 2 diabetes are in-adequate, limited to only two approved drugs (insulin and metformin) and the promotion of healthy lifestyle. In an adult with PWS, treatment with Glucagon-like peptide 1 (GLP-1) receptor agonist and analog has showed improvement in glycemic control.
Conclusion
Young person with type 2 diabetes is an evolving disorder in children, adolescents and young adults with distinctive challenges in both research and clinical care. To maintain the glycemic control in adolescents with PWS is an uphill task.

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P42

Newly diagnosed diabetes – incidence, presenting features and lessons learnt

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Introduction
The incidence of type 1 diabetes (T1DM) is increasing, affecting approximately 1 in 500 children and young people (CYP) under 19 years of age. The diagnosis of diabetes, as well as initial investigations and management is standardised, based on national guidance. Initial education and management have huge importance for long-term glycaemic control. We review the practice in our hospital, to establish our compliance and any deviations from the guidelines. We also look at whether there were any opportunities for earlier diagnosis and to reduce the incidence of newly diagnosed CYP presenting in diabetic ketoacidosis (DKA).
Methods
Retrospective analysis of clinical notes, discharge letters and lab reports.
Results
Over 12 months (October 2017-September 2018) there were 29 CYP newly diagnosed with T1DM in <19-year olds. Time to presentation from onset of symptoms varied from 3 days to 2 months. Polyuria and polydipsia were the commonest symptoms, with weight loss in a third. 4 CYP presented to healthcare professionals over the previous 1–2 weeks with similar symptoms. 3 of the 4 later presented in DKA. In total 12 CYP presented in DKA, 2 with severe and 10 with mild/moderate DKA. Length of stay varied from 0 to 4 days. 79% were positive for IA2 or GAD autoantibodies or both. 1 CYP was positive for TPO antibodies and 1 CYP was positive for anti-TTg antibodies at diagnosis. 93% received education from the specialist diabetic team prior to discharge, the rest from nursing and medical staff. Approximately 38% of CYP were carbohydrate counting at discharge.
Conclusions
These data demonstrate that there was a wide range of time between onset of symptoms and diagnosis. There was a missed opportunity for an earlier diagnosis in 4/29 CYP, 3 of whom later presented in DKA, highlighting the importance of ongoing education and awareness in primary care and the general public, to facilitate prompt diagnosis. We will continue to campaign for increased awareness of the symptoms of new onset of diabetes through participating in education sessions. We always feedback to colleagues in primary care for delayed diagnoses. This approach is important to be considered at regional and national level.

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P43

Continuous glucose monitoring/flash glucose monitoring in type 1 diabetes. Local unit experience at Glan Clwyd Hospital, Wales

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Background
Use of Continuous Glucose Monitoring (CGM) or Flash Glucose monitoring (FGM) has increased in children with type 1 diabetes without a conclusive evidence of sustained improvement in HbA1c. Aims: To assess whether use of CGM/FGM improves HbA1c. To review admissions, complications and impact on the quality of life.

Methods
Retrospective study of 33 Type 1 diabetic patients on CGM/FGM. Data collected from the case notes and Twinkle database system. A survey questionnaire was sent to parents/patients to assess the impact on quality of life.
Results
Indications for starting CGM/FGM were severe hypoglycemia, age and parental anxiety, reduced hypoglycaemic awareness, difficult glycaemic control and professional sports. Patients were divided into four baseline HbA1c cohorts, <53 mmol/mol ($n=6$), 54–69 mmol/mol ($n=17$), 70–85 mmol/mol ($n=6$) and >85 mmol/mol ($n=4$). Most patients in the first two cohorts showed no significant improvement or slight increase in HbA1c at 6 and 12 months. In 70–85 mmol/mol cohort, 33% had significant reduction in HbA1c at 6 months (>11 mmol/mol). 100% patients with baseline HbA1c of >85 mmol/mol showed significant reduction in HbA1c at 6 months. There was a significant reduction in number of hospital admissions from diabetes related problems during the 12 months period after using CGM/FGM in comparison to the 12 months period prior to CGM/FGM use (3 vs 12, 75% reduction). On Patient/parent satisfaction survey, majority stated that they were very satisfied with the use of CGM and it improved their quality of life. 14% reported problem with signal loss and in one patient the sensor was broken and embedded in the skin requiring surgical removal.
Conclusion
Patients with baseline HbA1c >70 mmomls/mol show significant reduction in HbA1c at 6 months after starting CGM/FGM. 75% reduction in hospital admissions. Broken sensor embedded in skin requiring surgical removal is an unusual complication which has not been reported before.

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P44

Treatment of paediatric diabetic ketoacidosis (DKA) with subcutaneous rapid-acting insulin: a UK centre, retrospective review of safety and efficacy data

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Introduction
The British Society of Paediatric Endocrinology (BSPED) DKA guidelines endorse the use of subcutaneous (SC) insulin in clinically well patients. In our institution, routine practice is to use SC insulin to manage DKA patients, without clinical evidence of shock. We present safety and efficacy data.
Methods
A retrospective review of electronic records was performed to identify episodes of DKA (pH <7.30 or HC03 <18 mmol/l and ketonaemia >3 mmol/l) managed with SC insulin, between 2011 and 2019. Cases managed with intravenous insulin or continuous subcutaneous insulin infusion (CSII) were excluded. Children without clinical shock (alert, with good peripheral perfusion, normal blood pressure at presentation) received an initial corrective dose of Novorapid insulin subcutaneously (0.1 units/kg <5 years, 0.2 units/kg >5 years), repeated every 4 h until readiness to eat was established. Children with nausea and vomiting received intravenous fluids. Descriptive characteristics including response to treatment and occurrence of complications in mild-moderate and severe DKA are presented.
Results
Sixty-nine cases of DKA were identified, of which 61 (88.4%) were managed with SC insulin. Eight episodes were excluded from the analysis: 4 cases managed with IV insulin, 3 cases with CSII, and 1 case of type 2 diabetes. Three patients were monitored on the paediatric intensive care unit. Mean age was 11.6 $\pm$ 4.2 years. Twenty-three (37.7%) episodes occurred in patients with new onset diabetes, thirty-six (59%) met criteria for mild-moderate DKA (pH$\leq$ 7.20), and 25 (41%) for severe DKA (pH$\leq$7.10). Resolution of DKA (pH$\geq$7.3; clinically well) occurred within 24 hours in 52 (85.2%) episodes; that is in 91.6% of mild-moderate and 76% of severe DKA episodes, and in 78.3% of new onset versus 89.5% of known diabetics. Recurrence of DKA, hypokalaemia and hypoglycaemia occurred in 4.9%, 9.8% and 24.6% of episodes respectively. Median length of stay was 2 days. No cerebral oedema, cardiac arrhythmia, or death occurred. No switch from subcutaneous to intravenous insulin was required.
Conclusion
SC insulin appears to be a safe and effective alternative to IV insulin, in children and young people with DKA, without clinical shock at presentation. Our data support results published from institutions worldwide.

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P45

Practical application and user experience of flash glucose monitoring in paediatric patients with type 1 diabetes

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Introduction
The FreeStyle Libre is increasingly employed in the management of T1DM. This audit examined if users are meeting the recommended competencies set out in the London prescribing guidelines, to ascertain if users are aware of and utilising inbuilt features of the Libre, to identify if user training can be enhanced, and to see if Libre use improves patients' quality of life as a result of Libre use.
Methods
The audit was conducted via a structured questionnaire, administered via phone interview by consenting users of the FreeStyle Libre.
Results
Eighteen Libre users participated in the audit (patient ages 7–17 years), among whom length of use ranged from 2 weeks to 3 years; 6 patients were on MDI and 12 were on CSII. Libre users showed a good familiarity with the features of the Libre; 94% of participants use the majority (>50%) of the in-built features of the Libre to gain an overall picture of their/their child's glucose levels and monitor or direct ongoing treatment. The three most utilised features are the logbook (89%), daily graph (89%), and average glucose (85%); all of which are deemed beneficial by the majority of participants. Only 67% of participants download their data. All participants feel the FreeStyle Libre is superior to conventional capillary blood glucose testing. Features of the Libre that enhance the users' quality of life were superiority to finger pricking (67%), use of trend arrows to help management (67%), allowing children to manage their own care (61%), convenience (56%), the ability to see patterns and analyse glycaemic control over time (50%), the ability to help parents monitor their child's glucose when they are apart (50%), and peace of mind/confidence in treatment (22%).
Conclusion
The FreeStyle Libre is considered life-changing technology by the majority of participants; the majority of inbuilt features are utilised by Libre users and deemed beneficial. Although recommended minimum competencies are confirmed as being met, future in house training will focus on how to maximise these features and emphasise the need to download data. The audit confirms many quality of life benefits for Libre users.

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P46

A regional UK audit between 2010–2018 of national quality indicators and surveillance of staffing levels in paediatric diabetes care units

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Introduction
The prevalence of diabetes continues to rise worldwide placing an increasing burden on the national health service. In 2012 a national Best Practice Tariff (BPT) was introduced in the UK and a National Peer Review Quality Assurance Programme was developed to drive improvements in diabetes care for children and young people. Our national audit from 2010 to 2018 aims to explore trends in paediatric diabetic care within the North West Diabetes Network and assess the impact of national quality initiatives.
Method
Data was collected from a regional survey in 2010, 2014 and 2018 from each of the 24 paediatric diabetes units (PDU) in the UK north west region for staffing levels. HbA1c outcomes were extracted from the National Paediatric Diabetic Audit (NDPA) for 2010–2019. We compared staffing levels with mean HbA1c and percentage of patients with HbA1C <58 mmol/mol in 2010, 2014 and 2019. Data was analysed using SPSS 24.0 statistical package.
Results
There was a significant increase in staffing levels for dedicated admin staff ($P<0.01$), consultants ($P=0.05$), dieticians ($P<0.01$), specialist diabetes nursing staff ($P<0.01$) and psychologists ($P<0.01$) across the network from 2010 to 2014 following BPT. However, between 2014 to 2019, there was only a

significant increase in staffing for administrative support ($P=0.04$). The mean HbA1C from PDUs and percentage of patients with HbA1C <58 mmol/mol were significantly improved between 2010 to 2014 but not from 2014 to 2018.
Conclusion
There had been a significant increase in staffing following BPT in multi-disciplinary diabetes teams across PDUs between 2010 and 2014 with similar improvements seen in HbA1c outcomes. However, between 2014 and 2019, staffing was only significantly increased for administrative support while mean HbA1c were not significantly improved. The audit shows that the driving force to produce better health outcomes does not solely depend on staffing levels of PDUs. In 2019, a UK National Quality Improvement Collaborative Programme was developed to support PDUs to transform their service using proven quality improvement methodologies. Tracking of national quality indicators and surveillance of staffing levels are essential in further understanding the role that quality initiatives play in driving better outcomes for diabetes care.

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P47

Patient directed carbohydrate counting from diagnosis – the Torbay experience

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In 2014 Torbay Hospital was a national outlier for diabetes control in the paediatric population. At this time a transformative quality improvement project which tracked the patient's journey through the service resulted in the introduction of carbohydrate counting from diagnosis. Whilst other hospitals had already adopted this approach the Torbay team introduced a system of care where the patient/parent lead the process of calculating carbohydrates and insulin doses from the point of diagnosis. The hope was that this would reduce the time spent in hospital during the diagnosis period and improve overall control at one year post diagnosis. This poster presents methodology and comparative data about length of hospital stay along with HbA1c data over the first year post diagnosis in the cohorts pre and post introduction of this change. This single change is cited as the most significant factor in moving our outcome over 4 years to a point we are no longer national outliers in our patient's overall HbA1c control (below).

Year	2014	2015	2016	2017
HbA1c	74	72	70	68

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Diabetes 5

P48

A rare complication of diabetic ketoacidosis: spontaneous pneumomediastinum with subcutaneous emphysema

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Introduction
Diabetic Ketoacidosis (DKA) is a medical emergency and major cause of mortality in children with type 1 diabetes (T1D). Careful evaluation is needed to identify expected and more unusual complications of DKA.
Case report
A 16 year old male with poorly controlled T1D presented with severe DKA; he reported excessive vomiting and had severe abdominal pain. He informed taking 'Ecstasy' (3,4-methylenedioxymethamphetamine; MDMA) twice in the preceding 72 h. Investigations revealed severe acidosis (pH 6.84), pre-renal failure (serum creatinine 137 μmol/l) and glycated Haemoglobin (HbA1c) >196 mmol/mol (>20%). X-rays excluded sub-diaphragmatic free air, but showed pneumomediastinum (PM) and subcutaneous emphysema of neck; CT demonstrated no convincing oesophageal tear. Urine toxicology showed MDMA traces and cannabinoids (patient later confided regular cannabis use). DKA management and a conservative surgical approach for possible oesophageal perforation were concurrently undertaken: nil by mouth (NBM); intravenous antibiotics for presumed mediastinitis; total parenteral nutrition (TPN) to promote oesophageal healing and prevent catabolism whilst NBM. Insulin titrated to glucose content of TPN, following DKA resolution. Enteral feeds re-started a week later, after contrast study demonstrated normal oesophageal appearances and no oesophageal leak. Patient and parents underwent intense diabetes re-education and patient referred to local addictions service. HbA1c improved to 115 mmol/mol (12.6%) by Day 12 with adequate insulin therapy.
Discussion
PM is a rare complication of DKA. Case reports describe PM following MDMA ingestion (without vomiting) possibly related to Valsalva manoeuvre during extreme physical exertion such as strenuous dancing. Severe vomiting can generate high intra-thoracic pressures (possibly intensified by recreational drug use) with alveolar over-distension and rupture, causing air tracking along bronchovascular bundles and PM. Hamman's syndrome refers to PM with subcutaneous emphysema and has excellent prognosis. Effort rupture of the oesophagus (Boerhaave's syndrome) has a high mortality from mediastinitis, necrosis and sepsis; distinguishing between the two entities can be challenging.
Learning points
Spontaneous PM is a rare complication of DKA.
- Careful assessment needed in DKA patients with epigastric, retrosternal, neck or chest pain
- DKA admission provides opportunity for re-education and improved glycaemic control; adolescents and families benefit from holistic, open dialogue.

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P49

Paediatric random glucose requests in primary care

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Background
NICE guidelines (NG18) state that paediatric patients aged <18 years old with suspected diabetes mellitus (DM) should be immediately referred to specialist care to confirm diagnosis and provide immediate treatment. The Nottingham University Hospitals (NUH) Paediatric Endocrine team advise primary care to investigate suspected hyperglycaemia using a POCT (point of care testing) glucose meter at the primary care facility to avoid the delay incurred by sending a sample to the laboratory. The aim of this study was to ascertain compliance with this advice and identify any cases where there was a potential delay in diagnosis.
Methods
Retrospective analysis (April 2018–April 2019) identified 1641 laboratory random glucose requests for patients <18 years of age in the Nottinghamshire area. A >7.8 mmol/l cut-off was used to identify patients who should have been referred immediately to secondary care for confirmation and treatment.
Results
The results ($n=1641$) identified 16 patients with glucose results >7.8 mmol/l, of which 5 had results >11.1 mmol/l; consistent with a diagnosis of DM (Type-1 DM: $n=4$, Type-2 DM: $n=1$). Five patients had confirmed delayed referrals, of which 2 patients presented in diabetic ketoacidosis (DKA). Of the remaining 11 patients (>7.8 – ≤11.1 mmol/l), 1 was a new diagnosis of Type 2 DM, 1 was a known case of DM and 9 patients were non-DM related or unknown requests. No hypoglycaemic (<2.6 mmol/l) patients were identified. 392 (23.88%) requests had DM specific symptoms (polyuria, polydipsia, tiredness, weight loss); 883 (53.80%) requests were non-DM related (routine screen, monitoring, abdominal pain, dizziness).
Conclusions
Primary care paediatric glucose requests showed lack of conformity to the recommended diagnostic pathway. 392 blood glucose requests were sent despite DM being considered as a differential which should have prompted a POCT glucose check. This increases risk of delayed diagnosis and management in children with undiagnosed Type 1 DM. Communication and training between NUH and primary care continues to be essential to improve standards of care but can be challenging to arrange with all CCGs across the region. In addition, an alert is now being set-up for electronic requests of glucose for primary care, encouraging the use of POCT glucose.

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P50

Use of flash glucose monitoring during hypo/hyperglycaemia and to guide insulin administration in paediatric patients with type 1 diabetes

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Introduction
Flash glucose monitoring is increasingly used in the management of T1DM. Although the FreeStyle Libre reduces the overall burden of conventional self-monitoring of blood glucose, capillary glucose should be checked at times of Libre-predicted extreme hypo/hyperglycaemia.
Methods
Consenting FreeStyle Libre users completed a structured questionnaire via phone interview. Users reported incidence of extreme hypo/hyperglycaemia (indicated by LO/HI outputs), subsequent actions taken, blood glucose levels correlating to LO/HI readings, use of Libre to guide insulin dosing, and any adverse outcomes directly linked to dosing insulin from Libre values.
Results
Seventeen Libre users participated (patient ages 7–17 years; MDI $n = 6$, CSII $n = 11$), length of Libre use ranged from 2 weeks to 3 years. 88% of participants report times the Libre indicated extreme hypo/hyperglycaemia by outputting 'LO' or 'HI'. All (100%) of those users check their/their child's capillary blood glucose when their Libre outputs LO/HI, in line with current recommended guidelines. 87% of users indicate their Libre readings are highly reliable in identifying extreme hypo/hyperglycaemia, as confirmed with blood glucose. Many users reported times their blood glucose levels were not as hypoglycaemic (53%) or hyperglycaemic (30%) as the Libre indicated. The majority of users (67% MDI, 100% CSII) use Libre readings to modify/guide insulin dosage; among users on CSII, 82% use Libre values always/almost always to determine insulin dosages. 93% of users report their/their child's blood glucose consistently responds as expected to insulin they dose from Libre readings. Two users (both MDI) reported times their child became hypoglycaemic after they dosed insulin based on Libre readings.
Conclusion
Participants report the Libre accurately predicts extreme hypo/hyperglycaemia, and 100% of those users check capillary blood glucose at that time. Instances of adverse events highlight the need for increased Libre training for certain users. As the majority of users dose insulin based on Libre readings, frequently only checking blood glucose for readings significantly out of their target range, clinicians should be aware of a potential gap between medical advice and practical use of the Libre.

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P51

A qualitative study evaluating solution focus brief therapy in improving delivery of diabetes care by healthcare professionals

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Introduction
It is essential that children and young people with diabetes are supported to manage their diabetes effectively to prevent the development of early complications. However, the common clinical challenge is difficultly in engaging adolescents and young people to achieve good glycaemic control in their diabetes management. Solution Focus Therapy (SFBT) has been found to be especially beneficial with children, adolescents and teenagers because it is a brief model translated to all age groups. With this in mind, it is of interest to discover the attitudes, experiences and common themes a paediatric diabetes team shares whilst using SFBT and how it impacts on their delivery of care. Currently there has been no research to evaluate any diabetes team's involvement with clinical health psychology. This qualitative study aims to evaluate the diabetes team's experiences from using SFT in their delivery of diabetes care, discovering aspects that assist their work and providing a greater insight into the use of SFBT in a paediatric diabetes setting.
Methodology
A qualitative descriptive design which was undertaken as method for describing the team's experiences with SFBT. Data was collected using semi-structured interviews within a specialist paediatrics diabetes team in the North West of England. The team consists of a Consultant Paediatrician, 3 specialist nurses, 1 patient educator and a specialist dietician. Face-to-face, semi structured interviews were conducted individually with each member. One independent researcher completed all interviews. Voice-recorded interviews were transcribed verbatim and analysed by another independent researcher using a thematic approach to identify main themes.
Results
It was found that SFBT used within the team, improved self-reported confidence, skills, trust and relationships with patients and their families. Additionally, each team member reflected how patient and their families have responded positively to the SFT approach.
Conclusion
Evaluating staff experiences of utilising SFBT in the delivery of paediatric diabetes care highlighted that a team's approach to SFBT is perceived to facilitate and support children, young people and their families in managing diabetes. The implications of SFBT for clinical practice and the dissemination of this approach to routine clinical practice should be explored.

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P52

A case of ischaemic stroke associated with severe DKA

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Introduction
Diabetic Ketoacidosis (DKA) is a known risk factor for ischaemic and haemorrhagic stroke in children and young people. Cerebral oedema may predispose to ischaemic or haemorrhagic brain injury, however not all cases of stroke are associated with cerebral oedema. This case illustrates severe complications of DKA including ischaemic stroke and cardiac arrest, and raises questions about fluid management in severe DKA.
Case report
We describe the case of an 8-year-old girl presenting as a new diagnosis of type 1 diabetes in severe DKA. Findings at presentation included a blood glucose level of 35 mmol/l, blood ketones 3.9 mmol/l, pH 6.75, bicarbonate 1.6 mmol/l and Base Excess −33.7. She had a fluctuating conscious level with a GCS between 9 and 13. Initial management included a 10 ml/kg fluid bolus of normal saline, followed by maintenance fluid as per BSPED 2015 guidelines. She was subsequently admitted to the paediatric intensive care unit and commenced on intravenous insulin at 0.05 units/kg/hr. A dopamine infusion was commenced for inotropic support in view of concerns regarding hypotension, tachycardia and poor peripheral perfusion. At 15 h after the initial presentation, left arm and leg weakness was noted, prompting an urgent CT head. This revealed a right thalamic infarct, with no evidence of cerebral oedema. Shortly after returning from the radiology department she had an asystolic cardiac arrest requiring 2 min of CPR and 1 dose of IV adrenaline. Insulin requirements increased up to a maximum of 0.24 units/kg/hour following these events, despite resolution in ketosis. Subsequent results include a normal coagulation screen and an MRI brain consistent with previous findings, showed an established right thalamic infarct.
Conclusions
Cerebral Ischaemic stroke is a known, but rare complication of DKA. Proposed mechanisms of elevated thrombosis risk in DKA include systemic inflammation, disordered coagulation, platelet activation and reduced blood volume and flow. This case describes thalamic stroke and cardiac arrest as severe complications of DKA. It raises questions regarding how to optimally assess fluid status and manage fluid resuscitation and replacement in severe DKA to prevent intracerebral complications.

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P53

Review of compliance and methods of carbohydrate counting in paediatric diabetic patients at District General Hospital

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Background
It has been proved that calculating the accurate amount of carbohydrate intake and good compliance in carb counting play a major role in in diabetes management.
Method
All patients who came to diabetes clinic at Hinchingbrooke Hospital in one-month duration were requested to complete the designed questionnaires anonymously and 17 patients/carers returned the results to the diabetes secretary. We asked about the methods they were using for carb counting, the frequency of carb counting at home and at school, the frequency of estimating the amount of carbohydrate and the frequency of skipping meal at school. In addition, we reviewed how they responded when the nutritional info was not available on the food package. Our aim is to analyse the compliance of carbohydrate counting and to provide the effective education and support to caregivers and patients.
Results
Out of the total 17 responses, 76%, which is 13 responses, were from parents and the rest was from patients. Remarkably, 82% of the total responses mentioned that they used carb and cal book and app. And when there was no nutritional info on food package, 35% of the total responders guessed the amount of carbohydrate using their previous experience while 31% of them relied on the Internet and 34% of them searched through the reference book. Surprisingly, 94% said that they did carb counting every time they ate at home whereas only 6% mentioned that they counted carb 1–3 times per day. However, the compliance dropped at school. 65% of the responders counted carb every time they ate at school while 6% counted carb less than one time per day or 1–3 times per week at school.
Conclusion
Even though the parents and patients aware that the compliance and accuracy of carb counting is vital in the glycaemic control, the encouragement and education on carb counting still need to be promoted at school.

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P54

A case of prolonged partial remission of type 1 diabetes

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Introduction
Newly diagnosed type 1 diabetes is characterized by a transient partial remission period ('honeymoon'), starting shortly after initiation of insulin treatment and during which the patient's requirement for exogenous insulin treatment declines. Improvement of peripheral insulin sensitivity as well as a partial beta-cell recovery with improved insulin secretion was speculating to contribute to the pathogenesis of this phenomenon.
Case
We describe a case of 18 year-old boy who was diagnosed with diabetes following a 2 week-history of polyuria and polydipsia at the age of 12 years and was commenced on insulin. His HbA1c on diagnosis was 76 mmol/mol and GAD antibodies were detected consistent with a diagnosis of type 1 diabetes. His diabetes was well managed with mean HbA1c of 51 mmol/mol on minimum insulin requirements of 0.4 units/kg per day over the following 6 years indicating unusually prolonged partial permission phase. He underwent further genetic investigations for MODY which were negative. However, his urine C-peptide/creatinine ratio was 0.91 nmol/mmol indicating preserved endogenous insulin secretion.
Conclusion
We present an 18-year-old adolescent, diagnosed at 12 years of age with type 1 diabetes, with spontaneous and partial remission sustained for more than 6 years. It is well documented that the residual β-cell function remained highest in the age-group of 10–15 years and this finding is comparable to our case. However further studies are required to determine which factors contribute to the partial and transient remission of type 1 diabetes in paediatric population.

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P55

Iatrogenic cardiac arrest and severe neurological complications in DKA (diabetic ketoacidodis)

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Cardiac complications including cardiac arrest in Diabetic Ketoacidosis (DKA) have been reported in adults but is not common in children. We present a case of a $3\frac{1}{2}$ year old child with new onset Type 1 Diabetes who presented in severe DKA and went into cardiac arrest needing prolonged resuscitation after starting insulin infusion due to rapid drop of serum potassium (K+). Serum K+ on presentation was 2.8 mmol/l and dropped to 1.5 mmol/l within 2.5 h of starting insulin leading to cardiac arrest. Although the child survived but ended up with a week in PICU and significant neurological deficit. Failure to acknowledge and properly manage hypokalemia in DKA can result in severe, symptomatic hypokalemia with detrimental effects on the neuromuscular and cardiopulmonary systems and warrants consideration to closely follow K+ levels during management.[1]
Reference
1. Shanlee M Davis, *et al*. Profound hypokalemia associated with severe diabetic ketoacidosis, *Pediatr Diabetes*. 2016 Feb; 17(1): 61–65.

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Diabetes 6

P56

Assessing the impact of continuous glucose monitoring (CGM) and flash glucose scanning (FGS) on HbA1c levels in paediatric diabetic patients

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Background
Advances in technology have led to new approaches in diabetes management. CGM has been associated with improvements in HbA1c, however, the evidence is limited and there are substantial cost considerations. The main aim of this audit was to assess the impact of CGM and FGS on HbA1c levels.
Method
A retrospective analysis of the use of CGM and FGS in paediatric patients under the care of the children's diabetes team at James Cook Hospital, Middlesbrough. Registers for patients started on CGM and FGS were used to identify patients, and electronic notes analysed. Patients were discounted from the HbA1c analysis if there was insufficient data. For CGM, a total of 23 patients were identified, 1 of whom was discounted. For FGS, 32 patients were identified and 16 were discounted. For both sets of patients, HbA1c levels were noted prior to starting CGM or FGS and after 6, 12 and 24 months of use. In this audit, we also analysed referral criteria for CGM by comparing with NICE guidance.
Results
After 6 months of use, the percentage of patients whose HbA1c level stayed the same or reduced after commencement of CGM/FGS was only 36% for CGM and 50% for FGS. For both groups, this percentage improved with longer use. This demonstrates a disappointing reduction in HbA1c despite use of this technology. However, the group of patients with longer duration of both CGM and FGS use achieved greater reductions in HbA1c. This may demonstrate more effective use of the technology by families over time. We must consider the limitations of this data, particularly patient numbers with increasing time-periods on CGM/FGS and regarding documentation. We should also consider other possible beneficial effects of the devices not assessed, such as reduced anxiety and improved awareness of hypoglycaemia. 82.6% of patients had documentation of compliance with NICE guidance.
Outcome
In the future, all families will complete a quality of life questionnaire when initiating CGM/FGS and annually during use. We will also clearly document; date when CGM/FGS initiated, education delivered in line with ACDC guidance and how NICE criteria were met.

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P57

A retrospective audit comparing diabetes control during summer and winter, in children with type 1 diabetes

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Introduction
Lifestyle, exercise and diet vary hugely between summer and winter months population-wide. We compared diabetes control in children with type 1 diabetes (T1D), during summer and winter months.
Methods
All children under 18 years with T1D attending our diabetes clinics were eligible. Those diagnosed within one year, changed insulin regimen between seasons or with incomplete data were excluded. Summer or winter months were defined by British Summer Time [25 March 2018–28 October 2018] or Greenwich Mean Time [29 October 2018–31 March 2019] use respectively. Clinical data for the previous year (glycated haemoglobin (HbA1c), weight, insulin dose and regimen) and HbA1c matched Diasend downloads (average glucose level, number of tests/day, proportion of tests in euglycaemia, hypoglycaemia and hyperglycaemia) was collected retrospectively. HbA1c and Diasend downloads within first 6 weeks of the season were not included, to avoid overlap between seasons.
Results
All 197 patients were audited; 97 excluded as diagnosis within 1 year (60), non-T1D (8), change in insulin regimen (2), over 18 years (1) and incomplete clinic data (26). Patients ($n=100$) ranged from 3 to 17 years (mean = 12.3, S.D. = 3.4). Paired sample *t*-tests were used to compare data in summer and winter months. Mean HbA1c (mmol/mol) in summer (mean = 63.6, S.D. = 12.2) was slightly lower than in winter (mean = 65.6, S.D. = 13.3), but not significant ($P=0.093$). Diasend downloads ($n=82$) revealed a significantly high percentage of tests in euglycaemia range (summer mean = 29.6, S.D. = 13.3; winter mean = 25.4, S.D. = 13.6) ($P=0.03$). There was significantly lower insulin dose used (units/day) in summer, both for bolus insulin (summer mean = 25.8, S.D. = 12.5, winter mean = 28.0, S.D. = 13.2) ($P=0.01$) and basal insulin (summer mean = 24.7, S.D. = 14.3, winter mean = 26.3, S.D. = 14.6) ($P=0.03$). But no difference noted when total insulin used was adjusted for weight (units/kg/day) between summer (mean = 0.9, S.D. = 0.3) and winter (mean = 0.9, S.D. = 0.2) ($P=0.94$).
Conclusions
Overall we found lower mean HbA1c in summer (by 2 mmol/mol), but it was not significant. There was greater proportion of tests in euglycaemia range in summer, which may explain the slightly lower mean HbA1c. Insulin requirements appeared lower in summer, but no difference noted when adjusted for weight. However, multiple factors affecting glycaemic control were not individually studied.

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P58

Quality improvement project assessing effect on diabetes control from the introduction of an empowerment tool to facilitate insulin self adjustment

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Introduction
We were one of ten paediatric diabetes teams taking part in the pilot RCPCH QI project initiated in Autumn 2017 and the sole representative from the North East of England. The project we chose was to enable and empower children, young people and their families to improve overall diabetes management, long term health and wellbeing through education and knowledge in adjusting insulin to improve blood glucose control.
Method
We created a bespoke diabetes empowerment tool giving advanced diabetes education and practical advice of how to make appropriate changes to insulin to improve HbA1c. After making improvements following focus group feedback the tool was given to all patients and families along with individualised education within clinic of how to use it. At the same time we set up a download clinic to encourage downloading of meters and pumps and promote communication with the team via email or telephone. We surveyed all patients before and after the QI project about self-adjustment and we assessed HbA1c from the start of the QI project, September 2017 to March 2019.
Results
Patients self-adjusting pre QI: (55 responses)
1. Never 18.18%
2. 3 monthly 14.55%
3. Monthly 18.18%
4. Weekly 29.09%
5. Daily 20%
Patients self-adjusting June 2019: (29 responses)
1. Never 31%
2. 3 monthly 13.79%
3. Monthly 17.24%
4. Weekly 13.79%
5. Daily 24%
Percentage of patients accessing download clinic June 2019: 60.7% of patients
HbA1c trend:
1. April to September 2017 64 mmol/mol
2. October 2017 to March 2018 63.5 mmol/mol
3. April to September 2018 58.75 mmol/mol
4. October to March 2019 58.75 mmol/mol
Conclusion
Overall the effect of involvement in the QI project has been an extremely positive one. Mean HbA1c had been static for two years until the dramatic reduction following the QI project. Despite positive feedback for the empowerment tool there are a significant number of our patient group who remain uncomfortable self-adjusting insulin and this must remain patient choice. We continue to develop our empowerment tool and are focussing on patients in the first 6 months of diagnosis to embed good practice early.

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P59

Audit on paediatric type 1 diabetes patients with HbA1c elevated >75 mmol/mol at a North West District General Hospital

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Introduction
Current NICE guidelines recommend that children and young people with Type 1 Diabetes Mellitus (T1DM) should aim for a target HbA1c $\leq$48 mmol/mol (6.5%) to reduce the risk of long-term complications. The National Paediatric Diabetes Audit (NPDA) shows that the number of young people under the paediatric diabetes service with HbA1c >75 mmol/mol at this District General Hospital has been consistently and significantly above both the North West and national average. This has serious future health implications for our patients and creates a persistent pressure on the service.
Aims
To assess the degree to which the recommendations from the previous audit (2017/18) have been implemented into current practice. To identify barriers to better glycaemic control and suggest recommendations for the diabetes service to put into practice to improve the management of patients with consistently high HbA1c.
Methods
All paediatric patients with two or more previous consecutive HbA1c >75 mmol/mol were identified from NEXUS. A number of patients parameters including age, sex, number of clinic visits and insulin regimen were analysed to assess for correlation with increasing HbA1c. All data collected was from the period 23 April 2018 to 23 April 2019.
Results
47 patients were identified as having their latest HbA1c >75 mmol/mol; 7 patients were excluded based on an isolated result. 22 females (54%) and 18 males (46%) were identified. 21/40 (52.5%) patients were in the 16–18 age-group compared to 40% and 43% in 2016/17 and 2017/18 respectively. All patients with HbA1c >130 mmol/mol were age 15–18 years. The proportion of children on multiple daily injections and continuous subcutaneous insulin infusion regimens was equivalent to the national average. All diabetes-related hospital admissions occurred in patients with HbA1c $\geq$100 mmol/mol. 9 patients had documented evidence of receiving alcohol and 25/40 patient were offered dietetic input.
Conclusions
The transition period (16–18 age group) appears to be a focus for deteriorating disease control. Higher HbA1c measurements observed in this group were associated with diabetes-related hospital admissions indicating the need for more extensive input. Documentation of dietetic input and alcohol education remains poor.

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P60

Audit on the management of diabetic ketoacidosis in children in 2 District General Hospitals: creation of a DKA pathway

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Introduction
Diabetic Ketoacidosis (DKA) is a common complication of Type 1 Diabetes (T1DM), accounting for around 21% of all diabetes related admissions. It is a major source of morbidity and mortality amongst children with T1DM. Delayed diagnosis, shock, renal failure, cerebral oedema and sepsis remain problematic. The aim of this project was to compare local management to best practice as per the British Society for Paediatric Endocrinology and Diabetes (BSPED), and provide intuitive ways to improve patient management.
Methods
A retrospective audit of the case notes of patients aged 0–16 attending A&E across two sites of the trust were identified using the clinical code 'Type 1 Diabetic with Ketoacidosis'. A 1 year period was analysed. Standards were set as per BSPED, which included correct diagnosis, correct fluid choice, initial fluid resuscitation including fluid calculations, timing of insulin, and monitoring of blood sugars, blood gases and neurological monitoring if appropriate.
Results
Overall twenty-four patients were admitted across our two sites (n total = 24). 96% of patients were correctly diagnosed and the average time to fluid initiation was 15 min. The average time between initiation of fluids to insulin was 1 h 23 min, although 12.5% of patients had their insulin started after 15 min of fluids. Around 30% of patients received a fluid bolus despite not being recorded as shocked. 83% of patients had appropriate fluids used including potassium. Only 60% of patients had hourly blood sugar monitoring and a minimum of 4 hourly blood gases/U&E monitoring. 58% of patients had their fluid calculations recorded. Around 80% were resuscitated over 48 h, and 90% had their fluids based on weight. 70% of those requiring neuro-obs received them as per protocol.
Conclusion
Whilst most patients were correctly diagnosed, there were many inconsistencies in DKA management. Therefore, we have implemented several measures to aid clinicians. Firstly, ensuring regular education of healthcare professionals on T1DM and DKA. Secondly, creating a DKA pathway to aid clinicians from the initial assessment to recovery of DKA. It will aid in diagnosis, initial fluid resuscitation, accurate fluid calculation and monitoring.

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P61

Our diabetes quality improvement initiative journey – ensuring an efficient and purposeful clinic experience...

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Our diabetes service was successful in the application to participate in the RCPCH Quality improvement initiative (2018–2019).
Our aims were
To identify strategies to enable teams to work collaboratively across multiple trust sites, 30 miles apart, covering a 50 mile radius. To undertake and complete projects in a timely and efficient manner to provide an equitable service across sites. To help maintain consistent improvement in HbA1c outcomes. To implement a programme of continuous education for children and young people with diabetes (CYPD) within the clinic.
To enhance the patient and families' clinic experience.
– To improve the percentage of care processes completed.
Consistent Information for patients was crucial – the team agreed for common goals and targets cross site and trained nursing and medical teams. We reviewed the current clinic situation by providing the previous year's PREMS questionnaire and monitored the patient journey in clinic. The clinic environment was altered to save time between various care processes and waiting times were used to provide micro-teaching to patients. All CYPD were handed out 'All About Me' handout which reinforced basics of diabetes management. We started offering CYPD the opportunity to download their glucose meter to diasend in clinic to encourage downloading at home. The number of patients downloading increased from 22 in March to 33 in May 2019. Comparison of random 5 patients who regularly downloaded prior to QI project, compared to 5 patients who never downloaded:
Group 1: Downloading average HBA1C was 56
Group 2: Not downloading average HBA1C was 71
All members of group 2 now downloading over a period of 3 months – average HBA1C now 57. We started using HbA1C tracker in clinic notes to monitor trends. One stop annual review clinic was set up to meet multidisciplinary team and undertake care processes. Safe management checklist to keep patient out of hospital was discussed in all annual review clnics.
Reflections
Team had Positive 'Go for it' attitude. QI huddles and Cross site meetings helped strengthen team bonding and boosted morale.
What next?
Consider a virtual clinic. Audit the management of patients a year after diagnosis. The journey continues...

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P62

Boy with type 1 diabetes and chronic idiopathic pancreatitis secondary to heterozygous variance for SPINK 1G

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13 year old lad diagnosed to have type 1 diabetes at the age of 18 months, moved to our area when he was about 5 years of age coming from a family with complex social background. His diabetes control has always been challenging with HBA1c generally above 70 mmol/mol and only occasionally going below 70. He was tried on multiple daily insulin (MDI), then insulin pump and then back to MDI – currently he is on Insulin degludec. He had recurrent admissions to the paediatric ward with tonsillitis and eventually had a tonsillectomy done. Subsequently he had multiple admissions with headache. He had lumbar puncture done to exclude idiopathic intracranial hypertension which was ruled out, later diagnosed to be migraines. He was initially on antimigraine prophylaxis with reported good effect and later came off this. He then presented with recurrent lower abdominal pains and eventually had an appendicectomy done histopathology of which showed non inflamed appendix. After a brief period of convalescence, he again represented with recurrent abdominal pain. He was noted to have persistently elevated creatinine with intermittently raised urea. Ultrasound abdomen and kidneys done showed normal kidneys and atrophic pancreas which was later confirmed by MRI. He was diagnosed to have chronic pancreatitis and was identified to have heterogeneous variant detected for SPINK 1G which is believed to have caused the acute on chronic pancreatitis. He has been started on selenium ACE. His faecal elastase was normal, however if he presents again with recurrent abdominal pain he would need review for exocrine pancreatic insufficiency. This young man has been challenging due to the complex family background, cared for by single mother with two other boys with challenging needs, tendency of mother to medicalise the boy and perhaps exaggerate symptoms with varying history to multiple professionals and the lad not that unwell each time he presented. Possibility of fabricated illness (FII) was and is still being considered but with the new diagnosis of chronic pancreatitis, this has now been put in the background though still being monitored. He is now diagnosed to have chronic kidney disease stage II.

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Learning from Mistakes and Miscellaneous

P63

The use of 'Hypopaks' in the investigation of hypoglycaemia in children

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Introduction
When hypoglycaemia (blood glucose <2.6 mmol/l) is detected in a child a 'Hypopak' is sent, which tests for blood glucose, lactate, hydroxybutyrate, insulin, growth hormone, cortisol, amino acids, acylcarnitines, and urine organic acids. We aimed to determine whether samples were sent appropriately and completely, and whether a diagnosis ensued.
Methods
All Hypopak samples received by the laboratory between 1/4/17 and 31/3/18 were reviewed. Samples with glucose ≥ 3 mmol/l or unrecorded were excluded. We used data handwritten on request forms and the Northern Ireland Electronic Care Record for information on the event and follow up.
Results
223 Hypopaks were received from 210 patients. 51% were from girls and 67% <3 years. Only 36% had complete results for all tests. 113 samples (51%) had glucose <3 mmol/l (3 samples <1 mmol/l), of these 83% had all endocrine tests completed. 25 samples (23 patients) had detectable insulin, 3 following dextrose administration and 9 from neonates. 10 patients had low/undetectable ketones. Of these, 1 had dumping syndrome, 1 was following dextrose, 1 had a metabolic disorder and the remainder were neonates. 24 samples (23 patients) had cortisol <450 nmol/l (mean and median both 212 nmol/l, range 24–435 nmol/l). Subsequently, 6 patients had a synacthen test (resulting in 2 diagnoses of ACTH deficiency), but 14 had no further testing. 3 patients had repeat cortisols sent (all >400 nmol/l). Defining sufficient growth hormone as 6.7 ng/ml, 76 samples had insufficient levels (6 samples <1 ng/ml). 1 patient is on growth hormone for septo-optic dysplasia (previously diagnosed) and 1 has IGF1 and IGFBP3 deficiency (not on growth hormone and had 5 samples sent). 14 patients with growth hormone <6.7 ng/mg are attending/have been discussed with Endocrinology. Following Hypopak investigations 2 patients were diagnosed with mitochondrial complex I deficiency.
Conclusions
Hypoglycaemia is most common in the <3 years age group but samples are frequently taken inappropriately and incompletely. Patients are often not followed up once the result is available and very few patients are diagnosed with an Endocrine or Metabolic disorder. We propose delaying analysis of some more expensive tests until blood glucose is confirmed <3 mmol/l and developing a guide for result interpretation and follow up.

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'Cognitive Bias – One of many'

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Cognitive bias is a systematic error in thinking that influences decision making and judgement. It occurs when people are processing and interpreting information given to them. Contemporary theories of clinical reasoning suggest a dual processing model, which consists of (i) a rapid intuitive component based on personal 'mind lines', heuristics, beliefs, judgements and preferences, and (ii) a slower logical and analytical component based on science and rationale. The rapid intuitive component is accurate for many decisions but is vulnerable to various cognitive biases. However evidence shows that most humans prefer to use this form of reasoning whenever possible. Cognitive biases (such as availability bias, framing, confirmation bias, the anchoring effect and premature closure, affective bias, blind obedience, and overconfidence) and personal traits (such as aversion to risk and ambiguity) may be associated with diagnostic inadequacies, medical errors and sub optimal management. The ultimate consequences of medical errors are avoidable hospitalisation, medication under use and overuse, and wasted resources that may lead to patient harm. We report a case of a fourteen year old boy who presented with polydipsia, polyuria, reduced appetite and weight loss. He was managed as a case of disordered eating in a Children and Adolescence Mental Health unit for a year; spending three months of that period as an inpatient on nasogastric tube feeding. Following review as a paediatric in-patient, he was found to have pituitary dysfunction and a CT scan showed hydrocephalus with an intracranial tumour involving pituitary and pineal gland which confirmed a germinoma on histology. Errors that stem from cognitive bias may be difficult to discuss because they are personal; and acknowledging them may feel like failure. Hence, improving our understanding and awareness of our own bias is an essential first step in enhancing our understanding of clinical decision making, improving patient care, informing future research and preparing clinicians for the cognitive rigours of clinical medicine.

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P65

Perplexing presentation of hypoglycemia

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Introduction
Ketotic hypoglycaemia is not an unusual presentation in preschool children particularly following gastroenteritis. Non-ketotic hypoglycaemia in a child is uncommon and could be due to endocrine or metabolic disorders.
Case report
Presentation: 4-year-old presented with fainting episode and hypoglycaemia as first episode. She was managed by the ambulance crew with oral glucose. Weeks later present to emergency department with non ketotic hypoglycaemia, associated with a mild viral respiratory illness. Hypoglycaemia screen was insufficient but not noticed before discharge. Treated with intravenous glucose and discharged home with a glucose meter and Dextrose tablets. She was admitted to ward following the concern from school about frequent hypoglycaemia around 0930 h at school. In the ward the patient continued to have hypoglycaemia mainly at late night or early morning she was on milk free diet, inhalers, antireflux, medications, emollients and antihistamines.
Investigations
Review of the blood glucose meter showed a trend of hypoglycaemia on weekday morning in school. No blood glucose readings on school holidays or weekends. day 3 of admission Blood glucose 1.8 mmol/l, ketones 0.2 mmol/l.
Background
Preterm, no hypoglycaemia concerns in neonatal period. In infancy frequent inpatient and outpatient for gastroesophageal reflux, faltering growth, food aversion, required nasal gastric tube feeding between 4 and 8 months of age She had neonatal follow up till 2 years of age. Recent outpatient review for co-ordination concerns and has been under follow up with gastroenterology ,respiratory and allergy clinic and awaiting psychologist referral for night terrors and urology referral Further results indicated the presence of exogenous insulin administration with low C-peptide. Further enquiry unravelled there was insulin accessible at home
Lessons learnt
- Detail of chronology of events including the pattern of the time of hypoglycaemic events.
- Detailed family history including medications available in the home and parent's profession.
- Significance of having single paediatrician and communicate with other professionals involved in the care of the child
- Discharge letter should include blood sugar monitoring plan, hypoglycaemia treatment plan ,care plan for school and early follow up in the clinic.

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P66

β-carotenaemia with secondary amenorrhea in a teenage athlete

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Introduction
Aurantiasis cutis is an asymptomatic condition characterised by yellow discolouration of the skin and is caused by high levels of β-carotene. Beta carotenaemia has frequently been associated with the development of menstrual disturbances in women but no causal link has been established.
Case report
We herein present a case of a 15 year old Caucasian girl (otherwise well, BMI 24) who presented with aurantiasis cutis together with a four month history of secondary amenorrhoea. Menarche was at the age of 12 and her cycle had been regular. Hyperbilirubinaemia was excluded and she had a normal renal and lipid profile and normal adrenal and thyroid function. She exercised regularly, consistently training up to ten hours a week for the regional hockey team. Despite being rich in fruit, vegetables and protein, her diet that was too 'healthy' as it was insufficient for her high energy expenditure and comprised on average 1700 kcal/day, 87% and 72% of the recommended fat and carbohydrate intake respectively. Her test results are shown in the table;

Test	Result
LH	0.7 U/l
FSH	5.8 U/l
E2	<66 pmol/l
Beta carotene	6.04 μmol/l (0.19–1.58)
Alpha carotene	1.2 μmol/l
Bone mineral density (DXA)	+2.1

Biochemistry results show low levels of gonadotrophins and oestradiol consistent with a diagnosis of hypogonadotrophic hypogonadism. As well as a raised β-carotene she had raised levels of lycopene, lutein and cryptoxanthin which all come from green leafy vegetables. Beta carotenaemia is most commonly caused by excessive dietary intake of β-carotene rich foods or dietary supplements. It can also be caused by diabetes mellitus, hypothyroidism, nephrotic syndrome, liver disease and a failure of enzymatic conversion of carotene to vitamin A.

Discussion and conclusions

The patient was found to have functional hypothalamic amenorrhoea resulting from insufficient calorie intake and excessive exercise. The patient's yellow skin was a result of β-carotenaemia due to excessive intake of raw vegetable and fruit. Although there are previous reported cases of adult patients with both presentations occurring together, no causal link has been established and are most likely related to the patient's lifestyle. Dietetic counselling has been provided and follow up is ongoing.

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P67

Using CRISPR/Cas9 gene editing to study the molecular mechanisms of congenital hyperinsulinism (CHI)

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Background

Congenital Hyperinsulinism (CHI) is characterized by the unregulated secretion of insulin in the presence of hypoglycaemia. The mutations in ABCC8 and KCNJ11, which encode the sulfonylurea receptor 1 (SUR1) and potassium inward-rectifying 6.2 (Kir6.2) subunits of ATP-sensitive potassium channel (K channel), are the most common identified cause of the condition. Defects in the HADH gene are responsible for SCHAD-HI, a rare form of the disease caused by the disruption of fatty acid oxidation.

Aims

Use the novel CRISPR/Cas9 gene editing technique to create a KO mouse cell model of Congenital Hyperinsulinism. The two genes of interest are ABCC8 and HADH. This cell model would be used for molecular and functional interrogation and may further aid in development of novel therapeutic drugs for CHI.

Methods

Single guide RNAs (gRNA) were designed to target both genes of interest. At the molecular level, the T7 Endonuclease assay and Sanger sequencing has been performed. Single cell cloning is currently under progress. Optimisation of ELISA using wild type (WT) and KO βTC6 cells to demonstrate glucose-stimulated insulin secretion (GSIS) and Western Blot analysis looking for reduced protein expression in KO cell population is being undertaken concurrently.

Results

Progress so far has addressed the optimisation of transfection conditions to deliver the gRNA. LPR nanocomplexes were used successfully in the transfection of βTC6 cells. The molecular validation of Abcc8 and Hadh KO models has been demonstrated by heteroduplexes in the T7 Endo assay. In addition, the optimisation of the ELISA insulin assay in wild type βTC6 cells has demonstrated a dose dependent GSIS which can be used as a standard to compare the GSIS from the KO cell model.

Conclusions

The results of our study so far has demonstrated the potential of the use of Cas9/gRNA system as an efficient reverse genetic tool in studying the molecular mechanisms underlying CHI. Future aims are to: conduct molecular interrogation to confirm the KO in Abcc8 and Hadh gene; and further, use the newly generated KO mutant cells to analyse the function of these genes and furthermore, to test and develop novel therapeutic drugs for CHI.

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P68

Mitochondrial disorders and endocrine dysfunction

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Mitochondrial disorders are the result of mitochondrial respiratory chain dysfunction and caused by mutations of genes encoded by the nuclear or the mitochondrial DNA. They affect approximately 1 in 5000 of the population and are the most common group of inborn errors of metabolism. Most of them involve multiple organ systems with predominant central nervous system features including ptosis, external ophthalmoplegia and sensorineural hearing loss.

Introduction

Endocrine dysfunction is caused by decreased intracellular production or extracellular secretion of hormones. Diabetes mellitus is the most frequently seen endocrine dysfunction followed by growth hormone deficiency, adrenal dysfunction, hypogonadism and hypoparathyroidism.

Case report

Our patient presented at 3 years of age with vomiting and collapse secondary to tonsillitis. Bloods showed hypoglycaemia, hyponatremia and metabolic acidosis. Cortisol was 239 nmol/l and ACTH was >1500 ng/l. Adrenal antibodies-negative. She was diagnosed with isolated glucocorticoid deficiency and commenced on hydrocortisone. At 8 years of age bloods showed mild hypoparathyroidism. She was also noted to have enamel hypoplasia, slow growth and intermittent diarrhoea. Autoimmune polyglandular syndrome type 1 was considered though there was no mucocutaneous candidiasis. Gene testing for anti IFN alpha IL-17 and 22 and common mutations in AIRE gene were negative. She was diagnosed with bilateral sensorineural hearing loss aged 10. At 11 years of age she was diagnosed with insulin dependent diabetes mellitus. GAD antibodies were strongly positive. Molecular genetic testing in Oxford did not identify any pathogenic variant in AIRE gene. At 16 years of age developed tremors in both hands. CT brain showed hypodensity in both globus pallidi. Mitochondrial disorder was considered as she was noted to have tremors, bradykinesia, rigidity and bilateral ptosis. Her fundal appearance was diagnostic of MIDD (Maternally inherited diabetes and deafness). Genetic testing showed single major mitochondrial DNA rearrangement due to deletion, likely sporadic. Final diagnosis: Mitochondrial disorder and insulin dependent diabetes mellitus.

Learning points

Early consideration of mitochondrial disorders in children presenting with multi organ involvement. Though diabetes mellitus is the common endocrine disorder, primary adrenal insufficiency has been reported prior to the onset of neurological symptoms.

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P69

Improving the patient journey in the children and young people diabetes clinics of the Cardiff and Vale Health Board

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Introduction
In the Cardiff and Vale (C&V) Health Board, there are 203 children and young people (CYP) under the care of the multidisciplinary team (MDT), 96% of whom have T1DM. Every CYP is offered four outpatient clinic appointments every year, one of which is an annual review. The majority of them are situated in the University Hospital Wales (UHW) site, whereas the University Hospital Llandough (UHL) clinic was introduced in 2016 for easier access for the CYP from the Vale area.
Objectives
– To improve the patient journey in the CYP diabetes clinics in the C&V Health Board.
– To identify functional and process bottlenecks in the patient journey and suggest potential improvement methods to the MDT.
Method
24 CYPs are followed through their journey in the UHW and UHL paediatrics diabetes clinics from registration to check out throughout a 6-week period (9 from UHW and 10 from UHL). The average time taken for each process and average total time taken are noted and illustrated on a patient journey timeline. Bottlenecks that interrupt the flow of the clinic resulting in delays are identified by direct observation and tabulated into a fishbone diagram.
Results
The MDT consultation takes the longest duration (30 min) out of all processes for both annual and routine reviews of both clinics – meeting the standard as stated in the National Paediatric Diabetes Network Guidance. The maximum time taken for the entire clinic process is 107 min in UHW and 57 min in UHL; the minimum time is 40 min and 31 min for UHW and UHL respectively. A total of 14 bottlenecks are identified which address the equipment and people involved, patient education, communication process, environment and general process of the clinics.
Conclusion
Several quality improvement suggestions, aiming to address the bottlenecks, are proposed to the MDT during a service meeting. Several interventions have been agreed to be implemented following discussion; evaluation on whether there are improvements to the efficiency, patient education and communication process in the clinics is required following implementation.

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P70

Audit of annual review investigations for girls with Turner's syndrome against the Turner's syndrome support society checklist

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Introduction
Turner's syndrome, also known as 45 X, or 45 X0, is characterised by the absence of one of the pair of X chromosomes. Clinical features are variable, and affected girls require regular review to identify and manage these. The Turner's Syndrome Support Society has produced a health checklist for the management of Turner's Syndrome, which provides a schedule for investigations. The aim of this audit was to evaluate whether we are meeting these standards.
Audit methodology
We performed a retrospective audit in January 2019 of all patients with Turner's syndrome, cared for in our District General Hospital. We identified patients using the local Endocrinology patient database, and then used paper and electronic notes to collect data from both the local DGH and regional tertiary unit.
Outcomes
9 patients were identified who had a diagnosis of Turner's Syndrome. 3 patients had classical X0 Turner's syndrome, 5 patients had mosaic Turner's syndrome and 1 had an abnormal X chromosome. At the most recent clinic visit, 89% of patients had height and weight recorded, but only 22% had BMI; blood pressure was recorded in 22%. 78% of patients had had thyroid function checked within the past 24 months, but only 11% had had thyroid antibodies, compared to 44% who had had coeliac antibodies. 11% had blood glucose checked within the past 12 months, but 33% had had HbA1c and IGF-1. Of the 4 post-pubertal patients, LFTs were checked in 50%. Bone age had not been investigated in the past 12 months in any patients, and it had never been done in 33%.
Conclusions
We are good at measuring height and weight, but could improve our blood test and bone age investigations to ensure that we meet recommendations. We plan to give a copy of the checklist to the patients' parents to empower them and act as a reminder, and to nominate 1 clinic appointment each year as an 'Annual review', during which this checklist should be consulted. We plan to re-audit 1 year following this implementation.

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P71

Intracranial hypertension secondary to severe obesity: case series

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Introduction
The prevalence of childhood obesity is continuing to increase, especially in more deprived areas. It is estimated that 28% of children are overweight or obese in England. Evidence has shown that obesity is associated with increased intracranial pressure (ICP) in adult and paediatric populations. We report three patients who presented with intracranial hypertension due to severe obesity.
Case 1
A fifteen-year-old girl presented with severe headaches and reduced vision following which she was noted to have papilledema. Her weight was 136.1 kg (+8.24 SDS) and BMI was 45.3 kg/m^2 (+3.81 SDS). She suffered from anxiety and found eating comforted her.
Case 2
A sixteen-year-old girl was noted to have asymptomatic papilledema following a routine optician review. Her weight was 114 kg (+5.98SDS) and BMI was 58.2 kg/m^2 (+4.46SDS). She had delayed puberty and her mother has type 2 diabetes mellitus.
Case 3
A nine-year-old girl presented with an eight week history of headaches, vomiting and diplopia and was noted to have papilledema. Her weight was 67.6 kg (+5.15SDS) and BMI was 35 kg/m^2 (+3.73SDS). Her mother has polycystic ovary syndrome and alopecia. None of the patients had features of Cushing's syndrome and investigations including thyroid function, HbA1c, liver function and lipid profile were normal. Oral glucose tolerance revealed insulin insensitivity. Brain imaging ruled out other causes for raised ICP. All patients underwent a lumbar puncture and the opening pressures were greater than 40 mm H2O (one patient needed multiple lumbar punctures). The patients were started on Acetazolamide and were given advice about lifestyle modification to aid weight loss. Two patients were commenced on metformin which was not tolerated and subsequently discontinued.
Conclusion
We describe three patients who have severe complications due to obesity. The exact mechanism of raised ICP due to obesity is unclear but evidence has shown that weight loss will reduce ICP. Lifestyle changes and metformin therapy were not successful in our patients. They continue to gain weight which is likely to further compromise their long-term health. Newer therapeutic options are urgently needed to manage morbid obesity. It may also be beneficial to screen obese patients for papilledema as one of our patients was asymptomatic.

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Pituitary

P72

Real-world safety data in children with Noonan syndrome treated with growth hormone: results from NordiNet®IOS and the Answer®Program

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Objective
To describe real-world safety data on growth hormone therapy (GHT) in paediatric patients with Noonan syndrome (NS) who were enrolled in NordiNet® IOS and the ANSWER®Program.
Introduction
Patients with NS have a high prevalence of cardiac defects and an increased risk for leukaemia and certain malignancies compared to the general population. Current safety data do not indicate an association of GHT with worsening of congenital cardiac defects or an increased risk for malignancies in NS patients; however, data are limited.
Methods
The long-term effectiveness and safety of Norditropin®, were evaluated in two non-interventional, multicentre studies. We report safety results for 412 paediatric patients with NS.
Results
31 safety events were reported in 21 patients. The majority 67% (21/31) were Non-Serious Adverse Drug Reactions. Most patients experienced a single event (16/21). One patient reported two Serious Adverse Drug Reactions. Under the MedDRA term, 'Neoplasms, benign, malignant and unspecified', four events were reported in three patients. Cardiovascular comorbidities were reported in 35 (8.5%) patients prior to GH start. After GH start, (potentially pre-existing) cardiovascular comorbidities were reported in five patients: unspecified cardiovascular disease ($n=3$), pulmonary valve stenosis ($n=1$) and ruptured abdominal aortic aneurysm ($n=1$); these events were all reported as comorbidities rather than Adverse Events. No other cardiac SARs, NSARs or SAEs not related to GHT were reported.
Discussion
In the current analysis, one cardiac safety event (ruptured abdominal aortic aneurysm) was reported. A recent randomised, double-blind, clinical trial of Norditropin®, in which cardiac function was monitored ($n=51$), showed no evidence of a negative effect of GH on cardiac function or structure. Furthermore, previous reports indicate that long-term GHT does not appear to have negative effects on the heart, in particular, ventricular wall thickness.
Conclusions
Real-world data from NordiNet®IOS and the ANSWER® Program support a favourable safety profile of GH therapy in patients with NS, specifically regarding cardiac safety events. As with other real-world studies, some comorbidities and safety events may have been under-reported.

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P73

Three novel Growth Hormone Receptor (*GHR*) splicing mutations causing a spectrum of Growth Hormone Insensitivity

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Introduction
Growth Hormone Insensitivity (GHI) is characterised by a triad of short stature (SS), IGF-1 deficiency and normal/high GH levels. 'Classical' GHI due to homozygous exonic *GHR* mutations results in extreme SS with dysmorphic and metabolic abnormalities. Heterozygous exon 9 *GHR* mutations are rare and exert dominant negative effects due to impairment of GHR dimerization/downstream signalling associated with a milder GHI phenotype. Only seven previous *GHR* dominant negative defects have been identified.
Objective
To identify the genetic cause of growth failure in undiagnosed patients with GHI phenotypes.
Design
Genetic variants were identified from our SS gene panel which interrogates coding and non-coding regions of known GHI genes using our established bioinformatics pipelines. Aberrant splicing was confirmed by *in vitro* splicing assays using an exon trap vector (pET01, MoBiTec GmbH, Germany).
Results
A heterozygous *GHR* variant (42718139T>G, c.810-15T>G) identified in Patient 1 was predicted to decrease splicing efficiency due to disruption of the polypyrimidine tract prior to exon 9. The strongest nearby alternative splice site was 26 bases 3' from the exon/intron boundary. The variant was inherited from his mother with a similar phenotype. A *de* novo heterozygous *GHR* variant (42718180T>G, c.836T>G) identified in Patient 2 was predicted to create a cryptic splice site within exon 9. Splicing assays confirmed the presence of mutant transcripts in both patients. Both novel variants cause frameshift and predicted premature truncation of *GHR* transcripts. Consistent with published reports, both had less severe growth failure than 'classical' GHI (height SDS -3.2 and -2.7, respectively). We also identified a novel homozygous *GHR* variant (42700940T>G, c.618+836T>G) in Patient 3. *In silico* analysis predicted donor splice site creation and *in vitro* splicing analysis confirmed inclusion of a 152bp pseudoexon. This causes frameshift and premature truncation of all GHR mRNA in keeping with his severe GHI phenotype (height SDS -7.5). We predict nonsense mediated mRNA decay and are currently testing this hypothesis.
Discussion
Three novel GHR splicing mutations contribute to our understanding of GHI. Our findings highlight the importance of considering dominant negative mutations in non-classical GHI and studying variation in deep intronic sequence as a cause of monogenic disorders.

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P74

STAT5B missense variant causing growth hormone deficiency with subclinical hypothyroidism and immune deficiency in a 13-year-old female: a case report

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Introduction
STAT5 proteins are components of the common growth hormone and interleukin-2 family of cytokine signaling pathway which is a critical molecule involved in growth hormone receptor (GHR) signal transduction, mediating the growth-promoting actions of the GHR. In addition to its role in GHR signal transduction, STAT5B is also involved in the immune system as an important mediator of interleukin-2 action and disruption of this signal transduction is responsible for T-cell function defects. Recently, there have been case reports on rare homozygous mutations in the signal transducer and activator of transcription 5B gene in patients with growth hormone insensitivity (GHI). We report a case of a 13-year-old female child who presented with short stature and recurrent chest infections whose evaluation revealed STAT5B missense variant.
Case report
A 13-year-old girl born of non-consanguineous marriage was referred to tertiary center in view of mildly elevated serum TSH levels. She had severe growth retardation, eczema along with chronic respiratory disease and features of chronic diarrhea on clinical evaluation. Because of the prolonged history of recurrent infections, chronic lung disease, and severe growth retardation, immuno-deficiency and GH deficiency or insensitivity was suspected. Her basal GH level was normal and IGF1 serum levels were extremely low. Hypothalamic–pituitary magnetic resonance imaging was normal. Moderate lymphopenia was observed with a reduced number of all evaluated cell lines. The levels of immunoglobulins were within the normal limits. Molecular analysis revealed homozygous missense variant of STAT5B gene which prognosticates probably damaging by bioinformatics techniques.
Conclusion
In summary, the presence of short stature in a child with chronic respiratory difficulties and immune dysfunction suggests growth hormone deficiency due to STAT5B pathological variants. Clinical and investigational dissociation for growth hormone deficiency associated with immunological defects are strongly suggestive of a mutation in STAT5B gene and should trigger an investigation for defects in this gene.

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P75

Growth and growth hormone abnormalities in bartter syndrome types 3 and 4

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Introduction
Bartter Syndrome types 3 and 4 (BS3/4) are rare tubulopathies, caused by *CLCNKB* and *BSND* mutations, which affect chloride channel function in the loop of Henle and distal convolute. Historically, with late presentation and poor disease control, patients had severe short stature. Multiple case reports have also found associations between BS3/4 and Growth Hormone deficiency (GHD). Our aim was to investigate growth and presence of GHD in a large contemporaneous BS3/4 cohort.
Method
Case notes were retrospectively reviewed for patients with BS3/4, seen by a UK paediatric nephrology service since 1984. Data collected included: anthropometry; endocrine testing and pituitary imaging results; GH treatment.
Results
26 BS3/4 patients, seen as children, were identified (currently aged 2–35 years). 16 patients were not referred to endocrinology, 10 of whom are post-pubertal with heights between 9th and 91st centiles. Ten (38%) children were/are seen by an endocrinologist; 9 underwent GH stimulation testing. Of those with abnormal tests ($N=6$), 5 received GH treatment: 4 for GHD (peak GH 0.9–2.4 mcg/l), 1 with GH neurosecretory dysregulation. GH increased growth velocity for most, but all have current/final height below 25th centile. Another has possible GH dysregulation (peak GH >40 mcg/l). The remaining stimulation tests showed: borderline low (6.7 mcg/l), normal (8 mcg/l) and borderline high (16.2 mcg/l) GH peaks. 4 children had MRIs. 2 GHD children had pituitary stalk thickening/possible thickening (one with absent posterior pituitary); 2 children with possible GH dysregulation (1 taking GH) had small anterior pituitary glands (with absent pituitary bright spot/optic nerve enlargement).
Conclusion
We report a high prevalence (23%) of GH disorders in BS3/4, with 20% of the cohort prescribed GH to date. Conversely, BS3/4 *per se* does not seem to cause growth failure, with many attaining normal final height. The pathophysiology of GHD is unknown, but may relate to the severe electrolyte/acid-base abnormalities in BS3/4. GH dysregulation is a novel finding in BS3/4, and the heterogeneity of pituitary images is striking and not previously reported. These suggest possible abnormalities in pituitary development, GH production and/or regulation in BS3/4.

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P76

A new frameshift mutation in immunoglobulin superfamily, member 1 (IGSF1) results in central hypothyroidism, delayed puberty and GH deficiency

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Background
Central hypothyroidism (CeHT) is uncommon in children. CeHT is often part of multiple pituitary hormone deficiency but can occur in isolation, and may occasionally be due to mutations in *TSHB, TRHR* or *IGSF1*, involved in TRH signalling. We present an adolescent with a novel truncating mutation of *IGSF1*.
Case presentation
A 15-year-old male was referred for pubertal delay, obesity and abnormal TFTs (FT4 (6.5 pmol/l [8.4–19.1], TSH 3.23 mU/l [0.3–5.0]). He was born breech, birth weight 3.7 kg ($+0.32$ SDS). At age 2, weight was 11 kg (-1.38 SDS), height 85 cm (-0.75 SDS), head circumference 52 cm ($+2.30$ SDS). Medical history: raised ALT and liver steatosis. Examination: Height 166 cm (-0.52 SDS), BMI 38.5 kg/m^2. Tanner staging P1G1A1, 8 ml testes. Investigations: LH 0.7 IU/l, FSH 4.1 IU/l, Testosterone 7.6 nmol/l, IGF1 11.2 ng/ml (13.5–66), prolactin 136 IU/l (90–300), AMH 28.1 (5.5–103). LHRH-test: peak LH 11.2, FSH 12.8. Bone-age was 1 year delayed. MRI showed a small pituitary gland. Levothyroxine was started and increased gradually. Primed glucagon test showed undetectable GH but with suboptimal FT4 (7.3 pmol/l). Later, a primed insulin tolerance test (ITT) showed a low GH peak (4.21 mcg/l). His growth and puberty progressed with quickly enlarging testes to 30 ml. Sequencing of *IGSF1* revealed a previously undescribed hemizygous pathogenic variant c.3343C>T p.(Gln1115*) causing frameshift and premature stop codon. The identified *IGSF1*-mutation is not described in GnomAD. It locates to the 12th Ig-like loop in the C-terminal domain, clustering with other frameshift mutations. The mutation likely leads to abnormal glycosylation and retention of shortened IGSF1 in the ER and may result in ER-stress response and cell death in the pituitary contributing to pituitary hormone deficiency, as previously described for GH1 mutations. Growth hormone deficiency (GHD) was evident on glucagon test and ITT, although difficult to interpret due to hypothyroidism and obesity. GHD may be transient given normalising height and IGF1, as seen previously.
Conclusion
We describe a novel frameshift *IGSF1* mutation, resulting in most previously described features: central hypothyroidism, macroorchidism, macrocephaly, delayed adrenarche and puberty, GHD, obesity, fatty liver disease and higher than average birth weight. This case adds to genotype-phenotype correlations and highlights the importance of careful assessment for a timely genetic diagnosis.

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P77

Observed effects of growth hormone doses on height in patients with Prader Willi Syndrome

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Introduction
Prader–Willi Syndrome (PWS) is a rare genetic disorder due to loss of paternally inherited genes on chromosome 15q11-13. It is characterised by neonatal hypotonia, childhood obesity, hypogonadism, cognitive and behavioural disabilities, and development of scoliosis. We aimed to review the impact of growth hormone (GH) doses, scoliosis and IGF1 levels on height gain in children with PWS.
Methods/design
Retrospective observational study of thirty-eight children with PWS on GH, from a tertiary paediatric centre, with up to 10 years follow-up. Data were collected on growth hormone doses, scoliosis, height SDS and IGF1 levels. IGF1 levels higher than 2 standard deviations classified as high. Height gain calculated from the height SDS before starting GH; including children restarting GH after a period of stopping.
Results
In the non-scoliosis group, mean GH dose was 23 μg/kg per day (S.D. 8). Mean height SDS gain was: -0.30 in the year before GH (baseline); $+0.70$ after 1 year on 15–25 micrograms/kg/day ($n=14$); and $+0.39$ on >25 μg/kg per day ($n=12$) (both $P<0.02$). In the scoliosis group, mean GH dose was 20 μg/kg per day (S.D. 6). Mean height SDS gain was: -0.33 at baseline; $+0.22$ after 1 year on 15–25 μg/kg per day ($n=12$) ($P=0.04$), and $+0.04$ on >25 μg/kg per day ($n=2$), ($P=0.09$). After 2 years on GH, the mean height SDS gain in all children: without scoliosis ($n=20$) was $+0.9$; and with scoliosis ($n=17$) was $+0.28$, ($P<0.03$). After 5 years, height SDS gain was $+1.24$ and $+1.02$, respectively ($P=0.62$). No significant differences in mean GH dose between the normal IGF1 group ($n=12$) and high IGF1 group ($n=23$), 19 μg/kg per day and 16 μg/kg per day, respectively ($P=0.47$). After 2 years on GH, mean height SDS gain was $+1.21$ in the normal IGF1 group and $+0.4$ in the high IGF1 group ($P<0.01$). After 5 years of treatment, the height SDS gain was $+1.15$ in normal IGF1 group and $+1.03$ in high IGF1 group ($P=0.7$)
Conclusions
Scoliosis and high IGF1 appeared to have minimal effects on height gain in the long term. Height gain on 15–25 μg/kg per day of GH was not inferior to higher doses. Further research to review whether lower GH doses may be used in future, and implications for side effects and cost-effectiveness.

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P78

Cranial diabetes Insipidus and anterior pituitary hormone deficiencies following 'minor' concussive sports head injury

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Introduction
Cranial Diabetes Insipidus (DI) presenting in children beyond infancy is most commonly associated with sellar/suprasellar tumours and severe traumatic brain injury or haemorrhage. Less frequent causes may be genetic or idiopathic. Exceptional cases may be associated with minor head injury. We present a case of post-concussive head injury with DI, and anterior pituitary hormone deficits.
Case
15 year old malesustained a concussive head injury (foot to head) playing rugby. Probable brief loss of conscious, and noted to have transient divergent squints before promptly transferred to local hospital emergency department. Neurological examination there reportedly normal; CT head no evidence haemorrhage/contusion injury.Patient allowed home. Overnight he developed nocturia, excessive thirst and progressive polyuria. Over next 3 months he would drink ~ 2.5 l water overnight, and 4–5 l daytime. He developed progressive daytime fatigue, stopped all sports and gym, would sleep in the afternoon after school, come home early or miss school through lack of energy. He experienced diffuse headaches, often felt nauseated on rising in the morning, and dizziness on standing. He shaved less frequently, lost appetite and weight. Referred to local Paediatrician at 3 months post-injury; investigations consistent with DI (Na 146 mmol/l x2, SeOsmo297/UOsmo 101), with normal Calcium and Glucose. Cortisol(1000 h) 61 nmol/l (Normal>150). While undergoing these tests he was admitted as an emergency with tonsillitis, tachycardic and prolonged capillary refill,looking exceptionally unwell. Overnight IV fluids were required to stabilise. MRI brain/pituitary revealed absent posterior pituitary bright signal; no other significant abnormality. On referral to our Endocrine service: Height 181.2 cm Weight 70 kg Additional investigations: Na 145 mmol/l, fT4 7 pmol/l/TSH 0.1 mIU/l, Cortisol < 30 nmol/l (1300 h),Testosterone 0.3 nmol/l, Prolactin 1900 mIU/l(NR < 410), IGF-1 16 nmol/l(6–68); BHCG/AFP undetectable. Pituitary MDT conclusion: Panhypopituitarism with DI secondary to stalk transection; raised Prolactin resulting from loss of dopaminergic inhibitory tone.Highly probable secondary to concussive head injury in view of coincident timing of DI symptom onset and lackof other pathology. Management:Hydrocortisone, DDAVP and Levothyroxine replacement with symptomatic relief; awaiting addition of testosterone and growth hormone.
Conclusion
Sports injury related concussion may rarely be associated with potential life threatening sequelae. Appropriate post-injury surveillance may be required.

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P79

A case of 17 years old beta thalassaemic boy with polyendocrinopathy secondary to hemosiderosis

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The main-stay management of Beta thalassaemia major is blood transfusion but this carries a risk of endocrinopathy from hemosiderosis in endocrine organs. Iron chelation therapy aims to mitigate this risk. Access to this therapy isn't available in some healthcare systems. Known Syrian refugee diagnosed with Beta thalassaemia major in infancy referred via the refugee medical services for thalassaemia management. There was previous history of intermittent transfusion support and poor chelation therapy management. Pallor, icterus, prominent maxillae, short stature, weight loss and delayed secondary sexual characteristics (A1, P2 G2, 3 ml testes bilaterally) were noted on examination.

Auxology

Parameters	Results	Centiles
Height	150.5 cm	< 0.4
Weight	46 kg	< 0.4

Investigations

Serum Ferritin	10 212 mg/l (23–540)
Follicle stimulating hormone	0.6 iu/l (1.0–10.0)
Testosterone level	0.4 mmol/l (9.4–37.0)
Sex hormone binding globulin	130 nmol/l (15–40)
Luteinising Hormone	0.5 iu/l (1–9)
IGF1	66 mg/l (105–346)
Prolactin	44 miu/l (50–400)
Cortisol	188 nmol/l (138–620)
17-Beta Oestradiol	72 pmol/l (0–130)
HbA1c	79 mmol/mol (< 42)

GHRH (Somatorelin) L-arginine stimulation test

Time	GH(mg/l)	IGF-1(mg/l)	Glucose mmol/l
−15	0.3	66	
0	0.4		9.2
30	12		12.1
60	6.3		12.4
90	3.2		11.4
120	1.4		11.0
150	0.5		

MRI abdomen/thorax: hepatic and myocardial iron overload, absent spleen, signal reduction for pancreas and bone marrow. MRI Pituitary: little signal intensity on T1-weighted imaging and no signal intensity on T2-weighted imaging in the anterior lobe. Overall appearance suggestive of pan-hypopituitarism 2nd to haemochromatosis. Bone age X-ray: Guryleich and pyle: 14–15 years old. Chronological age is 18 years. Spine bone density 0.691 g/cm^2 with *Z*-score of −4.0 Management: Iron chelation due to severe risk of heart failure: IV Desferal at 60 ml/kg/day 24 h, 7 days/week, Deferiprone 100 mg/kg per day. Endocrine management: Genotropin 1.6 mg (0.035 mg/kg per day) for a year, Testosterone 75 mg, monthly for 6 months. Diabetes management: Degludec and Insulin Aspart, total daily dose 46 Units. A case of Beta thalassaemia major and long-term suboptimal treatment leading to T1DM, partial hypopituitarism (growth hormone deficiency, hypogonadotropic hypogonadism) secondary to hemosiderosis demonstrating endocrine sequelae and subsequent endocrine management ameliorated the comorbidity.

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Thyroid

P80

Incomplete isosexual precocious puberty with macroadenoma: a rare presentation of primary hypothyroidism (Van Wyk-Grumbach Syndrome)

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Introduction
Precocious puberty occurs is associated with initial increase in linear growth and acceleration of bone maturity presenting as advanced bone age with early epiphyseal fusion which ultimately results in short stature. 'Van Wyk Grumbach Syndrome' (VWGS) is a rare syndrome associated with incomplete isosexual precocious puberty and macroadenoma seen in cases of longstanding, untreated hypothyroidism is associated with a delayed bone age .Complete resolution of all the features is seen after starting thyroid hormone replacement therapy.
Case report
An 8-yr-old girl child presented with history of cyclical vaginal bleeding for last 2 months. Her weight was 29 kg (75th–90th centile) and height was 119 cm (at 10th–25th centile). Her breast was tanner stage 4 with no axillary or pubic hair. Hormonal investigations revealed high FSH 3.02 mIU/ml (0.30–2.00 mIU/ml); low LH: 0.02 mIU/ml (< 0.10–6.00 mIU/ml); elevated Prolactin: 195.46 ng/ml (2.80–29.20 ng/ml), TSH: 750 μIU/ml (0.35–5.50 μIU/ml); low T3: 28.83 ng/dl

(60.00–181 ng/dl) and low T4: 0.06 μg/dl (4.50–12.60 μg/dl). CEMRI Brain showed enlarged sella with a suprasellar mass suggestive of macroadenoma measuring 1.6(1.5 cm. Her radiological investigations revealed bone age of 5 years (Greulich and Pyle's atlas). USG whole abdomen was normal. USG neck showed no abnormality. Anti TPO levels were <28.0 U/ml (<60.00 U/ml). Levothyroxine supplementation was started following which FSH, Prolactin and Thyroid Function Tests returned to normal levels. Repeat CEMRI Brain after 10 months showed complete resolution of macroadenoma. Vaginal bleeding stopped after 2 cycles and she again started having regular menstrual cycles at 12 years of age. At 13 years of age, her weight is 60 kg (90th–97th centile) and Height is 148 cm (at 25th centile) and having Tanner stage 4 Breast development with regular menstrual cycles. Mechanism postulated in VWGS which was attributed to a hormonal overlap in pituitary feedback mechanism. TSH, FSH, LH and human chorionic gonadotropin (hCG) are glycoprotein hormones which share a common alpha subunit but different beta subunits. Thus, TSH, in high concentrations, stimulates the FSH receptor leading to an increase in gonadal size and precocious puberty.

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P81

The neonatal screen that cried Wolff

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Introduction
Hypothyroidism is one of the major causes of preventable mental retardation. Neonatal screening aids in the prompt diagnosis of newborns with congenital hypothyroidism. There are other clinical conditions that can alter thyroid function during the newborn period, including exposure of high iodine concentrations.
Case presentation
One day old female born at 37 3/7 weeks of gestational age by C-section with imperforated anus and congenital heart disease was transferred to our children's hospital within the first day of life for a hybrid cardiac procedure of bilateral pulmonary artery banding and PDA stenting. She had an Illinois Neonatal screen done at 36 h of life that was normal. Her cardiac surgery was performed at 10 days of life, where she was exposed to iodine products transdermally. At 14 days of age, she had a repeat Illinois Neonatal screen that was positive for congenital hypothyroidism with a TSH of 78 mIu/ml (normal < 20 mIu/ml) and reflex total T4 of 5.4 ug/dl (normal is > 8 ug/dl). No family history of thyroid disease; mother was healthy during pregnancy and was not on medications that could affect baby's thyroid function. Subsequent serum laboratory testing confirmed a TSH of 74.3 mIu/ml and Free T4 of 0.6 ng/dl (6.0 ug/dl). Patient was diagnosed with Wolff–Chaikoff effect, which is the phenomenon of transient hypothyroidism caused by exposure to high doses of iodine (iodine containing contrast agents or topical antiseptics). Pediatric Endocrinology was consulted and she was started on 25 mcg of levothyroxine PO daily. The patient was last seen at 21 months of age by Pediatric Endocrinology. She is still on the initial dose of levothyroxine and her thyroid labs have been within normal limits for an infant. She will likely not require lifelong thyroid supplementation.
Conclusion
Risk of hypothyroidism among neonates must be considered seriously after large iodine exposure and monitoring for transient hypothyroidism should be performed. It is thus recommended that attempts should be made to reduce the amount of iodine used during procedures and to carefully monitor thyroid function in all neonates exposed to an excess of iodine.

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P82

Siblings with multinodular goiter and autoimmune thyroiditis

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Introduction
It has been documented that autoimmune thyroiditis (AT) predisposes to the development of papillary thyroid cancer (PTC). The presence of chronic inflammation was thought to act as an initiating factor in carcinogenesis. Moreover elevated levels of TSH found in hypothyroid patients with AT were speculated to stimulate follicular epithelial proliferation and thereby promote the development of PCT.
Case
We describe a case of two sisters aged 12 year and 14 year who were diagnosed with multinodular goitre and hypothyroidism secondary to AT two years prior to their referral to tertiary endocrine centre for further investigation and management of their multinodular goitre. They both had positive TPO antibodies and were commenced on levothyroxine. A repeat thyroid ultrasound and fine needle aspiration (FNA) on 14 year-old girl confirmed features consistent with AT (Thy2). She's remained asymptomatic and stable on the same dose of levothyroxine 75 mcg once daily. However her 12 year-old sister was found to have hypoechoic nodule 7×1.3 mm with multiple hypoechoic foci, compatible with calcification on a repeat thyroid ultrasound. Her FNA raised a high suspicion of PTC. A repeat USS and FNA confirmed metastatic PTC. Therefore she had an elective total thyroidectomy with neck dissection followed by radioactive iodine ablation few weeks later which didn't reveal pathological uptake. Postoperatively she developed a temporary hypocalcaemia managed with calcium, vitamin D and alfacalcidol, which were gradually weaned down when her PTH recovered and calcium normalised. Moreover her levothyroxine was gradually increased to 125 mcg once daily in order to suppress TSH < 0.1 mU/l.
Conclusion
We present an interesting case of two siblings with multinodular goitre and hypothyroidism secondary to AT, one of which developed PTC on a background of thyroiditis. Although PTC is rare in childhood and caused association between AT and PTC remains elusive, based on evaluation of current literature, it would be prudent to rule out malignancy in nodular autoimmune thyroiditis. Therefore it is recommended the thyroid ultrasound and FNA to be performed by experienced radiologist, especially when there is a suggestion of abnormal follicle appearance, which will help to confirm the diagnosis and initiate an early referral for surgical intervention.

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P83

Congenital hypothyroidism: screening, diagnosis, treatment & follow up – evaluation of service provided in a District General Hospital

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Background
Screening for Congenital hypothyroidism is part of National New-born screening program. Each District General Hospital is required to have a Congenital Hypothyroidism Service with a Lead Paediatrician and a Deputy to provide seamless service to babies with suspected congenital hypothyroidism and their families. National guidelines and service standards exist to guide setup, operation and auditing of this service.
Aim
We aim to benchmark the performance of our congenital hypothyroidism service against local and national guidelines.
Materials and methods
We studied timeliness of organising physical review, blood tests, scans, initiation of treatment and follow up of these patients. We planned it as a retrospective audit including all patients referred with suspected congenital hypothyroidism between 2002 and 2018. The list of patients was cross-checked with Regional Screening Laboratory to ensure all cases were included. The data was collected from hospital notes and laboratory system computers using a standardised pro forma. Results were analysed and presented in graphical form.
Results
Total 38 cases were identified. In 100% cases, contact with family was made within 48 h of receiving notification from screening laboratory. All patients were seen and started on treatment if required within 48 h of notification (66% seen on the same day and 34% seen on the next day). The starting dose of levothyroxine was correct as per guidelines in 100% of the cases. The future clinic follow-up scheduling did not conform to the national guidance. This was felt to be secondary to reduced capacity in out-patients clinic. However, 100% of these patients had blood tests done and dose change actioned on telephone.

Conclusion
Overall, our service achieved excellent performance in initial workup and initiation of treatment of all cases. However, future follow up scheduling needs improvement. This is one area where the concept of Virtual Clinic can deliver good results. The local team is in discussion with the Trust to pilot Video clinics in this service.

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P84

Deficiency of vitamin D as a potential factor of the development of Graves' disease in children and adolescents

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Goal
To determine the level of vitamin D and its pathogenetic role in children with Grave's disease living in the territory of Uzbekistan. The study included 16 children and adolescents of 9–17 years old with the first time identified Grave's disease. The control group included 12 children without thyroid pathology. The concentration of total vitamin D, TSH, fT4 and Antibodies to TSH receptors (TRAb) in serum was determined using a Cobas e 411 Hitachi closed-type immunochemical analyzer from HoffmanLeRoche (Switzerland) and its reagents. Vitamin D deficiency was determined at its serum level <20 ng/ml, insufficient at a level of 20–30 ng / ml. Statistical processing of the results was performed using the Microsoft Statistica 6.1. The significance of differences was established at $P<0.05$.
Results
At the time of the first treatment, all children with Grave's disease had a pronounced clinic of moderate thyrotoxicosis in a state of decompensation, all patients have high TRAb values, the interval of which was 2.5–40.0 IU/l with a median (Me) of 11.6. Despite the fact that the number of sunny days per year exceeds 300, the content of vitamin D (15.7 ± 4.7 ng/ml) in children with newly diagnosed Grave's disease was significantly lower than the control group (29.3 ± 4.8 ng/ml, $P<0.05$). All children with thyrotoxicosis had an indicator of vitamin D in the serum of less than 30 ng/ml, while a pronounced deficiency of vitamin D was detected in 68.8% (11), the remaining 31.2% (5) had insufficient levels. In the control group of children with vitamin D deficiency it was not diagnosed, but 66.7% (8) had insufficient serum levels. The results of the correlation analysis indicate the presence in patients with Grave's disease significant feedback between the content of vitamin D and the level of TRAb ($r=-0.38$; $P<0.05$).
Conclusion
Low levels of vitamin D may be the primary factor involved in the pathogenesis of the disease. Further in-depth study of this problem is needed in order to develop effective methods of treatment of Grave's disease in children.

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P85

Paediatric Graves disease – management in a District General Hospital

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Background
Graves disease is the most common cause of hyperthyroidism or thyrotoxicosis in children. The prevalance is 1 in 10 000 among children. It is important to reinforce the awareness amongst clinicians as patients can present with wide range of clinical symptoms. The range of presentations in our study included a child treated for one year for Attention Deficit Hyperactivity Disorder (ADHD) to a child who had diarrhoea and abdominal pain and presented as appendicitis initially.
Methods
Retrospective review of notes and clinic letters of 15 patients who presented as hyperthyroidism in last 6 years (2013–2019). Inpatient and outpatient notes along with lab results were used for data analysis.
Results
11/15 patients were confirmed to have Graves disease. 2 patients had false elevation due to Assay Interference. 1 had Hashimoto Thyroiditis and 1 had hyperthyroidism diagnosed on annual review of coeliacs disease. Age at diagnosis of our cohort ranged between 4 and 15 years, with age of 11–14 years for children with Graves. 9/11 children with Graves disease were clinically thyrotoxic and required beta blockers, 5/11 had eye signs at presentation. Thyroid stimulating immunoglobulins (TSI) or TSH receptor Antibodies (TRAB) were used for confirmation of Graves. Ultrasound Scans were done in cases of Graves disease which confirmed Thyroiditis. They were normal in Hashimotos thyroiditis. Antithyroid medications (ATM) were started initially on 13/15 patients.1-not started due to assay interference and the other was clinically and biochemically euthyroid. 3/11 had definitive treatment, 1 patient underwent total thyroidectomy and 2 had radioiodine ablation. 6/11 children are having ongoing dose titration with carbimazole and 2 children currently on block and replacement. Tertiary referral was done in 11/15 cases.
Conclusion
We have relatively large group of patients with Graves Disease for our population. Patient presentation was mostly with typical symptoms and signs but was nonspecific in few others leading to a delay in diagnosis. Most of our patients are treated with Dose titration (DT) regime.Emerging evidence suggests that longer treatment on ATM might increase chance of remission.One of our patients who underwent thyroidectomy had in situ papillary carcinoma.

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