Association of British Clinical Diabetologists
&
Welsh Endocrine and Diabetes Society
Spring Meeting "Now that's what I call diabetes and endocrinology"
Hilton Cardiff, 23rd & 24th April 2015

POSTERS

1 Whole genome sequence based analysis of thyroid function

Peter N. Taylor1, Eleonora Porcu2,3,4*, Shelby Chew5*, Purdey J. Campbell5*, Michela Traglia6,, Suzanne J. Brown5, Benjamin H. Mullin5,7, Hashem A. Shihab8, Josine L. Min8, Klaudia Walter9, Yasin Memari9, Jie Huang9, Michael R. Barnes10, John P. Beilby11,12, Pimphen Charoen13,14, Petr Danecek9, Frank Dudbridge13, Vincenzo Forgetta15,16, Celia Greenwood15,16, Elin Grundberg17,18, Andrew D. Johnson19, Jennie Hui11,12, Ee M. Lim5,11, Shane McCarthy9, Dawn Muddyman9, Vijay Panicker5, John R.B. Perry20,21, Jordana T. Bell21, Wei Yuan21, Caroline Relton8, Tom Gaunt8, David Schlessinger22, Goncalo Abecasis4, Francesco Cucca2,3, Gabriela L. Surdulescu21, Wolfram Woltersdorf23, Eleftheria Zeggini9, Houfeng Zheng15,16, Daniela Toniolo6,24, Colin M. Dayan1, Silvia Naitza2, John P. Walsh5,7, Tim D. Spector21, George Davey Smith8, Richard Durbin9, J. Brent Richards15,16,21, Serena Sanna2, Nicole Soranzo9, Nicholas J. Timpson8*, Scott G. Wilson5,7,21* and the UK10K Consortium25. * Authors contributed equally.*

1) Thyroid Research Group, Institute of Molecular & Experimental Medicine, Cardiff University School of Medicine, Cardiff University, Cardiff, United Kingdom:2) Istituto di Ricerca Genetica e Biomedica (IRGB), Consiglio Nazionale delle Ricerche, c/o Cittadella Universitaria di Monserrato, Monserrato, Cagliari, Italy; 3) Dipartimento di Scienze Biomediche, Università di Sassari, Sassari, Italy; 4) Center for Statistical Genetics, Biostatistics Department, University of Michigan, Ann Arbor, MI, USA; 5) Department of Endocrinology and Diabetes, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia; 6) Division of Genetics and Cell Biology, San Raffaele Research Institute, Milano, Italy; 7) School of Medicine and Pharmacology, University of Western Australia, Crawley, Western Australia, Australia; 8) MRC Integrative Epidemiology Unit at the University of Bristol, University of Bristol, Bristol, United Kingdom; 9) Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, United Kingdom; 10) William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom; 11) Pathwest Laboratory Medicine WA, Nedlands, Western Australia, Australia; 12) School of Pathology and Laboratory Medicine, University of Western Australia, Crawley, Western Australia, Australia; 13) Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, United Kingdom; 14) Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; 15) Department of Medicine, Jewish General Hospital, McGill University, Montréal Québec, Canada; 16) Departments of Human Genetics, Epidemiology, and Biostatistics, Jewish General Hospital, Lady Davis Institute, McGill University, Montréal Québec, Canada; 17) Department of Human Genetics, McGill University, Montreal, QC H3A1A5, Canada; 18) McGill University and Genome Quebec Innovation Centre, Montreal, QC H3A1A5, Canada; 19) Cardiovascular Epidemiology and Human Genomics Branch, National Heart, Lung and Blood Institute, Bethesda, MD, USA; 20) MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine,Box 285, Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge, United Kingdom; 21) Department of Twin Research and Genetic Epidemiology, King's College London, London, United Kingdom; 22) Laboratory of Genetics, NIA, Baltimore, MD 21224, USA; 23) Facharzt für Laboratoriumsmedizin, Geschäftsführer amedes Ost, Halle/Leipzig GmbH, Leipziger Chaussee 191f, 06112 Halle (Saale), Germany; 24) Institute of Molecular Genetics–CNR, Pavia, Italy

Objective
The genetic architecture of thyroid function is poorly understood. We aimed to identify genetic variants, including rare variants, associated with thyrotropin (TSH) and free thyroxine (FT4) using whole genome sequencing (WGS) data from the UK10K Consortium.

Methods
TSH and FT4 levels were standardized adjusting for age, age^2 and sex. We analyzed data from two UK10K cohorts (ALSPAC and TwinsUK N=2,287) and used an additional collection with WGS data (SardiNIA) and deeply imputed datasets (imputed to a joint 1000genomes and UK10K reference panel) to perform a meta-analysis for common variants (MAF >1%) associated with TSH and FT4 (N=16,335). We undertook analysis of exonic rare variants (MAF <1%) using sequence kernel association testing (SKAT) in 40 candidate genes and performed genome-wide complex trait analyses (GCTA) to explore the extent that common SNPs (MAF>1%) explained the variance in TSH and FT4.

Results
For TSH we report a novel variant at *SYN2* (MAF=23.5%, P=6.15x10^{-09}) and a new independent variant in *PDE8B* (MAF=10.4%, P=5.94x10^{-14}). Expression quantitative trait locus analysis revealed our variant at *SYN2* modulates gene transcription in adipose, skin and whole blood cells. Methylation profiles revealed evidence for methylation quantitative trait locus effects for our novel variant in *PDE8B* (P=4.38x10^{-07}). For FT4 we identified a low frequency variant in 18q11 (MAF=3.2%, P=1.27x10^{-09}) tagging a rare functional variant in *TTR* (MAF=0.4%, P=2.14x10^{-11}). SKAT analysis revealed a novel association with FT4 in chromosome *NRG1* (P=2.53x10-06). GCTA analysis estimated common SNPs (MAF>1%) explained 24% (95%CI 19, 29) and 20% (95%CI 14, 26) of TSH and FT4 variance, respectively (P=<0.0001).

Conclusion
Our results demonstrate that increased coverage in WGS population association studies allows detection of both common and rare variants in thyroid function. Common variants collectively account for over 20% of the variance in TSH and FT4; a substantial advance on estimates from earlier genome-wide association studies.

2 Reliability of a post partum fasting glucose in the management of women with gestational diabetes

Peter N Taylor1,2, Gautam Das1, Arshiya Tabsum1, Elizabeth Bradley1, David Burberry1 Dawn Lee 1 Piero Baglioni1, Anthony Robinson3, Onyebuchi E Okosieme1,2
(1)Endocrinology and Diabetes Department, Prince Charles Hospital, Cwm Taf University Health Board, Merthyr Tydfil; (2) Institute of Molecular and Experimental Medicine, Cardiff University School of Medicine, Cardiff; (3) Department of Diabetes and Endocrinology, Royal United Hospital, Bath.

Context
International guidelines recommend that all women with gestational diabetes should undergo a 6 weeks post-partum oral glucose tolerance test (OGTT), however UK guidelines recommend performing a fasting glucose initially.

Methods
Retrospective analysis of all postnatal OGTTs performed for women with gestational diabetes who were managed at Prince Charles Hospital, Merthyr Tydfil (2011-2014) and the Royal United Hospital, Bath (1993–2007). We assessed the utility of the postnatal fasting glucose in identifying persistent abnormalities of glucose tolerance in these women.

Results
We analysed 165 postnatal OGTTs of which 9 women had diabetes (5.5%) and 16 had IGT (9.7%). If only women with a fasting glucose of >6.0 mmol/l were selected to undergo an OGTT just 18.1% of individuals would require one. However this approach only had a sensitivity of 88.9% for diabetes and 37.5% for impaired glucose tolerance. Reducing the glucose threshold to >5.1 mmol/l improved sensitivity but resulted in almost half of individuals requiring an OGTT. Both fasting and 2 hour glucose levels in the pregnancy OGTT were strongly associated (p<0.001) with the 2 hour glucose value in the post-partum OGTT, but did not substantially enhance sensitivity and specificity.

Conclusion
In our study population a fasting glucose is an imperfect measure in determining who should undergo an OGTT post-partum. The addition of data from the pregnancy OGTT did not improve the prediction of abnormal glucose tolerance. Our data supports the approach adopted in the WHO guidelines, that a postnatal OGTT should be undertaken in all women with gestational diabetes.

3 Dapagliflozin is more effective in the most poorly controlled diabetic patients

T Min1, 2, A Dixon2, A Mallipedhi1, P Varnavas2, C McIver1, D Price1, J Stephens1, J Harvey2
1Department of Diabetes and Endocrinology, Morriston Hospital, Swansea, SA6 6NL; 2Department of Diabetes and Endocrinology, Wrexham Maelor Hospital, Wrexham, LL13 7TD

Aims
Dapagliflozin reduces HbA1c, body weight and blood pressure in type 2 diabetes. Trials have mostly recruited patients with modest elevations of HbA1c. We investigated its effect in patients with severely impaired glycaemic control.

Methods
A prospective observational trial was conducted in secondary care clinics in Wrexham and Swansea. Dapagliflozin was added to whatever other therapy patients were taking including insulin and GLP1 agonists. Results in patients whose baseline HbA1c was ≥9.5% (poorly control) were compared with those whose HbA1c was <9.5% (moderate impairment).

Results
133 patients (64% male) have so far undergone their first follow-up visit. Mean age was 57.55 ± 8.3 years and mean duration of diabetes was 11.1 ± 6.6 years. For the whole group pre-treatment mean HbA1c was 10.0 ± 1.4% and mean body weight 103.8 ±17.9kg. Mean duration of treatment was 6.0 ± 2.6 months. The mean difference in HbA1c was -1.3% with 95% CI (-1.0 to -1.5%) (p <0.001). Mean body weight was decreased by 2.3kg with 95% CI (1.7 to 2.9kg) (p <0.001). Insulin total daily dose reduced from 96.8 to 86.6 (p<0.001). SBP reduced 3.7mmHg (p=0.013); DBP reduced 2.6mmHg (p=0.004). In those with moderate impairment (n=48) HbA1c reduced from 8.6 to 8.0% (p<0.001). In poor control group (n=85) HbA1c reduced from 10.8 to 9.2% (p<0.001). Using linear modelling there was an interaction (p<0.001) indicating significantly greater response in patients with poor glycaemic control.

Conclusion
The effect of dapagliflozin on HbA1c is greatest in patients with the worst glycaemic control.

4 Correlations between cardiovascular risk factors and TBPI v Doppler in patients with type2 diabetes

L Lomova-Williams1, A Mallipedhi1,2, D E Price1, R Thomas1, C Ferguson1,2, S Bain1,2, J W Stephens1,2
(1)Department of Diabetes & Endocrinology, Morriston Hospital, ABM University Health, Swansea SA6 6NL; (2) Diabetes Research Group, Institute of Life Sciences, Swansea University SA2 8PP.

Aims: To investigate the correlations between cardiovascular risk factors and toe brachial index pressure (TBPI) v. US Doppler. Cardiovascular risk factors were assessed by using UKPDS Risk Engine.

Methods: We looked at cardiovascular risk factors (age of patients, duration of diabetes, gender, HbA1c, SBP, DBP, lipids, smoking, ethnicity and whether there was history of AF for patients) using UKPDS Risk Engine and compared the results to TBPI in both feet and posterior tibialis (PT) and dorsalis pedis (DP) US Doppler.

Results: A total of 49 patients who underwent TBPI measurement were divided in 3 subgroups: TBPI<0.3, TBPI 0.3-0.5 and TBPI>0.5. We found that UKPDS risk factor was not higher in those with abnormal TBPI (34.4 (17.3), 38.2 (19.1), 27.8 (17.0) accordingly (p 0.62). We also compared cardiovascular risk factors in 99 patients with monophasic, biphasic and triphasic doppler sounds. There was no significant difference observed in those patients (25.4 (16.6), 23.6 (14.7) and 18.7 (11.8) accordingly (p 0.49). Of particular interest there was good correlation between TBPI and doppler sounds in both feet.

Conclusions: There was no association between TBPI and changes in doppler signal and cardiovascular risk factors, therefore these investigations should be performed regardless to cardiovascular risk factors. There was good correlation between TBPI and doppler in both feet thus patients with abnormality in one foot are likely to have abnormality in the other.

5 Pancreatic Enzyme supplmentation in diabetes

Witczak JK, Evans PJ
Royal Gwent Hospital, Aneurin Bevan Health Board

Background and aims
Pancreatic enzyme supplementation appears to improve symptoms and quality of life of patients with pancreatic exocrine insufficiency (PEI) but it is not clear what effect it has on glycaemic control. Our aim was to establish if pancreatic enzyme supplementation led to any improvement or deterioration in HbA1c in patients who were diagnosed with PEI secondary to diabetes.
Methods
Out of 2420 patients who were tested for PEI in our trust between 2010 and 2013 we selected 56 excluding those with history of alcohol excess, pancreatic malignancy, pancreatic surgery or gallstone pancreatitis. Data were collected on age, sex, diabetes type, presenting symptoms and radiological findings. Patients were then subdivided into two groups: those who received pancreatic enzyme supplementation and those who did not. HbA1c was assessed at diagnosis and at 12 months (+/-3 months) follow up.
Results
Mean age at diagnosis was 64 years (range 36-90). The most common presenting symptoms of PEI were: diarrhoea (46%), bloating/abdominal pain (34%) and weight loss (27%), whilst steatorrhea was only reported by 10.7% of patients. Seventeen patients (30.3%) had severe PEI with faecal elastase below 15 microgram/gram stool. Of those who had reduced pancreatic exocrine function (faecal elastase below 200 microgram/gram stool), only 36 patients (64%) were commenced on pancreatic enzyme supplementation with mean HbA1c at baseline of 70 mmol/mol and one year later: 69 mmol/mol.
Conclusions
Although our study was observational and retrospective in nature, it appears that pancreatic enzyme supplementation has neither beneficial nor negative effects on HbA1c.

6 Local pregnancy and foetal outcomes in GDM in Gloucestershire

Emily Renninson, Sarah Murray, Tripti Mahajan
Diabetes and Endocrinology Department, Gloucester Royal Hospital, Great Western Road, Gloucester GL1 3NN

An audit for service and therapy evaluation in Gestational Diabetes Mellitus (GDM) at Gloucestershire Royal Hospitals Trust was conducted to provide data regarding local pregnancy and foetal outcomes and to ascertain if management changes have improved outcomes in the longer-term.

A total of 63 women with GDM who attended Antenatal Clinic from April 2013–March 2014 were compared with outcomes of 38 women that attended the same clinic in April 2005–March 2006. Blood glucose (BG) targets have been changed from fasting glucose <7mmols, 2 hours postprandial BG <8mmols; to fasting glucose <6mmols, 2 hours postprandial BG <7mmols. Education for primary care, a specialist nurse GDM clinic, regular intensive dietetic advice and a postnatal fasting glucose 'reminder' letter are now well established.

The number of patients seen annually with GDM has increased each year (almost doubling in 10 years). Tighter glycaemic control means more patients receive hypoglycaemic agents (37% to 77%), resulting in less macrosomic babies (28% to 6%). Significantly fewer emergency caesarean sections are being performed ($p = 0.08$) with the majority now being born by spontaneous vertex delivery (39% to 56%). Reduction in perinatal complications provides a cost advantage to subsidise the GDM clinics. Only 6% babies were admitted to the Special Baby Care Unit. 81% women had their 6 week postnatal fasting glucose, 15.7% of these were abnormal, which suggests they have at least impaired glucose tolerance. Identification and alteration of lifestyle behaviours has significant benefits for the long-term morbidity of the mother and foetus and must be encouraged.

7 Cardiovascular risk prediction in subjects at high risk of type 2 diabetes mellitus: Do different risk predictors give the same results

L Lomova-Williams1, A Mallipedhi1,2, R Tristham3, G Lake3, J W Stephens1,2

(1) Department of Diabetes & Endocrinology, Morriston Hospital, ABM University Health, Swansea SA6 6NL; (2) Diabetes Research Group, Institute of Life Sciences, Swansea University SA2 8PP; (3) Clydach Primary Care Centre, Clydach, Swansea, SA6 5LN.

Introduction
Identifying cardiovascular (CV) risk is essential in the management of patients at high risk of developing type 2 diabetes. Methods routinely used in primary care to estimate CV risks include:- Framingham, QRISK CVD, JBS3, ASSING. The aim of this study was to examine for differences in 10-year predicted CV risk using these methods in a sample of patients identified within a primary care practice known to be at high-risk of developing type 2 diabetes.

Methods
An electronic search was made within the local primary care practice database for subjects identified to be at high-risk for type 2 diabetes. Demographic and routine clinical measurements were recorded and 10-year CV risk calculated using the 4 above methods.

Results
We identified 148 subjects (age 61±9.7, BMI 29±6.1, HbA1C 40±3.6, QDiabetes score 11±8.9). Of these, further analysis was undertaken on 125 subjects without manifest CVD. The median [interquartile range] for 10-year CV risk were as follows: Framingham 11 [7-18], QRISK 9 [4-16], JBS3 9 [4-14], ASSING 10 [6-16]. We grouped subjects into low (≤10%), intermediate (10-20%) and high (≥20%) CV risk groups. Significant differences were observed with respect to the proportion of subjects in each risk group. The percentage of subjects within each group who scored high-risk (≥20%) were as follows:- Framingham 16.7%, QRISK 17.2%, JBS3 11%, ASSING 9.6% ($p<0.0001$).

Conclusion
Significant differences exist between routinely available risk engines to predict 10 year CV risk in patients at high-risk of type 2 diabetes. These marked differences may affect the prescription CV modified drugs.

8 Clinical testing of an internet web based tool for risk assessment and management of IP with diabetes

M Choudhary, K Boregowda, H Bolusani & A Roberts
Department of Diabetes and Endocrinology, University Hospital of Wales, Cardiff

In 2014 a pilot diabetes digital risk assessment tool was designed to categorise in-patients with diabetes at risk of adverse events such as hypoglycaemia and diabetic Ketoacidosis. The aim was to review patients who were at risk of adverse glycaemic related events and develop an online system of in patients with diabetes to enable a reduction in paper load in the inpatient diabetic service and develop a focused team approach to at risk patients.

Information including, type and duration of diabetes, medication, and reason for admission was collected onto the database. Blood sugars were assessed and a risk score of 1-7 was allocated for the patient based on their current glycaemic control. Patients with a higher risk score received an intervention by the diabetes team, which was recorded. Patients' risk score was reassessed following the intervention to see if an improvement in their risk had been made following intervention.

This is the first digital risk assessment tool developed in the University Hospital Wales. The pilot project will eventually lead to a paper free system with the future aim to link in patient blood sugar testing and create a virtual diabetes intervention service in hospital.

9 All Wales audit and real world outcomes on the use of Dapagliflozin in the management of T2DM

V S Eligar1, M Nassrullah1,S Zouras2, S Rice2, A Kalhan1, A Roberts1 and H Bolusani1
1University Hospital of Wales, Cardiff, 2Prince Philip Hospital

Aim: Dapagliflozin is the first SGLT2 inhibitor licensed to be used in type 2 diabetes. The purpose of the planned audit is to determine the patient groups in which Dapagliflozin is prescribed across secondary care hospitals in Wales and the real world outcomes of this treatment.

Methods: Hospitals involved in the audit will record baseline data when Dapagliflozin is initially prescribed and repeat data collection by recalling the patient following 6 months treatment with the agent. The anonymised data sets will be collected locally by the registrars and collated centrally at the University Hospital of Wales.

Data collected will include the patient's age and gender, duration of diabetes and current diabetes treatment. Each patient will have their weight, HbA1c and Creatinine /eGFR recorded at each visit. It will be recorded if Dapagliflozin is an additional agent or substituted in the therapy regime, and for what. Hypoglycaemic events and any adverse effects encountered will be documented. If Dapagliflozin treatment is withdrawn over that time then the reasons for this will be recorded.

Conclusion: Preliminary data analysis showed that Dapagliflozin produced a significant reduction in body weight and HbA1c in almost all the patients. A significant minority of patients had to stop treatment as a result of side effects including osmotic symptoms, urinary and genital infections which however seem to be slightly higher in comparison to clinical trials. Our data suggests that Dapagliflozin is well tolerated and effective in the management of patients with type 2 diabetes in clinical practice.

10 Type 2 diabetes, basal Insulin and the experience of hypos: Insights from the patient perspective

Jen Nash1, Amar Ali2, Grace Vanterpool3, Philippa Hammerton4, Richard Hudson5
1) Chartered Psychologist with the British Psychological Society, Director of 'Positive diabetes'; (2) GPWSI Diabetes, Oakenhurst Surgery, Blackburn; (3)Diabetes Nurse Consultant, London Northwest Healthcare NHS Trust; (4)RedLeaf Research Limited, Guildford; (5)Sanofi, Guildford, United Kingdom

Introduction
Glycaemic control is generally poor amongst basal insulin patients and hypoglycaemic events significantly affect daily routine, including work productivity. A person's experience of their diabetes can be affected by HbA1c targets and injection frequency, but these are often neglected. Better symptom control may lead to improved adherence and quality of life. This study aimed to capture patient experience on basal insulin and determine the impact of injection frequency.
Methods
Eligibility criteria included age ≥18 years, English literacy, diagnosis of type 2 diabetes and current basal insulin treatment. Participants recorded adverse events and completed standardised treatment satisfaction (DTSQs) and adherence scales (MMAS-8). The survey was conducted on-line in the UK during July 2014.
Results
The majority (84%) of participants (n=499, 61% male, 81% < age 65) experienced a hypoglycaemic event in the previous year, half of whom didn't report this to an HCP due to feelings of resignation or self-reproach. Similarly fear of hypoglycaemia was a barrier to titration for 40% of people. Despite the burden of hypoglycaemia only 13% of patients felt permitted to influence therapy change. A quarter of participants felt their blood sugars were unacceptably high but a third recently missed a dose. 20% didn't take their insulin for other reasons. Once daily regimens were associated with fewer hypos, tighter glycaemic control and higher adherence.
Conclusions
Hypoglycaemic events and fear of hypoglycaemia may influence adherence and patient experience. Shared decision approaches to treatment between healthcare professionals and patients (potentially addressing injection frequency), may lead to increased satisfaction, treatment adherence and better disease management. Clinical consultations are time pressured but this need not be a barrier to increasing patient empowerment.

Sponsored by Sanofi.

11 Awareness of driving regulations and safe driving requirements for people with Insulin treated diabetes: Health Care Professional Perspectives

Thinzar Min
Diabetes Department, Morriston Hospital, Swansea

Background and Aim: There are variations in clinical practices and deficiencies in knowledge regarding DVLA recommendations and requirements, amongst health care professionals (HCP). The aim of this study

is to assess the experience of primary and secondary HCPs and their clinical practice regarding the current DVLA guidance on driving and diabetes.

Method: A web-based anonymous questionnaire was sent to HCPs in 10 hospitals, 10 general practices and all the specialist registrars (SpR) in diabetes in Wales. The questionnaire included six case scenarios that are loosely adapted from clinic encounters. The answers are based on DVLA guidance and given in multiple-choice format.

Results: 64 HCPs completed the survey. Nearly 75% of HCPs reviewed 5 or more of patients per week. Over 90% of HCPs had consistent recommendations for newly diagnosed T1DM car driver. A small percentage (3%) of HCPs did not know that those who are on insulin are eligible to apply for Group 2 licence if they meet the DVLA's criteria whereas a third would recommend continue driving without further assessment. 10% of HCPs would recommend a lorry driver with impaired hypoglycaemia awareness continue driving. Worryingly up to 20% of health care professionals confused between the cutoff blood glucose level for definition of hypoglycaemia i.e. 4 mmol/L and the recommended minimal blood glucose level for safe driving i.e. 5 mmol/L.

Conclusion: Clinical practice regarding medical fitness to drive for people with insulin-treated diabetes was not consistent among health care professionals.

12 Experience with Dapagliflozin at the Royal Cornwall Hospital

Michael Gilroy
Endocrinology and Diabetes, Royal Cornwall Hospital Treliske, Truro

Dapagliflozin (Forxiga) became the first sodium-glucose cotransporter 2 (SGLT2) inhibitor to be introduced into clinical practice in the UK. We report our early findings on the improvement in HbA1c and weight loss in a cohort of patients initiated on Dapagliflozin at specialist diabetes outpatient appointments.
We under took a first pass review of hospital case notes and biochemical tests for 80 patients with poorly controlled type 2 diabetes seen in outpatient clinics and started on Dapagliflozin.
HbA1c follow up data was available for 59 of 80 patients demonstrating improvement of 10.8mmol/mol (range +22 to -48mmol/mol). Weight loss data was available for 28 of 80 patients with a mean weight loss of 6.5kg (range +1.7 to -16.6kg).
Our experience to date indicates that Dapagliflozin is effective at improving glycaemic control and results in weight loss greater than reported in the clinical trials.

13 HES data, patient experience and local statistics - can peer reviews of diabetes foot care services improve outcomes

Richard Paisey
Horizon Centre, Torbay Hospital, Torquay, TQ2 7AA

Introduction: National statistics have highlighted high amputation rates in diabetes in the South Western region of the UK. Age, ethnicity, a legacy effect of retirement and rurality may all be influential but local detail is lacking.
Aims: Sequential peer review of all CCG areas in the region to investigate causes of avoidable amputations.
Methods: Initial reviews took place between 2010 and 2013 under the aegis of NHS Diabetes. The review team comprised two lead podiatrists a diabetologist and a commissioner. The reviews focussed on the Hospital MDT with a report from community podiatry. From 2013 more formal repeat reviews have been undertaken by two diabetes specialists, two lead podiatrists, a vascular and/or orthopaedic surgeon and an NHS England quality improvement lead. Preliminary information on podiatry staffing, MDT staffing, Practice Care and variation in amputation rates within CCG is sought. The one day visit includes interviews with four patients, review of 10 unselected sets of notes, discussion with the community foot protection team, Practice and CCG representatives and the members of the MDT.
Results: Twelve CCG areas were reviewed in the first visits. Examples of good practice included health worker support for podiatrists, rotation of community podiatrists into the MDT, orthotics and orthopaedics integration in the MDT, prompt dispatch of summary letters to patient, practice and community podiatry and job planning for MDT staff. However these attributes were not universal. Concerns included no MDT, very long podiatry waiting lists, lack of orthotics and insufficient administrative support. The repeat reviews 18 to 24 months later have shown that 3 of 10 Trusts/community areas have maintained good major

amputation rates 4 of 10 have improved to below national average major amputation rates. All areas have begun to organise a rolling programme of education for community and primary care staff.
Conclusions: Peer review of diabetic foot services in the South Western Region has identified much good practice to share and varied local problems. Changes in local services introduced have improved outcomes in less than 2 years.

14 Audit of the outcomes of adding an SGLT2 inhibitor to Insulin in sub optimally controlled T2DM patients

L S Cozma, S Benjamin, S Roy-Chawdhury
Diabetes Centre, Princess of Wales Hospital, ABMU Health Board, Bridgend, South Wales

Aim:
To review the outcomes of adding a SGLT-2 inhibitor (dapagliflozin or canagliflozin) to insulin in type 2 diabetic patients in a secondary care setting. To assess which patients benefited most from the combination and identify baseline predictors of response.

Methods:
We analysed 27 patients (19 male, 8 female), on the combination for at least 3 months, with full data at baseline and follow-up. Dapagliflozin or canagliflozin were commenced in obese subjects (BMI ≥30), on a stable insulin regimen, with an HbA1c >8.0%, unlikely to benefit from further up titration of insulin in view of continuing weight gain.

Age at baseline (mean ± SD) was 57.6 ± 6.9 years and diabetes duration was 13.9 ± 6.7 years. Five (18.5%) subjects were on basal insulin, 18 (66.6%) were on a premixed insulin regimen (twice or thrice a day) and 4 (14.9%) patients were on basal bolus. 25 (92.6%) patients were on metformin, 3 (11.1%) were on sulphonylureas and 5 (18.5%) were on DPP-4 inhibitors or GLP-1 agonists.

Results:
Follow-up time (mean ± SD) was 5.9 ± 2.4 months. HbA1c improved by 1.1% (8.4 ± 1.4% vs. 9.5 ± 1.4%), weight dropped by 1.7% i.e. 1.9kg (109.9 ± 17.3kg vs. 111.9 ± 17.8kg) and BMI decreased from 38.4 ± 5.1kg/m2 to 37.8 ± 4.8kg/m2. Total daily insulin dose decreased by 7 ± 28 units (median 0U, minimum -96U, maximum +43U).

8 (29.6%) patients lost over 3% of body weight and 16 (59.3%) improved their HbA1c by over 1%. Only 5 (18.5%) subjects achieved both parameters. Frequency of insulin injections remained unchanged.

A higher baseline HbA1c predicted a larger decline in HbA1c but did not predict the change in weight or reduction in insulin dose. Baseline weight did not predict any parameters at follow-up.

Conclusion:
Adding an SGLT-2 inhibitor (dapagliflozin or canagliflozin) to insulin in obese diabetic subjects leads to significant improvements in HbA1c in the majority of patients with an associated weight loss of around 1.7%.

15 Weight change and sustained improvement in glyceamic control over 5 years in patients with T2DM on U500 Insulin

Umesh Dashora, Erwin Castro
Conquest Hospital, Hastings

19 patients with Type 2 DM with insulin resistance were commenced on U500 between January 2009 and August 2012. The effect on HbA1c, weight and patient satisfaction is presented from 2014.

Results: Prior to the intervention these patients required a mean dose of 443 units (range 300-944) with an average of 10 injections (range 6-19) a day and had mean weight 122 kg (range 80.5-180.2) & HbA1c 10.8% (95 mmol/mol) (range 7.1-15.2).

After three months of starting U500, the mean HbA1c reduced by 1.7% in 9 patients but two patients had an increase of 0.4% and 0.3%. At 6 months the mean reduction was 2.4% with improvement in 10 patients

whereas one patient had an increase of 0.1%. Most recent data from 2014 reflect a sustained effect, as the mean reduction of HbA1c remains at 2.43% (range 0.4%-4.9%). All ten patients show HbA1c improvement compared to baseline.

In 2014, eight patients had baseline weight. Three patients lost weight (1.2 kg, 3.6 kg and 4.6 kg), whilst five patients gained weight on average 16.9 kg (range between 6-28.7 kg). There was cost saving of £ 12538 calculated for 10 patients in using U 500 insulin for one year. Doses required will be discussed.

All the patients using U500 reported satisfaction with the treatment especially due to the reduction in the frequency of insulin injection.

Conclusion: The use of U500 has a role in the management of severely insulin resistant patients who are either waiting or not qualified for bariatric surgery.

16 Injection site reaction secondary to GLP1 therapy

P Srivatsava, K Boregowda, M Choudhury, Aled Roberts & Hemanth Bolusani
Department of Diabetes and Endocrinology, University Hospital of Wales, Cardiff

A 54 year-old lady with a 12 year history of type 2 diabetes mellitus presented with an erythematous slightly indurated maculopapular rash. The patient had been started on Byetta (Exenatide) 4-6 weeks prior to the onset of the rash. An injection-site reaction is a recognized complication of Byetta therapy and has an estimated prevalence of 0.2 – 1%. These are observed more frequently with the longer acting preparations like Bydureon in comparison to Byetta with nodule formation reported as the formulation contains a dissolvable suture-like material. The precise pathogenesis remains unclear, but possible mechanisms include immune reaction to GLP1 or excipients of the injection solution and this is supported by the fact that injection-site reactions were observed in 14.2% of antibody-positive patient's vs 3.1% of antibody-negative patients treated with Bydureon. Although most injection site reactions tend to decrease in frequency with continued treatment, a persistent or worsening reaction has been described. Symptomatic eruptions however can be treated with cold compresses, oral antihistamines, or nonsteroidals. After the discovery of injection site reaction, our patient discontinued GLP 1 treatment and the areas of erythema gradually diminished over a 3 month period.
Although unproven, it is important to remember that the antibody formation may potentially result in attenuation of the native GLP1 response with resultant failure to achieve adequate glycemic control. This however will need to be explored further.

17 Hyperglycemia post pancreas transplantation in a case of Alstrom's syndrome with diabetes

M Choudhary, K Boregowda, A Roberts, H Bolusani & C Dayan
Department of Diabetes and Endocrinology, University Hospital of Wales, Cardiff

We present the case of a 38 year old gentleman with Alstrom's syndrome and diabetes who underwent a pancreas transplant in 2005 and renal transplant in 2006. Following a successful transplant his glycaemic control began to deteriorate since 2012. His HbA1c was 70mmol/l in 2013 and c-peptide levels were 3992. He was commenced on Metformin and advised lifestyle changes in view of his high BMI and visceral adiposity. Subsequently his glycemic control improved and his recent HbA1c was 42mmol/l (January 2015). This patient's central adiposity along with the c –peptide levels suggested that the deterioration in this patient's glycaemic control was more likely to be result of impaired insulin sensitivity, the predominant feature of Alstrom's syndrome, rather than failure of the pancreas transplant.

Alstrom's syndrome is a rare condition which is inherited in an autosomal recessive manner. The mutation in ALMS1 (Alstrom syndrome protein 1) leads to premature protein truncation and ciliary dysfunction.

Endocrinological manifestations include obesity which is an early and consistent feature observed in nearly all affected individuals, growth hormone deficiency in isolation or in combination with other pituitary hormone deficiencies has been reported and may account for the short stature. Insulin resistance and hyperinsulinemia have been observed in most patients during childhood with most going on to develop type 2 diabetes.

Awareness of the condition is important especially due to its rarity and its variable manifestations over a period of time.

18 Cushungs Syndrome in assocaition with Osteoporosis

Pranav Kumar, Maneesh Udiawar, Santosh Shankarnarayan, David Price
Morriston Hospital , Swansea SA6 6NL

A 55 year old man was referred to the orthopaedic clinic with a 12 month history of sciatica and reduced sensation in left calf. He had gained 3 stone in weight and had symmetrical loss of muscle mass in both his lower limbs. He had been diagnosed with hypertension 18 months ago.
Plain X-ray exam showed multiple wedge fractures in the thoracic and lumbar vertebrae. MRI spine showed T9 fracture. CT thorax showed multiple healed rib fractures bilaterally and pubic rami fracture in association with vertebral fractures. A 45 mm left adrenal mass was also noted prompting a referral to the Endocrine clinic.
Clinical examination showed proximal muscle weakness, cushingoid facies, central obesity, purple striae and skin thinning.
24 hour Urine free cortisol was 625umol. Overnight dexamethasone test showed unsuppressed cortisol of 740. ACTH was unmeasurable. Serum Testosterone was 3.2 with a normal prolactin.
A diagnosis of Cushing's syndrome was made and patient was admitted for unilateral laparoscopic adrenalectomy. He was commenced on Hydrocortisone replacement and Alendronic acid.
Cushing's syndrome often presents with typical signs and symptoms of hypercortisolism. Osteoporosis is an association due to reduced osteoblast activity though presentation with multiple fractures is not common but has been associated with adrenal dependent Cushing's Syndrome.

19 The weekly injection: A practical soultion to an old crisis

Peter Taylor1,2, Arshiya Tabasum1, John Geen1, Gina Sanki1, Brian Tennant1, Andrew Aldridge1, Onyebuchi Okosieme1,2 and Gautam Das1
(1) Endocrinology and Diabetes Department, Prince Charles Hospital, Cwm Taf University Health Board, Merthyr Tydfil; (2)Institute of Molecular and Experimental Medicine, Cardiff University School of Medicine, Cardiff.

An 82 year-old female was admitted through the emergency department after being found on floor by her relatives. She had a background history of hypothyroidism (2006) and was on levothyroxine 75 µg once a day. On clinical examination, she was found to be unkempt, confused, bradycardic, hypothermic and had a low GCS and was barely arousable. Her initial biochemistry revealed a TSH of > 100 mU/L and FT4 of 1.5 pmol/L which supported a diagnosis of Myxoedema coma. She was resuscitated and was commenced on IV liothyronine, hydrocortisone and levothyroxine via NG tube.

Her clinical course deteriorated over the next few days. She developed pulmonary oedema consequent to an acute coronary syndrome (*hs*troponin increased by 570% over 9 hours to 780 ng/L) and was managed in the CCU and then in ITU where she needed diuresis, ionotropic support and assisted ventilation. A CXR revealed cardiomegaly, pulmonary congestion and an echocardiogram showed impaired diastolic function. Interestingly, her earlier TFT's showed a TSH of 27.21 mu/L and FT4 of 12.1 pmol/L (11 months ago) which reflected a picture of poor compliance/inadequate dose. These results were issued to the GP requestor with a suitable advisory comment from the biochemistry department.

It was apparent the patient was non compliant with levothyroxine and she recovered gradually with IV liothyronine and oral thyroxine preparation under close supervision. Her TFT's improved and her FT3 was maintained in the lower half of the reference range. Her TFT's were monitored regularly and have been summarised below: She was maintained on IV liothyronine for longer than originally intended, as it became apparent that she was pouching and spitting out her levothyroxine, with FT4 struggling to normalize.

After careful consideration, and given the need for long-term control we sought advice from international experts where IM levothyroxine was recommended. She was therefore managed from day 50 on IM levothyroxine 200 mcg once a week with good results. She has made continual neurological progress and was discharged to a rehabilitation hospital.

Day	TSH (mu/L)	FT4 (pmol/L)	FT3 (pmol/L)
On Admission	>100	1.5	
Day 5 in ITU	46.4	4.4	4.5
Day 17 in ward	17.6	10.6	3.0
Day 47	1.68	10.4	3.8
Day 65	3.03	19.3	

This report highlights the complex management of myxodema coma and the potential to use IM levothyroxine in individuals with poor absorption or compliance.

20 An unexplained case of chronic back pain: A large Pheochromocytoma in a 55 year old women

Stamatios Zouras, Sam Rice, Jayne Evans, Tom N W Evans
Prince Philip Hospital, Mawr Dafen Road, Llanelli, Carmarthenshire

Introduction: Low back ache is a common complaint and especially in the absence of red flag symptomatology it can be considered as benign.
There are only a few cases reported with pheochromocytoma presenting with back pain as the main symptom.

Clinical case: We report a case of a 55-year-old woman with a past medical history of osteoarthritis who presented with chronic mechanical back pain under the Rheumatology team. They reported normal clinical examination and a blood pressure of 120/70 mm Hg at the time.
Lumbar sacral spine x-rays were requested and showed calcification in the left paravertebral region. Follow up CT and MRI scan showed an 8.3 cm left adrenal mass with a cystic and hemorrhagic component, interestingly, visible on imaging of lumbar spine in 2009 and 2013 suggesting very slow growth rate.
Twenty-four urine collection showed raised urine metadrenaline 22.07umol/24h (<2.00) and normetadrenaline output at 14.24umol/24hr(<4.00).
Patient underwent left laparoscopic adrenalectomy after adequate alpha and beta blockade. The operation was uneventful.

Conclusions: There are cases that the clinical presentation may differ considerably from those in whom the tumor is suspected based on signs and symptoms. Pheochromocytoma, the ”great mimic”, can present like musculoskeletal disease so patients with new spinal pain warrant a routine radiological examination. Pheochromocytoma is a true imaging chameleon. Clinicians and radiologists should be aware of this rare entity.