

# ABCD Autumn Meeting Abstracts

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The ABCD meeting at the Holiday Inn Brighton Seafront in November 2016, saw another strong selection of research, service improvement work and clinical cases submitted for presentation. The top scoring abstracts are included here and the remaining can be found online at [www.bjd-abcd.com](http://www.bjd-abcd.com)

## Compatibility and safety of faster-acting insulin aspart used in continuous subcutaneous insulin infusion therapy in patients with type 1 diabetes

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Ultra-fast-acting insulins may be advantageous for patients on continuous subcutaneous insulin infusion (CSII). The primary objective of this randomised, double-blind trial was to evaluate CSII compatibility of faster-acting insulin aspart (faster aspart) and insulin aspart (IAsp) in 37 adults with type 1 diabetes ( $HbA_{1c}$   $7.5 \pm 0.7\%$ ). After a 2-week run-in period with IAsp, subjects received either faster aspart ( $n=25$ ) or IAsp ( $n=12$ ) for 6 weeks. Compatibility was evaluated by the number of microscopically confirmed infusion-set occlusions and potential occlusions prompted by indirect observations. Laboratory microscopic and macroscopic evaluation of infusion sets and reservoirs was performed after routine (every 72 h) and premature infusion-set changes. Short-term efficacy endpoints were also evaluated. After 6 weeks, no microscopically confirmed occlusions were observed in either treatment arm (of the 219 sets evaluated). Seven possible infusion set occlusions were reported by five subjects using faster aspart, compared with none with IAsp. None of these were associated with an observed plug; six cases were prompted by unexplained hyperglycaemia and one by leakage. Evaluation was possible in three cases, but showed no colour change or particle or crystal formation. Minimal particles, classified as 'unlikely related to insulin', were detected after routine changes on two occasions with faster aspart. The estimated mean change from baseline in  $HbA_{1c}$  favoured faster aspart, but was not significantly different from IAsp (treatment difference:  $0.14\%$  [95% CI:  $-0.40;0.11$ ]). No safety issues were found. In conclusion, faster aspart was compatible with CSII use and demonstrated a trend towards improved glycaemic control.

## Estimating the potential risk reduction of Type 2 diabetes mellitus (T2DM) complications if systolic blood pressure (SBP) targets were to be lowered

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### Aims

Recent trial evidence assessing the advantages of targeting a SBP level lower than 140mmHg suggests benefits may occur in people without diabetes to 120mmHg, but not in individuals with T2DM.

To investigate this discord, we simulated the potential benefits of lowering SBP targets in a T2DM population.

### Methods

We used the UKPDS Outcomes-Model v2 to estimate 10-year event rates for T2DM complications: myocardial infarction (MI), stroke, blindness, amputation, and all-cause mortality. We used baseline data from 5,717 T2DM participants in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin Study. Risk factor values were held constant over 10 years in 5 simulations, each with a different allocated cohort SBP level between 160 and 120mmHg. Cumulative relative risk reductions (cRRR) at each 10mmHg decrement were compared using Kruskal-Wallis tests.

### Results

Patients were mean age 66years,  $HbA_{1c}$  7.3%, LDL-cholesterol 2.3mmol/l, HDL-cholesterol 1.12mmol/l, median T2DM duration 9.8years, with 28.3% women, 66.6% White ethnicity and 52.7% with history of smoking.

From a 160mmHg baseline, imposing SBP levels of 150mmHg, 140mmHg, 130mmHg and 120mmHg produced cRRRs of 2.2%, 4.5%, 7.0%, & 10.0% for MI; 12.5%, 24.8%, 35.6%, & 44.9% for stroke; 5.4%, 10.9%, 16.2%, & 20.9% for blindness; 7.4%, 14.7%, 21.6%, & 27.4% for amputation; 1.4%, 2.8%, 4.1% & 5.2% for all-cause mortality, respectively ( $p<0.001$  in all cases).

### Conclusions

These simulated outcomes provide guidance on the potential benefit of targeting progressively lower SBP values from a baseline of 160mmHg to 120mmHg. Benefits may continue at lower levels, but should be balanced against possible adverse hypotensive effects.

## Does glycaemic control improve in adults with type 1 diabetes after attending CarbAware, a novel, 3-hour, structured-education course?

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**Background:** Structured education is important to support self-management of type 1 diabetes. A one-off, 3 hour, education course for adults with type 1 diabetes (CarbAware) was designed. We aimed to assess whether attendance at CarbAware could improve diabetes control and promote self-management.

**Methods:** The CarbAware curriculum, delivered by a specialist dietician, includes carbohydrate counting. A blood glucose meter with bolus calculator function (Aviva Expert, Roche) was demonstrated and provided to each participant.  $HbA_{1c}$  levels were measured at baseline,  $\geq 3$  months and  $\geq 12$  months after CarbAware. Participant questionnaires completed immediately before and after attending CarbAware were analysed ( $n=103$ ).

**Results:** From February 2014 to July 2015, 336 adults (52% male)

attended CarbAware. At baseline, mean  $\pm$  SD HbA<sub>1c</sub> levels (mmol/mol) were 75.2  $\pm$  18.4, and 23% participants reported using carbohydrate counting to adjust bolus insulin doses. The mean change in HbA<sub>1c</sub> (mmol/mol) after  $\geq$ 3 months was -2.3 (95% CI 0.6-4.0,  $p < 0.01$ ,  $n = 292$ ), and after  $\geq$ 12 months was -3.3 (95% CI 0.2-6.5,  $p < 0.05$ ,  $n = 96$ ). After CarbAware, 85% attendees reported being 'very confident' or 'fairly confident' to carbohydrate count using food labels (vs. 38% at baseline,  $P < 0.05$ ); 1% attendees reported being 'not confident' to carbohydrate count by weighing food (vs. 45% at baseline,  $P < 0.05$ ); and 45% participants intended to increase blood glucose monitoring.

**Conclusion:** Patients with type 1 diabetes attending CarbAware had small but sustained improvements in HbA<sub>1c</sub>. Glycaemic control remained sub-optimal in most attendees. This low-cost course significantly improved reported confidence to self-manage diabetes. The course feedback was universally positive.

### Significant reduction of hypoglycaemia in patients with type 2 diabetes with insulin degludec compared with insulin glargine U100: a randomised, double-blind, crossover trial (SWITCH 2)

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SWITCH 2 was performed to demonstrate that treatment with the long-acting basal insulin degludec (IDeg) is associated with a lower risk of hypoglycaemia compared with insulin glargine U100 (IGlar) in patients with type 2 diabetes (T2D).

In this double-blind, treat-to-target crossover trial including two treatment periods of 32 weeks, each comprising a 16-week titration followed by a 16-week maintenance period, 721 patients with T2D were randomised 1:1 to once-daily IDeg/IGlar or IGlar/IDeg. Patients included were previously treated with basal insulin  $\pm$  oral antidiabetic drugs and had  $\geq$ 1 hypoglycaemia risk factors. The primary endpoint was the rate of overall\* hypoglycaemia in the maintenance periods. Other endpoints included the rates of nocturnal\*\* hypoglycaemia and severe\*\*\* (requiring third-party assistance, externally adjudicated) hypoglycaemia in the maintenance periods. Hypoglycaemia endpoints were also assessed for the full treatment period. HbA<sub>1c</sub> reductions were similar with IDeg versus IGlar. In the maintenance period, treatment with IDeg resulted in a significant 30% lower rate of overall hypoglycaemia and a significant 42% lower rate of nocturnal hypoglycaemia versus IGlar (both  $p < 0.0001$ ). Similar significant reductions were seen in the full treatment period (23% and 25%, respectively), where there was also a significant 51% lower rate of severe hypoglycaemia for IDeg versus IGlar ( $p < 0.0306$ ). Adverse event rates were similar with IDeg and IGlar. Compared with IGlar, IDeg resulted in a consistent reduction in hypoglycaemia in patients with T2D previously treated with basal insulin.

\*Severe or BG-confirmed ( $< 3.1$  mmol/L) symptomatic hypoglycaemia; \*\*Severe or BG-confirmed ( $< 3.1$  mmol/L) symptomatic nocturnal (occurring 00:01–05:59) hypoglycaemia; \*\*\*ADA 2013 definition.

### An integrated multidisciplinary diabetic renal service improves patient care and provides efficiency savings Dr. Parizad Avari, E Lewington-Gower, K Shapriya, T Cairns, A Pokrajac.

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**Background:** Patients with diabetes mellitus (DM) and chronic kidney disease (CKD) require an integrated approach to treat their metabolic disorders, complications, and cardiovascular risk factors. Equally pertinent is excluding alternate causes of CKD. We established a combined diabetes-renal service to optimise management for such patients, with a virtual MDT.

**Methodology:** Retrospective study identified 88 patients (59 male), age 68years (+/-14years) with DM and CKD who attended the service over 3-years. Patients were referred from diabetes or renal clinics, and discussed in an MDT (diabetes and renal physician). We looked into: pointers and causes of CKD other than diabetic nephropathy, screening for complications, CV risk management and cost-efficiency of the service.

**Results:** Patients had median HbA<sub>1c</sub> 63mmol/mol IFCC [range 39-131mmol/mol], Hb 117g/dL [range 81-153mmol/mol] and eGFR 33mL/min [range 5-85mL/min]. Prior to service entry 28/88 patients did not have screening for bone disease.

Following the MDT, 51/88 patients were assigned to be seen in both speciality clinics, 23/88 were followed-up within diabetes clinic only and 7/88 in renal clinic only. Remaining patients were referred to the community/GP/other Trust. There were 300 outpatient appointments in the year prior to service entry, with a reduction in the consecutive year to 262 appointments. At a cost of approximately £200 per clinic, this equates to total savings of £7600 per population (£86 per patient/year).

**Conclusions:** An integrated approach enhances patient management in ensuring access to the appropriate specialist clinics, but also minimises outpatient visits and improves efficiency within the NHS.

### A case of extreme subcutaneous insulin resistance Dr Pei Chia Eng, Dr Sushmitra Chakrabarti, Dr Keith Steer

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A 52-year old Indian man was referred to our service with 9 years history of type 2 diabetes since 2007 and poor glycaemic control. His HbA<sub>1c</sub> was 98 mmol/mol despite being treated with multiple oral hypoglycaemic agents and 250 units of four daily subcutaneous insulin injections. He has no diabetes related complications. He has a BMI of 31 kg/m<sup>2</sup>, a blood pressure of 130/78 mm Hg. Investigations for secondary causes of insulin resistance were carried out. His 24 hours urinary cortisol was normal at 24 nmol (1-124), IGF1 of 25.6 nmol/L (12.2 -30), testosterone of 9.9 nmol/L and his overnight dexamethasone suppression test was normal. His fasting glucose level was 10.5 mmol/L and his fasting insulin was 228 pmol/L with a C-peptide level of 1036 pmol/L indicating a normal ratio of 1:5 and his anti insulin antibodies were negative. We intensified his insulin regimen. Canagliflozin, metformin, Pioglitazone and Sitagliptin were added to improve glycaemic control leading to improvement of HbA<sub>1c</sub> to 70 mmol/mol. Further enquiry led to him being referred for sleep studies as his Epworth score was 17. Obstructive sleep apnea (OSA) is typically associated with conditions that increased insulin resistance and insulin sensitivity may improve with continuous positive airway pressure therapy. We have also referred him for consideration of bariatric surgery despite relatively modest BMI. We

want to highlight the wide differential of causes of insulin resistance, the challenges it bring to diabetes management and the need to use a multimodal approach in the management of insulin resistance.

### Severe hyperlipidaemia due to nephrotic syndrome in a diabetic patient

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Secondary hyperlipidaemia often provides a clue to the underlying systemic disease. Although common in patients with diabetes mellitus, one should think of other causes if there is a poor response to HMG CoA reductase inhibitors in a diabetic patient with good glycaemic control.

We present the case of a 68 year old patient with longstanding well controlled Type 2 diabetes (HbA<sub>1c</sub> 44-60mmol/mol), and new onset severe hyperlipidaemia (cholesterol 9.3mmol/l) co-incident with the development of hypoalbuminaemia and nephrotic range proteinuria. The hyperlipidaemia was unresponsive to statin therapy. Subsequent renal biopsy confirmed systemic AL amyloidosis – lambda type (light chain amyloidosis). SAP scintigraphy showed a large amyloid load within the liver, spleen and kidneys but no definite cardiac involvement on echocardiography. He completed six cycles of weekly combination velcade chemotherapy with a 51% reduction in his post-chemotherapy total serum total cholesterol compared to his pre-chemotherapy levels.

The causes of secondary hyperlipidaemia are numerous but they often demonstrate a distinctive lipid signature dependent on the underlying pathogenetic mechanisms. The characteristic lipid profile in nephrotic syndrome differs from that typical of diabetes and is well described in the literature. It includes elevated total cholesterol, triglycerides, very-low-density lipoprotein and low-density lipoprotein cholesterol levels. There is little literature on the lipid profile in amyloid nephropathy.

This case highlights that an atypical lipid profile unresponsive to statin therapy in a patient with well controlled Type 2 diabetes requires further evaluation. It emphasises the importance of urine protein quantification and of amyloid nephropathy as a cause for severe dyslipidaemia.

### A case of adrenocortical insufficiency in a patient with stable liver cirrhosis

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A 76-year-old male with a background of chronic liver disease (CLD), presented with a one week history of lethargy, confusion, vomiting and instability. He was on furosemide 40mg and spironolactone 150mg daily for recurrent ascites. On examination, he was oriented, euolemic, BP 130/78mmHg with no postural drop. Chest, abdominal and neurological examinations were unremarkable.

Investigations revealed a hyponatraemia of 110mmol/L, potassium of 5.8mmol/L with stable renal function (urea 8.7;eGFR 80). He had low albumin of 31g/L, correlated with Child-Pugh class-A CLD. Serum osmolality was 242mOsmol/Kg and urinary osmolality was 361mOsmol/Kg; urinary sodium was 39mmol/L. His anterior pituitary profile was normal. His early morning cortisol was 68nmol/L

and subsequent short synacthen test (SST) demonstrated a basal cortisol of 65nmol/L, with a blunt response to synacthen (30minute:204nmol/L; 60minute:252nmol/L). The CXR showed no abnormalities and recent CT was reported as normal adrenal glands. Spironolactone was discontinued and hydrocortisone therapy was commenced and sodium improved to 131mmol/L.

Our case illustrates adrenal insufficiency (AI) in the context of CLD. In CLD, cortisol-binding-globulin and hepatic cortisol synthesis are reduced and therefore free-cortisol assays are recommended for diagnosis as total-serum cortisol overestimates AI. Furthermore, a low-dose SST is preferred for diagnosis in patients with stable CLD. Consensus treatment guidelines are not available, however in critically-ill patients with AI, glucocorticoid replacement reduces mortality and vasopressor dependence. Additionally, 1-year survival rates in non-critically ill patients with cirrhosis with and without AI were 69% and 95% respectively. Therefore, although there is controversy, treatment in this group should be considered.

### Arrhythmias in an obese patient with diabetic ketoacidosis

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We present the case of a 38 year old, obese man (BMI 60 kg/m<sup>2</sup>), who presented with osmotic symptoms. He had ketoacidosis and a new diagnosis of diabetes mellitus was made. He was managed in a level 2 facility with fixed-rate intravenous insulin, 0.1 U/kg, as per national guidelines: 18 U/h, weight 182 kg. His progress was complicated by hypokalaemia and hypophosphataemia; he had new atrial flutter with a rapid ventricular rate. Intravenous potassium and phosphate were given in an attempt to manage his tachyarrhythmia, but the insulin rate was unchanged. He was later transferred to the Cardiac Care Unit and required DC cardioversion as the atrial flutter continued despite correction of electrolyte imbalance.

Changes in patient demographics, with increasing prevalence of obesity and other insulin-resistant states, have led to changes in the management of DKA to FR111 calculated on weight. The Joint British Diabetes Societies guidelines suggest that giving more than 15 units of insulin per hour should be only with specialist advice. Our patient's tachyarrhythmia will have been driven by electrolyte deficiencies, hypokalaemia more so than hypophosphataemia; the high dose of insulin will have precipitated hypokalaemia. The hypophosphataemia in DKA tends to be due to inter-compartment shifts rather than absolute deficiency; its association with correction of atrial tachyarrhythmias is less clear than hypokalaemia. We recommend that greater care should be exercised with the dosing of insulin in obese patients with DKA in order to avoid dysrhythmias.

### GAVE a little, gain a lot

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We present the case of a 60-year-old man with type 2 diabetes for 12 years. Extreme insulin resistance led to him requiring 130 international units of insulin daily by 2 years after diagnosis. Glycaemic control was poor with HbA<sub>1c</sub> ranging from 70 to 90 mmol/mol. Other metabolic parameters were suboptimal despite maximal medical treatment with hypertension, dyslipidemia and obesity. Poor

cardiovascular profile was compounded by a sedentary lifestyle. Anti-GAD and anti-islet antibodies were negative, excluding type 1 diabetes.

In addition, gastric antral vascular ectasia (GAVE) was diagnosed 4 years ago. He required frequent endoscopic interventions to control his disease, requiring almost 60 procedures in 4 years. However, endoscopic treatment proved ineffective and he became transfusion dependent for two years ago, requiring transfusions every 3 weeks. Measurement of glycaemic control using fructosamine showed it continued to be poor. Surgery was performed as definitive treatment of GAVE and consisted of a partial gastrectomy (Roux-en-Y).

Postoperatively, he made excellent progress and required no further blood transfusions or endoscopies. Furthermore, insulin requirement significantly reduced such that it was discontinued a year after surgery. Taking metformin and sitagliptin, HbA<sub>1c</sub> fell to 46 mmol/mol. Post-operative BMI was 32.8 compared with 39.4 kg/m<sup>2</sup> prior to surgery. His blood pressure and lipid profile became maintained within the diabetic target ranges. In summary, we present the unusual case of a poorly controlled patient with diabetes, who optimised his glycaemic control via a fortunate and unintended byproduct of surgery.

**An audit of sodium-glucose cotransporter 2 inhibitor (SGLT2i) use in a specialist community service: are the NICE Technology Appraisal (TA ) guidelines too restrictive?**

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**Introduction:** The Knowsley Community Diabetes service provides a consultant and diabetes specialist nurse delivered service in a community setting. The contract requires that we report on compliance with local and national prescribing guidance.

**Aim:** To audit compliance with NICE technology appraisals for SGLT2i drugs and to assess the benefit of these drugs on glycaemic control and other parameters.

**Methods:** SGLT2i treatment was initiated for 32 patients with type 2 diabetes seen between April and September 2015. Pre treatment parameters and the latest data available as of 15 January 2016 was obtained from hospital and GP notes, and laboratory systems.

**Results:** 17/32 (53%) were fully compliant with NICE TA guidance. In 9/15 patients prescribed SGLT2i outside of guidance, the reason was reluctance to start insulin and in 3/15 patients weight control was stated. Data on treatment was available for an average of 24 weeks. Mean pretreatment glycated Hb was 79.7 mmol/mol (range 51-111) and last available mean glycated Hb was 66.5 mmol/mol. (range 42-90). Mean weight was 105.6 kg before treatment and 100.3 kg after. Mean systolic blood pressure (BP) improved by 6 mmHg and diastolic BP by 2 mmHg.

Glycated Hb reduction in patients prescribed outside guidance was greater than in patients prescribed within guidance (17 mmol/mol vs 9 mmol/mol). Reductions in weight, systolic BP and diastolic BP were seen in both groups.

**Conclusion:** SGLT2i initiation can result in equivalent or greater reduction in glycated Hb in patients who would not receive these drugs if guidance were strictly adhered to.