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Obesity Update 2019 Endorsements:

Society for Endocrinology
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Speaker Abstracts

A Year in Review: What Are the Highlights?

OU1

Is obesity pharmacotherapy finally coming of age?

John Wilding
University of Liverpool, Liverpool, UK.

Obesity is a chronic relapsing disease with significant adverse implications for current and future health. Whilst guidelines recommend first line treatment with lifestyle interventions that include restriction of energy intake, increased physical activity and behavioural modification, these only demonstrate an average decrease of 3–5% initial body weight over 12 months, and weight regain is common. Bariatric surgery is effective, but is generally only offered to people with more severe obesity (usually defined as a BMI $>$ 40-kg/m^2, or $>$ 35 kg/m^2 if significant complications are present; it may be offered to those with a BMI $>$30 kg/m^2 in those with recent onset type 2 diabetes). Surgery may result in significant complications and is not suitable for everyone. Pharmacotherapy should be considered an adjunct to lifestyle intervention and may help bridge the efficacy gap between lifestyle and surgery. Current anti-obesity agents available in the USA (not all are approved in Europe or other countries) include the peripherally-acting intestinal lipase inhibitor, orlistat, and the centrally acting drugs, which work to modulate various aspects of appetite regulation. These include the $5HT_{2c}$ receptor agonist lorcaserin, a combination of the mu opioid antagonist naltrexone with bupropion, phentermine as monotherapy, or in combination with topiramate, and liraglutide, a GLP-1 receptor analogue that is also approved at lower doses for use as glucose lowering agent in type 2 diabetes. These agents provide approximately 3–6% greater weight loss than lifestyle intervention alone over 12 months or more treatment duration. Adverse effects depend on the mode of action, and regulators have focussed on cardiac and neuropsychiatric safety given previous problems with older (now withdrawn) medicines for weight loss such as sibutramine and rimonabant. Lorcaserin was recently shown to be safe from a cardiovascular perspective, and data with the lower dose of liraglutide in people with diabetes suggests cardioprotection in those at high risk. The recently reported results of a phase 2 trial with the GLP1 agonist semaglutide are promising and suggest even greater weight loss is possible with some approaches. Future developments will likely target multiple pathways in an attempt to optimise efficacy and approach the weight loss seen with surgical approaches.

DOI: 10.1530/endoabs.61.OU1

OU2

Update on fatty liver: assessment and treatment

Philip Newsom[1,2]
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Non-alcoholic fatty liver disease is a condition characterised by deposition of fat within the liver and can be associated with progressive inflammation and fibrosis (NASH). Up to 30% of the population may have NAFLD and yet only a small proportion will have progressive disease. This means that accurate stratification of at risk patients is required to ensure best use of NHS resource. The talk will describe the diagnostic modalities that can be used to identify patients including algorithms and imaging modalities. Weight loss has been shown to be effective in reducing steatosis and inflammation, although challenges remain with maintaining weight loss. There are no licensed pharmacotherapies for NAFLD but there is a burgeoning trial portfolio globally and also in the UK which promises the offer of new therapies soon. The talk will focus on current treatment modalities being explored.

DOI: 10.1530/endoabs.61.OU2

OU3

Novel endoscopic techniques for the treatment of obesity

BuHussain Hayee
King's College Hospital NHS Foundation Trust, London, UK.

The twin epidemics of obesity and type 2 diabetes represent a major challenge to healthcare service provision worldwide. It has long been recognised that, while surgery is effective in treating both conditions, only a tiny proportion of patients who might be eligible can access appropriate services and even fewer actually undergo treatment. Furthermore, there exists a significant treatment gap on the continuum of risk:efficacy between diet and lifestyle and surgical interventions. A panel of endoscopic metabolic therapies show increasing promise in bridging this gap safely and effectively. The American Society of Gastrointestinal Endoscopy has ratified a number of these interventions as effective, in the setting of a multidisciplinary service. Dr Hayee will summarise the clinical landscape in endoscopic therapies and current areas of interest, focussing on those currently available as well as areas of research and development.

DOI: 10.1530/endoabs.61.OU3

Plenary 1: Can It be Healthy to be Overweight? Is so When?

OU4

Can it be healthy to be overweight? If so when?

Katarina Kos
Royal Devon and Exeter NHS Foundation Trust, University of Exeter, Exeter, UK.

Being overweight or obese is by many people considered a lifestyle choice. It is primarily us healthcare professionals who worry about the health impact of obesity, however are we always right? Whom should we consider at risk and when should we (try) to intervene? Is there something like healthy obesity? This talk is aimed to reflect and understand what happens with adipose tissue when we gain weight, how it copes with surplus energy and how it links with obesity and its complications. We will discuss if there are any genes we need to consider when assessing obesity risk and whether being overweight is as we get older? How can one be obese and metabolically healthy? Eventually, you might be surprised, I will tell you that fat tissue is one's friend if it is well looked after.

DOI: 10.1530/endoabs.61.OU4

Debate: Will Metabolic Surgery Replace Pharmacotherapy for the Treatment of T2 Diabetes?

OU5

Very low calorie diets for the treatment of Type 2 diabetes and obesity are a waste of time -DEBATE

Tricia Tan & Abd Tahrani
Imperial College London, London, UK.

Very low calorie diets (VLCD) have been a time-honored means of losing weight for many decades. The DiRECT trial has put VLCD back in the limelight and now NHS England and Scotland have committed resources to piloting VLCD as an intervention for Type 2 diabetes. Is this premature, or is it the solution for the tsunami of Type 2 diabetes that we face? Prof Tricia Tan and Dr Abd Tahrani will debate the utility of VLCD in the treatment paradigm of Type 2 diabetes.

DOI: 10.1530/endoabs.61.OU5

Symposium: The Role of Weight Loss in Managing Type II Diabetes

OU6

Intensive dietary lifestyle interventions in type 2 diabetes

Adrian Brown
University College London, London, UK.

Dietary and physical activity lifestyle change remain key components in the management of type 2 diabetes. With dietary factors being of paramount importance. Despite this there remains controversy and confusion on which dietary method or pattern is the most effective in the management of a person's glycaemia and weight, meaning that patients and clinicians struggle on which way

to turn. This session will briefly examine the current dietary guidelines for type 2 diabetes. What is the best dietary approach? Should a low carbohydrate diets be the primary dietary option for those with type 2 diabetes. In addition with calls that diabetes remission should now be an outcome target for those with recently diagnosed diabetes, what dietary options are available to achieve this? And finally linking with new evidence within the field.

DOI: 10.1530/endoabs.61.OU6

OU7

Weight lowering treatments in type 2 diabetes

Clifford Bailey
Aston University, Birmingham, UK.

Excess adiposity, especially in visceral depots, is a major driver of insulin resistance, fatty liver and hyperglycaemia in type 2 diabetes mellitus (T2DM). Treatment guidelines for T2DM emphasise lifestyle measures (principally diet and exercise) with pharmacotherapy as additionally required to achieve glycaemic control. Therapeutic strategies ideally assist weight control, avoid hypoglycaemia and address cardiovascular, renal and other risks. Metformin (weight neutral), which counters insulin resistance and offers several of these requirements is usually initial pharmacotherapy. Dipeptidyl peptidase-4 inhibitors (weight neutral), which prevent the rapid breakdown of endogenous incretin hormones and potentiate nutrient-induced insulin release are often introduced next. However, the weight-lowering properties of sodium/glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) encourage use of these agents for obese patients. SGLT2 inhibitors reduce reabsorption of filtered glucose by the proximal tubules of the kidney, creating a therapeutic glucosuria of 50–90 g/day (200–360 kcal) often enabling $>5\%$ weight loss. Since the mechanism is independent of insulin, SGLT2 inhibitors can be combined with other agents at most stages of T2DM provided glomerular filtration is adequate. The osmotic diuresis generated by SGLT2 inhibitors may improve blood pressure control, and large outcome trials have identified cardio-protective and reno-protective benefits. GLP-1RAs increase meal-related insulin secretion, suppress prandial glucagon secretion, slow gastric emptying and exert a satiety effect which promotes weight loss, often $>5\%$. Currently available GLP-1RAs are administered by daily or once weekly subcutaneous injection, and an orally administered GLP-1RA is advanced in development. Fixed-ratio combinations of insulin with a GLP-1RA can reduce/prevent the weight gain associated with insulin therapy, and hybrid and chimeric peptide sequences that activate receptors for GLP-1, gastric inhibitory peptide, glucagon, gastrin, oxyntomodulin and peptide YY are advancing in development.

DOI: 10.1530/endoabs.61.OU7

OU8

Metabolic surgery as a treatment for type 2 diabetes

Dimitri Pournaras
Southmead Hospital, North Bristol NHS Trust, Bristol, UK.

The evidence base for obesity surgery in the context of diabetes will be briefly presented introducing the concept of surgery for the metabolic syndrome. The shift from treating morbid obesity to treating obesity associated morbidity will be discussed. Data on long-term outcomes after weight loss surgery will be presented demonstrating that recurrence of type 2 diabetes following initial remission is an issue. The need for intensive treatment of type 2 diabetes postoperatively with reduction in cardiovascular risk will be highlighted. The paradigm of cancer treatment with multimodal treatment, surgical and medical will be discussed. Comparative data of best medical therapy compared to best medical therapy combined with weight loss surgery will be presented. The need to focus on hard endpoints such as micro-vascular complications as an outcome measure after weight loss surgery will be suggested, as with all other treatment modalities used for type 2 diabetes. The shift of the focus from weight loss maintenance to obesity associated disease control will be highlighted.

DOI: 10.1530/endoabs.61.OU8

Plenary 2: CVOT's in Obesity - Where Are We Coming from, Where Are We Going

OU9

CVOT's in Obesity - Where are we coming from, where are we going?

Nick Finer
University College London, London, UK.

Cardiovascular disease is the leading cause of death globally and obesity is a major risk factor either directly or through its complications such as diabetes, dyslipidaemia and hypertension. While the residual risk after treating these complications is diminishing, obesity can drive risk through, for example causing systemic and paracrine inflammation. Weight loss either through dietary and behaviour change, anti-obesity medications and bariatric surgery has been shown to be beneficial in reducing risk, or in some circumstances cardiovascular events, but the experience from cardiovascular outcome trials (CVOT) of anti-obesity medications is limited and disappointing. Obesity CVOTs will be reviewed and future perspectives discussed.

DOI: 10.1530/endoabs.61.OU9

Oral Communications

Case Discussions: Complex Clinical Cases 1.0

CD1.1

Lifestyle intervention enhances weight loss and metabolic control in GLP-1RA-initiating subjects with T2DM

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We retrospectively studied the effect on BMI and metabolic control (HbA1c within therapeutic targets) of structured lifestyle intervention associated with glucagon-like-1 receptor agonists (GLP-1RA) compared to GLP-1RA alone in patients with Type 2 diabetes (T2DM).
Materials and method
The anthropometric and clinical data of 525 T2DM patients who started therapy with GLP-1RA were collected in a comprehensive database with follow-up of 24 months. According to our protocol, behavior therapy is offered to all cases first attending our institution. Behavioral treatments were carried out within 6 months of GLP-1RA treatment and were classified either as elementary nutrition education (ENE, 5 group sessions) or as cognitive-behavior treatment (CBT, 12 group sessions). The primary endpoint was weight loss ($\geq$5% initial body weight); secondary endpoint was A1c target achievement ($\leq$7%). Patients with out at least 12 months follow up, who changed T2DM drug treatment or interrupted GLP-1RA treatment were excluded from the analysis. In total, 255 (146 male) patients were selected, 191 only received GLP-1RA treatment and 64 accepted either ENE ($n=21$) or CBT ($n=43$).
Results
Body weight decreased significantly in all groups in the course of the 2-yr follow-up ($P < 0.001$). Mean weight loss was 6.5, 5.2 and 3.1% for CBT, ENE and GLP-1RA alone at 1-year, respectively, and increased to 8.3, 6.7 and 3.3% at 2-year follow-up. At logistic regression analysis the participation into a CBT program increased the probability of both 5 and 10% weight loss at 12 months (OR 2.67; 95% CI, 1.20–5.95 and OR 7.62; 95% CI 2.77–20.95, respectively), after correction for age and gender. The results on 5 and 10% weight loss were maintained at 2 years (OR 5.91; 1.84–18.97 and OR 4,99; 1.19–20.96). HbA1c decreased in all groups, more significantly in the CBT group (-1.39% vs -0.87 in GLP-1RA alone at 12 months; $P=0.045$; -1.09% vs -0.85 at 24 months).
Conclusions
The results indicate that intensive lifestyle intervention exerts a significant effect on both body weight and metabolic control in subjects initiating a GLP-1RA treatment. Lifestyle- and GLP-1RA-associated weight loss are likely to produce mutual reinforcement.

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CD1.2

Diabetes Intervention Accentuating Diet and Enhancing Metabolism (DIADEM-I): a randomised controlled trial to examine the impact of an intensive lifestyle intervention consisting of a low-energy diet and physical activity on body weight and metabolism in early type 2 diabetes mellitus: preliminary findings

Odette Chagoury[1,2], Hadeel Zaghloul[1,3], Shahrad Taheri[1,2] & DIADEM-1 Study Team[1]
[1]Weill Cornell Medicine, Doha, Qatar; [2]Weill Cornell Medicine, New York, New York, USA; [3]King's College London, London, UK.

Introduction
Increasing evidence shows that type 2 diabetes mellitus (T2DM) could be reversible and that this is related to weight loss. Significant weight loss achieved through bariatric surgery or medically can result in diabetes remission. Diabetes remission is more likely to occur in those who are younger, have shorter duration of disease, and are on fewer diabetes medications. The impact of using a low energy formula-based diet in combination with physical activity on T2DM in younger patients with early T2DM has not been tested. DIADEM-1 is a randomized controlled trial comparing such an intensive lifestyle intervention (low energy diet with physical activity) with best medical care (BMC; lifestyle advice and medical optimization for body weight and diabetes). We report early 3-month findings from DIADEM-1.
Methods
Subjects ($n=112$) with early T2DM ($<=3$ years) and obesity (BMI$>=$ 27 kg/m^2) aged 18–50 years were recruited into the Diabetes Intervention Accentuating Diet and Enhancing Metabolism – 1 (DIADEM-1) randomised controlled clinical trial. Subjects were randomized into the ILI and BMC groups. All participants received baseline and 3-month assessments including anthropometric measurements, and collection of fasted blood samples. Key outcomes are reported from 3 months into the study.
Results
There were no baseline differences between the ILI and BMC groups. About 1/3 of participants were women. At 3 months, there was significant weight loss in the ILI group compared to the BMC group (ILI 12.89 Kg; 95%CI: 11.04–14.74 Vs BMC 3.17 Kg 95%CI: 2.27–4.07; $P<0.0001$). The ILI group had significantly lower fat mass (bioimpedance) at 3 months (ILI 27.55 Kg 95%CI:24.30–30.80 Vs BMC 35.62 Kg 95%CI:31.73–39.52; $P=0.0024$), but no difference in muscle mass, suggesting that muscle mass was preserved. HbA1c was significantly lower in the ILI group despite no/lower medications for T2DM (ILI 5.8% 95%CI:5.5–6.0% Vs BMC 6.4% 95%CI:6.1–6.7%; $P=0.0016$).
Conclusion
It is possible to achieve significant weight loss and diabetes improvement/remission in younger patents with early T2DM using an ILI that combines a low energy diet though meal replacements with physical activity. It remains to be seen if this effect is sustained.

DOI: 10.1530/endoabs.61.CD1.2

CD1.3

Weight outcomes, by baseline BMI category, in patients referred to a commercial weight management programme

Josef Toon, Sarah Bennett, Amanda Avery & Jacquie Lavin
Slimming World, Derby, UK.

Introduction
Slimming World on Referral (SWoR) is a well-established partnership with NHS and local government commissioners, which provides a cost-effective, 12-week, tier-2 weight management intervention for patients, some of whom may meet NICE criteria for tier 3 services. This analysis examines weight loss outcomes by baseline BMI at 3, 6 and 12 months.
Methods
Referrals to Slimming World were made through 80 locally-commissioned schemes across England. Data for analysis included directly measured weight, self-reported height and attendance. Patients were classified as 'continuers' if they continued to attend SW after their initial referral period. Analysis of co-variance (ANCOVA) was used to investigate the effect of baseline BMI category on weight loss outcomes at 3 months.
Results
The number of patients referred to SW between January and December 2016, who met inclusion criteria was 27,733. Of these, 43.1% ($n=11,950$) had a starting BMI of $>25^{-2}$ and 56.9% of patients ($n=15,783$) had a starting BMI >35 kg/m^2, which, in the presence of co-morbidities, meets NICE guidance for tier-3 weight management services Mean starting BMI for patients was 37.0$\pm$ 6.0 kg/m^2 ranging from 25.0 to 83.3 kg/m^2 with 15.6% males. Mean attendance for patients was 9.7 ($\pm$3.8) sessions over the 12-week referral period. Mean % weight loss for the $>25^{-2}$ BMI category vs the >35 kg/m^2 BMI category at 3, 6 and 12 months was 5.7$\pm$3.8 vs 5.6$\pm$3.8, 10.1$\pm$5.5 vs 10.0$\pm$5.9 and 11.9$\pm$6.8 vs 13.0$\pm$8.3, respectively. After adjusting for gender and age, ANCOVA revealed no significant differences between BMI categories ($P>0.05$), with clinically significant weight loss achieved at 3 months for both groups and even larger clinically important weight losses for continuers.
Conclusions
A number of patients referred to SW had baseline BMIs >35 kg/m^2. Meaningful weight losses were achieved for patients at 3-months, even in patients who may be eligible for tier 3 weight management services. Those who continued to attend post the 12-week referral continued to lose clinically significant amounts of weight.

DOI: 10.1530/endoabs.61.CD1.3

CD1.4

Frequency of Type 2 Diabetes Mellitus in persons with different types of obesity, data of prospective observation

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Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences, Russian Federation, Novosibirsk, Russia.

Objective
To evaluate the chance of developing new cases of Type 2 diabetes mellitus (DM) in obese people in the population sample of the city of Novosibirsk aged 45–69 years.

Materials and methods
The analysis included 2464 people, including 586 (23.7%) men and 1878 (76.2%) women without DM. This sample was formed from the base of the international project HAPIEE surveyed from 2003 to 2005. When conducting a re-screening of the same sample in 2006–2008. The prevalence and risk of developing new cases of DM in obese people with and without metabolic syndrome (MetS) were analyzed (according to NCEP ATP III criteria). Persons with obesity, but without MetS are designated as: «Metabolically healthy obesity» (MHO). According to the screening survey for 2003–2005 the group of obese people without MetS was 1237 people, and the group of people with obesity and MetS was 1227.
Results
Over the observation period, new cases of DM in people with MHO were determined 6.6%, (82 people), while in the group of obesity with MetS, the frequency of newly diagnosed DM was 17.1%, (210 people), p MetS, new cases of DM were detected 2.5 times more often than in the group of MHO; men have a greater risk of developing diabetes in comparison with women.

DOI: 10.1530/endoabs.61.CD1.4

Case Discussions: Complex Clinical Cases 2.0

CD2.1

Factors related to Non-Alcoholic Fatty Liver Disease (NAFLD) measures in obese subjects with early Type 2 Diabetes mellitus

Hadeel Zaghloul[1,2], Odette Chagoury[1], Barbara McGowan[2,3], Shahrad Taheri[1] & DIADEM-1 Study Team[1]
[1]Weill Cornell Medicine, Doha, Qatar; [2]King's College London, London, UK; [3]Guys and St Thomas NHS Trust, London, UK.

Introduction
T2DM (type 2 diabetes mellitus) appears to worsen the course of NAFLD (Non-Alcoholic Fatty Liver Disease) and NAFLD can make diabetes management more challenging. Long-term, NAFLD can lead to liver fibrosis, steatohepatitis, cirrhosis, and end-stage liver disease. This study aimed to examine factors associated with NAFLD measures in early T2DM.
Methods
Subjects ($n=144$) with early T2DM ($<=3$ years) and obesity (BMI$>=$ 27 kg/m^2) aged 18–50 y were recruited into the Diabetes Intervention Accentuating Diet and Enhancing Metabolism – 1 (DIADEM-1) randomised controlled clinical trial. All participants received baseline assessments including anthropometric measurements, collection of fasted blood samples, and measurement of liver steatosis and fibrosis using the FibroScan.
Results
The mean liver controlled attenuation parameter (CAP) for subjects was 329 dB/m and the mean liver stiffness score was 7.2 kPa. Linear regression was used to determine the relation between steatosis and liver stiffness with cardio-metabolic factors, adjusting for age and gender. Both steatosis and liver stiffness were associated with body weight, body mass index (BMI), waist and neck circumference, fat mass, fat percentage, systolic blood pressure, insulin levels, HOMA-IR, and AST levels. Also, steatosis was correlated with HbA1c, fasting glucose, diastolic and mean arterial blood pressures, ALT and albumin-creatinine ratio. Only liver stiffness was correlated with the AST to platelet ratio (APRI).
Conclusion
NAFLD features are associated with measures of adiposity, insulin resistance, and cardiovascular health in obese individuals with early T2DM. NAFLD should be evaluated routinely in those with obesity and early T2DM as addressing NAFLD may result in improved cardio-metabolic outcomes.

DOI: 10.1530/endoabs.61.CD2.1

CD2.2

Simultaneous islet cell and kidney transplant in a patient with Type 1 Diabetes and End-Stage Renal Failure after Roux-en-Y gastric bypass

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Background
Severe obesity, BMI $\geq$40 kg/m^2, confers a greater risk for graft loss and mortality among renal transplant patients. Transplantation provides a better survival and quality of life in overweight dialysis patients. Higher BMI is associated with progressively increased risk of CKD stages 4–5, hazard ratio of 3.10 (CI 2.95–3.25) for BMI $\geq$35 kg/m^2. A recent meta-analysis found pre-transplant BMI $<$30 kg/m^2 is associated with positive outcome measures, including mortality and graft rejection. Indeed, certain transplant centres (London), have categorically suggested a cut-off BMI $<$ 30 kg/m^2 before consideration for transplant, but overall there is insufficient evidence to demonstrate that intentional weight loss pre-transplantation improves post-transplant outcomes. Roux-en-Y gastric bypass (RYGB) supports excellent weight loss (in the range of 50–60% excess weight lost at 1 year). It is clear that this is an area which requires further study. We report a rare case of simultaneous kidney and islet cell transplant in a patient post-RYGB.
Case Report
58-year old female with a 22-year history of type 1 diabetes and severe obesity (BMI 45.4 kg/m^2; weight 126.6 kg, 51.8% fat mass) had a RYGB 9 years previously; weight lost 32.1 kg (25.4% of baseline weight), and although glycaemic control improved (HbA1c 97 mmol/mol reduced to 69 mmol/mol), she had erratic glycemic control and significant concerns over hypoglycemia unawareness (scored 7 on Clark questionnaire & 5 on Gold questionnaire). She subsequently developed end-stage renal failure (ESRF), classed as CKD G5A3 and received peritoneal dialysis. Insulin pump therapy was discussed, but a donor became available and she safely underwent simultaneous islet and cadaveric donor kidney transplant, with a BMI of 33.4 kg/m^2. She reaped benefits in terms of glycaemic control (HBA1c 38 mmol/mol), markedly reduced insulin requirement (70 units to 20 units/day of insulin; random C-peptide 513 pmol/l), reduction of frequency of hypoglycaemia and maintenance of weight loss. Such an approach offers feasible treatment option for post-bariatric surgery patients with ESRD and unstable diabetes.

DOI: 10.1530/endoabs.61.CD2.2

CD2.3

Exploring the roles of Annexin A1 in adipocytes using an *in vitro* model of obesity

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Introduction
Adipose tissue oxygen consumption and blood flow are altered in obesity inducing local tissue hypoxia. Hypoxia affects several biological functions including adipogenesis, inflammation, insulin resistance and metabolism affecting the overall degree of adiposity. The expression of Annexin A1 (ANXA1); an anti-inflammatory protein, increases in the adipose tissue in response to obesity and further increases in the subcutaneous adipose tissue of old obese individuals compared to young obese individuals however, the roles of ANXA1 in the adipose tissue or obesity are unclear.
Aim
The aim of this study was to investigate the potential roles of ANXA1 in adipocytes using an *in vitro* model of obesity.
Methods
Differentiated SGBS cells were treated with and without 10 μM AC2-26 peptide and incubated in hypoxia (1% O_2) for 24 hours to achieve obesogenic conditions. Gene expressions were analysed via RT-qPCR and normalised against GAPDH. Statistical analysis was preformed using GraphPad Prism version 5. Statistical significance was determined using T test at 95% level.
Results
AC2-26 treatment differentially regulated the expression of genes involved in the insulin signalling pathway, adipocytokine signalling pathway, PPAR signalling pathway, metabolism and inflammation. SREBF1 ($P=0.0253$, $n=3$), FASN ($P=0.0125$, $n=3$), SLC2A4 ($P=0.0278$, $n=3$) and IRS1 ($P<0.0001$, $n=3$), TNF ($P=0.0429$, $n=3$), LEP ($P=0.0400$, $n=3$), NAMPT ($P=0.0039$, $n=3$), RETN ($P<0.0001$, $n=4$), ACOX1 ($P=0.030$, $n=3$), DPP4 ($P=0.0170$, $n=3$), IGFR1 (0.0394, $n=3$) and CD36 ($P=0.0305$, $n=3$) were significantly downregulated. ADIPOQ ($P=0.0073$, $n=3$), PPARA ($P=0.0303$, $n=3$) and IL-6 ($P=0.0072$, $n=3$) were significantly upregulated.
Summary
The regulation of genes in response to acute AC2-26 indicate a protective role of ANXA1 in obesity and inflammation and provide a novel strategy to prevent the development of obesity associated inflammation and metabolic diseases. The results of this study further indicate an insulin sensitising role of ANXA1.

DOI: 10.1530/endoabs.61.CD2.3

Poster Presentations

P001

GLP-1 agonist use in the management of obesity in Type 2 Diabetes: an Irish tertiary hospital experience

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Background
In Clinical Trials, Glucagon-like peptide-1 (GLP-1) receptor analogs liraglutide and semaglutide have been shown to cause weight loss, reduced systolic blood pressure, effectiveglycemic control with low rates of hypoglycemia, in patients with type 2 diabetes. Through a retrospective clinical study, the authors aimed to assess the clinical effectiveness of GLP-1 receptor agonists in the management of obesity in patients with Type 2 Diabetes.
Methods
Patients attending St. James's Hospital, Dublin, Ireland who were prescribed GLP-1 receptor agonists (June 2016–December 2018) were assessed both at baseline and first post-initiation visit were included in the analysis. The primary endpoints were weight loss and reduction in glycatedhemoglobin (HbA1c) from baseline. Secondary endpoints were frequency of hypoglycemic events as well as systolic Blood Pressure.
Results
Data from 205 patients are reported (baseline HbA1c 77 mmol/l, mean age 62 years, diabetes duration 8.8 years, 66.8% male). Mean body weight change was −2.4 kg in Liraglutide group and −2.8 kg in Semaglutide group. Mean change in HbA1c from initiation to first visit was −0.7% in Liraglutide group and −0.9% in semaglutide group, while and change in SBP was −2.0 mmHg in both groups. Transient gastrointestinal side effects were experienced by 11.9% of patients, more commonly in the Liraglutide group. The number of patients experiencing minor hypoglycemic events was low (5.7%) and no major events were reported.
Conclusion
GLP-1 receptor agonists such as liraglutide and Semaglutideresulted in weight loss in Obese type 2 Diabetic patients. They also provided improved glycemic control accompanied by improved blood pressure control and low incidence of hypoglycemia. Patient satisfaction were higher and side effects less in the Semaglutide group compared to the Liraglutide group.

DOI: 10.1530/endoabs.61.P001

P002

Metabolic changes post Roux-En-Y Gastric Bypass: one year prospective study

Kleopatra Alexiadou, Preeshila Behary, Joyceline Cuenco, George Tharakan, Oluwaseun Anyiam, David Hope, Haya Alessimii, Sirazum Choudhury, Chedie Doyle, Ahmad Rabie, Ahmed Ahmed, Steve Bloom & Tricia Tan
Imperial College, London, UK.

Background
Bariatric surgery is currently the most effective treatment for weight loss. Its metabolic effects of weight loss and improvement of type 2 diabetes are mediated mainly through the postprandial elevation of gut hormones such as GLP-1, which suppresses food intake and improves insulin secretion.
Aim
To characterize the longitudinal changes in fasting and postprandial secretion of glucose, insulin and gut hormones (GLP-1 and GIP) in patients before and after Roux-en-Y gastric bypass (RYGB).
Subjects and Methods
Twenty-one obese patients with type 2 diabetes (Age: 48.2±13.2 years, BMI: 43.2±6.2 kg/m^2) were studied before and at 1, 3 and 12 months after RYGB. Glucose, Insulin, GLP-1 and GIP levels were measured at fasting state and during a Mixed Meal Tolerance Test.
Results
There was a significant reduction in fasting and postprandial levels of glucose and insulin as early as 1 month post-RYGB. An earlier peak of glucose and insulin was observed at 30 minutes as opposed to the one at 60 minutes prior to bariatric surgery. There was a steady increase in peak GLP-1 levels secreted in response to a mixed meal test (MMT) with time after surgery with an earlier peak at 15 minutes versus the peak seen at 30 minutes preoperatively. There was no significant difference in GIP responses to MMT before and after surgery.
Conclusions
Our results confirm, in concordance with the literature, a reduction in fasting and postprandial glucose and insulin levels and an increase in postprandial secretion of GLP-1 after surgery which increases in magnitude with time whereas there is no significant change in GIP secretion with surgery. Interestingly, there is an earlier peak of GLP-1 levels followed by an earlier peak of glucose and insulin levels post-RYGB.

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P003

The benefits of non-surgical weight management on weight and glycaemic control in people with complex diabetes: a primary care service evaluation of clinical outcomes at 12 months

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Optimising glycaemic control and reducing risk of associated co-morbidities in the patient with complex diabetes and obesity presents a number of challenges in primary care. This study evaluates weight and HbA1c changes at 12 months (primary outcomes) and blood pressure, lipid and medication changes (secondary outcomes) in people with diabetes referred by the diabetes specialist practice nurse (DSN) to a weight management group. The DSN identified patients who would benefit from the weight management intervention (Slimming World, SW) held within the practice setting. Referred patients attended the funded weekly group sessions for up to 12 weeks. On completion, patients were offered a second 12 week referral, if they had achieved a ≥3% weight loss, to attend a locally run SW. The DSN recorded age, gender and baseline data for weight, height, HbA1c, systolic and diastolic blood pressure (SBP & DBP), total cholesterol (TC), LDl cholesterol (LDlc), HDl cholesterol (HDlc), triglycerides (TG) and medication. These measures were then repeated at 3–6 months and 12 months post intervention. A post-intervention questionnaire determined how useful patients found the group, the support they received, accessibility of the group and dietary and lifestyle changes. Sixty-nine patients, mean age 60.5 (10.05) years, achieved a mean weight loss of 5.5 (5.16) %, reduction in BMI (37.7 (6.11) to 35.9 (6.30) kg/m^2, $P<0.001$) and HbA1c levels (62.8 (12.85) to 55.0 (13.02) mmol/mol, $P<0.001$) at 12 months. 81.2% of patients reduced their HbA1c levels. Small reductions were observed in BP and triglycerides with six patients reducing their diabetes medications. Twenty patients completed the questionnaire: 95% found the intervention/support very useful and 80% the group accessible. Unhealthy snacking habits reduced ($P<0.001$) and going for walks increased ($P<0.001$) with fewer people avoiding moderate activity ($P<0.05$). Despite being a chronic, progressive condition, this service evaluation found that referral from primary care to a community based weight management programme was successful in supporting patients with established diabetes to improve their diet and physical activity levels and lose weight and improve their glycaemic control 12 months later. Improvements in cardiovascular risk factors with some patients being able to reduce their medication were also seen.

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P004

Evidence of aberrant inflammation in patients with Lipodystrophy

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Introduction
Lipodystrophy is a rare medical condition with a varied etiology that is characterised by a complete or partial loss of adipose tissue, which can be generalised, partial or localised. Patients have altered secretion of adipokines, such as, Leptin and Adiponectin. Ectopic lipid accumulation is common and leads to metabolic complications associated with insulin resistance (IR) such as, diabetes mellitus (DM) and hypertriglyceridemia. Levels of circulating inflammatory markers are also altered; increase in proinflammatory cytokines, such as, TNF-α and IL-6 and decrease in anti-inflammatory proteins, such as, IL-10 are observed. Annexin A1 (AnxA1) is an anti-inflammatory/pro-resolution protein secreted by the adipose tissue and is decreased in obese individuals. Although obesity is opposite to lipodystrophy, they share similar metabolic alterations and cytokine profiles. Therefore, it was hypothesised that plasma AnxA1 levels are also decreased in lipodystrophy patients.
Aim
To investigate the plasma AnxA1 levels and C-Reactive protein (CRP) concentrations in lipodystrophy patients.

Methods
The plasma concentration of AnxA1 and CRP were measured using a specific Enzyme-linked immunosorbent Assay. Data obtained was analysed using GraphPad Prism version 5 and a four-parameter logistic curve. Statistical significance was determined using T test at 95% level.
Results
Plasma AnxA1 levels were significantly decreased in lipodystrophy patients in comparison to healthy controls (0.24 ng/ml $\pm$0.243 S.D., $n=9$ and 1.24 ng/ml $\pm$ 0.878 S.D., $n=19$ respectively, $P=0.003$). Conversely, Plasma CRP levels are significantly increased in lipodystrophy patients in comparison to healthy controls (3.26 μg/ml $\pm$3.10 S.D., $n=9$ and 1.35 μg/ml $\pm$1.46 S.D., $n=19$ respectively, $P=0.03$).
Conclusion
Lipodystrophy patients display an aberrant inflammatory balance, which may contribute to their dysfunctional glycaemic control.

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P005

Metabolic health and different body composition phenotypes in a Maltese cohort

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It is known that a subset of obese individuals do not exhibit features of the metabolic syndrome (Met-S); these are referred to as being metabolically healthy obese (MHO) individuals. Conversely there are other individuals who although have a normal BMI are insulin resistant and exhibit some of the features of the Met-S and are termed as being metabolically unhealthy normal weight (MUHNW) individuals. This study aims to identify the prevalence of metabolic health among a different array of body composition phenotypes in a randomly selected cohort and to identify potential predictors of metabolic health. This was an observational cross sectional study. Subjects with a BMI[2] were considered normal weight and subjects with BMI >25 kg/m^2 were considered overweight or obese. Individuals having two or less features of the Met-S (as per NCEP ATPIII criteria) were deemed as being metabolically healthy. The subjects were then classified into one of the following body composition phenotypes: Metabolically healthy normal weight (MHNW); metabolically unhealthy normal weight (MUHNW); metabolically healthy obese (MHO) and metabolically unhealthy obese (MUHO). A total of 343 individuals were recruited. 64% were female and a median age of 41 years. There were 26.5% MHNW; 0.88% MUHNW; 50%MHO; 22.5% MUHO subjects. In the obese cohort there was a higher percentage of MHO females and higher percentage of MUHO males. There were significant difference in a wide range of anthropometric and biochemical parameters in between the MHO and MUHO cohorts. In the normal weight cohort 96% were MHNW of whom 80% were female. There were only 3 female MUHNW individuals. There were no significant differences in anthropometric parameters between the two cohorts. Receiver operating characteristic analysis showed that BMI, neck and arm circumference and waist index (WI) all had very good discriminative power to predict metabolic health. In conclusion, there was a high percentage of obese subjects within the recruited population. This is in keeping with recent data showing Malta to have a high prevalence of obesity. A quarter of the studied population were metabolically unhealthy and certain bedside parameters (BMI, arm circumference and WI) can be used to predict metabolic health.

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P006

Recognition of the healthcare professional role pharmacy is playing in the management of weight and Type 2 Diabetes

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Background
The role of weight loss in the management and prevention of type 2 diabetes has grabbed the attention of the media and the NHS, supported by the extremely positive DROPLET trial results. Very Low Calorie Diets (VLCDs) are being recognised as a valuable treatment option for type 2 diabetes, with a qualified healthcare professional closely involved. The NHS has announced plans for a pilot project in 2019 to establish the feasibility of this approach within the NHS structure. Current Healthcare Experience - Pharmacy. I have assisted many people with weight management, in pharmacies since 2004. Data from the 1144 people who have used my VLCD option shows 991 people losing 5% or more of their initial weight, with a mean of 11.98% (range 5% to 58%). From the median, half of these dieters lost over 10%. Among this cohort, 80 people had an initial BMI in excess of 40 kg/m^2 (40 in excess of BMI 43). The mean weight loss in these 80 dieters was 16.03%. Of the 15 dieters who initially presented with type 2 diabetes, all experienced remission in the early days of their programme, attributed to the recognised rapid weight loss and rapid blood glucose normalisation seen with VLCDs. A significant number of diabetics were unnecessarily excluded by GPs refusing permission to significantly reduce prescribed hypoglycaemics which is essential to prevent hypoglycaemia. Effective weight loss programmes, like mine, are time consuming, with availability and flexibility essential. Surgery staff and GPs are already under extreme pressure, with any imposed limitations likely to dilute diet effectiveness and possibly compromising availability. Hundreds of other pharmacists are already offering VLCDs. Their medical knowledge, flexibility and extended availability is critical to establish effective weight loss and long-term weight management. These are features almost impossible to replicate in a surgery setting.
Conclusion
Diabetics do not have to wait for the outcome of the NHS trial. Pharmacists are effectively treating weight now. The overall acceptance of pharmacy-led VLCDs by the NHS and general practice, will help a much larger number of diabetic patients and like my pharmacy programme, at no cost to the NHS.

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P007

25-hydoxy vitamin D and cardio-metabolic risk factors in obesity with early Type 2 Diabetes mellitus

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Introduction
Type 2 Diabetes Mellitus (T2DM) and obesity are a serious health challenge. Obesity and metabolic disorders are associated with cardiovascular risk. Several studies have suggested that low vitamin D status contributes to insulin resistance. This study aimed to explore vitamin D and its relationship with cardio-metabolic risk factors in those with early T2DM.
Methods
Early T2DM subjects ($N=139$) with early T2DM, $\leq$ 3 years, were recruited into the study. Assessments included are anthropometry, waist circumference, neck circumference, blood pressure measurements and samples collection. Diastolic blood pressure was measured. 25-hydroxyvitamin D was measured. Linear regression adjusted for age was used to examine the relationship between vitamin D and cardio-metabolic parameters.
Results
25-hydroxy vitamin D levels were significantly negatively associated with diastolic blood pressure ($\beta-0.1873$; $P=0.006$), mean arterial pressure ($\beta-0.145$; $P=0.02$), and insulin levels ($\beta-0.117$; $P=0.04$) after adjusting for age. There were no significant associations between 25-hydroxy vitamin D levels and waist circumference, fat mass, lipids, HbA1c, and heart rate).
Conclusions
The preliminary results showed that 25-hydroxy vitamin D levels were related to mean arterial pressure, insulin levels and diastolic blood pressure. The nature of the relationship between vitamin D metabolites and identified cardio-metabolic factors remains to be determined.

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P008

Evaluating the effect of seaweed and alginate enriched cheeses on wellbeing outcomes in a nutritional intervention study (pilot study)

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Background
Obesity is a public health problem, associated with several non-communicable diseases, lower psychosocial well-being and elevated risk of death. Managing obesity with Orlistat (a lipase inhibitor) has shown gastrointestinal side effects. Seaweed and its extract alginate, have shown lipase inhibition, which could help with weight loss. Therefore, adding alginate or seaweed into a cheese could decrease dietary lipids digestion and absorption and therefore reducing body weight.
Objectives
The aims were; firstly, assess the acceptability, palatability, and ease of incorporation chesses containing seaweed and alginate into an habitual diet, secondly to examine their effect on gastrointestinal wellbeing functions.
Design
Thirty-seven healthy participants completed the study (21 females), filled in daily food intake and daily and a weekly GI wellbeing questionnaire during 4 weeks of intervention by consumed their normal habitual diet for one week, they consumed alginate cheese for one week, consumed seaweed cheese for one week, and consumed control cheese for one week.
Results
There was no statistically significant difference between the baseline food consumed and the dietary food intake (calories, carbohydrate, fat, and protein) during consuming the alginate, seaweed, and control cheeses. There was no significant change to the GI wellbeing (the participants feeling of alert, fullness, bloatedness, flatulent, irritable) during consuming all the study cheeses. There was no significant correlation between the total macronutrients consumed during the study for any of the cheeses and the wellbeing questions asked of participants at the end of each day.
Conclusion
We can conclude that alginate and seaweed were acceptable and eating theses cheeses had no impact on the health of GI wellbeing.

Keywords: Alginate, pancreatic lipase, obesity, gastrointestinal (GI).
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P009

The effect of high protein meal on Glycaemic Indices and Gut Hormones Profiles in patients with Post-Bariatric Hypoglycaemia

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Post–bariatric surgery hypoglycaemia (PBH) is a metabolic complication of bariatric surgery. Symptoms of post-bariatric hyperinsulinaemic hypoglycaemia may develop from 6 months to years after surgery, and typically present 1 to 3 hours after a meal. The incidence of post bariatric hypoglycaemia is estimated to be 0.2–11%,[1,4] but the actual incidence is unknown due to the vague symptoms and lack of diagnostic criteria for the diagnosis of post-bariatric hypoglycaemia. To make a definitive diagnosis of post-bariatric hyperinsulinaemic hypoglycaemia, a patient must have symptoms, laboratory values that support the diagnosis and the symptoms must be relieved by carbohydrate ingestion (Whipple's triad). The management of PBH includes dietary modification (less carbohydrate and more protein) and pharmacotherapy using calcium channel blockers, alpha-glucosidase inhibitors and somatostatin analogues which are often poorly tolerated. In extreme cases, some patients undergo partial pancreatectomy, which may not resolve hypoglycaemia. With regard to post-bariatric surgery nutrient intake, the American Society of Metabolic and Bariatric Surgery[2] recommends protein intake of at least 60–80 g/day, while other guidelines suggest 1.5–2.1 g/kg of ideal weight. In our cohort of patients, we will be comparing OGTT and MMT as provocative tests for hypoglycaemia. In addition, we seek to evaluate the effect of high protein meal comprising of 70% protein, 15% carbohydrate and 15% fat on glycaemic indices and gut hormone profile.
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