Abstract book

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Abstracts

Contents; first 8 abstracts are presented in order of presentation, remainder in order of submission

Title:	**12-week combined polyphenol supplementation: indications for sex-specific differences in gut microbiome-host metabolism interaction in individuals with overweight and obesity**
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Abstract:	**Introduction**: Alterations in gut microbiota composition and functionality are related to obesity-related metabolic diseases. We previously showed that polyphenol supplementation exerts beneficial effects on host metabolism, which may be mediated through changes in the gut microbiota. However, it is not fully clear whether and how polyphenols impact gut microbiota composition, and whether this is sex-specific. Here, we investigated the interactions between combined polyphenol supplementation, fecal microbiota profile, and associations with tissue-specific insulin sensitivity, substrate oxidation and skeletal muscle mitochondrial function in men and women. **Methods**: In a double-blind, randomized, placebo-controlled study, 18 men and 19 women with overweight/obesity received either epigallocatechin-3-gallate and resveratrol (EGCG+RES, 282 and 80 mg/day) or placebo for 12 weeks. Before and after the intervention, fecal samples were collected, tissue-specific insulin resistance was determined by a two-step hyperinsulinemic-euglycemic clamp, fasting/postprandial substrate oxidation by indirect calorimetry, and skeletal muscle mitochondrial oxidative capacity by *ex vivo* respirometry. **Results**: Baseline microbiota composition of specific genera ($q < 0.2$) and phyla (Verrucomicrobia, $q = 0.02$) were significantly different between men and women. Overall, 12-week EGCG+RES supplementation did not induce significant changes in fecal microbiota composition ($q > 0.05$) and α- and β-diversity ($p = 0.69$ and $p = 0.95$ respectively). However, baseline abundance of specific microbial genera highly correlated with polyphenol-induced changes in skeletal muscle oxidative capacity in men ($p < 0.05$), but not in women. **Conclusion**: Our findings suggest that combined polyphenol supplementation has no effect on fecal microbiota composition in individuals with overweight/obesity. However, baseline microbiota composition may be more predictive for changes in metabolic outcomes in men compared to women. Future studies investigating gut microbiome-host metabolism interactions in humans should therefore consider employing a sex-specific approach. **1. Conflict of interest: None disclosed.** **2. Funding: Several authors (1) work under the auspices of TiFN, a public - private partnership on precompetitive research in food and nutrition.**

Title:	**Dietary butyrate promotes intestinal GLP-1 release to reduce appetite and induce fat oxidation via central GLP-1 receptor signaling**
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Abstract:	**Introduction:** The prevalence of obesity has been increasing steadily and requires efficient therapeutic strategies to reduce energy intake and/or increase energy expenditure. We recently showed that dietary butyrate reduces energy intake and increases energy expenditure by activating brown adipose tissue (BAT) as dependent on the gut-brain neural circuit. In the present study, we aimed to elucidate the involvement of central GLP-1 receptor signaling in the metabolic benefits induced by dietary butyrate. **Methods:** Male APOE*3-Leiden.CETP mice, a well-established translational model for human-like cardiometabolic disease, received a high-fat diet (HFD; 60% of total calories derived from lard and 0.25% cholesterol) with or without 5% (w/w) sodium butyrate for 12 weeks, while receiving an intracerebroventricular infusion of the GLP-1 receptor antagonist Exendin-(9-39) or vehicle during the final 4 weeks. Energy metabolism was assessed by indirect calorimetry and nutrient partitioning was assessed by intravenous injection of glycerol tri[^{3}H]oleate-labeled triglyceride-rich lipoprotein-like particles and [^{14}C]deoxyglucose. **Results:** Dietary butyrate increased GLP-1-positive cells in the ileum (+33%), as well as activated GLP-1 in plasma (+41%), accompanied by a reduction in food intake (-15%), body weight gain (-73%) and fat mass (-57%). Also, dietary butyrate increased fat oxidation (+~30%) at the expense of glucose oxidation (-~85%), and increased [3H]oleate uptake, e.g., by BAT (+~50%). Intracerebroventricular infusion of Exendin-(9-39) abolished the effect of butyrate on food intake and largely attenuated the effects on nutrient oxidation, without affecting the effects on body weight gain, fat mass and nutrient partitioning. **Conclusion:** Dietary butyrate stimulates the intestinal GLP-1 release and reduces appetite and increases fatty acid oxidation at the expense of carbohydrate oxidation via central GLP-1 receptor signaling, while butyrate improves nutrient partitioning and activates BAT independent of central GLP-1 receptor signaling.

Title:	**Timing of physical activity is associated with reduced insulin resistance, but not with liver fat content**
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Abstract:	**Introduction:** In addition to total physical activity, timing of physical activity may be important for metabolic health. Therefore, our aim was to examine if objectively assessed timing of physical activity was associated with reduced liver fat content and insulin resistance. **Methods:** In the Netherlands Epidemiology of Obesity (NEO) study, physical activity was assessed using activity sensors. Participants were categorized as being most active in the morning (06-12h), afternoon (12-18h), evening (18-24h), or as having a similar distribution of moderate-to-vigorous-physical activity (MVPA) throughout the day. We examined differences in HOMA insulin resistance (n=777) and the amount of liver fat content, as assessed by MR spectroscopy (n=206), for total MVPA and for the subgroups of timing of MVPA using linear regression analysis, adjusted for demographic and lifestyle variables including percentage of body fat. Associations of timing of MVPA were additionally adjusted for total MVPA. **Results:** We analysed data of 777 participants (42% men with a mean (SD) BMI of 26.2 (4.1) kg/m^2), age 56 (4) years. Total MVPA (-5% [95% CI: -10;0%] per hour), but also timing of MVPA was associated with reduced insulin resistance: compared with participants with a similar distribution of MVPA, insulin resistance was reduced in participants who were most active in afternoon (-18% [95% CI: -33;-2%]) or evening (-25% [-49;-4%]), whereas it was similar (-3% [-25;14%]) in those most active in morning. Timing of MVPA was not associated with liver fat content. **Conclusion:** Performing most MVPA in the afternoon or evening was associated with up to 25% reduced insulin resistance compared with having a similar distribution of activity throughout the day. Prospective studies are warranted to examine timing of physical activity in relation to risk of type 2 diabetes. **1. Conflict of interest: n/a** **2. Funding:** We acknowledge the support from the Netherlands Cardiovascular Research Initiative, an initiative with support from the Dutch Heart Foundation (CVON2014-02 ENERGISE) and from the Netherlands Organisation for Health Research and Development (ZonMw) Partnership Diabetes

Title:	**Pancreatic uptake of radiolabelled exendin as a measure of beta cell mass in type 2 diabetes before and after gastric bypass surgery (RYGB)**
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Abstract:	**Introduction:** Targeting glucagon-like peptide-1 receptor by ^{68}Ga-labelled-exendin-4 (EX) is a promising tool for beta cell imaging. In type 2 diabetes mellitus (T2DM), the role of beta cells in onset and course, and in remission after RYGB is not clear. This study aims examining beta cell function (BCF) and mass (BCM) in patients with T2DM pre- and post-RYGB. **Methods:** Thirteen patients were included between December 2017 and September 2019. Oral glucose tolerance test (OGTT) and EX-PET/CT were performed pre- and one year post-RYGB. Total pancreatic EX uptake (kBq/injected MBq) was measured on PET/CT as measure for BCM. **Results:** Currently, analysis was completed in nine patients: six female, mean age: 54 years, mean T2DM duration: 12 years. Six patients had insulin therapy (104±53IU/day) and three metformin (1-2g/day). Postoperatively, BMI and HbA1c decreased (39±4.7 to 27±3.7 kg/m2 and 63±10 to 47±17 mmol/mol). Preoperatively, pancreatic EX uptake was lower in insulin than metformin group (1.55 vs. 2.95, p=0.017). C-peptide response during OGTT was smaller in insulin than metformin group (1.1 vs. 2.9 nmol/l, p=0.015). In the insulin group, one patient had complete remission (no antidiabetics, normal HbA1c), two patients had little improvement (insulin or sulfonylurea, unchanged HbA1c) and three patients were in between. Pancreatic uptake increased to 2.29 (p=0.025), and seems related to the degree of improvement: Three patients with largest improvement had relative increases of 56-340%, compared to 8-30% in patients with least improvements. All metformin patients had complete remission and average EX uptake decreased to 2.5. **Conclusion:** As could be expected, BCF and BCM were lower in patients with insulin-dependent compared to noninsulin-dependent T2DM. Decreased EX uptake in metformin patients possibly reflects reduced beta cell hyperplasia. Contrary, increased uptake in insulin-dependent patients may indicate recovered BCM. Visualizing BCM in T2DM has not been described before and underlying mechanisms in remission need further investigation. **1. Conflict of interest: none** **2. Funding: none**

Title:	**Changes in long-term appetite-regulating hormones in response to a combined lifestyle intervention for obesity**
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Abstract:	**Introduction:** Altered levels of appetite-regulating hormones have been observed in obesity which may be both cause and consequence of the disease. Weight loss is often accompanied by normalizations of long-term adiposity signals (such as leptin, insulin and adiponectin), but findings concerning short-term appetite regulators after weight loss vary across interventions (e.g. very low calorie diets vs. exercise). Moreover, it is unclear whether such weight-loss-induced alterations reflect a disposition for weight regain. Here, we investigated changes in appetite-regulating hormones in response to a combined lifestyle intervention (CLI) and whether hormonal changes during initial weight loss predict subsequent weight gain. **Methods:** For 41 patients, data on fasting serum levels of appetite-regulating hormones (leptin, insulin, adiponectin, GIP, PP, PYY, CCK, FGF21, AgRP) were available. Hormone levels were correlated to BMI and compared across three time points: T0 (baseline), T1 (after 10 weeks; initial weight loss) and T2 (after 75 weeks; weight loss maintenance). **Results:** At T0, hormone levels were not associated with BMI. BMI decreased significantly from T0 (40.13 kg/m^2±5.7) to T1 (38.2 kg/m^2±5.4) which was maintained at T2 (38.2 kg/m^2±5.9). Leptin and insulin were both significantly decreased at T1 and T2 compared to T0. Adiponectin was increased at T2 compared to T1. PP was significantly decreased at T2 compared to T0. Other hormones were not altered. T0-T2 BMI decrease correlated positively with T0-T2 decreases in leptin, insulin and increases of adiponectin, but no other hormone. T0-T1 increases of adiponectin were associated with T1-T2 increases of BMI. **Conclusion:** A 75-week CLI was associated with beneficial changes in the long-term energy regulators adiponectin, leptin and insulin, but no changes in most short-term appetite-regulators. The decrease in PP might point towards a slightly more orexigenic disposition. However, only initial increases in adiponectin were associated with subsequent weight gain. **1. Conflict of interest:** Nothing disclosed **2. Funding:** Netherlands organization for scientific research (NWO), Elisabeth foundation

Title:	**Benefits of exercise in addition to diet in people with overweight or obesity and type 2 diabetes: a systematic review and meta-analysis**
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Abstract:	**Introduction:** Lifestyle interventions including hypocaloric diet and exercise are the first choice weight loss strategy for overweight/obese individuals with type 2 diabetes (T2D). However, the additional effect of exercise on top of diet is not clear. This systematic review and meta-analysis aimed to evaluate the added value of exercise in addition to hypocaloric diet on body weight, body composition, and metabolic health in this population. **Methods:** We searched Embase, Medline, Web of Science, and Cochrane Central databases and performed a meta-analysis on 10 available randomized controlled trials, covering 11 (sub)studies that compared the effect of hypocaloric diet plus exercise with hypocaloric diet alone in overweight/obese individuals with T2D. Outcomes were body weight, BMI, waist circumference, body composition, fasting glucose, and HbA1c. **Results:** Exercise interventions consisted of (brisk) walking or jogging, resistance training, football training, or cyclo-ergometer training, and had a median duration of 12 weeks (range 2-52 weeks). Meta-analysis showed an estimated mean difference of -1.04 kg [95% CI -2.39; 0.30] for weight (n=802), -0.48 kg/m^2 [95% CI -0.88; -0.08] for BMI (n=783), -1.74 cm [95% CI -4.73; 1.24] for waist circumference (n=635), -2.29 kg [95% CI -6.13; 1.54] for fat mass (n=120), -0.16 kg [95% CI -1.43; 1.10] for fat-free mass (n=93), 0.20 mmol/l [95% CI 0.01; 0.40] for fasting glucose (n=732), and -0.02 % [95% CI -0.22; 0.18] for HbA1c (n=802). There were limited data available on anti-diabetic medication. **Conclusion:** Adding exercise to a hypocaloric diet results in a further reduction of BMI, without showing additional benefit on body weight or composition. The unexpected smaller reduction in fasting glucose by the combined intervention is hard to interpret without data on anti-diabetic medication. Adding exercise to hypocaloric diet has potential for beneficial health effects in people with overweight/obesity and T2D. More high quality studies are needed to confirm this. **1. Conflict of interest:** None to declare **2. Funding:** Not applicable

Title:	**Impact of the COVID-19 pandemic and related lockdown measures on lifestyle behaviours and wellbeing in children and adolescents with severe obesity**
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Abstract:	**Introduction:** COVID-19 lockdown measures have large impact on lifestyle behaviours and wellbeing of children (including adolescents ≤18 years). We investigated the impact on eating styles and behaviours, physical activity (PA), screen time, and health-related quality of life (HRQoL) in children with severe obesity. **Methods:** During the first COVID-19 wave (April 2020), questionnaires and semi-structured telephone interviews were conducted in children with severe obesity treated at our obesity centre. The Dutch Eating Behaviour Questionnaire – Child (DEBQ-C), Paediatric Quality of Life Inventory (PedsQL™), and Dutch PA Questionnaire were filled out by child and/or parents, and changes in pre-pandemic vs. lockdown scores were assessed. Qualitative analyses of interviews were performed conform the Grounded Theory. **Results:** Ninety families were approached; 83 families included. Mean age of the children was 11.2 years (SD 4.6), 52% were female, mean BMI SD score was +3.8 (SD 1.0). On group level, no changes in eating styles, HRQoL or (non-educational) screen time were observed, but weekly PA decreased (Δ-1.9 hr/wk [range -17 to +22.5], p=0.02), mostly in adolescents. In 51% of the population, mean weekly PA decreased to ≤2 hours/week. Children with high emotional and external eating during lockdown or pre-existent psychosocial problems had the lowest HRQoL scores (p<0.01). Increased demand for food was frequently observed in children <10 years, often attributed to loss of daily structure and perceived stress. Families who reported comparable (n=15) or improved eating behaviours (n=11) attributed this to already existing strict eating schemes. **Conclusion:** We show differing responses to COVID-19 lockdown measures in children with severe obesity, with unfavourable changes in PA on group level and in eating styles and HRQoL in substantial minorities. Children with pre-existent psychosocial problems, or pre-pandemic high external or emotional eating were most at risk, and should be targeted to minimize negative physical and mental health consequences. **1. Conflict of interest:** None **2. Funding:** Elisabethfonds; Hartstichting:CVON2016-07LIKE

Title:	**Concomitant glucose-dependent insulinotropic receptor (GIPR) and glucagon-like peptide-1 receptor (GLP1R) agonism stimulates triglyceride-rich lipoprotein metabolism and attenuates atherosclerosis development**
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Abstract:	**Aim:** Tirzepatide, a dual GIP/GLP-1 receptor agonist was recently shown to cause robust weight loss in patients with Type II Diabetes (Frias *et al.* 2018). Since GIPR agonism stimulates lipolysis in white adipose tissue (WAT) and GLP1R agonism promotes brown adipose tissue (BAT) thermogenesis, we hypothesized that GIPR agonism combined with GLP1R agonism enhances the fatty acid (FA) flux to BAT to facilitate thermogenesis, thereby alleviating dyslipidemia and attenuating atherosclerosis development. **Methods:** Dyslipidemic female APOE*3-Leiden.CETP mice were fed a Western-type diet and received a daily subcutaneous injection with either vehicle, a GIPR agonist (GIPFA-085; 300 nmol/kg/day), a GLP1R agonist (GLP-140; 30 nmol/kg/day) or both agonists for up to 10 weeks. Body weight and body composition were monitored throughout the study by echoMRI. At the end of the study plasma triglycerides (TGs) and cholesterol were measured in 4h fasted plasma samples, and TG-rich lipoprotein (TRL) metabolism was assessed using injection of glycerol tri[^{3}H]oleate and [^{14}C]cholesteryl oleate-labeled TRL-like particles. In the aortic valve region, atherosclerotic lesions were scored. **Results:** GLP1R agonism lowered body weight (-2.0 g) and fat mass (-1.8 g), while it increased the uptake of VLDL-TG-derived FA by BAT (+157%) compared to vehicle. On all of these parameters, concomitant GIPR and GLP1R agonism outperformed GLP1R agonism alone (body weight -2.8 g; fat mass -2.3 g; VLDL-TG derived FA uptake by BAT +191%, compared to vehicle). Concomitant GIPR and GLP1R agonism, but not GLP1R agonism or GIPR agonism alone, tended to lower plasma TG levels (-46%) and markedly increased hepatic TRL-remnant uptake (+67%). Importantly, concomitant GIPR and GLP1R agonism decreased atherosclerotic lesion progression (-35% severe lesions). **Conclusion:** Concomitant GIPR and GLP1R agonism stimulates TRL lipolysis and clearance more than the individual agonists and correspondingly attenuates atherosclerosis development. Current studies evaluate the effects of co-treatment on atherosclerosis in an obese setting. **1. Conflict of interest:** HQ and TC are employees and shareholders of Eli Lilly and Company. Eli Lilly and Company have no role in study design, data collection and analysis, or decision to publish. **2. Funding:** PCNR is supported by a Lilly Research Award Program (LRAP) Award.

Title:	**The impact of Personalized Lifestyle Advice on type 2 diabetes remission as compared to usual care in newly diagnosed type 2 diabetics in the primary care setting in Hillegom, the Netherlands**
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Abstract:	**Introduction:** Previous research has shown that T2D pathophysiology may determine the response to lifestyle interventions. Therefore, a T2D subtyping method is proposed, that determines the diabetic phenotype based on the response to an oral glucose tolerance test (OGTT) and establishes which pathophysiology should be addressed. In the present exploratory study we assessed the effectiveness of this subtyping approach and subsequent personalized treatment in ameliorating T2D in a primary care setting. **Methods:** Sixty subjects, newly diagnosed with either prediabetes or T2D and not taking diabetes medication, completed the intervention. Retrospectively collected data of 60 T2D patients were used as controls. An OGTT was performed to assign subjects to one of seven T2D subtypes according to their BCF and presence of hepatic and/or muscle IR. Subsequently, subjects were allocated to one of seven personalized lifestyle treatments, consisting of either a dietary, exercise or combined 13-week intervention. **Results:** Body weight ($p<0.01$) and HbA1c ($p<0.01$) were significantly reduced after 13 weeks in the intervention group, but not in the control group. The intervention group achieved 81.6% remission after 13 weeks (fasting glucose ≤6.9 mmol/L and HbA1c < 48 mmol/mol); for the control group this was 22.0%. However, only 32% obtained a healthy subtype (normal BCF without IR) after 13 weeks of intervention. **Conclusion:** In this study, we show that personalized diagnosis and subsequent tailored lifestyle intervention for T2D in a primary care setting is more effective in improving T2D-related parameters than usual care. Additionally, our results show that the underlying pathology of T2D may not be resolved in subjects with normalized FPG and HbA1c. Therefore, we propose that the current definition of diabetes remission may need to be adapted. **1. Conflict of interest:** None **2. Funding:** TNO

Title:	**Beneficial alterations in the inflammatory phenotype of monocytes in patients with obesity after a combined lifestyle intervention**
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Abstract:	**Introduction** Obesity is associated with chronic, low-grade inflammation, in which monocytes play an important role. In this study, we compared monocyte subset composition between a group of patients with obesity and healthy controls. Next, we followed the patients during a 75-week combined lifestyle intervention (CLI, consisting of dietary advice, exercise, and components of cognitive behavioral therapy) and assessed the subsequent effects on their monocyte subsets and inflammatory immunophenotype. **Methods** Monocyte counts and subsets (classical monocytes (CM), intermediate monocytes (IM) and non-classical monocytes (NCM)) were assessed using flowcytometry in 81 patients with obesity (mean BMI 37.2 Kg/m^2, 80.2% female) and 14 healthy controls (50% female). Similar measurements as well as inflammatory marker profiles were determined after 10 and 75 weeks of CLI in a subgroup of patients. **Results** Patients with obesity had significantly lower absolute and relative intermediate monocyte counts than controls ($p<0.001$ for both). In patients who completed the first 10 weeks (n=51), absolute and relative IM counts increased (+28.8% and +0.9%, $p<0.05$ & $p<0.01$), but this was not significant after 75 weeks (n=35, +17% and +0.2%, $p=0.879$, $p=0.206$) After 10 weeks, CD14 expression by CM and IM, CD16 expression by IM and NCM and IREM2 expression by all subsets decreased ($p<0.01$). After 75 weeks, the expression levels of CD14, CD16 and CD64 were still decreased compared to baseline, whereas IREM2 increased to levels higher than baseline. **Conclusion** Absolute and relative counts of intermediate monocytes, considered pro-inflammatory, are lower in patients with obesity than in controls. These cells increase during the initial phase of a lifestyle intervention. Expression of multiple cell surface markers, indicative of cellular activation, decrease persistently during this intervention. Together, these findings suggest an altered inflammatory status of monocytes in patients with obesity, which is beneficially affected upon combined lifestyle intervention. 1. Conflict of interest: none 2. Funding: Vidi grant from the Netherlands Organization of Scientific Research NWO (grant number: 91716453) and Elisabeth Foundation, a non-profit foundation supporting academic obesity research.

Title:	**Liver-specific fibroblast growth factor 21 overexpression attenuates diet-induced hepatic steatosis and inflammation**
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Abstract:	**Introduction:** Fibroblast growth factor 21 (FGF21) is considered a promising therapeutic agent for obesity and T2D and we recently showed that FGF21 protects against atherosclerosis (Cardiovasc Res 2020). Since the role of FGF21 in NASH currently remains elusive, we aimed to investigate the effects of liver-specific FGF21 overexpression on NASH development in APOE*3-Leiden.CETP mice, a well-established model mimicking NASH initiation and progression in humans. **Methods:** Male APOE*3-Leiden.CETP mice were intravenously injected with an AAV8 vector encoding a murine optimized FGF21 coding sequence, or a non-coding AAV8 vector, after which they were fed a high fat (60%) and high cholesterol (1%) diet for 11 weeks. At the end of the study, histological and flow cytometry analyses were performed to assess hepatic steatosis and inflammation. **Results:** Hepatic FGF21 overexpression lowered body fat mass due to reduction of both white (-69%) and brown (-31%) adipose tissue weight, which was accompanied by improved hypertriglyceridemia and hyperglycemia. Moreover, FGF21 largely reduced hepatic lipid droplet content (-85%), resulting in lowered liver weight (-50%). FGF21 markedly improved hepatic steatosis (-94%) as indicated by reduced hepatic macro- and micro-vesicular steatosis as well as hepatocellular hypertrophy. Furthermore, FGF21 reduced the number of hepatic inflammatory foci (-53%) and crown-like structures (-80%). Flow cytometry analysis further identified that FGF21 prevented Kupffer cell activation and protected against hepatic monocyte infiltration (-51%). **Conclusion:** Hepatic FGF21 overexpression prevents lipid and pro-inflammatory immune cell accumulation within the liver, thereby ameliorating hepatic steatosis and inflammation. We have thus provided evidence to support the clinical use of FGF21 in the treatment of NASH. **1. Conflict of interest:** LM, WK, PA, OS, IY, PXR are employees of AstraZeneca. **2. Funding:** This work was supported by the Diabetes Fonds (2015.81.1808 to MRB), NWO (VENI 91617027 to YW); ZonMW (Early Career Scientist Hotel grant 435004007 to YW); the Novo Nordisk Foundation (NNF18OC0032394 to MS), and CVON (GENIUS-2).

Title:	**Effects of Glucagon-Like-Peptide-1 analogue treatment in genetic obesity**
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Abstract:	**Introduction:** Obesity is highly prevalent and comes with serious health burden. In a minority, there is a genetic cause for the obesity which is often therapy-resistant. Furthermore, it is still unclear whether bariatric surgery is less successful in genetic obesity. Liraglutide is a Glucagon-Like-Peptide-1 (GLP-1) receptor agonist or GLP-1 analogue, showing positive effects on metabolic parameters, satiety and weight loss in lifestyle-induced obesity. We present our experiences of GLP-1 analogue treatment in patients with genetic obesity disorders. **Methods:** Adults with overweight or severe obesity and a molecularly proven genetic cause were treated with liraglutide 3,0 mg daily, in addition to ongoing intensive supportive lifestyle treatment. Anthropometrics, metabolic parameters, resting energy expenditure (REE), side effects, and subjectively reported satiety and quality of life were assessed. **Results:** Two patients with a heterozygous pathogenic melanocortin-4-receptor variant and two patients with 16p11.2 deletion syndrome, ranging in age between 21-32 years and in BMI between 28.1-55.7 kg/m2 at baseline, were treated. At end of follow-up, ranging between 33 weeks and 12 years, a mean change in BMI and waist circumference was observed of -5.7±3.8 kg/m2 and -15.2±21.1 cm, respectively. All patients reported better quality of life, three of them also reported improved satiety. Moreover, improvement of metabolic parameters was seen. No clear effect on REE was observed. Two patients experienced mild side effects, e.g. nausea and stomach pain, for a few weeks. **Conclusion:** We here show beneficial effects of GLP-1 analogues on weight, metabolic parameters, and quality of life in four patients with genetic obesity. Satiety improved in three of the four patients. All patient achieved at least the clinically relevant 5-10% weight loss. Our findings suggest that GLP-1 analogues might be an effective treatment option, in addition to a healthy lifestyle, for patients with genetic obesity. **1. Conflict of interest:** none **2. Funding:** none

Title:	**Illness Perceptions and Health-related Quality of Life in Individuals with Obesity**
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Abstract:	**Introduction:** To understand how individuals (self-)manage obesity, insight is needed into how patients perceive their condition and how this perception translates into health outcomes (e.g., health-related quality of life, HRQOL). Our objectives were (1) to examine illness perceptions in individuals with and without obesity, and (2) to investigate associations of these perceptions with physical and mental HRQOL. **Methods:** In a cross-sectional analysis of the Netherlands Epidemiology of Obesity Study (n=6,568; 56% women), illness perceptions were assessed using the Brief Illness Perception Questionnaire and HRQOL was assessed using the 36-Item Short-Form Health Survey. We used overall and abdominal obesity criteria to define obesity. We investigated associations of illness perceptions with HRQOL using BMI-stratified multivariable linear regression analyses, adjusted for age, sex, education, pre-existing cardiovascular disease, diabetes, and mental health disorders. **Results:** Compared to those without obesity, individuals with obesity believe to a higher extent that their condition had more serious consequences [Mean Difference (95%CI): 1.6 (1.2-1.9)], persisted for a longer time [0.9 (0.2-1.5)], manifested in more symptoms [3.1 (2.6-3.5)], caused more worry [3.6 (3.2-4.0)] and emotional distress [1.0 (0.6-1.5)], but was more manageable with medical treatment [1.6 (0.8-2.4)]. They perceive to a lesser extent that they had personal control [-2.5 (-3.0,-2.0)] and understanding [-3.1 (-3.7,-2.5)] regarding their condition. These negative perceptions were more pronounced in individuals with overall obesity, but less strong in individuals with abdominal obesity. Stronger negative illness perceptions were associated with impaired physical and mental HRQOL. **Conclusion:** Individuals with obesity perceived their conditions as threatening, and this seemed somewhat stronger in individuals with overall obesity than those with abdominal obesity. Strategies that aim to change negative perceptions of obesity into more adaptive ones, as well as self-management regarding the impact of obesity, may improve patients' coping strategies and consequently health outcomes including HRQOL. **Word Count (excluding title, authors, and affiliations): 295** 1. **Conflict of Interest: None** 2. **Funding: None**

Title:	**The relation between cortisol and anthropometric measurements throughout lifespan: a systematic review and meta-analysis**
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Abstract:	**Introduction**: Recently, studies report associations between long-term glucocorticoid levels in scalp hair (HairGC) and obesity. The aim of this systematic review and meta-analysis was to investigate the relation between HairGC and anthropometrics and to explore possible moderators of this association. **Methods**: We searched the Medline, Embase, Cochrane, Web of Science, Scopus, Cinahl, PsycInfo, and Google Scholar databases for articles that relate HairGC to measures of adiposity (date 11-16-2020). Primary outcomes were correlations between hair cortisol (HairF) and cortisone (HairE), and anthropometrics. Pooled correlation coefficients were calculated using random effects models. Assessment of heterogeneity was performed using the I^2 statistic. Exploratory moderator analyses were performed with subgroup analyses and meta-regression. **Results**: We identified 150 cohorts, comprising a total of 37,107 individuals. For BMI, the pooled correlation for HairF was 0.121 (95% CI 0.083-0.158, n=26,941; I^2 94.2%, p<0.001) and for HairE 0.108 (95% CI 0.047-0.167, n=7,250; I^2 52%, p<0.01). For WC, the pooled correlation for HairF was 0.111 (95% CI 0.058-0.164, n=10,290; I^2 63%, p<0.01) and for HairE 0.200 (95% CI 0.137-0.264, n=2,198; I^2 0%, p=0.42). For WHR, the pooled correlation for HairF was 0.102 (95% CI 0.040-0.163, n=6,865; I^2 27%, p=0.14) and for HairE 0.261 (95% CI 0.195-0.330, n=1,314; I^2 0%, p=0.40). A higher percentage of male participants was related to stronger correlations with WC (p<0.001), but not with BMI and WHR. Mean age, mean BMI, mean HairGC levels of the cohorts, and used laboratory techniques (immunoassays vs mass spectrometry-based assays) did not significantly moderate the pooled correlations. **Conclusion**: This unique, large meta-analysis demonstrates that long-term endogenous glucocorticoids show consistent correlations to measures of obesity, despite a large heterogeneity between cohorts. Strongest associations were found between HairE and WC and between HairE and WHR, suggesting that glucocorticoid levels in the high-normal range may contribute to or reflect the state adiposity. **1. Conflict of interest:** None Disclosed. **2. Funding:** Elisabeth Foundation; Netherlands Organization of Scientific Research NWO, Grant/ Award Number: 91716453

NASO Board: Layout has been modified to fit all content onto a single page, as requested.