Abstract book

2025

NASO Scientific Spring meeting

April 09, 2025, Oudaen Utrecht

Abstracts

Contents; first 12 abstracts are presented in order of presentation during the meeting (in total 6 orals and 6 pitches), remainder in alphabetical order of first author, as indicated on this and next page.

Oral and pitch presentations

Other included abstracts 2025 (in alphabetical order)

Investigating the quasi-causal association between the obesogenic environment and obesity: a twin study.
Berntzen BJ, Beulens JWJ, Lakerveld J

Zooming in on the inter-individual variability in treatment effectiveness for overweight and obesity.
Vanbrabant, E., Hesen, J., Mironiuc, C., Jordan, S., Goossens, G., Lemmens, L., Shapovalova, Y., & Roefs, A

Long-acting glucagon receptor agonism increases circulating triglyceride levels in diet-induced obese mice
Jamie I. van der Vaart, Mariëtte R. Boon, Patrick C.N. Rensen, Sander Kooijman, Robin van Eenige

A supportive tool for general practitioners to manage children with overweigh and obesity in primary care: a mixed-method evaluation study.
Van der Velden, MAM, Van Tilborg-den Boeft, M, Buis, S, Jansen, W, Bindels, PJE, Van Middelkoop, M

Real world effect of personalized lifestyle treatment advice on health outcomes at one year follow-up in children who visit a specialized obesity clinic with severe obesity.
van der Walle EPL, Welling MS, Abawi O, van Eck J, Meeusen R, Vos M, Brandsma AE, Beelen MLR, Oosterman JE, Boon MR, van Rossum EFC, de Groot CJ, van den Akker ELT

The role of 3D visualisation based on CT in diagnosing internal herniation after RYGB
T. Veerbeek, S. Hillebrink, F. Intema, L.N. Deden, E.J. Hazebroek

The narcolepsy drug γ-hydroxybutyric acid improves metabolic dysfunction in existing and developing obesity through altering the gut microbiota.
Zhang S*, Liu C*, Zwaan M, Verhoeven A, Schinkelshoek M, Wang Y, Giera M, Boon MR, Rensen PCN, Schönke M

Title:	**Brown fat activation improves plasma lipid levels and energy expenditure independent of timing**
Authors:	van Buuren MDH[1], Rensen PCN[1], Van Eenige R[1], Kooijman S[1]
Affiliations	*[1]Division of Endocrinology, Department of Medicine, and Einthoven Laboratory for Experimental Vascular Medicine, Leiden University Medical Center, Leiden, the Netherlands*
Abstract: (max 300 words)	**Background:** Brown fat combusts lipids to produce heat, and stimulating its activity has potential as treatment for obesity-linked cardiometabolic atherosclerotic cardiovascular diseases including atherosclerosis. Interestingly, we previously showed in mice that brown fat metabolic activity shows a strong day-night rhythm, with high uptake of triglyceride-derived fatty acids from the circulation at wakening. Here, we studied whether brown fat activation at onset of sleeping (Zeitgeber time (ZT) 22) or wakening (ZT10) is more effective in increasing energy expenditure, decreasing fat mass and improving dyslipidemia. **Methods:** Female APOE*3-Leiden.CETP mice were fed a Western-type diet and treated with β3-adrenergic receptor agonist CL316243 or vehicle for four weeks at ZT22 or ZT10. Energy expenditure was monitored in calorimetric cages and body weight, body composition and plasma lipid levels were determined. At the end of the study, uptake of radio-labeled triglyceride-derived fatty acids and cholesteryl esters by brown fat was assessed. **Results:** CL316243 treatment decreased fat mass, regardless of time of administration (ZT22 -36%; ZT10 -32%). This coincided with a higher energy expenditure (ZT22+32%; ZT10 +23%) and increased fat oxidation (ZT22 +32%; ZT10 +48%) in the 12 hours after treatment. Interestingly however, CL316243 treatment at ZT22 but not at ZT10 increased the uptake of triglyceride-derived fatty acids (+40%) and cholesteryl esters (+119%) by brown fat. Nonetheless, CL316243 lowered plasma triglyceride levels 16 hours after administration in both conditions (ZT22 -41%; ZT10 -42%), and CL316243 treatment at ZT10 furthermore lowered plasma cholesterol levels 4 hours after treatment (-29%). **Conclusions:** Brown fat activation, using C316243, increases energy expenditure and fat oxidation, decreases fat mass and lowers plasma triglycerides to a similar extent, independent of timing. Given that C316243 administration at ZT10 but not at ZT22 also lowered plasma cholesterol levels, further investigation is warranted to determine the long-term effects of timed brown fat activation on atherosclerosis development. **1. Conflict of interest:** No conflict of interest **2. Funding:** This project is funded by the Hartstichting, Senior Scientist Dekker Grant

Title:	**Differential modulation of melanocortin-4 receptor signaling by serotonin receptors HTR1B and HTR2C**
Authors:	Rodríguez Rondón A.V.[1], Garcia de Lima A.G.[1], Delhanty P.J.D.[1], Visser J.A.[1]
Affiliations	*[1]Dept. of Internal Medicine and Obesity Center CGG, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands*
Abstract: (max 300 words)	**Introduction:** G protein-coupled receptors (GPCRs) in hypothalamic neurons, such as melanocortin-4 receptor (MC4R) and the serotonin receptors, HTR1B and HTR2C, are important mediators of appetite and energy regulation. Loss-of-function (LoF) variants in MC4R are associated with monogenic obesity in humans. Interactions between GPCRs modulate their signaling mechanisms. Since MC4R, HTR1B and HTR2C are co-expressed in hypothalamic neurons, we aimed to discover whether serotonin receptors modulate signaling of wild type (WT) MC4R and obesity-associated MC4R variants. **Methods:** HEK293 cells were transiently transfected with expression plasmids encoding WT or variant MC4R and empty vector, WT HTR1B or HTR2C, and stimulated with α-MSH. The effects of the serotonin receptors on MC4R cell surface expression and α-MSH-stimulated cAMP response were measured using bioluminescent assays. We assessed WT and three obesity-associated MC4R variants (T150I, F262L, and V255A), previously categorized as complete-LoF, partial-LoF, and WT-like, respectively, based on their cAMP responses to α-MSH. **Results:** HTR1B suppressed maximal cAMP responses of WT MC4R and variant V255A by 69±1% and 62±8% ($p<0.001$), respectively. HTR1B decreased WT MC4R cell surface expression by 29±3% ($p<0.001$) but not of the variants. Unlike HTR1B, HTR2C potentiated maximal cAMP responses of WT MC4R and variants F262L and V255A by 82±2%, 31±5% and 114.2±3% respectively ($p<0.05$), but not of T150I. However, HTR2C increased the cell surface expression of T150I by 60±2% ($p<0.05$) to levels of WT MC4R, but had no effect on WT MC4R, or variants F262L and V255A. **Conclusion:** Our results show that serotonin receptors HTR1B and HTR2C oppositely modulate MC4R signaling. These findings suggest that MC4R may heterodimerize with serotonin receptors impacting cell surface expression and possibly the interaction with downstream signaling proteins. Furthermore, our results show that these serotonin receptors alter signaling of MC4R variants. Unraveling the underlying mechanism may aid to understand the impact of MC4R variants in monogenic obesity. **1. Conflict of interest:** **2. Funding:**

Title:	**Partitioning of the polygenic risk score for body mass index reveals eight biological mechanisms**
Authors:	Vlaming P[1], van Rooij JGJ[1], van Meurs JBJ[1], Visser JA[1]
Affiliations	[1]Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands.
Abstract: (max 300 words)	**Introduction:** Obesity is a major global health issue arising from a combination of environmental factors and genetic predisposition. The latest genome-wide association study (GWAS) has identified 941 susceptibility variants for body mass index (BMI). However, translating variants to genes and biological pathways remains a major challenge. Here, we clustered BMI GWAS variants based on variant-trait associations and determined their potential biological relevance to obesity. **Methods:** We applied hierarchical clustering of 941 BMI variants (GIANT meta-analysis) and variant-trait associations using the GWAS catalog. To evaluate biological relevance, we constructed weighted, partitioned polygenic risk scores (PRS) per cluster and associated each z-scaled PRS with body composition, body fat, energy intake and components of Metabolic syndrome in the Rotterdam Study (N=3941). All associations were adjusted for age and sex. **Results:** We identified eight clusters containing variant-trait associations indicative of body fat, inflammation, blood pressure, lean mass, metabolic syndrome, childhood BMI, insomnia and educational attainment. The body fat and inflammation partitions were associated to all body composition and body fat measurements, with the highest effect sizes for BMI (body fat: β=0.565, p=1.6e-17, inflammation: β=0.414, p=3.0e-10) and body fat percentage (body fat: β=0.689, p=8.3e-12, inflammation: β=0.466, p=3.1e-6). Furthermore, the blood pressure partition was the only partition significantly associated with systolic (β=1.145, p=5.0e-4) and diastolic (β=0.714, p=7.5e-5) blood pressure. **Conclusion:** Our study suggests that variant-trait associations can partition the BMI PRS into biologically relevant mechanisms. Greater understanding of these mechanisms could help to identity novel molecular pathways regulating metabolism, thereby improving prevention and treatment of obesity and its comorbidities. **1. Conflict of interest:** none **2. Funding:** none

Title:	**Ultra-processed food consumption and BMI, weight gain and overweight in young children in the Netherlands: the GECKO Drenthe birth cohort**
Authors:	Yang J[1], Navis G[2], Corpeleijn E[1].
Affiliations	*[1]Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands*; *[2]Department of Internal Medicine, Division of Nephrology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands*.
Abstract: (max 300 words)	**Introduction:** Ultra-processed foods (UPFs) are related to increased risk of overweight and obesity in adults, but less is known about this association in children. This study examined the association between UPF consumption at 3 years and the BMI, increase in BMI and overweight/obesity at 10-11 years in Dutch children. **Methods:** Of 1091 children (50.2% male) from the GECKO Drenthe birth cohort, dietary intake was assessed using a 71-item Food Frequency Questionnaire (FFQ) at 3 years. Food items were categorized according to the NOVA classification system and the proportion of UPF (NOVA-4) in total daily food weight was calculated. Height and weight were measured to determine BMI z-scores and increase in BMI-z between 3 and 10/11 years, normalized for age and gender. Overweight/obesity was defined by IOTF criteria. Regression models were adjusted for potential confounders. **Results:** The mean UPF intake at 3 years was 786 ± 310 g/d (52% of total food weight). The prevalence of children with overweight/obesity at 10/11 years was 16.2%. The top UPF categories consumed were sugary beverages, sugary dairy products, and carbohydrate-rich staple foods. Children in the highest quartile of UPF consumption demonstrated a higher BMI z-score at 10-11years (β = 0.16; 95% CI: 0.01 to 0.31; $P < 0.001$) and a greater increase in BMI z-scores from 3 to 10/11 years (β = 0.16; 95% CI: 0.01 to 0.31; $P < 0.001$) compared with those in the lowest quartile, independent of total energy intake and other confounders. No significant association was observed with overweight/obesity status at 10/11 years. **Conclusion:** Higher UPF intake at 3 years was associated with higher BMI z-scores and a greater increase in BMI z-scores at 10/11 years. This study suggests a high UPF intake in early childhood may contribute to long-term weight gain, emphasizing the importance of early dietary habits. 1. **Conflict of interest:** The authors declare to have no conflict of interest. 2. **Funding:** The GECKO Drenthe birth cohort was funded by an unrestricted grant of Hutchison Whampoa Ltd, Hong Kong and supported by the University of Groningen, Well Baby Clinic Foundation Icare, Noordlease, Paediatric Association Of The Netherlands, Youth Preventive Health Care Drenthe, the European Union's Horizon 2020 research and innovation programme (LIFECYCLE, grant agreement No 733206, 2016), and Foundation Vrienden Beatrix Kinderziekenhuis, Groningen, The Netherlands.

Title:	**The clinical utility of polygenic risk scores: insights from an obesity cohort**
Authors:	van Uhm J[1,2,*], Vos N[3,4,*], van Weelden W[3,4,*], Bulthuis EP[3,4], Kleinendorst L[3,4,5], Nijman J[3], Genome of the Netherlands Project, Sie D[6], Sistermans E[3,4], Mannens MM[3,4], van den Akker ELT[1,2], van Rossum EFC[1,7], Jansen PR[3,4,8,#], van Haelst MM[3,4,5,#]
Affiliations	*1 Obesity Center CGG, Division of Endocrinology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands, 2 Department of Pediatrics, Division of Endocrinology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands, 3 Amsterdam UMC, University of Amsterdam, Department of Human Genetics, Amsterdam, the Netherlands, 4 Amsterdam Reproduction and Development Research Institute, Amsterdam, the Netherlands, 5 Emma Center for Personalized Medicine, Amsterdam UMC, Amsterdam, the Netherlands,6 Department of Bioinformatics, Amsterdam UMC, Amsterdam, the Netherlands, 7 Department of Internal Medicine, Division of Endocrinology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands, 8 Department of Complex Trait Genetics, Center for Neuroscience and Cognitive Research (CNCR), VU University, Amsterdam, the Netherlands*
Abstract: (max 300 words)	**Objective:** We investigated whether suspected genetic obesity can be partially explained by high polygenic risk scores (PRS) and whether these scores help identify patients with a high probability of monogenic obesity. **Methods:** We evaluated the utility and predictive value of BMI PRS in a clinical cohort of 83 patients referred for suspected rare genetic obesity. BMI PRS were computed from clinical SNP array data using summary statistics from the largest BMI GWAS (N = 681,275) and compared to 498 Dutch population controls (Genome of the Netherlands, GoNL). We stratified the cohort into patients without detected rare genetic variants (OBE-NV) and those with confirmed or likely pathogenic variants (OBE-RV). We assessed the association between PRS and BMI variability. **Results:** The clinical obesity cohort exhibited significantly elevated BMI PRS compared to controls ($P < 0.001$), indicating a strong polygenic contribution to obesity. Patients without an identified rare variant (OBE-NV) had significantly higher PRS than those with confirmed monogenic obesity (OBE-RV; $P < 0.05$). The predictive model for monogenic obesity achieved moderate accuracy (AUC = 0.69). Regression analyses revealed that, across the entire cohort, a one standard deviation increase in PRS was associated with a 0.29 standard deviation increase in BMI. Subgroup analyses showed a stronger association in patients with rare pathogenic variants (0.54 SD increase) compared to those without (0.24 SD increase), highlighting the differing roles of common and rare genetic factors. **Conclusions:** Our findings demonstrate that BMI PRS can elucidate the genetic etiology of obesity in patients with suspected genetic obesity and serve as a valuable first-tier diagnostic tool. By identifying patients with a high likelihood of carrying rare pathogenic variants, PRS can improve patient stratification and guide personalized management strategies. These results underscore the potential clinical utility of integrating polygenic risk assessment into the diagnostic workflow for genetic obesity effectively.

Conflict of interest:

The authors declare no conflict of interest.

Funding:

JU's PhD is funded by the OBCT project (www.obct.nl), which has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No. 101080250. Views and opinions expressed are, however, those of the author(s) only and do not necessarily reflect those of the European Union. Neither the European Union nor the granting authority can be held responsible for them.

The institute of Wenneke van Weelden receives funding from Rhythm Pharmaceuticals for research about Bardet-Biedl syndrome.

P.R.J. was funded by the Netherlands Organization for Scientific Research (VENI project 09150162010138). This study uses Genome of the Netherlands data. A full list of the investigators is available from www.nlgenome.nl. Funding for the project was provided by the Netherlands Organization for Scientific Research under award number 184021007, dated July 9, 2009, and made available as a Rainbow Project of the Biobanking and Biomolecular Research Infrastructure Netherlands (BBMRI-NL). The sequencing was carried out in collaboration with the Beijing Institute for Genomics (BGI). Included in the GONL cohort are samples from the following cohorts: The LifeLines Cohort Study (http://www.lifelines.nl), and generation and management of GWAS genotype data for it is supported by the Netherlands Organization of Scientific Research (NWO, grant 175.010.2007.006), the Dutch government's Economic Structure Enhancing Fund (FES), the Ministry of Economic Affairs, the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the Northern Netherlands Collaboration of Provinces (SNN), the Province of Groningen, the University Medical Center Groningen, the University of Groningen, the Dutch Kidney Foundation and Dutch Diabetes Research Foundation; for sponsorship of the EMC Ergo Study please refer to (http://www.ergo-onderzoek.nl/wp/); the LUMC Longevity Study was supported by a grant from the Innovation-Oriented Research Program on Genomics (SenterNovem IGE01014 and IGE05007), the Centre for Medical Systems Biology and the National Institute for Healthy Ageing (Grant 05040202 and 05060810), all in the framework of the Netherlands Genomics Initiative/Netherlands Organization for Scientific Research; for sponsorship of the VU Netherlands Twin Register please refer to www.tweelingenregister.org.

Title:	**A fast(ing) way to cardiometabolic health: investigating the effects of fasting-mimicking diet on gut microbiota in patients with type 2 diabetes**
Authors:	Kovynev A[1,2], Schoonakker MP[3], van den Burg EL[3], van Peet P[3], Schönke M[1,2], Pijl H[1], Rensen PCN[1,2], Zeller G[4] and Ducarmon QR[4]
Affiliations	[1]Division of Endocrinology, Department of Medicine, [2]Einthoven Laboratory for Experimental Vascular Medicine, [3]Department of Public Health and Primary Care, and [4]Leiden University Center for Infectious Diseases, LUMC, Leiden, The Netherlands
Abstract: (max 300 words)	**Introduction:** Fasting-mimicking diets (FMDs) are emerging as a new form of periodic fasting diets to improve cardiometabolic outcomes and combat obesity, by inducing the effect of fasting while still providing several meals a day. It is known that the gut microbiome undergoes extensive remodeling during extreme short-term fasting periods, but long-term effects of FMDs on the microbiome have not been described. Here, we investigated the effects of a year-long periodic FMD intervention on the gut microbiome of individuals with type 2 diabetes (T2D). **Methods:** Over twelve months, individuals with T2D either followed a standard of care treatment (n=42) or followed an FMD for five consecutive days a month using meal replacement products (n=49), in addition to standard care. Fecal samples were collected at baseline, right after the first FMD cycle and after twelve months, and were subjected to metagenomic shotgun sequencing. Successful treatment outcome was defined as a decrease in glucose-lowering medication dosage without HbA1c changes. **Results:** Directly after the first FMD cycle, gut microbial beta-diversity was significantly altered. FMD increased the relative abundance of *Akkermansia muciniphila* and other short-chain fatty acid producers, which are likely beneficial for individuals with T2D. The ratio between genes encoding enzymes involved in mucin and fiber digestion was not changed, while it is negatively affected in more severe caloric restrictions. One year of FMD significantly improved glycemic management in 53% of participants, compared to 8% in the control group, and resulted in sustained microbial changes, with an increased abundance of butyrate-producing metabolic pathways. At endpoint, gut microbial composition of individuals with improved glycemic management was significantly different from those without improvement. **Conclusion:** Both acute and prolonged FMD beneficially alter the gut microbiome of individuals with T2D, warranting further studies on the causal role of the gut microbiome in the effect of FMD on T2D. **1. Conflict of interest:** None **2. Funding:** The project was co-funded by Health~Holland, Top Sector Life Sciences & Health, and the Dutch Diabetes Foundation (project LSHM17040-PTO). L-Nutra contributed the formula diet and a small part of the funding.

Title:	**Personalized dietary fibre mixtures based on *in vitro* microbial SCFA production reduce insulin resistance (HOMA-IR) in individuals with prediabetes and overweight/obesity**
Authors:	Larik GNF[1]*, Hamari N[1]*, Maurer Sost M[2] , van Kalkeren CAJ[1] , Holst JJ[3], Blaak EE[1], Canfora EE[1] *shared first authorship
Affiliations	[1]Department of Human Biology, Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Center+, Maastricht, the Netherlands; [2]Centre for Healthy Eating & Food Innovation (HEFI); Maastricht University-Campus Venlo, 5928 SZ Venlo, The Netherlands Department of Biomedical Sciences; [3]Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark.
Abstract: (max 300 words)	**Introduction:** The gut microbiota ferments dietary fibres into short-chain fatty acids (SCFAs), which can improve host metabolism. However, long-term supplementation of single isolated dietary fibres showed inconsistent metabolic benefits, emphasizing the role of individual differences in microbial fermentation capacity. This study aimed to investigate the effects of a personalized fibre mixtures (PFM), designed to enhance gut microbial SCFA production, on insulin sensitivity. **Methods:** This randomized, placebo-controlled, double-blind parallel study included 44 individuals with overweight/obesity (body mass index (BMI) 28–40 kg/m², age 35–70 y) with prediabetes and/or insulin resistance. Anaerobic faecal samples were screened using an *in vitro* colon model (TIM-2) to determine a PFM that maximized SCFA production. Participants were randomized to receive either 24g of the *in vitro*-defined PFM (n=22) or a control fibre (galacto-oligosaccharides, n=22) daily for 12 weeks. Peripheral insulin sensitivity (primary outcome) was assessed via hyperinsulinemic-euglycemic clamp, alongside other metabolic parameters. **Results:** No differences in peripheral insulin sensitivity (M-value) were observed between groups. However, PFM decreased fasting insulin (Δ -0.98 ± 2.48 vs 0.90 ± 2.96 mU/L, P=0.037), HOMA-IR (Δ -0.27 ± 0.65 vs Δ 0.22 ± 0.76, P=0.036), body weight (Δ -0.28 ± 2.3 vs Δ 1.37 ± 1.5 kg, P=0.014), and BMI (P=0.017) with a trend toward reduced body fat mass (P=0.073) compared to control. The PFM increased plasma branched-chain fatty acid isovalerate (P=0.030) and a trend toward increased isobutyrate levels (P<0.1) compared to control. No differences were observed in energy expenditure, substrate oxidation, blood lipids, inflammatory markers, gut-derived hormones, or plasma and faecal SCFAs. **Conclusion:** PFM supplementation did not affect peripheral insulin sensitivity but slightly decreased body weight and reduced HOMA-IR, suggesting a beneficial effect on hepatic insulin sensitivity compared to control treatment. Thus, Personalized fibre approaches may help improve metabolic health in individuals at high risk for type 2 diabetes. **1. Conflict of interest:** the authors declare no conflict of interest **2. Funding:** Research relating to this abstract was funded by the Dutch Diabetes Association (Diabetes fonds) (DFN nr 2019.81.010)

Title:	**A 12-week dietary fiber intervention targeting distal colonic saccharolytic fermentation affects circulating immune cells in individuals with overweight/obesity**
Authors:	van Deuren T[1], van Kalkeren CAJ[1], Jocken JJ[1], Temmerman L[2], Blaak EE[1], Wouters K[3]
Affiliations	*1Department of Human Biology, Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Center+, Maastricht, the Netherlands'* *2Department of Pathology, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center+, Maastricht, the Netherlands* *3Department of Internal medicine, Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Center+, Maastricht, the Netherlands'*
Abstract: (max 300 words)	**Introduction**: Dietary fibers may mitigate obesity-associated disruptions in the microbiota-immune axis and chronic low-grade inflammation through short-chain fatty acid (SCFA) production. Evidence suggests SCFA administration to the distal, rather than the proximal colon, may lead to beneficial metabolic health outcomes. However, as fibers are fermented throughout the colon, protein fermentation increases, producing metabolites commonly linked to adverse metabolic health effects. Thus, we investigated the effect of potato-fiber/pectin supplementation (Fiber), which induces high distal SCFA production *in vitro*, on circulating immune cells in individuals with overweight/obesity. **Methods**: Individuals with overweight/obesity were given an eucaloric high-protein diet (25%E, 45% plant-based) and randomly assigned to receive either 15 grams of Fiber (n=17) or an isocaloric placebo (maltodextrin) (n=20) daily for 12 weeks. Inflammatory markers were assessed, and flow cytometry was used to analyze changes in the abundance of various circulating immune cells including granulocytes and monocyte, natural killer (NK)-, NKT-, B-, and T-cell subsets at baseline, 6, and 12 weeks. **Results**: After 12 weeks, circulating granulocyte concentrations were significantly increased by Fiber (p=0.005) compared to placebo. Additionally, the reduction in IL-6 was abolished by Fiber (p=0.025) and the reduction in Th1:Th2 ratio (p=0.052) tended to be attenuated compared to placebo. After 6 weeks, Fiber attenuated the increase in natural killer T (NKT) cells (p=0.046), specifically $CD8^{-}CD4^{-}$NKT cells (p=0.001), compared to placebo. Δgranulocytes positively correlated with the ΔC-reactive protein in the Fiber group, while ΔNKT cells inversely correlated with ΔIL-8 in the placebo group after 12 weeks, highlighting intervention-specific associations. **Conclusion**: Adding a fiber mixture to a high protein diet to steer distal colonic fermentation resulted in increased granulocytes and attenuated the reduction in IL-6 and Th1:Th2 ratio compared to placebo. Overall, the high (45% plant-based) protein diet without additional fiber mediated more potent anti-inflammatory effects. **1. Conflict of Interest:** None Disclosed **2. Funding:** NWO and Carbohydrate Competence Center (part of Next Food Collective; private-public partnership including industrial partners Royal Avebe U.A., Nutrition Sciences N.V. and Sensus (Royal Cosun Group).

Title:	**The impact of steering fiber fermentation towards the distal colon on insulin sensitivity and cardiometabolic health in individuals with overweight: 12-week randomized controlled trial (DISTAL-study)**
Authors:	van Kalkeren, C.A.J.[1]; van Deuren, T.[1]; Blaak, E.E.[1]
Affiliations	[1]Department Human Biology, Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Center+, Maastricht, The Netherlands'
Abstract: (max 300 words)	**Introduction:** The gut microbiome ferments dietary fibers, producing short-chain fatty acids (SCFA) known to improve cardiometabolic health. Previous work showed that administering SCFAs to the distal colon can improve cardiometabolic health. However, most fibers are fermented proximally, leading to increased protein fermentation in the distal colon, reducing SCFAs and increasing proteolytic metabolites, associated with detrimental health effects. Increasing distal saccharolytic fermentation while inhibiting proteolytic fermentation through a fiber supplement that increased distal SCFA production *in vitro* might therefore improve insulin sensitivity and metabolic health in individuals at risk of type 2 diabetes (T2D). **Methods:** This 12-week RCT investigated daily 15-gram potato-fiber and sugar beet pectin supplementation (fiber) versus isocaloric placebo (maltodextrin), added to a high-protein diet (25E% protein; 45-50% plant-based) on peripheral insulin sensitivity (2-step hyperinsulinemic-euglycemic clamp) in adults at risk of T2D (30-75y, BMI 28-40kg/m^2). Secondary outcomes included hepatic and adipose tissue insulin sensitivity, body composition, microbial composition, and energy metabolism. **Results:** 40 participants completed the intervention. Peripheral insulin sensitivity tended to decrease after fiber intake, while placebo increased (ΔGlucose disposal per unit insulin -0.004±0.016 vs 0.005±0.018, p=0.081). Additionally, fiber intervention prevented an increase in protein oxidation (Δ0.000±0.014 vs 0.010±0.011 g/min, p=0.048) and reduced insulin-stimulated CHO oxidation, compared to placebo (Δ-0.010±0.080 vs 0.026±0.050 g/min, p=0.027). Body composition, microbial composition, and fecal and circulating metabolites did not change after 12 weeks. **Conclusion:** Fiber supplementation with a high-protein diet (45-50% plant-based) did not improve but tended to decrease (peripheral) insulin sensitivity. Reduced protein oxidation after fiber intervention may suggest a reduced bioavailability of dietary amino acids. More research on underlying mechanisms, including microbial composition and functionality, will follow. **1. Conflict of Interest:** None **2. Funding:** NWO and Carbohydrate Competence Center (part of Next Food Collective; private-public partnership including industrial partners Royal Avebe U.A., Nutrition Sciences N.V. and Sensus (Royal Cosun Group).

Title:	**Unraveling the Impact of Daily Life Stress and Glucocorticoid Regulation on Cardiometabolic Health**
Authors:	Robin Lengton[1], Susanne Kuckuck*[1], Mariëtte R. Boon*[1], Johanneke E. Oosterman[1], Brenda W.J.H. Penninx[2], Elisabeth F.C. van Rossum[1] * Shared second authorship
Affiliations	*[1]Obesity Center CGG, Department of Internal Medicine, Division of Endocrinology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands* *[2]Department of Psychiatry and Amsterdam Public Health, Amsterdam UMC, Vrije Universiteit, Amsterdam, The Netherlands*
Abstract: (max 300 words)	**Background:** Chronic stress is linked to cardiometabolic diseases through increased glucocorticoid exposure, but the impact of daily life stress on glucocorticoid regulation and cardiometabolic health remains underexplored. This study investigates these associations. **Methods:** We included 870 participants from the Netherlands Study of Depression and Anxiety (NESDA) (64.7% female, median age 47.0 years) without a psychiatric disorder diagnosis in the six months prior to study. Daily life stress was assessed using the Daily Hassles questionnaire (DHQ). Salivary cortisol was analyzed for 1-h awakening cortisol (4 time points), evening cortisol and diurnal slope. Also an overnight 0.5 mg dexamethasone suppression test was performed. Associations between DHQ, glucocorticoid measures, and cardiometabolic health were studied using logistic and linear regressions. **Results:** After multivariable adjustment, each SD increase in DHQ score was associated with 1.38-fold (95%CI 1.07;1.77) higher odds for cardiovascular disease (CVD), but not diabetes, metabolic syndrome, or obesity. DHQ scores were not associated with glucocorticoid measures. However, each SD increase in cortisol suppression ratio was associated with 1.37-fold (95%CI 1.08;1.72) higher CVD risk, but not diabetes, metabolic syndrome, or obesity. No interactions between DHQ and glucocorticoid measures on CVD risk were observed. **Conclusion:** A higher cortisol suppression ratio, indicating increased glucocorticoid sensitivity, and increased daily hassles were independently associated with increased CVD risk. The absence of interaction between these factors suggests they influence CVD risk through separate pathways, highlighting the need for further research to better understand stress mechanisms and identify “stress profiles” most at risk for developing cardiometabolic diseases. **1. Conflict of interest:** All authors declare that they have no relevant financial interests or disclosures to report. **2. Funding:** This work is funded by Stress in Action. The research project ‘Stress in Action’: www.stress-in-action.nl is financially supported by the Dutch Research Council and the Dutch Ministry of Education, Culture and Science (NWO gravitation grant number 024.005.010). EFCvR is also supported by a Vidi grant from the Netherlands Organization of Scientific Research NWO/ZONMW (grant number: 91716453).

Title:	**Dietary environmental impact and its association to the development of overweight and obesity in young children: the GECKO Drenthe cohort.**
Authors:	Zou, J.[1], De Boer, E.W.[1], Vellinga, R.E.[2], Corpeleijn, E.[1]
Affiliations	*[1]Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.* *[2]National Institute for Public Health and the Environment (RIVM), The Netherlands.*
Abstract: (max 300 words)	**Introduction:** The growing global population demands a shift towards sustainable diets that are healthy, environmentally friendly, acceptable, and affordable. In this study we explore the environmental sustainability of diets in young children and relate this to the development of overweight. **Methods:** In the GECKO Drenthe cohort, dietary intake was derived from a validated 71-item food frequency questionnaire designed for children aged 2-12 years, filled in by parents, when children were 3 years old. Diet-induced Greenhouse Gas Emissions (GHGE) and Blue Water Consumption (BWC) were calculated using Lifecycle Assessment data by the RIVM and adjusted for the total amount of food consumed, for total, solid, and liquid food consumption. BMI Z-score, the change in BMI Z-score, and overweight/obesity (by IOTF criteria) were derived from height and weight measured by trained nurses. **Results:** The final analysis included 893 children (50.2% male) of which 13% developed overweight/obesity at 10/11 (10.6±0.4) years old. The mean GHGE from solid and liquid foods were 1.88±0.58 (mean±SD) and 0.57±0.29 kg CO2eq./day, respectively. The mean BWC from solid and liquid foods were 27±8 and 15±14 liter/day, respectively. After adjusting for potential confounders, GHGE per kg of solid foods in the highest tertile was associated with a higher BMI Z-score (β=0.159 (95% CI 0.001, 0.318)) and a higher weight gain (delta BMI-Z, β=0.21 (0.06, 0.35)) at 10/11 years old, compared with the lowest tertile. Both GHGE (OR=1.83 (1.06, 3.16)) and BWC (OR=1.69 (1.01, 2.84)) per kg of solid foods in the highest tertile compared with the lowest tertile were related to a higher risk of developing overweight/obesity. **Conclusion:** A less sustainable diet among young children was associated with a higher risk of developing overweight and obesity in later childhood. Promoting sustainable dietary habits may bring benefits to young children in preventing overweight and obesity. **1. Conflict of interest:** None Disclosed. **2. Funding:** JZ is supported by a joint fellowship from the China Scholarship Council and University of Groningen (no. 202307720064). The GECKO Drenthe birth cohort was funded by an unrestricted grant of Hutchison Whampoa Ltd, Hong Kong and supported by the University of Groningen, Well Baby Clinic Foundation Icare, Noordlease, Paediatric Association Of The Netherlands, Youth Preventive Health Care Drenthe, the European Union's Horizon 2020 research and innovation programme (LIFECYCLE, grant agreement No 733206, 2016), and Foundation Vrienden Beatrix Kinderziekenhuis, Groningen, The Netherlands.

Title:	Mental Health Changes After 4 Months Treatment with the GLP-1 Analogue Liraglutide
Authors:	Susanne Kuckuck[1,2], Nina van Gerwen[3], Maryam Kavousi[2], Brenda W.J.H. Penninx[4], Mariëtte R. Boon[1], Elisabeth F.C. van Rossum[1]
Affiliations	*[1] Department of Internal Medicine, Erasmus MC, University Medical Center Rotterdam* *[2] Department of Epidemiology, Erasmus MC, University Medical Center Rotterdam* *[3] Department of Biostatics, Erasmus MC, University Medical Center Rotterdam* *[4] Department of Psychiatry, Amsterdam Neuroscience and Amsterdam Public Health, Amsterdam UMC, Vrije Universiteit Amsterdam*
Abstract: (max 300 words)	**Introduction:** Obesity is commonly associated with mental health problems, including depression and anxiety as well as impaired psychological wellbeing. The glucagon-like peptide-1 (GLP-1) analogue liraglutide is effective in promoting weight loss, but its impact on mental health outcomes remains poorly understood in patients with obesity. This study aimed to evaluate the effects of 4 months liraglutide treatment on mental health and psychological wellbeing in patients with obesity. We also investigated potential associations between weight loss and changes in mental health parameters. **Methods:** We evaluated 98 patients with obesity (72% women) treated with liraglutide. Mental health was assessed using the Hospital Anxiety and Depression Scale ('HADS', range 0-42 for total score, 0-21 for anxiety and depression subscale) at baseline (T0) and after 4 months (including the initial uptitrating phase of 4 weeks and the subsequent 3 months of treatment with the highest tolerable dose). Psychological well-being was evaluated via the OBESI-Q questionnaire (range 0-100). At both time points, we also assessed body weight, body mass index (BMI) and waist circumference. **Results:** After 4 months of liraglutide treatment, body weight (-7.4 ±5.7 kg) and BMI (-2.5 ±1.9 kg/m2) were significantly reduced, along with decreased waist circumference (-5.0 ±9.3 cm), all $p<0.001$. We saw decreases in the HADS total score (-2 ±5, $p<0.05$) as well as depression subscore (-1 ±3, $p<0.05$) and anxiety subscore (-1 ±3, $p<0.08$). OBESI-Q psychological wellbeing increased (+5 ±15, $p<0.05$). Changes in all mental health parameters were correlated with changes in BMI and waist circumference significantly or in trend (all $p<0.1$). **Conclusion:** In patients with obesity, we observed improvements in mental health and psychological well-being after 4 months of liraglutide treatment at the highest tolerable dose. Those changes were paralleled by changes in BMI and waist circumference, suggesting that the improvements are at least partly mediated by weight loss. **1. Conflict of interest:** None disclosed. **2. Funding:** These authors are supported by Stress in Action. The research project 'Stress in Action': www.stress-in-action.nl is financially supported by the Dutch Research Council and the Dutch Ministry of Education, Culture and Science (NWO gravitation grant number 024.005.010).

Title:	**Investigating the quasi-causal association between the obesogenic environment and obesity: a twin study**
Authors:	Berntzen BJ[1,2,3], Beulens JWJ[1,2,3], Lakerveld J[1,2,3]
Affiliations	[1]Department of Epidemiology and Data Science, Amsterdam UMC, De Boelelaan 1117, Amsterdam, the Netherlands; [2] Amsterdam Public Health, Health Behaviors and Chronic Diseases, Amsterdam, the Netherlands; [3] Upstream Team, Amsterdam UMC, De Boelelaan 1117, Amsterdam, the Netherlands
Abstract: (max 300 words)	**Introduction:** Twins can be considered quasi-experimental controls for genetic and early life environmental factors. This study aimed to investigate the association between the obesogenic environment and body mass index (BMI), independent of familial factors shared by twins. Secondarily, we assessed whether the obesogenicity of the environment moderates the genetic contribution to BMI. **Methods:** This cross-sectional study included 2764 adults (77% female, mean [SD] age 40 [15]) from the Dutch Twin Registry (2009-2022), totaling 1382 twin pairs: 998 monozygotic (MZ) and 366 same-sex dizygotic (ssDZ). We enriched the NTR dataset with the Dutch Obesogenic Built Environment CharacterisTics (OBCT) index, consisting of four constructs: 1) food environment; 2) walkability index; 3) drivability index; and 4) sport facilities. The OBCT-index was calculated within a 1000-meter circular Euclidean buffer surrounding twins' residential addresses and ranged from 0-100 (higher scores indicate greater obesogenicity). Linear regression models analyzed individual (i.e., all ssDZ and MZ twin individuals) and pairwise (i.e., intrapair differences in MZ pairs) associations between the OBCT-index and BMI. Univariate and moderated twin models assessed the gene-environment relationship between the OBCT-index and BMI. **Results:** Living in a 10% higher OBCT-index environment was associated with a mean [95% CI] 0.15 [0.07, 0.24] kg/m^2 higher BMI in individuals (R^2 = 0.4%). However, this association was attenuated and nonsignificant in the pairwise MZ twin analyses (R^2 = 0.01%). The genetic contribution to BMI variation decreased from 82% to 35% between the lowest and highest intrapair OBCT-index difference. **Conclusion:** A more obesogenic environment was modestly associated with higher BMI, but this was explained by familial confounding. However, increasing intrapair differences in obesogenicity appeared to reduce genetic contributions to BMI variation. **1. Conflict of interest:** None disclosed **2. Funding:** The OBCT project is funded by the European Union's Horizon Europe research and innovation programme under grant agreement No. 101080250.

Title:	Zooming in on the inter-individual variability in treatment effectiveness for overweight and obesity.
Authors:	Vanbrabant, E.[1], Hesen, J.[1], Mironiuc, C.[1], Jordan, S.[1], Goossens, G.[2], Lemmens, L.[1], Shapovalova, Y.[3], & Roefs, A[1].
Affiliations	1. Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, the Netherlands 2. Department of Human Biology, Institute of Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Centre+ 3. Institute for Computing and Information Sciences, Radboud University Nijmegen, Nijmegen, the Netherlands
Abstract: (max 300 words)	Introduction: Obesity remains a major global health issue, and the effectiveness of standardized lifestyle interventions on average is not optimal, with large interindividual differences in achieved weight loss. This study aims to gain insight into this large interindividual variability. In the present analyses, we investigate how lifestyle behavior assessed in daily life (Ecological Momentary Assessment; EMA), motivation, coach-coachee relationship, and intervention satisfaction may explain inter-individual variability in treatment effectiveness. Method: 113 participants with overweight or obesity were included in the present analyses (of a total of 400 participants ultimately to be included). Participants were randomized to a 6-month intensive lifestyle intervention (ILI) or a 6-month information control condition (INFO). At baseline, a comprehensive profile was created, including biological, psychological, environmental, behavioral and personal variables, and anthropometric measures were obtained. In addition, at baseline and post-intervention, participants completed 3 weeks of EMA, including measures of food craving, intake, mood states, sleep quality, and physical activity. Body weight and waist-to-hip ratio are (self-)measured both at baseline and post-intervention. Results: As expected, average weight loss was larger in the ILI (M = -4.14%, n=56) than in the INFO group (M = -1.59%, n=57), t(df) = 3.1779 (103.6), p = 0.002, and interindividual variability was large (ILI: -17,7% to +6,3%; INFO: -14,6% to +5,6%). Further analyses are currently ongoing, which investigate how motivation, coach-coachee relationship, treatment satisfaction and daily lifestyle may explain inter-individual variability in weight change. Preliminary analyses showed large inter-individual variability in daily lifestyle and showed that participants who benefited most from treatment showed improvements in different daily lifestyle behaviors (e.g., healthier food choices). Conclusion: The large inter-individual heterogeneity in treatment effectiveness and daily lifestyle calls for a personalized approach to lifestyle interventions for obesity. Conflict of interest None disclosed. Funding This research was funded by a VICI grant from the Dutch Research Council (VI.C.211.010) awarded to Prof. Dr. Anne Roefs.

Title:	**Long-acting glucagon receptor agonism increases circulating triglyceride levels in diet-induced obese mice**
Authors:	Jamie I. van der Vaart[1,2], Mariëtte R. Boon[1,2], Patrick C.N. Rensen[1,2], Sander Kooijman[1,2], Robin van Eenige[1,2]
Affiliations	*1Dept. of Medicine, Div. of Endocrinology; 2Einthoven Laboratory for Experimental Vascular Medicine*
Abstract: (max 300 words)	**Introduction:** Glucagon is well-studied for its role in glucose metabolism. However, its involvement in lipid metabolism, in particular the context of obesity, remains less explored, although current evidence indicates that glucagon stimulates fatty acid oxidation in the liver. This study is aimed at evaluating the effects of a long-acting glucagon receptor agonist on lipid fluxes in diet-induced obese mice to better understand its potential role in obesity. **Methods:** Diet-induced obese male C57BL/6N mice were fed a Western diet (40% fat, 40% sucrose) and were treated every three days with a glucagon receptor agonist (GFA-015; 10 nmol/kg) or vehicle for 2 weeks. Body weight, body composition, and 4h-fasted plasma triglyceride levels were monitored throughout the study. At the end of the treatment period, VLDL production and VLDL catabolism were assessed. **Results:** Compared with vehicle treatment, treatment with the glucagon receptor agonist reduced fat mass (-16%), without affecting food intake. Interestingly, the glucagon receptor agonist increased plasma triglyceride (TG) levels (+64%). Mechanistically, the glucagon receptor agonist did not impact plasma clearance of intravenous injected VLDL-like particles, but enhanced VLDL-ApoB production (+51%) while decreasing VLDL-TG (-18%) production. **Conclusion:** Our preliminary results show that long-acting glucagon receptor agonism increases plasma TG levels, accompanied by hepatic overproduction of lipid-poor VLDL particles. We anticipate that smaller VLDL are lipolyzed less efficiently by lipoprotein lipase (LPL) on peripheral tissues, thereby increasing circulating TG levels. An increase in circulating TG levels should be considered in the development of glucagon receptor agonists for the treatment of obesity.

Title:	**A supportive tool for general practitioners to manage children with overweigh and obesity in primary care: a mixed-method evaluation study.**
Authors:	Van der Velden, MAM[1,*], Van Tilborg-den Boeft, M[1], Buis, S[1], Jansen, W[2,], Bindels, PJE[1], Van Middelkoop, M[1].
Affiliations	*[1]Department of General Practice, Erasmus MC Medical University Center Rotterdam, The Netherlands;* *[2]Department of Public Health, Erasmus MC Medical University Center Rotterdam, The Netherlands.*
Abstract: (max 300 words)	**Introduction:** In the Netherlands, general practice could be an ideal setting to identify and address overweight and obesity in children since it is the first point of care. A tool to support general practitioners (GPs) to identify, address and refer children with overweight and obesity was developed in co-creation with GPs and parents. The aim of this study was to evaluate the feasibility of this tool in general practice. **Method:** A mixed-methods design was performed. GPs applied the tool in daily practice from March to June 2024. Interviews qualitatively explored GPs' experience's with the application of the tool in practice, challenges faced, and further optimization and implementation strategies. All interviews were conducted online, digitally recorded, transcribed and thematically analyzed. Electronic Health Record Data (EHRD) were used to extract the number of reported children with overweight/obesity in general practice during the 3-month study period. These were compared with registration from the same 3 months in 2023. **Results:** Eight practices participated in this study of which 12 GPs were interviewed. Most GPs perceived the tool as user-friendly and were satisfied with the tool's content. GPs particularly appreciated the BMI-calculator, example sentences for weight-related conversations with parents and children, and the intervention map. Furthermore, GPs reported an improved feeling of confidence and alertness regarding overweight in children. Though, GPs reported barriers such as a short study period, limited consultation time, and poor findability of the tool. The EHRD showed that within the eight practices, 32 children with overweight/obesity were registered in the period of 2024, compared to 24 children in the same period of 2023. **Conclusion:** This study indicates that a supportive tool has the potential to support GPs in managing children with overweight and obesity. To successfully implement the tool in general practice, modifications are needed to overcome the identified barriers. **1. Conflict of interest:** none disclosed **2. Funding:** Stichting Theia

Title:	**Real world effect of personalized lifestyle treatment advice on health outcomes at one year follow-up in children who visit a specialized obesity clinic with severe obesity**
Authors:	van der Walle EPL[1 2], Welling MS[1 2 3], Abawi O[1 2], van Eck J[1 2], Meeusen R[1 3], Vos M[1 3], Brandsma AE[4], Beelen MLR[4], Oosterman JE[1 2 3], Boon MR[1 2 3], van Rossum EFC[2 3], de Groot CJ[1 2 5], van den Akker ELT[1 2]
Affiliations	*[1] Obesity Center CGG, department of Pediatrics, division of Pediatric Endocrinology, Erasmus MC, University Medical Center-Sophia Children's Hospital Rotterdam, Rotterdam, the Netherlands.* *[2] Center of expertise for genetic obesity, Erasmus University Medical Center Rotterdam and Amsterdam University Medical Center Amsterdam, The Netherlands* *[3] Obesity Center CGG, department of Internal Medicine, division of Endocrinology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands.* *[4] Obesity Center CGG, department of Pediatrics, Maasstad Hospital, Rotterdam, the Netherlands.* *[5] Department of Pediatrics, IJsselland Hospital, Capelle aan den IJssel, the Netherlands.*
Abstract: (max 300 words)	**Introduction:** Treating childhood obesity is challenging, especially in children with severe obesity. This observational study at a specialized, tertiary obesity clinic examines the effect of personalized treatment advice on health outcomes in children with severe obesity after one year of follow-up (FU). **Methods:** Children (0-18 years) referred to Obesity Center CGG until January 2024 with at least one-year FU were included. All underwent standardized diagnostic assessments, after which a multidisciplinary, personalized treatment plan was made involving local healthcare professionals. This plan focussed on lifestyle, including exercise and nutritional advice. Patients treated with anti-obesity medication during FU were excluded. Weight, height, waist circumference (WC), validated questionnaires and cardiometabolic parameters were assessed at baseline and FU. A subgroup analysis was performed for patients with confirmed genetic obesity. **Results:** A total of 671 patients were included (mean age 10.6 ±4.09 years, 57% girls), with a mean FU of 1.25 ±0.23 years. Mean BMI SDS decreased from 3.78 ±0.95 at baseline to 3.60 ±0.95 at FU ($p<0.001$), with 16% of the patients achieving ≥5% BMI reduction. Mean WC SDS decreased from 3.30 ±0.90 to 3.14 ±0.82 ($p<0.001$). At baseline, impaired fasting glucose was present in 7%, impaired glucose tolerance in 20%, type 2 diabetes in 1%, dyslipidaemia in 44%, elevated ALT in 27% and vitamin D deficiency in 53%. Analyses for cardiometabolic risk factors at FU are in progress. The subgroup of 98 patients (14.6%) with genetic obesity showed a similar decrease in BMI SDS (from 3.73 ±1.53 to 3.59 ±1.30, $p=0.026$) and WC SDS (from 3.30 ±1.50 to 3.13 ±1.05, $p=0.025$). **Conclusion:** Personalized lifestyle treatment advice has limited but significant positive impact on BMI and WC in children with severe obesity, including those with genetic obesity. However, most of the children remain in the category of obesity with elevated weight related health risk.
	1. Conflict of interest: no disclosures **2. Funding:** no funding

Title:	**The role of 3D visualisation based on CT in diagnosing internal herniation after RYGB**
Authors:	T. Veerbeek[1,2], S. Hillebrink[1,3], F. Intema[4], L.N. Deden[1,4], E.J. Hazebroek[1,2]
Affiliations	*[1]Vitalys, part of Rijnstate Arnhem, Department of Bariatric surgery; [2]Wageningen University and Research, Human Nutrition and Health; [3]Department of Multi-modality Medical Imaging, University of Twente; [4]Department of Radiology and Nuclear Medicine*
Abstract: (max 300 words)	**Introduction:** Internal herniation (IH) is a severe complication after Roux-en-Y gastric bypass surgery (RYGB) and requires a diagnostic laparoscopy (DLS). Diagnosing IH is challenging and often involves abdominal Computed Tomography (CT). However, the diagnostic accuracy of CT is poor. This may lead to unnecessary DLS. In this study, we explore the benefit of three-dimensional (3D)-visualisations based on CT to improve diagnosing IH and prevent unnecessary surgeries. **Methods:** In this retrospective cohort study, we included all RYGB-patients that were suspected for IH and had a DLS and abdominal CT performed between January 2019 and June 2024. Based on the outcome of DLS, the presence of IH was defined and classified. 3D-visualisations based on CT were generated, demonstrating characteristics including the location and orientation of the staples used to close the mesenteric defects and the vasculature of the intestines. These characteristic CT-markers were expected to benefit the IH-diagnosis. The diagnostic accuracy of these CT-markers was calculated and compared to the original CT report. **Results:** In total, 74 patients were included (57 females, mean age 44.6 years, mean BMI before RYGB 41.4 kg/m^2, mean BMI before CT 28.1 kg/m^2, total weight loss [TWL] 31.5%). The accuracy of the original CT report was 70.3 (sensitivity of 67.3%, specificity of 77.2%, positive predictive value [PPV] of 87.5% and negative predictive value [NPV] of 50%) and a moderate agreement was found between CT and DLS-outcome (κ= 0.386, p<.001).The accuracy of the CT-markers was 83.8 (sensitivity of 90.4%, specificity of 68.1%, a PPV of 87.0% and NPV of 75%). A moderate agreement was found between CT-markers and DLS-outcome (κ= 0.601, p<.001). **Conclusion:** The CT-markers seem to be beneficial in diagnosing IH as the diagnostic accuracy improves, compared to the original CT report. Further studies should include larger sample sizes and focus on exploring clinical use and implementation of the CT-markers. 1. Conflict of Interest None Disclosed 2. Funding No funding to report

Title:	**The narcolepsy drug γ-hydroxybutyric acid improves metabolic dysfunction in existing and developing obesity through altering the gut microbiota**
Authors:	Zhang S[1,2*], Liu C[1,2*], Zwaan M[1,2], Verhoeven A[3], Schinkelshoek M[1,2], Wang Y[1,2,4], Giera M[3], Boon MR[1,2], Rensen PCN[1,2,4], Schönke M[1,2] *co-first authors
Affiliations	[1]Department of Medicine, Division of Endocrinology, LUMC, Leiden, The Netherlands; [2]Einthoven Laboratory for Experimental Vascular Medicine, LUMC, Leiden, The Netherlands; [3]Center for Proteomics and Metabolomics, LUMC, Leiden, The Netherlands; [4]Med-X institute, Center for Immunological and Metabolic Diseases, and Department of Endocrinology, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an Jiaotong University, Xi'an, China.
Abstract: (max 300 words)	**Introduction:** γ-hydroxybutyric acid (GHB), used in the treatment of narcolepsy type 1, is known to counteract narcolepsy-induced increase in body weight. Here, we aimed to unravel the underlying mechanisms in mice, which could inform the development of drugs for obesity and related cardiometabolic diseases. **Methods:** Male wild-type mice (C57BL/6J background) were treated with either GHB or vehicle by daily oral gavage for 8 weeks, either after 8 weeks of high-fat diet (HFD) feeding ('existing obesity') or with concurrent HFD feeding ('developing obesity'). To elucidate the role of gut microbiota in beneficial cardiometabolic effects observed, we next performed fecal microbiota transplantation (FMT) from GHB-treated donor mice to untreated recipient mice fed a HFD during 6 weeks. **Results:** While GHB attenuated fat mass gain and improved glucose control only in existing obesity, GHB alleviated HFD-induced hepatic steatosis in both existing and developing obesity. This was accompanied by improved hepatic mitochondrial function, evidenced by upregulated hepatic expression of mitochondrial respiratory complexes and increased circulating levels of acetyl-carnitine. In addition, GHB alleviated HFD-induced adipose tissue dysfunction and beneficially remodeled the gut microbiota composition, enriching anti-inflammatory and succinate-producing microbes along with increased succinate concentration in the caecum. FMT attenuated HFD-induced body weight gain accompanied by improved hyperglycemia, hepatic steatosis and hepatic inflammation in recipient mice. Since GHB levels were similar in feces of GHB and vehicle-treated donor mice, these effects were not caused by transplantation of GHB but revealed the causal contribution of gut microbiota in the beneficial cardiometabolic effects of GHB. **Conclusion:** GHB promotes metabolic health in obesity, accompanied by improved hepatic mitochondrial function, which is at least in part explained by an altered gut microbiota composition, potentially through microbiota-derived metabolites. **1. Conflict of interest:** None Disclosed. **2. Funding:** Research relating to this abstract was funded by the Novo Nordisk Foundation (to M.S.), the Netherlands Cardiovascular Research Initiative (to P.C.N.R.) and the Chinese Scholarship Council (to S.Z.).