# 1. Content

1. Content ........................................................................................................................................................ 1
2. Programme ................................................................................................................................................... 2
3. Investigators/Participants with abstracts .................................................................................................. 6
4. Biographic sketches - Speakers ............................................................................................................. 17
5. Short summary of speaker’s talk ............................................................................................................. 20
6. Speakers/Chairs ......................................................................................................................................... 24
7. Organising Committee .............................................................................................................................. 25
8. Sponsors .................................................................................................................................................... 26
2. Programme

Day 6 September

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:45-09:00</td>
<td>Zoom Call Opens – grab a coffee</td>
</tr>
<tr>
<td>09:00-09:30</td>
<td>Welcome, practical information, meet &amp; greet</td>
</tr>
<tr>
<td></td>
<td><strong>Dr Agatha Van der Klaauw</strong>, Wellcome-MRC Institute of Metabolic Science (UK) &amp; Managing Director <strong>Tore Christiansen</strong>, Danish Diabetes Academy (DK)</td>
</tr>
<tr>
<td></td>
<td><strong>Session I</strong> Eating behaviour – the brain/ body and the policy</td>
</tr>
<tr>
<td></td>
<td>Chair: <strong>Dr Rajalakshmi Lakshman</strong>, MRC-Epidemiology Unit University of Cambridge (UK)</td>
</tr>
<tr>
<td>09:30-10:20</td>
<td>Key points from webcasts and Questions &amp; Answers:</td>
</tr>
<tr>
<td></td>
<td>Life course of childhood obesity and role of family unit</td>
</tr>
<tr>
<td></td>
<td><strong>Professor Daniel Witte</strong>, Aarhus University (DK)</td>
</tr>
<tr>
<td></td>
<td>Genetic influences on eating behaviour</td>
</tr>
<tr>
<td></td>
<td><strong>Dr Clare Llewellyn</strong>, University College London</td>
</tr>
<tr>
<td></td>
<td>Intrauterine environment and childhood obesity risk – insights into mechanisms</td>
</tr>
<tr>
<td></td>
<td><strong>Dr Laura Dearden</strong>, Wellcome-MRC Institute of Metabolic Science, (UK)</td>
</tr>
<tr>
<td>10:20-10:35</td>
<td>Tea &amp; Coffee break</td>
</tr>
<tr>
<td></td>
<td>Chair: <strong>Professor Jens Meldgaard Bruun</strong>, Steno Diabetes Center Aarhus (DK)</td>
</tr>
<tr>
<td>10:35-11:50</td>
<td>Four oral presentations from Early Career Researchers (ECRs)</td>
</tr>
<tr>
<td></td>
<td>1. High fat high sugar diet during pregnancy induces metabolic, inflammatory and redox alterations independent of changes in maternal body composition</td>
</tr>
<tr>
<td></td>
<td><strong>PhD Student Alejandro Candia</strong>, University of Cambridge (UK)</td>
</tr>
<tr>
<td></td>
<td>2. Protocol for “Young adults with early-onset obesity treated with semaglutide” - a randomized double blind placebo-controlled clinical trial</td>
</tr>
<tr>
<td></td>
<td><strong>Postdoc Eva Winning Lehmann</strong>, <strong>PhD Student Simon Birk Kiaer Jensen</strong>, <strong>PhD Student Christian Rimer Juhl</strong>, University of Copenhagen (DK)</td>
</tr>
<tr>
<td></td>
<td>3. Serum uric acids is associated with childhood obesity</td>
</tr>
<tr>
<td></td>
<td><strong>PhD Student Dorthe Dalstrup Jakobsen</strong>, University of Aarhus (DK)</td>
</tr>
</tbody>
</table>
4. Genetic variation of appetite-regulating hormones associated with body size in childhood  
PhD Student **Malene Revsbech Christiansen**, University of Copenhagen (DK)

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:50-13:30</td>
<td>Lunch</td>
</tr>
</tbody>
</table>
| 13:30-14:30   | Debate: Food addiction: Biology vs behaviour  
**Christina Horsager Pedersen**, Aalborg University Hospital (DK)  
Dr **Agatha Van der Klaauw**, Wellcome-MRC Institute of Metabolic Science (UK) |
| 14:30-14:45   | Tea & Coffee break                                                      |

Chair: **Professor Niels Jessen**, Steno Diabetes Center, Aarhus (DK)

Three oral presentations from Early Career Researchers (ECRs)

<table>
<thead>
<tr>
<th>Time</th>
<th>Oral Presentations</th>
</tr>
</thead>
</table>
| 14:45-15:40   | 1. The potential of future clinical examinations of food cue responsiveness in children  
PhD Student **Hanne Pedersen**, Steno Diabetes Center Copenhagen (DK)  
2. The vicious cycle of obesity – association between maternal weight and health, fetal growth and childhood overweight  
PhD Student **Magnus Møller**, University of Aarhus (DK)  
3. Target discovery for obesity using machine learning on individual patient journeys  
Postdoc **Rikke Linnemann Nielsen**, Novo Nordisk Research Centre Oxford (UK) |

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>15:40-15:45</td>
<td>Closing remarks</td>
</tr>
</tbody>
</table>
Day 7 September

08:45-09:00  Zoom Call Opens – grab a coffee

Session II  Energy expenditure – the brain/ body and the policy

Chair: Professor Jens Meldgaard Bruun, Steno Diabetes Center Aarhus (DK)

09:00-09:30  Key points from webcasts and Questions & Answers:

Evidence based interventions in childhood obesity
Professor Signe Torekov, University of Copenhagen (DK)

Metabolic Flexibility links adipose tissue dysfunction to metabolic diseases
Dr Sam Virtue, University of Cambridge, (UK)

Chair: Dr Erika Ikeda, Centre for Diet and Activity Research (CEDAR), MRC Epidemiology Unit (UK)

09:30-10:00  Key points from webcasts and Questions & Answers:

Physical activity patterns in children and adolescents in Denmark
Professor Anders Grøntved, University of Southern Denmark (DK)

Promoting physical activity in young people: child’s play?
Dr Esther van Sluijs, Centre for Diet and Activity Research (CEDAR)-MRC Epidemiology Unit, University of Cambridge (UK)

10:00-10:15  Tea & Coffee break

10:15-10:45  Kahoot Quiz

Chair: Professor Ken Ong, MRC Epidemiology Unit, University of Cambridge (UK)

10:45-11:45  Three oral presentations from Early Career Researchers (ECRs)

1. Socioeconomic differences in the family food home environment, and associations with childhood obesity – A pilot and feasibility study
Postdoc Dr Andrea Smith, University of Cambridge (UK)

2. Early prevention and predictors of obesity in children exposed to gestational diabetes during pregnancy
PhD Student Maja Thøgersen, Steno Diabetes Center Copenhagen and Aarhus University (DK)

3. Characterisation of G-protein coupled relaxin/insulin-like family peptide receptor 4 (Rxfp4)-expressing cells in the mouse hypothalamus
PhD Student Orla RM Woodward, University of Cambridge (UK)
11:45-13:30 Lunch

Chair: Professor Ken Ong, MRC Epidemiology Unit, University of Cambridge (UK)

13.30 – 13.50 The Novo Nordisk Foundation Initiative Promoting Healthy Weight in Children and Adolescents
Professor Arne Astrup, Novo Nordisk Foundation (DK)

13.50 – 14:10 A tale of two countries: How government policymaking works in reality in the UK versus Denmark and the role scientific evidence plays
Dolly Theis, MRC Epidemiology Unit, University of Cambridge (UK)

14.10-14:30 Joint discussion

14.30-14:45 Tea & Coffee break

14:45-15:15 Open Discussion - Moving forward: How can we start?
Professor Sadaf Farooqi, Wellcome-MRC Institute of Metabolic Science, University of Cambridge (UK) & Managing Director Tore Christiansen, Danish Diabetes Academy (DK)

15:15-15:30 Closing remarks, evaluation & farewell
### 3. Investigators/Participants with abstracts

<table>
<thead>
<tr>
<th>Abstract</th>
<th>Name</th>
<th>Place of Enrolment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1</td>
<td>Alejandro Candia</td>
<td>University of Cambridge (UK)</td>
</tr>
<tr>
<td>1-2</td>
<td>Andrea Smith</td>
<td>University of Cambridge (UK)</td>
</tr>
<tr>
<td>1-3</td>
<td>Eva Winning Lehmann, Simon Birk Kjaer Jensen, Christian Rimer Juhl</td>
<td>University of Copenhagen (DK)</td>
</tr>
<tr>
<td>1-4</td>
<td>Dorthe Dalstrup Jakobsen</td>
<td>Aarhus University (DK)</td>
</tr>
<tr>
<td>1-5</td>
<td>Hanne Pedersen</td>
<td>Steno Diabetes Center Copenhagen (DK)</td>
</tr>
<tr>
<td>1-6</td>
<td>Magnus Møller</td>
<td>Aarhus University (DK)</td>
</tr>
<tr>
<td>1-7</td>
<td>Maja Thøgersen</td>
<td>Aarhus University (DK)</td>
</tr>
<tr>
<td>1-8</td>
<td>Malene Revsbech Christiansen</td>
<td>University of Copenhagen (DK)</td>
</tr>
<tr>
<td>1-09</td>
<td>Orla RM Woodward</td>
<td>University of Cambridge (UK)</td>
</tr>
<tr>
<td>1-10</td>
<td>Rikke Linnemann Nielsen</td>
<td>Novo Nordisk Research Centre Oxford (UK)</td>
</tr>
</tbody>
</table>
High fat high sugar diet during pregnancy induces metabolic, inflammatory and redox alterations independent of changes in maternal body composition.

Alejandro A. Candia¹, Samantha C Lean¹, Edina Gulacsi¹, Amanda Sferruzzi-Perri¹

¹Centre for Trophoblast Research, Department of Physiology, Development and Neuroscience, Physiology Building, Downing Site, University of Cambridge (UK)

Diets high in fat and sugar (HFHS) can induce obesity. Obesity induces oxidative stress and a low-grade inflammatory state. During pregnancy, it increases the risk of metabolic complications. This study aimed to examine the effect of HFHS diet on maternal metabolism, oxidative stress and inflammatory state. We found mice fed a HFHS diet (3x fat, 2x sugar of control diet) had higher adiposity pre-pregnancy. Due to adipose hyper-mobilization in pregnant HFHS dams, their adiposity matched control dams by end of pregnancy. HFHS dams were hyperglycemic and glucose intolerant. They also had reduced insulin and elevated insulin sensitivity. HFHS dams had lower plasma triglycerides, elevated resistin and tendencies for lower leptin, IL-5, IL-10 and IL-17 but higher IL-1α and IL-6 and antioxidant capacity. HFHS dams exhibited hepatic steatosis and decreased glycogen, catalase and phospho-NFκB/total NFκB. They also had a tendency for increased hepatic 3-Nitrotyrosine and reduced/total glutathione suggesting an increased response against oxidative stress. Thus, a HFHS diet induces metabolic, inflammatory and redox alterations in the mother during pregnancy that are independent of changes in body composition. These data are important as maternal body weight change is the current clinical indicator for risk of metabolic problems in pregnancy.

References:
2. Lumeng et al. (2011).
Socioeconomic differences in the family food home environment, and associations with childhood obesity – A pilot and feasibility study

Dr Andrea Smith1,2, David Boniface2, Dr Mark Spires3, Dr Daisy Bradbury3,4, Prof Corinna Hawkes3* & Dr Clare Llewellyn2
1 MRC Epidemiology Unit, University of Cambridge, Cambridge (UK)
2 Research Department of Behavioural Science and Health, UCL, London (UK)
3 Centre for Food Policy, City, University of London, London (UK)
4 Sandwell and West Birmingham NHS Trust, Birmingham (UK)
*Joint senior authorship

Background
The prevalence of childhood obesity has increased in England despite decades of targeted policies. Inequalities are stark and widening. The Family Food Experience Study-London (FFES-L) aims to understand how the contexts into which existing interventions on diet are delivered impact families across the socioeconomic spectrum.

Methods
Socioeconomically diverse families (n=1000; with a child aged 4-11) from London boroughs with existing obesity prevention interventions will be invited to complete an interview-survey on eating behaviour and family food culture (incl. child BMI). Families will be recruited via 150 schools in wards in the top and bottom 25% of the Income Deprivation Affecting Children Index. A pilot study tested the feasibility of the sample design, recruitment, materials and survey length.

Results
The survey element of the FFES-L was feasible but recruitment challenging (11/46 target families recruited). Mean interview length was 72 min, exceeding the 1 h target. This was seen for families where English was not the primary language (80 vs 60 min). Feedback raised concerns about the comprehension of the consent section and few survey items. Presence of an informal translator and simplified wording were implemented.

Conclusion
Contextual factors in the family home warrant consideration when commissioning interventions to avoid widening inequalities in childhood obesity. The revised FFES-L survey will identify these salient factors in deprived households.
Protocol for “Young adults with early-onset obesity treated with semaglutide” - a randomized double blind placebo-controlled clinical trial.

Eva Winning Lehmann MD PhD†, 2*, Simon Birk Kjaer Jensen, Msc.†, 2, Christian Rimer Juhl†, 2, Torben Hansen‡, MD, DMSci‡, Jens J. Holst, MD, DMSci†, 2, Jens-Christian Holm, MD, PhD§ and Signe S. Torekov†, 2, PhD
†Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen; Denmark
2 The Novo Nordisk Foundation Center for Basic Metabolic Research, Section for Translational Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
‡ The Novo Nordisk Foundation Center for Basic Metabolic Research, Section for Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
§ Department of Pediatrics, Holbæk University Hospital, Denmark
Corresponding author: Eva Winning Lehmann, e-mail: epwi@sund.ku.dk

Background and aim:
The increment in prevalence rate for obesity is particularly pronounced among children and adolescents. Generally, lifestyle interventions to treat childhood obesity have yielded disappointing results, and 25% of children do not respond to structured lifestyle interventions, despite vigorous efforts. Thus, new effective treatment strategies are urgently required. Accordingly, the aim of the study is to treat young adults with obesity, who have been resistant to structured lifestyle intervention with the GLP-1 RA semaglutide + lifestyle intervention.

Material and methods:
This is an investigator-initiated, randomized, placebo-controlled trial. We will recruit 150 young adults (age 18-23) from The Children’s Obesity Clinic (TCOC), Department of Paediatrics, Holbæk Hospital. Based on their response to lifestyle changes (TCOC Protocol) we will divide them in two groups: 1) Non-responders: 75 young adults (BMI>30 kg/m²) who have not succeeded in losing weight (BMI SDS reduction <0.1) and remain obese and 2.) Responders: 75 young adults, who have succeeded in losing weight (BMI SDS reduction >0.5) and no longer obese (BMI<30 kg/m²). Non-responders will be randomized 2:1 to either semaglutide 2.4 mg/weekly or placebo for 68 weeks. The primary endpoint is change in BMI from randomization to end-of-treatment.

Perspectives:
Obtaining a clinically relevant weight loss in this patient group, will be an important break-through for the many treatment resistant adolescents, who otherwise have a dire prognosis.
Serum uric acids is associated with childhood obesity

Dorthe Dalstrup Jakobsen\textsuperscript{a,b}, Lea Brader\textsuperscript{c}, Jens Meldgaard Bruun\textsuperscript{a,b,d,e}

\textsuperscript{a}Steno Diabetes Center Aarhus, Aarhus University Hospital, Denmark, \textsuperscript{b}Department of Clinical Medicine, University of Aarhus, Denmark, \textsuperscript{c}Arla Innovation Centre, Global Nutrition, Aarhus, Denmark \textsuperscript{d}Medical Department, Randers Regional Hospital, Randers, Denmark, \textsuperscript{e}Department of Nutrition, Exercise, and Sports, University of Copenhagen, Denmark

Background and aim:
Dyslipidemia and hyperglycemia may be associated with childhood obesity and are key markers in prediabetes, type 2 diabetes and metabolic syndrome in children. A relationship between uric acids (UA) and obesity has been established in adults but the relationship in children remains obscure. The aim of this study was to investigate the relationship between obesity (i.e. BMI-SDS) and UA in children.

Material and methods:
Children were recruited from multicomponent-overnight lifestyle camps in Denmark as a part of an ongoing cluster-randomized trial. All children had anthropometrics assessed at baseline and a blood test was collected from the children willing to have blood drawn. Correlations were investigated using Pearson's correlation or Spearman’s correlation.

Results:
Fifty-nine children (age 9-14) with a mean BMI-SDS of 2.6 are currently included and thirty-four children have agreed to a blood test. A positive correlation was found between BMI-SDS and UA $r(32)=0.50$; $p=0.003$, total lipids $r_s=0.37$; $p=0.030$, LDL $r(32)=0.43$; $p=0.012$, and HbA1c $r(31)=0.36$; $p=0.042$. A negative correlation was found between BMI-SDS and HDL $r(32)=-0.56$; $p=0.001$.

Conclusion and discussion:
The novel finding in this ongoing study is a strong association between baseline UA, childhood obesity and metabolic markers (i.e. HbA1c). Could this imply that UA may be a key biomarker in diagnosing prediabetes, T2D and metabolic syndrome in children?
The potential of future clinical examinations of food cue responsiveness in children

Hanne Pedersen, Steno Diabetes Center Copenhagen, Gentofte, Denmark

Background:
More knowledge of the biobehavioral responses to food cues is important to understand factors contributing to food choice, excess food intake and the obesity epidemic. We examined how behavioral biometric responses differed when presented to foods varying in fat and taste and explored how biometric signatures to food cues were related to food reward and intake.

Methods:
We developed the Steno Biometric Food Preference Task to examine implicit and explicit responses to food cues. In a cross-sectional study in 100 adults with normal weight, we assessed biometric responses (concurrent eye tracking, electrodermal activity and facial expressions) and food reward to visual food stimuli from different food categories.

Results:
Differences were found in participants' visual attention (eye tracking) to food categories. We found that visual attention (during forced choice paradigm) was associated with subsequent food reward and intake. Attention, arousal or facial expression (during passive viewing) were not associated with food reward or intake, except for an association between negative valence and explicit liking such that less liked foods elicited stronger negative facial expressions.

Conclusions/discussion:
The findings indicate that biometric responses to food cues predict both food reward and actual food intake. There is a great potential in applying this methodology in children to examine their responses to food cues. How should the task be adapted to this target group?
P 1-6 Magnus Møller

The vicious cycle of obesity – association between maternal weight and health, fetal growth and childhood overweight

Magnus Møller, Dept. of Obstetrics and Gynecology, Aarhus University, Aarhus, Denmark.

Background and aim
The prevalence of childhood obesity is increasing in Denmark and world-wide. Many overweight children and adolescents remain overweight their entire life, putting them at increased risk of morbidity. Genetics and maternal health before and during pregnancy, fetal growth, nutrition and family socioeconomics all have an impact on the risk of childhood overweight but the interaction and timing of growth and overweight remain largely unexploited. We aim to investigate these causes of childhood overweight and their relation to later risk of overweight or obesity in the child and explore the importance of timing of overweight.

Material and methods
By a unique combination of data on maternal health and fetal ultrasound scans collected during pregnancy and data collected on children by specialty child health nurses during home-visits in Aarhus, we have information on 40,000 children and their families. We will explore the effects of fetal growth, maternal diabetes, pre-pregnancy weight, gestational weight gain and breastfeeding on childhood overweight and explore the importance of interplay and timing of these predictors.

Results
First results expected in spring 2022.

Conclusions and discussion
We expect to gain new knowledge on the early life predictors and causes of childhood overweight. I am interested in input on combining obstetric and postnatal data and the possibilities of combining epidemiological studies with biomarker research and the challenges involved.
Early prevention and predictors of obesity in children exposed to gestational diabetes during pregnancy

Maja Thøgersen, PhD student
Steno Diabetes Center Copenhagen and Aarhus University, Denmark

Background and aim
Children exposed to gestational diabetes (GDM) during pregnancy are at significant high risk of developing obesity and other cardiometabolic risk factors throughout life. Efforts to prevent childhood obesity should begin in early life. However, profound knowledge on the complexity of predictors and strategies targeting obesity prevention in GDM-exposed offspring are limited or inconclusive. This PhD aims to investigate risk- and protective factors of obesity development in children exposed to GDM during pregnancy, to target avenues for early prevention.

Material and methods
The project includes three studies: 1) A systematic review of interventions measuring obesity in GDM exposed offspring, 2) A large nationwide register-based study investigating biological, social and cultural predictors of childhood obesity including the modifying role of breastfeeding on the association between GDM and childhood obesity, 3) A secondary effect evaluation of a health promotion intervention for women with prior GDM and their families (the Face-it study), on the child’s obesity risk in the first year of life.

Results
Not available yet

Conclusions and discussion
This interdisciplinary project uses different data and study designs. Nationwide register data is collected by healthcare nurses, translated into research and new knowledge is returned to healthcare nurses to inform future prevention efforts. Also, development of the cross-sectional Face-it intervention is a collaborative process including user involvement of the target group and health professionals from Danish hospitals, municipalities and research institutes.
Genetic variation of appetite-regulating hormones associated with body size in childhood

Malene Revsbech Christiansen
Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark

Background and aim:
Children with obesity, a growing issue, are 5 times as likely to stay obese in adulthood, adding to the global burden of obesity. Being overweight as a child might also lead to earlier onset of puberty and unfavourable conditions later in life. Genetic variants (SNPs) can influence development of obesity by regulating the levels of a hormone involved in appetite and energy expenditure, leptin (LEP) and its receptor (LEPR). How big implication, these SNPs have on childhood body size, are not yet determined. We thus examine how alleles regulating LEP and LEPR levels associate with childhood adiposity.

Material and methods:
We used the UK Biobank where participants were asked to self-report body size compared to peers at age 10. In addition, we looked at puberty onset (age of menarche and age of first voice break and facial hair). We used SNPs associated with LEPR (rs2767485) and LEP (rs10487505) and examined their impact on these traits using linear, logistic and ordinal models. The effects were examined for each SNP separately, in addition to the combination of risks alleles.

Results:
Both rs2767485, rs10487505 and a combination of the alleles were significantly associated with body size at age 10 in multiple models, thus increasing the chances of being plumper compared to peers at age 10 when having the risk alleles. The results remained significant in boys and girls separately. In addition, risk alleles were associated with an earlier onset of puberty.

Conclusions and discussion:
Genetic predisposition to higher levels of leptin and lower levels of leptin receptor are significantly associated with a plumper body size at age 10 in subjects from the UK. In addition, the SNPs are associated with earlier puberty. We aim to validate the results in other cohorts and are happy to collaborate.
Relaxin family peptide receptor 4 (RXFP4), a Gαi/o-couple receptor, is thought to regulate ingestive behaviour as Rxfp4 knock-out mice have altered meal patterns and food preferences. In this study, the Rxfp4-Cre reporter mouse was used to identify and characterise Rxfp4-expressing cells in the brain. Rxfp4-expressing cells were identified in multiple brain regions, with distinct populations observed in the hypothalamus primarily in the ventromedial hypothalamus (VMH) and lateral and medial mammillary nuclei. Single-cell RNA-sequencing of hypothalamic Rxfp4-expressing cells identified both glutamatergic and GABAergic cells. Hypothalamic Rxfp4-expressing neurons were found to express several neuropeptide receptors (Glp-1R, Cckar, Cnr1, Mc4r and Nmur2) known to be involved in feeding. Employing neuronal circuit mapping techniques, we found that Rxfp4-expressing neurons in the VMH (Rxfp4VMH) receive projections from a small number of hypothalamic regions associated with homeostatic food intake, and project to multiple forebrain regions including regions of the reward system. Targeting and activation of Rxfp4VMH neurons using Cre-dependent AAVs expressing Gq-coupled Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) decreases intake of highly palatable meals. These findings indicate that Rxfp4VMH neurons may influence digestive behaviour through regulating homeostatic and hedonic feeding pathways and may be a pharmacotherapeutic target for childhood obesity.
Target discovery for obesity using machine learning on individual patient journeys

Rikke Linnemann Nielsen
Postdoc, Department of Computational Biology, Novo Nordisk Research Centre Oxford, Oxford, UK.

Background and aim
Obesity is a complex chronic disease with differing sub-groups of People with Obesity (PwO) given individual disease progression, response to treatment, and development of complications. We define context-dependent phenotypes of obesity and related comorbidities and use machine learning (ML) models to enable discovery of PwO subgroups, and identification of driving features.

Material and methods
UK Biobank data were transformed into phenotypes of obesity progression and trajectories towards complications, in people with and without a type 2 diabetes diagnosis. ML models were trained for classification of phenotype endpoints, integrating genotype and diverse longitudinal patient data such as physical activity, biomarkers, drug medication, and socio-economics.

Results
In one example, models discriminated a subgroup of PwO developing osteoarthritis (ROC-AUC:0.69, n=55,422) that were explained by typical clinical risk factors in combination with self-reported poor health ratings.

Conclusions and discussion
Ongoing work explores translation of patient signatures to identify predictors of disease progression, develop personalised intervention strategies and discover precision target candidates for obesity drug discovery. Similar modelling approaches can be applied to identify childhood patient subgroups with different risk of obesity, response to treatment and complications to enable biomarker and target discovery in early life.
4. Biographic sketches - Speakers

Astrup, Arne
Professor Arne Astrup, MD, DMSc. Is program Director at The Novo Nordisk Foundation in Denmark responsible for the establishment of a “National Center For a Healthy Weight” 2021. He was Head of Department of Nutrition, Exercise and Sports, University of Copenhagen, from 2012-20 with 300 staff and 1,200 students, and Chief Consultant at the Unit for Clinical Nutrition Research, Bispebjerg Frederiksberg University Hospital. Under Arne Astrup’s leadership the Department of Nutrition, Exercise and Sports ranked as the world’s number one sports and nutrition research environment 2018 in the Global Ranking of Sport Science Schools and Departments of the internationally recognised Shanghai Ranking.
Arne Astrup has previously been Chairman of the State Council for Nutrition, and for international research organisations. Major scientific areas are appetite regulation, treatment of obesity, type 2 diabetes, and cardiovascular disease, and diseases where nutrition and physical activity play a role. He is also interested in bridging nutrition, gastronomy and health, and has written a large number of popular diet books, which have been published in many countries, including the United States, Australia and Germany.
Discovered in 1996, together with Professor Jens Holst, that GLP-1 is a satiety hormone in humans, and was a driving force behind the prohibition of industrially produced trans fats in foods in Denmark in 2004. Arne Astrup publishes frequently in journals such as British Medical Journal, Lancet, Nature and New England Journal of Medicine. He has supervised 39 PhD students to date. Among University of Copenhagen scientists Arne Astrup is ranked number 5. His H-index is 100 (Google Scholar H-index 133 with 94700 citations). Astrup was created Knight of the Order of Dannebrog in 1999 By the The Queen Margrethe II, and Knight of the First Order of Dannebrog in November 2012.

Dearden, Laura
I undertook my PhD with Dr Nina Balthasar at the University of Bristol studying hypothalamic glucose sensing mechanisms. After my PhD I obtained a Sir Henry Wellcome post-doctoral fellowship to work jointly between Professor Sue Ozanne’s lab at the University of Cambridge and Dr Sebastien Bouret’s lab at the University of South California to combine their expertise in developmental programming and hypothalamic development respectively. This allowed me to pursue my research focused on how an obese pregnancy alters the fetal development of hypothalamic feeding centres, resulting in altered feeding regulation and subsequent obesity in these animals.

Llewellyn, Clare
Dr Clare Llewellyn is Associate Professor of Obesity in the Department of Behavioural Science and Health at University College London, where she leads the Obesity Research Group and the Gemini twin cohort. After an initial career in the pharmaceutical industry, she retrained as a Psychologist, undertaking an MSc and PhD in Health Psychology at UCL, and post-doctoral training at UCL and King’s College London. Her research interests are to understand how genetic and environmental factors interact to influence weight gain, eating behaviour and eating disorders, and to develop novel obesity prevention interventions. As part of an MQ funded fellowship she is examining links between childhood appetite, parental feeding practices, and the onset of adolescent eating disorders. With support from the Medical Research Council she is developing a digital obesity prevention intervention focused on infancy, with colleagues from the University of Cambridge. She leads the ‘early years’ work stream for the UK Obesity Policy Research Unit, funded by the National Institutes of Health Research. She also holds funding from the EU, the ESRC and NIHR for research into links between early diet and early weight gain, social deprivation and childhood obesity, and parental feeding practices and child eating behaviour. Clare is passionate about science communication and has published three evidence-based practical books for caregivers about feeding during the early years.
Pedersen, Christina Horsager
Christina Horsager Pedersen, MD, obtained the PhD degree based on a project entitled “Food addiction comorbid to mental disorder” in December 2020. In the PhD-project she investigated whether food addiction could represent a link between mental illness and obesity – a hypothesis, which was confirmed. The influence of mental illness on physical health/obesity (and vice versa), is the main focus of her research and she is interested in exploring how these conditions may interact and share common risk factors and etiological pathways. Currently she is employed at the Department of Child - and Adolescent Psychiatry, Aalborg University Hospital, where she has started specialist training to become a child and adolescent psychiatrist. She is currently planning a new research project aimed at investigating the role of food addiction in “difficult-to-treat” obesity, prediabetes and diabetes.

Theis, Dolly
Dolly Theis is in the final year of her PhD at the MRC Epidemiology Unit in the University of Cambridge. Her research focuses on what influences government obesity policy in England, how government policymaking works in reality, how governments use and understand scientific research, and the particular role policy entrepreneurs play. Prior to her PhD, Dolly led the childhood obesity and grassroots sport research at the Centre for Social Justice think tank and was a parliamentary researcher in the House of Lords. Dolly co-founded 50:50 Parliament's cross-party #AskHerToStand campaign which helps women get selected and elected. She is an ambassador of military veterans charity Forward Assist and ex-offenders employment charity Tempus Novo.

Sluijs, Esther van
Dr Esther van Sluijs is an MRC Investigator leading the ‘Behavioural Epidemiology and Interventions in Young People’ programme at the MRC Epidemiology Unit, University of Cambridge. Her team conducts observational research to further enhance the understanding on where, when and how physical activity and dietary interventions in young people may be implemented. This evidence is translated in the development and evaluation of innovative and holistic behavioural change programmes and interventions to promote behaviour change in young people. She has been an expert advisor on young people’s physical activity promotion guidelines for IOC and NICE and a member of the expert working group for the recent update of the UK physical activity guidelines.

Torekov, Signe
Prof Torekov has led seminal studies showing that patients with obesity have low levels of the appetite-inhibiting hormone GLP-1 (Færck and Torekov et al, Diabetes 2015), but that sustained weight loss increases GLP-1 and may thus normalize appetite (lepsen et al, Torekov, European Journal of Endocrinology 2016). GLP-1 receptor agonist (GLP-1RA) treatment was superior to low-calorie-diet regarding sustained weight loss reduction in blood glucose and increased availability of the appetite-inhibiting hormone leptin (lepsen et al, Torekov, International Journal of Obesity 2015). The Torekov group also showed that treatment with GLP-1RA prevents bone loss during weight loss (lepsen et al, Torekov, JCEM 2016) and that successful maintenance of weight loss involves instrumentalization of eating (Christensen et al Torekov, Obesity Facts 2017). The discovery, that GLP-1RA is an efficient treatment for patients with the most common form monogenic obesity caused by mutations in the appetite-regulating receptor MC4R (lepsen et al, Torekov, Cell Metabolism 2018; Cell Report Medicine 2020; and Gastroenterology 2021), has led to clinical practice change. Recently, the Torekov group finished a large randomized, placebo-controlled trial of 215 individuals with obesity to investigate the efficacy of one-year treatment with either exercise (WHO guidelines), GLP-1RA, or a combination of the two for healthy weight loss maintenance after a 13 kg diet-induced weight loss. The combination therapy was superior in terms of additional weight loss, insulin sensitivity, cardiorespiratory fitness and emotional well-being (Lundgren et al Torekov, The New England Journal of Medicine, 2021).
Prof Torekov has published 63 papers (13 first and 23 last authorships) in high-ranking journals including last authorships in *The New England Journal of Medicine*, *Cell Metabolism*, *Circulation*, *Gastroenterology* and more. She also received the Anders Jahre Medical Prize for young researchers.

**Van der Klaauw, Agatha**
I completed my medical training and PhD in classical neuroendocrinology at Leiden University in the Netherlands. After foundation jobs in General Medicine and Endocrinology at Leiden University Medical Centre as a academic clinical fellow, I joined the Institute of Metabolic Science in Cambridge in 2011, first as a Bernard Wolfe Research Fellow and in 2013 as a Wellcome Postdoctoral Clinical Fellow. In 2017, I became a Specialty Registrar in Metabolic Medicine at the Addenbrooke's Hospital Trust, Cambridge, followed by Clinical Lecturer in Metabolic Medicine at the Institute of Metabolic Science of the University of Cambridge in 2019. My research interest is the neurobiology of human energy balance, in other words how the brain regulates body weight and energy expenditure in humans. Outside work I love practising yoga and reading, but most of all playing and running outside with our three young children.

**Virtue, Sam**
I am research associate in the laboratory of Antonio Vidal-Puig. My main focus is on metabolic flexibility. I study how using the wrong nutrients at the wrong times leads to metabolic disease, focusing on how adipose tissue controls nutrient storage and supply to other organs. I also study fatty acid remodelling and how it impacts on physiology and metabolic disease, and I also have a long-standing interest in improving the translatability of mouse physiology to humans.

**Witte, Daniel**
Daniel R. Witte is Professor of Diabetes Epidemiology at the department of Public Health, Aarhus University and Steno Diabetes Center Aarhus. His main research interest is studying the pathophysiological mechanisms that drive the transition from normal glucose control via pre-diabetes to diabetes and the early stages of its complications at the population level. He has a special focus on longitudinal trajectory analyses and analysis of clustering of diabetic complications. His work uses data from several large longitudinal studies, such as the Inter99 and ADDITION trials, the ADDITION-PRO and Whitehall II cohorts, as well as routine medical and population registers which allow the enrichment of cohort datasets with data on the long-term consequences of diabetes and its clinical management. Daniel studied medicine and completed a PhD in clinical epidemiology at the University of Utrecht, the Netherlands, followed by 5 years as MRC clinical research fellow at the department of Epidemiology and Public Health, University College London. Between 2008 and 2012 he led the diabetes epidemiology group at Steno Diabetes Center Copenhagen. Between 2012 and 2014 he worked at the Luxembourg Institute of Health. In January 2015 he was appointed Professor of Diabetes Epidemiology at Aarhus University, Denmark based on a grant from the Danish Diabetes Academy. He is the recipient of the 2017 Harry Keen award from the International Diabetes Epidemiology Group.
5. Short summary of speaker’s talk

Astrup, Arne

Title: The Novo Nordisk Foundation Initiative: Establishment of “Healthy Weight Centre”
Novo Nordisk Foundation has an ambition to establish a national centre for healthy weight (HWC) based on the vision: All children have the right to grow up with a healthy weight and to maintain it throughout life. Children are not personally responsible for developing overweight, but they must live with the psychological, social and health-related consequences of their overweight. The aim is therefore to create the best possible framework for ensuring that children have the best start in life, physically and mentally.
The HWC will promote a healthy weight in children and their families through the establishment of strong partnerships with research and implementation partners, as well as with other partners, who jointly will focus on the following initiatives:

• **New knowledge**: Create the basis for effective initiatives and knowledge-based changes through interdisciplinary research and development.

• **Knowledge-based change**: Create changes through effective initiatives and supplementary and competence development and further education for professions working with children and their families.

• **Knowledge sharing**: Create, collate and disseminate evidence-based knowledge, nationally and globally.

HWC will comprise of both a physical centre and of the activities of the partners, that will be initiated and co-funded by the centre. The initiatives in the centre will be based on:

• **A broad methodological approach**, including classical health and natural science research, with observation studies, proof-of-concept studies in controlled environments, and interdisciplinary feasibility studies in real-life settings, with an aim to develop new, effective interventions of benefit to children.

• **Implementation projects in society** based on existing and new knowledge of effective initiatives, and involving interdisciplinary research, including implementation research, public health science, social sciences, health economics, etc.

HWC have started activities, such as research projects and an alliance, as an independent department in NNF, and will later become an independent unit, e.g. under a ministry or as a public-private partnership. In addition to a physical knowledge centre, binding, mission-driven partnerships will be established with several Danish and international stakeholders to secure research and implementation in order for new knowledge and methods to be implemented in Denmark, e.g. municipalities and regions.

Dearden, Laura

Title: Intrauterine environment and childhood obesity risk – insights into mechanisms
In the Ozanne lab we are interested in how the environments we experience early in life affect our health later in life. In particular, we are interested in how in utero exposure to maternal obesity programs an increased risk of cardio-metabolic disease in offspring as they grow up. In my talk I will share some of our recent data showing
how maternal obesity impacts on development of the fetal hypothalamus, and is associated with changes in key neuronal populations in the adult hypothalamus that may underlie the increased food intake and obesity in these animals.

Grøntved, Anders

Title: Detailed physical activity patterns in Danish children and adolescents: descriptive investigations of relevance for obesity prevention

An important starting point for a long-term coordinated effort to tackle insufficient physical inactivity among children and adolescents is to provide timely and valid detailed monitoring data. In this talk, I will provide an overview of our recent effort to combine and harmonize physical activity data obtained in five distinct population-based studies of Danish children and adolescents (n=6,500) in the period from 2016 to 2019 using similar methodology based on combined trunk- and thigh worn accelerometry (full 24-hour recordings for 7 days). Our investigations have provided a detailed insight into children’s engagement in sitting, standing, walking, running, and non-specific physical activity of light, moderate, and vigorous intensity during school hours and leisure time. Our data point to relevant domains of children’s habitual activity patterns, that could be targeted in future population-wide efforts to change obesogenic behaviors.

Llewellyn, Clare

Title: Genetic and environmental influences on children’s eating behaviour

Eating behaviour (EB) is about far more than simply what we eat. It characterises how we eat, why we eat, and our relationship with food. Our understanding of children’s EB was revolutionised in 2001 when Professor Jane Wardle published the Child Eating Behaviour Questionnaire (CEBQ), which was the first comprehensive psychometric instrument measuring 7 distinct EBs in children. Three ‘food approach’ traits characterise an avid appetite, and a greater interest in food: ‘food responsiveness’ (FR), desire to eat when prompted by palatable foods; ‘enjoyment of food’ (EF), reward experienced from eating; ‘emotional overeating’ (EOE), eating more in response to negative emotions. Four ‘food avoidance’ traits characterise a smaller appetite, and a lower interest in food: ‘satiety responsiveness’ (SR), fullness sensitivity; ‘slowness in eating’ (SE), eating speed; ‘emotional undereating’ (EUE), eating less in response to negative emotions; ‘food fussiness’ (FF), pickiness. FR, EF, SR, and SE are measurable from the earliest period of life during exclusive milk-feeding and can be measured using an infant version of the CEBQ (the Baby Eating Behaviour Questionnaire). Four of these traits reflect appetitive processes controlled by the homeostatic (SR, SE) and hedonic (FR, EF) appetite systems involving gut hormones, adipokines and the central nervous system; FF, EOE and EU are psychological. Large individual differences in EBs emerge after we are born, track throughout childhood, and are robustly associated with adiposity and weight gain. We have used two twin studies (Gemini; the Twins Early Development Study) to test the hypothesis that individual differences in EBs have a strong genetic basis, and mediate part of the well-established genetic influence on weight – so-called Behavioural Susceptibility Theory. The appetitive traits (FR, EF, SR and SE) have a strong genetic basis during infancy and childhood, with heritability estimates between 53% and 84%. The genetic influence on FF increases significantly from toddlerhood (54%) to early childhood (83%), while the sizeable influence of the shared environment that is observable in toddlerhood (31%) disappears. In contrast to these EBs, individual differences in emotional over-and under-eating are shaped almost entirely by the shared environment during toddlerhood (87% to 91%) and early childhood (71% to 77%), with very low genetic influence on either EB (3% to 10%). These findings indicate that the EBs that reflect homeostatic (SR, SE) and hedonic (FR, EF) appetitive processes may be behavioural endophenotypes that mediate genetic susceptibility to obesity. On the other hand, emotional eating is largely learned during early life. Research is needed to establish how best to modify children’s EBs during early life.
Pedersen, Christina Horsager

Title: Food addiction and childhood obesity

Food addiction (FA) is a phenotype characterized by an addiction-like attraction to highly processed foods with a high content of refined carbohydrates and fat. FA is likely to be involved in the development of overweight and obesity, often having its onset in childhood and adolescence. The Food Addiction Denmark (FADK) project found FA to be relatively prevalent in adults from the Danish general population (9%), and even more prevalent in adults with most mental disorders, and in adolescents with affective and psychotic disorders. Importantly, FA was associated with obesity in both adults and adolescents, and with T2D in adults. Thus, FA in children and adolescents may increase the risk of obesity and thereby also the risk of developing T2D in adulthood. Therefore, FA could represent a potential early target for prevention and treatment of childhood obesity, and of particular relevance in those with mental disorder, where obesity indeed is a tremendous problem.

Theis, Dolly

This talk will explore how UK government policymaking works in reality, what conditions are likely to lead to policy change and a specific look at how the Childhood Obesity Plan came about in England as a case study. It will also highlight the role of ‘policy entrepreneurs’ and how they manage to be such effective and influential policy actors.

Torekov, Signe

Children and adolescences with obesity and evidence-based effects of obesity treatment interventions in children and adults

Accelerating obesity levels, with a tenfold increase in four decades among children, pose a serious threat to human health, as children with early-onset obesity have a very high risk of developing morbid obesity, type 2 diabetes and cardiovascular disease already as young adults. The current treatment of childhood obesity involving lifestyle and behavioral change has shown low to moderate effect of reducing obesity. In adults with obesity low-calorie diets, GLP-1 analogues, exercise and gastric bypass have all showed clinical relevant effects on reducing obesity. However, given the high risk of weight regain when/if treatment is subsided, preventing development of overweight and obesity early in childhood seem to be crucial when it comes to battling the obesity epidemic.

Van der Klaauw, Agatha

Overeating of food high in dietary fat and sucrose leads to obesity. Eating behaviour in humans is complex. Decisions about what to eat and when to eat involve availability of food as well as intrinsic properties of food such as taste, texture, and palatability of food in addition to biological cues such as hunger and satiety.

Food choice or selection on the basis of biological needs is a very well conserved behaviour across species. Studies in various animal model have shown that food intake of dietary macronutrients such as proteins, fats and carbohydrates, is adjusted to meet nutritional requirements. This happens through complex interactions between hormones and nutrients from the gut and liver with defined brain regions. I will discuss these entero-endocrine and neural pathways that underly dietary macronutrient selection and preference in animal models and humans. I will show that the preference for dietary fat and sucrose has a strong biological basis, that we need to understand in order to effectively address overconsumption of dietary fat and sucrose.
Van Sluijs, Esther

In her talk, Esther will discuss the most recent evidence on physical activity promotion in young people and discuss some of the key challenges for effectively changing physical activity behaviour in young people.

Virtue, Sam

Metabolic flexibility is the capacity to switch between using carbohydrates and lipids as fuels, and its loss is termed metabolically inflexibility. Metabolic diseases including obesity and diabetes are characterized by metabolic inflexibility. Importantly, metabolic inflexibility has been shown to manifest prior to the development of detectable insulin resistance or hyperglycemia, suggesting that it is an early stage event in the development of diseases such as diabetes. This talk will provide an introduction the concept of metabolic flexibility and cover how it can be assessed and the phenotypes that manifest as a result of a loss of metabolic flexibility. In particular I will discuss how adipose tissue can control nutrient usage on a daily basis, and how a loss adipose tissue lipid-handling results in metabolic inflexibility and ultimately metabolic disease.

Witte, Daniel

**Title: The family unit and the life-course of obesity**

Development of obesity throughout the life-course has a strong social component. Although many of the health behaviours linked to obesity are highly influenced by the close social circle (e.g. eating, exercise, sleep), the current standard approach in epidemiology and clinical studies is to regard individuals as independent. We have shown clear concordance between spouses for different markers of obesity and diabetes risk. This implies that there is strong potential to improve risk detection and lifestyle interventions by taking the family as the unit rather than the individual. As most health behaviours have a strong learned component, this family approach may be a promising avenue for the prevention of childhood obesity.
## 6. Speakers/Chairs

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrup, Arne</td>
<td>Novo Nordisk Foundation (DK)</td>
</tr>
<tr>
<td>Bruun, Jens Meldgaard</td>
<td>Steno Diabetes Center Aarhus (DK)</td>
</tr>
<tr>
<td>Farooqi, Sadaf</td>
<td>Wellcome-MRC Institute of Metabolic Science, University of Cambridge (UK)</td>
</tr>
<tr>
<td>Dearden, Laura</td>
<td>Wellcome-MRC Institute of Metabolic Science (UK)</td>
</tr>
<tr>
<td>Grøntved, Anders</td>
<td>University of Southern Denmark (DK)</td>
</tr>
<tr>
<td>Ikeda, Erika</td>
<td>Centre for Diet and Activity Research (CEDAR), MRC Epidemiology Unit (UK)</td>
</tr>
<tr>
<td>Jessen, Niels</td>
<td>Steno Diabetes Center Aarhus (DK)</td>
</tr>
<tr>
<td>Lakshman, Rajalakshmi</td>
<td>MRC-Epidemiology Unit, University of Cambridge (UK)</td>
</tr>
<tr>
<td>Llewellyn, Clare</td>
<td>University College London (UK)</td>
</tr>
<tr>
<td>Ong, Ken</td>
<td>MRC Epidemiology Unit, University of Cambridge (UK)</td>
</tr>
<tr>
<td>Pedersen, Christina Horsager</td>
<td>Aalborg University Hospital (DK)</td>
</tr>
<tr>
<td>Sluijs, Esther van</td>
<td>Centre for Diet and Activity Research (CEDAR), MRC Epidemiology Unit (UK)</td>
</tr>
<tr>
<td>Theis, Dolly</td>
<td>MRC Epidemiology Unit, University of Cambridge (UK)</td>
</tr>
<tr>
<td>Torekov, Signe</td>
<td>University of Copenhagen (DK)</td>
</tr>
<tr>
<td>Van der Klaauw, Agatha</td>
<td>Wellcome-MRC Institute of Metabolic Science (UK)</td>
</tr>
<tr>
<td>Virtue, Sam</td>
<td>University of Cambridge (UK)</td>
</tr>
<tr>
<td>Witte, Daniel</td>
<td>Aarhus University (DK)</td>
</tr>
</tbody>
</table>
7. Organising Committee

Bruun, Jens Meldgaard, Professor
Department of Clinical Medicine, Steno Diabetes Center Aarhus (DK)

Farooqi, Sadaf, Wellcome Principal Research Fellow and Professor of Metabolism and Medicine
Wellcome-MRC Institute of Metabolic Science, University of Cambridge (UK)

Husum, Jette Education Manager, Danish Diabetes Academy (DK)

Ikeda, Erika Dr, Postdoctoral Fellow
Centre for Diet and Activity Research (CEDAR), Behavioural Epidemiology and Interventions in Young People, MRC-Epidemiology Unit, University of Cambridge (UK)

Jessen, Niels Professor, Head of Research,
Department of Clinical Medicine and Department of Biomedicine, Aarhus University (DK)

Lumsdon, Angela, Metabolic Network Co-ordinator, University of Cambridge (UK)

Lakshman, Rajalakshmi Dr, Clinical Senior Research Scientist
Centre for Diet and Activity Research (CEDAR), Behavioural Epidemiology and Interventions in Young People
MRC-Epidemiology Unit, University of Cambridge (UK)

Ong, Ken Professor, Programme Leader, Early Life Aetiology and Mechanisms of Diabetes and Related Metabolic Disorders
MRC-Epidemiology Unit, University of Cambridge (UK)

Van der Klaauw, Agatha Dr, NIHR Clinical Lecturer
Wellcome-MRC Institute of Metabolic Science, University of Cambridge (UK)
8. Sponsors

UNIVERSITY OF CAMBRIDGE

Cambridge Metabolic Network

Danish Diabetes Academy
Funded by the Novo Nordisk Foundation
Danish Diabetes Academy

CMN-DDA PhD & Postdoc Course: Childhood Obesity – An interdisciplinary approach to prevention and treatment

6-7 September 2021

Online Course