Dear Colleagues,

On behalf of the organizing committee, it is my pleasure to welcome you to Oulu to participate in the 3rd Paula Rantakallio Symposium on Birth Cohorts and Longitudinal Studies. The first Paula Rantakallio Symposium was held in 2014 in Oulu to honor late Professor Rantakallio, the pioneer in Epidemiological Birth Cohort Studies and the founder of NFBC.

We are very grateful to all of the speakers whose presentations will describe the broad spectrum of excellent research performed in the NFBC and other birth cohorts all over world. We also wish to acknowledge all researchers who contributed to our abstract book and present their work as posters further illustrating the wide variety of ongoing epidemiological research on birth cohorts.

We hope the conference will be memorable and that you will all participate the Dinner on Thursday 14th of June 2018 in Hotel Lasaretti. Let’s have fruitful discussions during the conference and during the dinner! Also, we hope you enjoy the midnight sun!

Olette lämpimästi tervetulleita!

On behalf of the organizing committee,

Juha Veijola, Chair

Organizing committee:
Marjo-Riitta Järvelin
Jouko Miettunen
Minna Ruddock
Sylvain Sebert
Juha Veijola
Tuula Ylitalo
# Conference on Epidemiological Birth Cohort and Longitudinal Studies – 3rd Paula Rantakallio Symposium

**Day:** Wednesday 13 – Friday 15, June, 2018  
**Place:** University of Oulu, Faculty of Medicine, Aapistie 5 A, 90220 Oulu

## Programme

### Day 1: June 13, 2018

**Chair,** Juha Veijola, University of Oulu, Finland

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<td>09.00–10.00</td>
<td>Welcome coffee and registration</td>
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| 10.00–10.15 | Opening remarks | Taina Pihlajaniemi, Professor, Vice rector, University of Oulu, Finland  
| 10.15–10.50 | Stress and chronic disease across the life course | Mika Kivimäki, University College of London, United Kingdom  
| 10.50–11.05 | Prenatal cigarette smoke exposure and DNA methylation changes in adulthood | Ville Karhunen, Imperial College London, United Kingdom  
| 11.05–11.20 | Investigating the impact of second-hand tobacco smoke exposure on DNA methylation and related health risks; the Avon Longitudinal Study of Parents and Children | Rebecca Richmond, University of Bristol, United Kingdom  
| 11.20–11.55 | First trimester origins of adult diseases | Vincent Jaddoe, Erasmus MC, Netherlands  
| 11.55–13.30 | Coffee |  
| 13.30–14.05 | Health consequences of life circumstances among men and women over the life course | Anne Hammarström, Uppsala University, Sweden  
| 14.05–14.20 | Longitudinal trajectories of physical activity from childhood to adulthood and their determinants: the Cardiovascular Risk in Young Finns Study | Tuija Tammelin, LIKES Research Centre for Physical Activity and Health, Finland  
| 14.20–14.50 | Coffee |  
| 14.50–15.05 | The origins project: a community project to restore global health | Desiree Silva, Telethon Kids Institute, Australia  
| 15.05–15.40 | Generalizability, representativeness and baseline selection in birth cohorts | Lorenzo Richiardi, University of Torino, Italy
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<td>The Finnish Gestational Diabetes Study (FinnGeDi)</td>
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<td><strong>Elina Keikkala, Oulu University Hospital and University of Oulu, Finland</strong></td>
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<td>15.55-16.30</td>
<td>Is the DOHaD paradigm applicable to Spinal Pain?</td>
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<td><strong>Anne-Marie Nybo Andressen, University of Copenhagen, Denmark</strong></td>
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<td>16.30 – 16.45</td>
<td>Physical fitness in adults born preterm - a study of 80,000 young men</td>
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<td><strong>Marjaana Tikanmäki, National Institute for Health and Welfare, Finland</strong></td>
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<td>16.45 – 17.00</td>
<td>Quantitative urine NMR metabolomics pipeline for large-scale systems epidemiology</td>
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<td><strong>Mika Ala-Korpela, Baker Heart and Diabetes Institute, Australia</strong></td>
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### Session I
**Chair, Jouko Miettunen**, University of Oulu, Finland

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<td>Coffee</td>
<td><strong>Mendelian randomization: an update</strong>&lt;br&gt;George Davey-Smith, University of Bristol, United Kingdom</td>
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<td>09.30 – 10.05</td>
<td>Session I</td>
<td><strong>Maternal early-pregnancy glucose-insulin metabolism, fetal growth and adverse birth outcomes: The generation R study</strong>&lt;br&gt;Romy Gaillard, Erasmus University Medical Center, Netherlands</td>
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<td>10.05 – 10.20</td>
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<td><strong>Metabolic changes in response to an oral glucose tolerance test in 4,620 middle-aged individuals; 46y follow-up of the Northern Finland Birth Cohort 1966</strong>&lt;br&gt;Qin Wang, University of Oulu, Finland</td>
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<td>10.20 – 10.35</td>
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<td><strong>The RECAP Preterm platform: the opportunities and challenges of bringing together data from European cohorts of children and adults born very preterm</strong>&lt;br&gt;Jennifer Zeitlin, French National Institute of Health and Medical Research, INSERM; France</td>
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<td>10.35 – 11.10</td>
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<td>11.10 – 12.40</td>
<td>Session I</td>
<td><strong>Challenging Lifecourse Approaches and their Implications – “New Research Concepts”</strong>&lt;br&gt;Marjo-Riitta Järvelin, Imperial College London, United Kingdom and University of Oulu, Finland</td>
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<td>12.40 – 13.15</td>
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<td><strong>Harmonized Zika Birth Cohorts as a nucleus for multicentre birth cohorts in Latin America and the Caribbean</strong>&lt;br&gt;Thomas Jaenisch, Section Clinical Tropical Medicine, Heidelberg University Hospital, Denmark</td>
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<td>13.15 – 13.30</td>
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<td><strong>Antisocial and borderline personality disorders in the adult offspring of antenatally depressed mothers in the Northern Finland 1966 Birth Cohort: Relationship to parental severe mental disorders</strong>&lt;br&gt;Tiina Taka-Eilola, University of Oulu, Finland</td>
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<td><strong>What studies of the NFBC have taught us about PCOS</strong>&lt;br&gt;Stephen Franks, Imperial College London, United Kingdom</td>
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<td>14.15 – 14.50</td>
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<td><strong>Dispositional Compassion and Individual’s Health</strong>&lt;br&gt;Mirka Hintsanen, University of Oulu, Finland</td>
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<td>14.50 – 15.25</td>
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<td><strong>Improved register data for cohort studies</strong>&lt;br&gt;Mika Gissler, National Institute for Health and Welfare, University of Turku, Finland and Karolinska Institute, Sweden</td>
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<td>15.25 – 16.00</td>
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## Day 3: June 15, 2018

**Session I**  
**Chair, Marjo-Riitta, Imperial College London, United Kingdom and University of Oulu, Finland**

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<td>09.30 – 10.05</td>
<td>Finnish large scale genomics studies: SUPER and FinnGen</td>
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<td><strong>Aarno Palotie, University of Helsinki, Finland and Harvard University</strong></td>
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<td>10.05 – 10.20</td>
<td>Continuous tracking of BMI from birth to adolescence reveals BMI acceleration during preschool age as critical risk factor for developing sustained obesity</td>
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<td><strong>Antje Körner, University of Leipzig, Germany</strong></td>
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<td>10.20 – 10.55</td>
<td>Epigenetic Epidemiology: Insights from birth cohort and longitudinal studies</td>
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<td><strong>Caroline Relton, University of Bristol, United Kingdom</strong></td>
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<td>10.55 – 11.10</td>
<td>Genome-wide association analysis on childhood body mass index reveals two new loci</td>
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<td><strong>Janine F Felix, Erasmus University Medical Center, Netherlands</strong></td>
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<td>11.10 – 11.25</td>
<td>Genetic study of pubertal height growth shows that the tempo of pubertal growth is correlated with adult health</td>
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<td><strong>Diana Cousminer, Children’s Hospital of Philadelphia and University of Pennsylvania, USA</strong></td>
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<td>11.25 – 11.40</td>
<td>A New Statistical Method to Estimate Maternal Genetic Effects on Perinatal Outcomes in Large Scale Genetic Studies</td>
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<td><strong>David M Evans, University of Queensland Diamantina Institute, University of Queensland, Brisbane, Australia, Integrative Epidemiology Unit, University of Bristol, Bristol, UK</strong></td>
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<td>11.40 – 11.55</td>
<td>Genetic study of birth weight resolves maternal and fetal genetic effects and their relevance to later life disease</td>
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<td><strong>Robin N Beaumont, Institute of Biomedical and Clinical Science, University of Exeter, Exeter, UK</strong></td>
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<td>11.55 - 12.05</td>
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<td><strong>Juha Veijola, University of Oulu, Finland</strong></td>
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Keynote speakers
Professor Mika Kivimäki

Professor Mika Kivimäki is an epidemiologist at University College London, UK, and University of Helsinki, Finland. He is the director of the British Whitehall II cohort study and leads the Individual-Participant-Data Meta-analysis in Working Populations (IPD-Work) consortium of 17 European cohort studies. The overarching aim of his research is to increase understanding on adulthood risk factors for impaired functioning and common chronic conditions, such as cardiovascular diseases, type 2 diabetes and dementia. Kivimäki has published more than 900 peer-reviewed papers, including state-of-the-art reviews and meta-analyses in the Lancet and Nature Reviews. A biographical interview of Prof. Kivimäki is available in Circulation 2012;126;f97-f102 at:

http://circ.ahajournals.org/content/126/17/f97.full.pdf+html
Stress and chronic disease across the life course

Email address: m.kivimaki@ucl.ac.uk

**Background** - The WHO Global Action Plan for the Prevention and Control of Non-Communicable Diseases targets established risk factors, including physical inactivity, tobacco use, heavy alcohol consumption, unhealthy diets, overweight, and raised blood pressure. However, a number of new risk factors have been proposed.

**Objective** - In this keynote, the most recent evidence for stress as a risk and prognostic factor for non-communicable diseases is reviewed. To cover the multiple roles of stress in disease pathology, the review is organized according to the disease process, from the development of subclinical disease and the acute triggering of clinical disorder to progression of the disease.

**Design** – A review of published studies.

**Results** – In prospective studies, stress has been linked to cardiometabolic diseases and depressive disorders, but no robust associations with site-specific cancers, all cancers combined, chronic obstructive pulmonary disease, asthma, Crohn’s disease or ulcerative colitis have been observed. Over the last 5-10 years, pooling of multiple datasets into mega studies has accelerated progress in research on stress as a risk factor for diabetes, coronary heart disease and stroke. Severe stressful experiences in childhood, such as physical abuse and household substance abuse, are associated with increased risk of multiple chronic conditions in adulthood. Adulthood stress has a modest role in cardiovascular disease aetiology among healthy individuals, but it seems to be a disease trigger in persons who already a high atherosclerotic plaque burden. Adulthood stress seems also to affect prognosis and outcome in those with pre-existing diabetes, cardiovascular or cerebrovascular disease.

**Conclusions** - Meta-analyses published during the past 5–10 years suggest that severe childhood stress can substantially damage mental and physical health. By contrast, adulthood stress might be an important risk factor in specific groups only, such as those with pre-existing cardiometabolic disease.
Professor Vincent Jaddoe

Paediatrician – Epidemiologist

Director Generation R Study; Project Coordinator EU Horizon2020 LifeCycle Consortium

Dr Jaddoe’s research is focused on how genetic variants and environmental exposures lead to maternal gestational complications, fetal and childhood developmental adaptation mechanisms, and risk factors for common diseases. His research is specifically focused on 3 main themes (1) maternal and fetal health; (2) early fetal and infant programming of common diseases; (3) genetics and epigenetics of common diseases in childhood; Most recent studies are focused on preconception and early pregnancy as critical periods for later life health outcomes. This life-course research is largely embedded in the Generation R Study, a population-based prospective cohort study among 10,000 pregnant women and their children. Since 2006, he is principal investigator of the Generation R Study at the Erasmus University Medical Center Rotterdam. His research is conducted in close collaboration with several international research groups. Genetic association studies are embedded in the Early Growth Genetics (EGG) Consortium and Early Growth and Longitudinal Epidemiology (EAGLE) Consortium, in which various cohorts combine their genome wide association studies efforts. Epigenetic association studies are embedded in the Pregnancy and Childhood Epigenetics (PACE) Consortium. Dr. Jaddoe is Project coordinator of the Horizon2020 EU LifeCycle - Project: Early life stressors and lifecycle health, in which European and Australian data from pregnancy and child cohort studies are combined into the EU Child Cohort Network. Dr Jaddoe received various national and European personal grants (ZonMw Klinische Fellowships, NWO-VENI, NWO- VIDI, ERC Consolidator Grant EMBRYOandLATERHEALTH).
First trimester origins of adult diseases

Email: v.jaddoe@erasusmc.nl

Preterm and small- or large-size born children have increased risks of cardiovascular disease and type 2 diabetes in adulthood. These intriguing observations strongly suggest that common diseases have at least part of their origins in early-life. Yet, the enormous potential for translation into population health strategies still needs to be fulfilled. To translate observational associations into innovative prevention strategies, it is urgently needed to disentangle the early-life critical periods, exposures and mechanisms. An accumulating body of evidence suggest that the preconception period and early pregnancy are critical for disease programming across the life course. Adverse exposures in these periods, leading to cardio-metabolic adaptations, predispose individuals to disease in later life and are clues for innovative population-based prevention strategies. Evidence from population-based studies on maternal factors during preconception and first trimester fetal development in relation to offspring growth and cardio-metabolic development will be discussed, with specific focus on early-life critical periods, life-style related exposures and mechanisms.
Professor Anne Hammarström

**Current position**
Professor of Public Health at Uppsala University

**Courses and Degrees Doctoral degree**
Medical Degree (M.D.) 1976, Uppsala University
Authorised physician 1977, Uppsala University
Specialist physician in social medicine 1989, in general practice 2004

**Doctoral Degree**
1986 at Karolinska Institute. Title: Youth unemployment and ill-health. Results from a two year follow-up study. Supervisor: professor Töres Theorell.

**Post doc appointment**
1998-99 One year post-doc at the department of Psychology and the department of Social Inquiry and Women’s Studies, University of Adelaide, Australia.

**Prior positions (2 most recent selected)**
2000-2016 Professor of Public Health, Umeå University
1993 – 2000 Senior Lecturer of Public Health, Umeå University

**Selected academic distinctions**
1996 – 99 Co-ordinator for a European project on unemployment and health (financed by EU)
1998 – 99 Visiting research fellow at the department of Psychology and the department of Social Inquiry and Women’s Studies, University of Adelaide, Australia
2006 Visiting professor, University of South Australia
2006 – 07 Chair of the Evaluation Committee of Public Health, Rehabilitation and Disability Science at the National Agency for Higher Education
2006 Member of the Swedish governments Scientific Working Committee
2006 – 07 Member of the Employment Conditions Knowledge Network, WHO Commission on the Social Determinants of Health
2006 – 09 Chair/Vice Chair of the Swedish Secretariat for Gender Research
2009 Award winner of Görel Bohlins’ prize for gender research
Health consequences of life circumstances among men and women over the life course

Email: anne.hammarstrom@pubcare.uu.se

**Background** - There is a need for a life-course perspective in research about gendered determinants of depressive symptoms.

**Objective** - This study analyses inequalities in depressive symptoms between men and women in four age groups (adolescence, youth, adulthood and mid-life), and identifies the extent to which social determinants explain the gap in symptoms between men and women in northern Sweden.

**Design** - The study is performed on the Northern Swedish Cohort, which consists of all pupils in their last year of compulsory school in 1981 the town of Luleå in Northern Sweden. The cohort has been followed over 27 years with extremely high response rate. Of those alive at age 43 in the original cohort (n=1071) 94.3 per cent participated (n=1010).

The cohort has been followed with extensive questionnaires at age 16, 21, 30 and 43.

**Results** - Over the life-course depressive symptoms were more common among women than among men. The largest gender gap was found at age 16. Socio-economic, school and labour market, interpersonal and physical factors explained a high proportion of the gap (88% at age 16, 77% at age 21, 64% at age 30 and 48% at age 43).

**Conclusions** - The health gap between men and women was mainly explained by the difference in access to economic and social resources. Thus, gendered health inequality is socially and politically produced and potentially avoidable.
Anne-Marie Nybo Andersen received her Medical Degree in 1988. After six years of clinical work, she became a full-time researcher in 1994. She obtained her PhD degree in 2001 with the thesis: Fetal death; Epidemiological studies, a research work carried out at the Danish Epidemiological Science Centre. She has been assistant and associate professor at University of Copenhagen (2000-2004), research director for child health at the Danish National Institute for Public Health (2004-2007), Professor of Epidemiology at University of Southern Denmark (2007-2010) and since 2010 she serves as Professor of Social Epidemiology at Department of Public Health, University of Copenhagen.

Her research group is working with maternal and child health, mainly using epidemiologic approaches but also some health services research. The group finds special interest in the fetal, childhood and long-term health effects of exposures in pregnancy, particularly gestational duration, social factors (including maternal and paternal age), infections and health behavior during pregnancy, reproductive immunology, and reproductive conditions among ethnic minorities in Denmark. Furthermore, the group takes an interest in development of epidemiologic methods, register-based research and in birth cohort studies.

Birth cohort research is a key interest, and Anne-Marie was part of establishing the Danish National Birth Cohort in 1995 and has since 2017 been the PI for this large-scale cohort with long-time follow-up. Further, she is founder and web administrator of www.birthcohorts.net, a resource used by researchers worldwide. Anne-Marie was a co-PI for the FP-7 project CHICOS, that built up a close scientific collaboration between more than 15 birth cohorts in Europe, taking advantage of large numbers and great diversity, resulting in a number of research projects addressing rare but important child health outcomes. Currently, she is leading the harmonization task in the Horizon2020 project LifeCycle, with the aim of improving causal inference from epidemiologic studies of childhood metabolic, respiratory, and mental health
Is the DOHaD paradigm applicable to Spinal Pain?

Email: amny@sund.ku.dk

**Background** - According to the most recent Global Burden of Disease Study, back and neck pains (BNP) were the leading causes of disability world-wide. The life-course approach has improved our understanding of the etiologies of some non-communicable chronic diseases, why this approach has been suggested as an important next step for research in musculoskeletal health.

**Objective** - The objective of this keynote talk is to discuss the opportunities for life-course studies of spinal pain in the birth cohorts set up around the turn of the century.

**Design** - The Danish National Birth Cohort has collected information about back and neck complaints in the recently completed 11-year and the currently running 18-year follow-up of the cohort, using the Young Spine Questionnaire. Early life influences (mode of delivery, anthropometry, childhood traumas, mental health/well-being and parental exposures) are investigated as risk factors acting via biological vulnerability, social patterns within the family, parental mental health, and acquired pain- and sick leave behavior through parental role models.

**Results** - Descriptives of back and neck complaints in 11-year olds will be presented, and the opportunities for a timely exploration of Developmental Origin of musculo-skeletal pain syndromes and preventive measures will be discussed.
Professor George Davey Smith is a clinical epidemiologist, director of the MRC Integrative Epidemiology Unit (IEU) at the University of Bristol and Scientific Director of the Avon Longitudinal Study of Parents and Children.

Professor Davey Smith’s research has pioneered understanding of the causes and alleviation of health inequalities; lifecourse epidemiology; systematic reviewing of epidemiological evidence; and the study of population health contributions of the new genetics. He is particularly interested in developing and applying Mendelian randomization approaches, interrogating the causal role of behavioral factors (such as alcohol consumption) and intermediate phenotypes on different health outcomes, such as cardiovascular diseases and type 2 diabetes.
I am a perinatal epidemiologist and tenured research director with at the Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Center for Epidemiology and Statistics Sorbonne Paris Cité at INSERM (French Institute for Health and Medical Research) in Paris. My research focuses on assessing the impact of the organization and quality of care on the health and development of babies born very preterm before 32 weeks of gestational age using multi-national prospective cohort studies. I am principal investigator of a H2020 project (SHIPS) on the use of evidence based medicine for the care and follow-up of very preterm infants in Europe and coordinate the work package on very preterm child cohort research as part of the H2020 project: Research on Children and Adults born Preterm (RECAP Preterm) Platform. I also coordinate the Euro-Peristat project, an EU initiative to develop maternal and infant health indicators that can be used for monitoring health on the national and European level. My third research interest is the management and consequences of fetal growth restriction for preterm and term births.

http://cvscience.aviesan.fr/cv/1647/jennifer-zeitlin
The RECAP Preterm platform: the opportunities and challenges of bringing together data from European cohorts of children and adults born very preterm

Email: jennifer.zeitlin@inserm.fr

Background - Very preterm infants constitute fewer than 2% of all births. Their survival has improved dramatically over past decades, but they face more health and developmental problems than children born at term. The RECAP Preterm project brings together European cohorts of very preterm or very low birthweight infants constituted since the 1980s to promote research on the consequences of very preterm birth. There are two research strands, one on outcomes up to early school age and the second on adult outcomes.

Objective - To present the opportunities and challenges of bringing together European very preterm cohorts and Nordic national registry studies for collaborative research on outcomes up to young adult age.

Design - Presentation of the cohorts in the RECAP Preterm project and priority research areas identified by cohort leaders, published studies from the cohorts, and external experts participating in a consultation process.

Results - Nineteen cohorts are part of RECAP Preterm and have produced over 500 publications. Most cohorts are area-based with inclusion of all eligible births, although follow-up rates vary greatly (50-90%). Follow-up schedules are heterogeneous as are instruments used to assess health and neurodevelopment. Rich clinical data exist for many cohorts, but biomarkers are mostly limited to adult studies and only few cohorts have genetic data. In childhood, the most studied longer-term outcomes are moderate to severe disability. RECAP Preterm research priorities focus on the impact of socio-economic and environmental conditions, uncommon exposures and outcomes, broadening the scope of outcomes to mental and physical health and quality of life and social adaptation outcomes as well as evaluating the longer term impact of perinatal care practices through the use of pooled datasets and national registry studies.

Conclusions - Many opportunities exist for building knowledge using the temporal and geographic diversity as well as the larger sample sizes enabled by pooling European cohorts; constraints relate to the logistic complexity of combining data on a common platform, including ethics and data management and the heterogeneity in outcome measures.
Lorenzo Richiardi is Associate Professor in Biostatistics and Epidemiology at the University of Turin, Italy. He graduated in medicine in 1999, specialized in biostatistics at the Milan University, and received his PhD in epidemiology at the Karolinska Institutet in Sweden.

His main research interests include cancer epidemiology, birth cohort research and causal inference methods. He is the principal investigator of the NINFEA birth cohort and member of the steering committee of the PICCOLIPIU birth cohort. Currently Lorenzo is responsible of the methodological workpackage of the Horizon2020 project LifeCycle. He teaches epidemiology and biostatistics in national and international courses and is currently co-director of the Residential Summer Course of Epidemiology of the European Educational Programme in Epidemiology.
Baseline recruitment in cohort studies is affected by intentional selection, due to the definition of the source population and corresponding inclusion criteria, as well as unintentional selection, due to baseline non-response or volunteering. These selection mechanisms may contribute to shaping the confounding pattern of the exposure-outcome relationship of interest, when both the exposure and at least one outcome risk factor affect or are associated with the probability of being a member of the cohort, thus introducing collider bias.

We will show these concepts using directed acyclic graphs and empirical examples. Using empirical examples based on the population of the Piedmont Region (4,000,000 inhabitants) we will show that collider bias due to the selection mechanism might alter the confounding pattern also when the source population is representative of the general population. We argue that every source population, either representative or selected, has its confounding pattern; efforts should be made to identify and control for the confounders of the relationship of interest in the study-sample.

When a cohort study aims at estimating the exposure-outcome causal effect in a specific population and at a specific time (i.e. generalizability matters only or mainly for that population) the sample should be representative of that population and analyses should aim at estimating the marginal rather than the conditional effect. This is for example relevant in presence of effect modification and/or when non-collapsible measures of association are used. We notice however that representative cohort studies are rarely analyzed using marginal methods.

In conclusion, the choice of the source population for a cohort study, including whether it should be representative of the general population or not, depends on several issues, including the study aim, its feasibility and efficiency, the expected completeness to follow-up, and control of confounding.
Marjo-Riitta Järvelin, MD, MSc, PhD, FFPM, is Professor and Chair in Lifecourse Epidemiology at Imperial College London (IC), UK, also holding a visiting professorship at Brunel University London, UK and a part-time professorship at the University of Oulu, Finland. She has been running large-scale population based studies for over 25 years, working on the genetic and early life environmental origins of multi-factorial diseases and disorders. She is a Scientific Director of the Northern Finland Birth Cohort (NFBC) research programme, and has an active role in research training as Director of Postgraduate Studies at School of Public Health, IC. Professor Järvelin has published over 700 original papers. She has been nominated on several prestigious visiting and collaboration awards, has received an award of Excellence in Genetic Epidemiology at Imperial College London, been honoured by the title, Epidemiologist of the Year in Finland and invited to join the Finnish Academy of Sciences.

Email: m.jarvelin@imperial.ac.uk

Over the last few years there has been increasing interest in (genetic) epidemiology conceptualizing disease aetiology within a life-course framework. Conventionally, chronic disease cohort studies recruit subjects in mid-life and follow them up for future disease end-points. Even when baseline measures include early life exposures, such as childhood socioeconomic position, these would usually be entered into a multivariable model without much attention to the temporal relationships.

In the DynaHEALTH H2020 program (www.dynahealth.eu), we have set out to explore a composite of biological and psycho-social factors that may predict premature ageing associated with metabolic adversities such as obesity and glycaemic health from early life onward. The analyses support a strong interplay of metabolic and psychosocial factors in establishing risk of premature ageing. Although the bio-psycho-social concept was introduced 40 years ago by Engel and acclaimed by the scientific community, it has yet to be successfully operationalized into research approaches and routine practice. The methodological challenge is to explore in-depth the life-long psycho-social wellbeing by taking into account metabolic measures, heritability, temporal relationships, interactions and causality, and how direct biological markers may be used as more “objective measures” of the impact of the environment on health. Statistical methods developed for life course studies are required to enhance the understanding of the aetiologies of the risk factors for more effective prevention and treatment. DynaHEALTH includes the potential to exploit the results for new technologies and strategies, adding to our understanding of the pathways related to healthy and active ageing, underpinning options for targeted, personalised healthcare.

*Understanding the Dynamic determinants of glucose homeostasis and psychosocial capability to promote Healthy and active ageing.*
Professor Stephen Franks

Stephen Franks trained in Internal Medicine and Endocrinology. He is Professor of Reproductive Endocrinology at Imperial College Faculty of Medicine (University of London) and Consultant Endocrinologist at St Mary’s and Hammersmith Hospitals, London. He is a former Chairman of the Society for Endocrinology (UK). He has both clinic and laboratory based programmes of research in the field of normal and disordered function of the hypothalamic-pituitary-ovarian axis. He has a major interest in polycystic ovary syndrome, which is not only the commonest cause of anovulatory infertility but is also a major risk factor for development of type 2 diabetes.
What studies of the NFBC have taught us about PCOS

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Background - Polycystic ovary syndrome (PCOS) is the commonest endocrine disorder in women and has both reproductive and metabolic effects. It is the most prevalent cause of infertility due to infrequent or absent ovulation, is associated with increased risk of type 2 diabetes and of markers of cardiovascular risk. Almost all such data have, however, been derived from clinic-based rather than population-based studies. Consequently, the impact of PCOS in the general population remains uncertain.

Objective - To discover the impact, in an unselected population of women, of symptoms PCOS (and/or PCOS diagnosis) on reproductive performance, metabolic health and mental health.

Design - Women with one or more symptoms of PCOS were identified within the 1966 NFBC cohort. Information about reproductive, metabolic and mental health, obtained from questionnaires, was supported by data (including endocrine and metabolic tests) from face-to-face visits for clinical assessment between the ages of 14 and 46.

Results - As expected, women with PCOS presented to clinics more frequently with infertility and had reduced fecundibility (increased time to first pregnancy) but had one child at least as often as in the reference population and family size (by age 46) was only slightly smaller. Furthermore, the rate of miscarriage was no greater than in the general population. Metabolic dysfunction in women with symptoms of PCOS was greatly influenced by the presence of obesity (which was significantly more common than in referents). Type 2 diabetes was more common in women with PCOS but only in those who were also obese. Women with PCOS suffered more often from anxiety and depression than referents.

Conclusions - Results from these population studies are largely in line with those from clinic-based studies but with important differences in the implications for both reproductive and metabolic health which give a new perspective to our understanding of this very common endocrine problem.
Mirka Hintsanen is Professor of psychology at University of Oulu, Finland (appointed in 2014). Hintsanen has received a PhD in psychology at the University of Helsinki, Finland (2007) and a PhD in educational sciences at the University of Tampere, Finland (2013). Hintsanen has led several funded large-scale research projects and is currently leading a four-year project on development of dispositional compassion funded by Academy of Finland. Hintsanen has well over 100 international peer reviewed publications. Finnish Academy of Science and Letters has awarded her Jutikkala Award. Her research focuses on personality, stress and health. Currently she is especially interested in the development and outcomes of individual’s compassion.
Dispositional Compassion and Individual’s Health

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**Background** – Compassion is related to better relationships and more constructive conflict resolution and it may be claimed as one of the building blocks of social harmony and humane society. It is clear that receiving compassion and acts of kindness are beneficial for the receiver, but it is less clear, whether feeling compassion towards others is beneficial or detrimental for the individual him/herself. The potential detrimental side is conceptualized e.g. in the term “compassion fatigue” that is used to describe exhaustion in encountering others suffering.

Compassion can be defined as concern for other’s suffering combined with a desire to alleviate this suffering. Thus, compassion includes a motivational component that is directed towards the well-being of other’s. Compassion is often confused with empathy, which is characterized by an ability to perceive and understand other’s feelings and thoughts, i.e. to put oneself in other’s shoes. Whereas, goodwill for others is written in the definition of compassion, it is not necessarily included in empathy.

**Objective** – In this presentation, I will review what is so far known about the associations of individual’s dispositional (trait like) compassion with the individual’s own health and well-being. I will also present some new findings on compassion as a predictor of health and well-being and shortly discuss the potential mechanisms behind these associations.

**Conclusions** – The limited research findings that exist indicate that in addition to being beneficial to others, compassion may also benefit the individual, who feels compassion towards others.
Dr Mika Gissler has a Master degree in Economic (1989) and Statistics (1992) at the University of Helsinki and he is a doctorate of Epidemiology at the University of Tampere (1999). He is a Research Professor and hold faculty appointments at the National Institute for Health and Welfare, the University of Turku, Finland, the University of Oulu, Finland, and Karolinska Institute, Stockholm, Sweden. His main research focus has been in utilization of routinely collected health and welfare registers with experience from all Nordic countries, and from several European and non-European countries, e.g. Germany, Estonia and Australia. Professor Mika Gisslers research interests include perinatal and infant health, childhood and adolescent health, sexual and reproductive health, mental health, migrant health and use of health care services. Increasingly, the studies have included a longitudinal component, usually from the prenatal period until adulthood.
Improved register data for cohort studies

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**Background** - The five Nordic countries have a long tradition of population statistics (since the 1700s) and health statistics (since the 1800s), even though the first real registers were initiated in the 1940-50s along with computer technology. Several data quality studies have shown the high quality and completeness of nationwide registers. All Nordic countries have introduced personal identification numbers, which enable technically uncomplicated record linkages. Data protection legislation has allowed the collection of register and their use in research without informed consents.

**Objective** - To present new possibilities for completing cohort data with register data.

**Results** - The Nordic countries have collected registers on cancers, infectious diseases, hospitalisations, deaths, births and congenital anomalies for decades. More recently, the collection of register data has been enlarged to cover prescriptions, primary health care, and the quality of treatment for various diseases and medical conditions. These new registers open novel possibilities to get reliable information for cohort studies without recall, reporting, or participation bias. They do not, however, give a complete picture. For example registers on social welfare services tend to be less developed than for health services. Also the possibilities to use data from electronic health records have been limited due to complex process to get access to the data and to get extraction from the national, regional or local databases.

**Conclusions** - The compilation and maintenance of health registers and their use in research is widely accepted, but critical voices are not uncommon. A major threat to the current register practice and for epidemiologic research is the tightening of data protection legislation. The consequences of the General Data Protection Regulation remain unknown. Finally, the use of sensitive register data in cohort studies is justifiable only when the studies serve widely acceptable aims and are designed and carried out to the highest possible standards of quality.
Aarno Palotie, M.D., Ph.D. is the research director of the Human Genomics program at FIMM. He is also a faculty member at the Center for Human Genome Research at the Massachusetts General Hospital in Boston and associate member of the Broad Institute of MIT and Harvard. He has a long track record in human disease genetics. He has held professorships and group leader positions at the University of Helsinki, UCLA, Wellcome Trust Sanger Institute, The Broad Institute of MIT and Harvard and the Massachusetts General Hospital. He has also been the director of the Finnish Genome Center and Laboratory of Molecular Genetics in the Helsinki University Hospital. He has served in numerous national and international boards, including the FIMM board. He has also chaired several large international research consortia and as a member or chair in national and international expert panels, including the International Headache Genetics Consortium (IHGC) and the SISu (Sequencing Initiative Suomi) consortium that combines all genome or exome wide sequence data produced from Finnish samples. Aarno Palotie has extensive experience in establishing, running and overseeing infrastructures both in research and clinical settings. In addition to running clinical laboratories and the Finnish Genome Center, he served as the director of Medical Sequencing and a member of the sequencing committee in the Sanger Institute, established and run the tissue array unit in UCLA and has been a key player in planning the National Genome Strategy and national biobanking strategies in Finland. He has published over 400 original publications, reviews and book chapters.
Human genetics has matured to a point where assessment of genotype-phenotype relationships can be performed in very large populations. These analyses can guide us to new disease associated pathways, inform about comorbidities, shared genetic background between diseases and their complications and potential novel drug targets. To achieve the next level of knowledge, we need larger and larger samples that have health data combined to genome data. Recently large biobanks have been launched to address this need. Nordic countries have collected standardized health service data for decades from every individual who uses these services. Such national registers include hospital and outpatient discharge data, cause of death data, prescription purchase and reimbursement data, cancer registers. These registers provide follow-up data over decades. Finland is also the largest population isolate in Europe. The small founder population, long isolation and rapid population growth have boosted a set of low frequency alleles to frequencies that make their statistical analysis meaningful. The longitudinal health data, the population structure and a favorable, well educated population, combined with genome data provide possibilities for unique study designs. I will describe two large studies, the SUPER study, which is a part of the Stanley Center of Psychiatric Research’s Global genetics initiative and the FinnGen Study, a large public private partnership. In the SUPER-study we are collecting 10 000 cases that have been diagnosed with psychosis, nationwide. We will analyze their genetic (GWAS and exome sequence data) and phenotype data and meta-analyze with other international cohorts. The FinnGen study aims to collect 500 000 Finns, representing 10% of the population and combined health register data with their genome (GWAS) variant data to improve our understanding of the genetic background of diseases. The FinnGen project is a collaboration of all Finnish biobanks, their stakeholders, University of Helsinki and seven large pharmaceutical companies.
Caroline Relton is a Professor of Epigenetic Epidemiology in the MRC Integrative Epidemiology Unit at the University of Bristol. She obtained a PhD in molecular genetics at Newcastle University in 1999 where she then held an academic position for 12 years, before moving to the University of Bristol in 2012. Caroline’s research focuses on understanding the role of both epigenetic variation in development and disease. The work of her group includes using population-based approaches to study epigenetic information as a biomarker of exposure and a predictor of disease. She has developed and applied causal analysis methods to understand the role of epigenetic processes as disease mechanisms and has led studies investigating the genetic architecture of DNA methylation variation. Her research spans multiple clinical areas from perinatal health to cancer. Caroline is also Director of the Bristol Population Health Science Research Institute.
Epigenetic variation is believed to play a role in mediating both the development of and adverse consequences of many diseases. Epigenetic mechanisms may be important determinants of health (where causality is important) or as useful biomarkers to help predict the occurrence and/or the consequences of disease (where causality is less important).

The presentation will provide an overview of epidemiological approaches to improve our understanding of the role of epigenetic variation in development and disease. These can be applied to explore causal pathways and to identify and validate epigenetic biomarkers. The use of Mendelian randomization to strengthen causal inference will be presented. Examples will be used to illustrate the use of DNA methylation as a biomarker of previous, long term exposure and as a predictive biomarker of future health outcomes.
ABSTRACTS (in alphabetical order)
O1 - Quantitative urine NMR metabolomics pipeline for large-scale systems epidemiology

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Background – Quantitative molecular data from urine are rare in epidemiology and genetics. NMR spectroscopy could provide these data in high-throughput, and it has already been applied in epidemiological settings to analyse urine samples, but quantitative protocols for large-scale applications are not available.

Objective – We give an initial demonstration of fully automated quantitative high-throughput metabolite analyses of human urine samples via NMR spectroscopy and introduce an open access quantitative pipeline of urine NMR metabolomics to facilitate large-scale epidemiological and genetic studies.

Design – We describe in detail how to prepare urine samples and perform NMR experiments to obtain quantitative metabolic information. Semi-automated quantitative lineshape fitting analyses were set up for 43 metabolites and applied to data from various analytical test samples and from 1,004 individuals from a population-based epidemiological cohort. Novel analyses on how urine metabolites associate with quantitative serum NMR metabolomics data (61 metabolic measures; n=995) were performed. In addition, confirmatory genome-wide analyses of urine metabolites were conducted (n=578). The initial fully automated quantitative regression-based spectral analysis is demonstrated for creatinine and glucose (n= 4,548).

Results – Intra-assay metabolite variations were mostly <5% indicating high robustness and accuracy of the urine NMR spectroscopy methodology per se. Intra-individual metabolite variations were large, ranging from 6% to 194%. However, population-based inter-individual
metabolite variations were even larger (from 14% to 1655%), providing a sound base for epidemiological applications. Metabolic associations between urine and serum were found clearly weaker than those within serum and within urine, indicating that urinary metabolomics data provide independent metabolic information. Two previous genome-wide hits for formate and 2-hydroxyisobutyrate were replicated.

**Conclusions** – Quantitative urine metabolomics data suggest broad novelty for systems epidemiology. A roadmap for an open access methodology is provided, including metabolite quantifications via an automated website.
P1 - Child Protection Actions among Children Born Preterm – The Contribution of Parental Socioeconomic Position; A Follow-up of the Finnish 1987-1990 Birth Cohort

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Background – Prematurity predisposes to out-of-home care (OHC) as a child protection action. Furthermore, parents of children born preterm have more often lower socioeconomic position, which may contribute to that risk.

Objective – The aim of this study was to assess whether parental socioeconomic position contributes to preterm subjects’ more frequent entries to OHC.

Design – We identified singletons (n=226,460) of five gestational age (GA)-categories born between Jan 1st 1987 and Sep 30th 1990 from the Finnish Medical Birth Register. Register of Child Welfare provided follow-up data, since Jan 1st 1991, (7870 first placements outside home, 3.5%) until 18th birthday. The data on parental highest attained socioeconomic position (through Dec 31st 2015) came from The Statistics Finland. We analyzed the effect of GA on OHC by Cox regression, stratified by index child’s (IC) birth year.

Results – Hazard Ratios (HRs) and Confidence Intervals (CIs) for OHC were compared to those born at full term (39 to 41 gestational weeks) with a model adjusted for child’s sex, maternal age, marital status, smoking in pregnancy, number of previous children (biological or adoptive) and her highest attained education. HRs for OHC were as follows: early preterm; 1.56 (95% CI 1.30 to 1.87), late preterm; 1.29 (1.16 to 1.44), and early term 1.14 (1.08 to 1.21). When further adjusted for parental highest achieved socioeconomic position (higher official or entrepreneur / lower official or laborer / other or unknown) the HRs attenuated as follows: early preterm; 1.32 (1.10 to 1.58), late preterm; 1.19 (1.07 to 1.33), and early term 1.10 (1.04 to 1.17).

Conclusions – As compared to full term children, children of other GA-categories are predisposed to out-of-home care. A considerable portion of that risk of preterm birth may be explained by parental socioeconomic position.
ABO blood groups are not the underlying cause for the link between ABO and cardiovascular disease

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Background – Multiple studies have found ABO blood groups to be associated with low-density lipoprotein (LDL) cholesterol and coronary artery disease (CAD). Large-scale genome-wide association studies (GWASs) have also robustly linked the ABO locus with LDL and CAD. However, the potential causal role of ABO antigen system in CAD remains unclear.

Objective – We aim to evaluate whether the ABO blood antigen system is associated with circulating lipoprotein, cholesterol and triglyceride measures, and whether ABO is causal for CAD.

Design – High-throughput NMR spectroscopy was used to quantify detailed lipoprotein subclass profile, circulating cholesterol and triglyceride measures in five Finnish population-based cohorts, comprising 22,270 individuals. Associations of these lipoprotein measures with genetically defined ABO blood groups and GWAS lead variant in the locus were assessed by linear regression adjusted for the relevant covariates. Additionally, metabolic associations were cross-adjusted for blood groups and GWAS lead variant.

Results – We observed that the GWAS lead variant remains robustly associated with metabolic measures after blood group adjustment. Using publicly available GWAS summary statistics data, we showed that the lipoprotein association in this locus is underlying the CAD risk as they share the genetic determinants. As the ABO locus has previously been linked with pancreatic cancer, we examine genetic sharing of risk between pancreatic cancer and CAD and observe that ABO harbors locus-specific sharing of genetic risk between these endpoints.
**Conclusions** – Our findings suggest that ABO is not the causal underlying factor for the CAD risk in this locus. The genetic sharing between LDL, CAD and pancreatic cancer, along with other lines of evidence, indicate that an alternative biologically relevant candidate gene in this locus would be carboxyl ester lipase (CEL), which is a pancreas specific enzyme that is involved in cholesterol absorption from intestine.
Background - In the general population, visuospatial associative learning starts to decline around the fourth decade of life, often as the first sign of age-related cognitive decline. Previous studies have shown that this cognitive function is also substantially impaired in a proportion of patients with schizophrenia.

Objective – To compare visual memory in two populations: a mid-life general population birth cohort, and patients with schizophrenia with the same mean age.

Design - A total of >5000 participants were drawn from the Northern Finland Birth Cohort 1966 (NFBC66) and the Finnish SUPER study of schizophrenia, part of the Stanley Global Neuropsychiatric Genomics Initiative. Visual learning and memory was assessed using CANTAB Paired Associative Learning Test (PAL). The effect on PAL scores of sociodemographic factors including sex, marital status and educational level were assessed in the two groups.

Results - Compared with the general population, the SUPER sample made more than twice as many errors on average, and also performed more poorly at the first attempt at each problem. In SUPER, males made slightly more errors and in NFBC66 substantially more errors than females. There were no differences in performance between ever-married and never-married participants in either population, but greater education predicted better performance in both samples.

Conclusions – Visuospatial memory is a marker of normal variation in midlife cognitive function, but is extremely heterogeneous in schizophrenia, where performance is characterized by a multimodal distribution not seen in the general population. Around a fifth of patients with schizophrenia have error scores similar to the top 50% of the general population, while around half show a substantial impairment. Immediate memory may be more impaired than learning over time in schizophrenia. Demographic factors affect memory scores similarly in schizophrenia and the general population.
O2 - Genetic study of birth weight resolves maternal and fetal genetic effects and their relevance to later-life disease

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Birth weight is a key determinant of pregnancy outcomes, an important predictor of newborn and infant survival, and is associated with adult cardio-metabolic disease risk. We previously reported an inverse genetic correlation between birth weight and cardiometabolic disease. However, fetal genotype is 50% correlated with maternal genotype, and may influence birth weight indirectly through the intrauterine environment. Here, we use a new statistical method based on structural equation modeling (SEM) to distinguish fetal and maternal genotypic contributions to birth weight in greatly-expanded GWAS meta-analyses, and elucidate birth weight-disease risk relationships.

In fetal and maternal GWAS, we identified 305 lead SNPs at 274 loci. Using SEM, we categorized SNPs into those with fetal genotype effects only (n=83), maternal only (n=45), directionally-concordant maternal and fetal effects (n=36), or directionally-opposing (n=24). Our findings implicate several fetal-specific (e.g. imprinted genes, insulin sensitivity and cardiovascular tissues) or maternal-specific mechanisms/tissues (e.g. metabolism of xenobiotics and connective tissues and bone) involved in the regulation of birth weight, and also mechanisms with directionally-opposing effects (e.g. insulin secretion, fasting glucose). Mendelian randomization indicated a causal effect of maternal blood pressure lowering offspring birth weight. The lack of a negative maternal birth weight genotype effect on later-life offspring SBP suggests the well-reported phenotypic association between birth weight and adult SBP is mediated not by intrauterine programming, but by SBP genotypes acting maternally to lower birth weight and then transmitted to the offspring to directly alter offspring SBP. Mendelian randomization also indicated causal effects of maternal insulin secretion lowering offspring birth weight; these same alleles are associated with lowered future risk of type 2 diabetes (T2D) when inherited by the fetus. Opposite effects were seen for fetal genotypes lending support to the Fetal Insulin Hypothesis.
P4 - Structural properties of the human corpus callosum: Multimodal assessment and sex differences

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\textbf{Background} – Corpus callosum is the main interhemispheric fiber tract in the human brain, consisting of about 200 million axons. Heterogeneity of its fiber composition suggests that cortical regions differ in the type of channels carrying information between their left-right homologues. Mutually connected cortical regions and the respective callosal fibers together present modules of interhemispheric information transfer that are affected by numerous pathological and developmental factors including prenatal exposure to maternal cigarette smoking.

\textbf{Objective} – To study callosal fiber composition and related cortical microstructure in the human brain and to assess the effects of prenatal exposure to maternal cigarette smoking.

\textbf{Design} – We modeled interhemispheric connectivity using diffusion tractography in a sample of 100 unrelated individuals from the Human Connectome Project. Those pairs of cortical regions and the callosal segments through which they are most consistently connected were included to form 6 modules. Then we assessed the similarity in structural values (MTR) in each of the 6 callosal segments and 16 cortical regions, as well as their inter relationship in 450 young adults from the Northern Finland Birth Cohort 1986.

\textbf{Results} – Callosal MTR correlated consistently with cortical MTR in all modules. Cortical MTR was found to be negatively correlated with cortical thickness in all but one cortical region, namely the precentral gyrus, primarily connected through the posterior part of the callosal body. This cortical site is also the only one to show significantly stronger effect in the correlation between cortical MTR and cortical thickness in those exposed prenatally to maternal cigarette smoking.

\textbf{Conclusions} – We speculate such a stronger correlation in this group may reflect greater variability in dendritic arborization.
Large-scale studies of height and pubertal timing have yielded hundreds of genetic associations, but the genetic variants that mediate differences in growth during adolescence are less explored. Here, we performed genome-wide association studies on longitudinally modeled height using Super-Imposition by Translation And Rotation (SITAR) growth curve analysis, which results in three parameters that describe each individual’s growth curve: \( a \)-size, which represents taller or shorter than the mean; \( b \)-timing, which represents the timing of the growth spurt earlier or later than the mean; and \( c \)-velocity, which is the tempo of the pubertal growth spurt, a property of pubertal growth that has not previously been subjected to genetic analyses. Here, we included 19,107 samples of European descent in the first round of meta-analyses. Additional study cohorts are still being added to the second version of the results, which will also include trans-ethnic data.

Thus far, we detected four genome-wide significant loci previously identified in EGG studies, including the \( EFEMP1 \) and \( SOCS2 \) loci (previously associated with height at age 10 in girls and 12 in boys), at \( LIN28B \) (previously associated with growth during late puberty), and \( GDF5 \) (previously associated with infant length). Here, these loci showed either steady effects on growth across childhood, from birth length to adult stature (for \( a \)-size), or affected growth during the pubertal growth spurt, possibly acting through effects on the timing of puberty (\( b \)-timing or \( c \)-velocity).

Next, we used LD Score Regression to investigate the genetic correlation of the SITAR parameters with traits and diseases. As expected, \( a \)-size was strongly correlated with body size traits, including birth weight and length, height at age 10/12, adult stature, and hip and waist circumference, while \( b \)-timing was highly correlated with the timing of puberty and body fat/BMI traits, as well as adult fasting insulin and 2hr glucose adjusted for BMI. Interestingly, however, \( c \)-velocity was correlated with both pubertal timing and anthropometric traits throughout the lifespan, but was also strongly correlated with measures of adult health, including glycemic traits (insulin, HOMA-IR), metabolites (HDL, VLDL concentrations), bone (femoral neck bone mineral density) and measures of lung function (forced vital capacity and forced expiratory volume) as well as lung cancer. These findings suggest that the tempo of pubertal development, often challenging to assess and thus overlooked in epidemiological studies, should be studied more in the context of adult health outcomes.
O4 - THE ORIGINS PROJECT: A COMMUNITY PROJECT TO RESTORE GLOBAL HEALTH

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Background - There is a pressing need to understand how the modern environment is contributing to the unsustainable health burden of non-communicable diseases. The ORIGINS community study is a collaborative project between Joondalup Health Campus and Telethon Kids Institute, funded by the Federal Government of Australia and a philanthropic organisation, Paul Ramsay Foundation.

Objectives - 1) To improve the health of the next generation. 2) To initiate and integrate harmonised nested clinical trials within this framework with include studies that positively change the ‘exome’. 3) To develop a robust biobank and databank repository of information which utilise new technologies to further this field of research.

Design - The ORIGINS project commenced in November 2016. It aims to recruit 10,000 women and their partners over a 5-year period, early in pregnancy, and follow their child for 5 years. We are collecting biological samples, routine data and web-based questionnaires at a range of time points. Strong community, local government and academic partnerships are key to this project.

Results - Currently we have recruited 1000 families, integrating and harmonising four nested studies from the onset, which include: a randomised controlled trial using prebiotics in pregnancy; an intervention study around early weight gain in pregnancy; antenatal and early post natal assessment tools to detect neurodevelopmental disorders with timely intervention, reducing cardiovascular risk in fathers, and understanding the impact of electronic use.

Conclusions - Developing a new community birth cohort with an emphasis on pregnancy and the early years with real time feed back and having nested clinical trials provides a novel way to develop future cohorts. The intent of this project is to increase research capacity, productivity, collaboration and translational impact on future generations. We also anticipate flow-on benefits for community cohesion and purpose, which will provide a sentinel example for tailored replication in other communities around the world – as part of interconnected grass-root strategies to restore global health.
P5 - Genetic architecture of early childhood growth phenotypes gives insights into their link with later obesity


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Background – Early childhood growth patterns are associated with adult metabolic health, but the underlying mechanisms are unclear. These observational associations may be explained by discrete genetic variants that could regulate developmental patterns during rapid growth in infancy compared to later growth periods in childhood. Alternatively, observational associations between early growth and later metabolic health may, in part, be explained by shared genetic factors.

Objective – To identify genetic variants associated with early growth phenotypes and their underlying mechanisms.

Design – We performed genome-wide meta-analyses and follow-up in up to 22,769 European children for six early growth phenotypes derived from longitudinal data: peak height velocity (PHV), peak weight velocity (PWV), age at adiposity peak (Age-AP ~9 months) and rebound (Age-AR), body mass index (BMI) at adiposity peak (BMI-AP) and rebound (BMI-AR ~5-6 years). We then performed additional downstream functional analyses to understand the possible functional mechanisms of the associated loci including eQTL analyses, genetic correlation and pathway analyses.
Results – We identified four associated loci \((P < 5 \times 10^{-8})\): \textit{LEPR/LEPROT} with BMI at AP, \textit{FTO} and \textit{TFAP2B} with Age at AR and \textit{GNPDA2} with BMI at AR. The observed AR-associated SNPs at \textit{FTO}, \textit{TFAP2B} and \textit{GNPDA2} represent known adult BMI-associated variants. The common variant at \textit{LEPR/LEPROT} associated with BMI-AP was not associated with adult BMI but was associated with \textit{LEPR} and \textit{LEPROT gene} expression, especially in subcutaneous fat \((P = 1.59 \times 10^{-6} \text{ & } P = 1.6 \times 10^{-89})\). We identified strong positive genetic correlations between early growth and later adiposity traits, and analysis of the full discovery stage results for Age-AR revealed enrichment for insulin-like growth factor 1 (IGF-1) signaling and apolipoprotein pathways.

Conclusions – This genome-wide association study supports mechanistic links between early childhood growth and adiposity in later childhood and adulthood, highlighting these early growth phenotypes as potential risk factors for obesity.
Genetic effects on perinatal traits may be mediated through the fetal or maternal genome or both. In this presentation we describe a new statistical method based on structural equation modelling that we use to partition genetic effects into maternal and fetal components. Our approach is flexible in that singletons, genotyped mother-offspring duos, and individuals reporting their own and their offspring’s phenotype can be simultaneously incorporated into the analysis. Importantly, our method can be applied either to individual-level genotype data, or to summary-level GWAS results data. Additionally when our model is applied across the genome, it can increase power to detect variants that have opposing maternal and fetal effects on perinatal traits. We describe the statistical properties of our approach, demonstrate that it yields unbiased estimates of maternal and fetal effects, and has low sensitivity to random measurement error. We will also illustrate our model via application to known and novel variants for birthweight using data from the UKBB and EGG consortium. We show that whilst most loci influence birthweight primarily through the fetal genome, there is a subset of SNPs that exert their effects predominantly through the mother’s genome, and a subset that exhibit maternal and fetal effects in opposite directions. Interestingly the loci that manifest opposing effects through maternal and fetal genomes include diabetes-associated loci. Our results are consistent not only with smaller and less powerful conditional regressions in genotyped mother offspring duos, but also with examples of opposing maternal and fetal contributions on birth weight of rare mutations influencing insulin secretion and glucose tolerance. Finally, we illustrate how our method can be run computationally efficiently across the genome and the resulting estimates used in a variety of downstream analyses like LD Score regression and Mendelian Randomization to provide important information on hypotheses like the Developmental Origins of Health and Disease.
P6 - Self-reported musculoskeletal pain in adults born early and late preterm; evidence from two Finnish birth cohorts

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Background – Individuals born preterm are at risk for later developmental problems and long-term morbidities. There is conflicting evidence regarding musculoskeletal pain in young adulthood.

Objective – We investigated the prevalence of self-reported musculoskeletal pain in young adults born across the range of preterm birth compared with a term-born reference group.

Design – From the Ester Preterm Birth Study and Arvo Ylppö Longitudinal Study, 184 individuals born early preterm (<34 weeks), 350 late preterm (34 to <37 weeks), and 641 born at term completed a questionnaire of musculoskeletal pain at mean age 24.1 (SD 1.4) years. Group differences were examined by logistic regression, adjusting for sex, age and source cohort (Model 1), potential early life confounders (Model 2), lifestyle covariates (Model 3) and depressive symptoms (Model 4).

Results – The late preterm group had lower odds for reporting neck pain (0.73; 95% confidence interval (CI): 0.56-0.96), which was further reduced when adjusting for potential early life confounders, lifestyle covariates and depressive symptoms (Model 4). Odds for reporting peripheral pain was 0.69 (95% CI: 0.48-0.99, Model 4) in the early preterm group. The odds for reporting any pain, shoulder, low back or widespread pain did not differ significantly between groups, although odds for reporting widespread pain was 0.77 (95% CI: 0.58-1.03, Model 4) in the late preterm group.

Conclusions – We did not find evidence of increased vulnerability to musculoskeletal pain in adults born early or late preterm. In contrast, our results suggest that adults born preterm have a slightly lower risk for reporting musculoskeletal pain, also when adjusted for lifestyle factors.
P7 - Poorer health-related quality of life in adults born with very low birth weight at 28 years of age; a follow-up of the NTNU Low Birth Weight Life cohort

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Background – Being born with a very low birth weight (VLBW:≤1500g) involves a high risk of developmental problems, but findings of health-related quality of life (HRQoL) in adulthood are mixed. We have previously reported lower HRQoL in VLBW individuals at 23 years, and declining HRQoL from 20 to 23 years in VLBW adults.

Objective – Examine whether VLBW individuals have poorer HRQoL compared with a term-born controls at 28 years, and whether their HRQoL shows a further decline from 23 to 28 years.

Design – Follow-up study of 51 VLBW (25 females/26 males) and 86 (48 females/38 males) term-born control members of the NTNU Low Birth Weight Life cohort at 28 years. Participants completed the Short Form 36 Health Survey (SF-36). Data on SF-36 were also available for 52 VLBW and 77 controls at 20 years, and 35 VLBW and 37 controls at 23 years. We used linear regression to analyze group differences, adjusted for age and sex, and linear mixed models to analyze changes across the three time points, adjusted for sex.

Results – At 28 years, the VLBW group had significantly lower scores for all but one domain (bodily pain, p=0.06). There were group differences in change over time for general health (p=0.003) and role limitations due to emotional problems (p=0.022). General health decreased from 20 to 23 years in both groups, but increased from 23 to 28 years in the control group only (p<0.001). The VLBW group had decreased scores for role-emotional from 20 to 23 years (p=0.019), but no further change from 23 to 28 years.

Conclusions – VLBW adults reported poorer HRQoL at 28 years compared with term-born controls. Between 20 and 28 years, differences between VLBW adults and term-born controls increased first in role limitations due to emotional problems and then in general health.
O6 - MATERNAL EARLY-PREGNANCY GLUCOSE-INSULIN METABOLISM, FETAL GROWTH AND ADVERSE BIRTH OUTCOMES: THE GENERATION R STUDY

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Background – Gestational diabetes is related to increased risks of perinatal complications. It is unknown whether maternal glucose-insulin metabolism, already in early-pregnancy, influences fetal growth and risks of adverse birth outcomes, and whether these effects are modified by maternal prepregnancy BMI.

Objective – To assess the associations of maternal early-pregnancy glucose-insulin metabolism with fetal growth and risks of adverse birth outcomes, in addition to maternal prepregnancy BMI.

Methods – In a population-based cohort among 6114 pregnant women, maternal glucose and insulin were measured in blood samples at a median 13.2 weeks of gestation (95% range 9.6-17.6 wks). HOMA-IR was calculated. We measured fetal growth in second and third trimester. We obtained maternal prepregnancy BMI by questionnaire and birth outcomes from medical records.

Results – Higher maternal early-pregnancy glucose, insulin and HOMA-IR were associated with higher estimated fetal weight from third trimester onwards, which led to a higher gestational-age-adjusted birth weight (p-values<0.05). Associations for insulin and HOMA-IR were explained by maternal BMI. Stratified analyses showed that only among obese women, higher maternal glucose was related to higher third trimester estimated fetal weight and gestational-age-adjusted birth weight (differences: 0.12 SDS (95% CI: 0.01, 0.23), 0.14 SDS (95%CI: 0.03, 0.24) per SDS increase in glucose, respectively). Higher maternal early-pregnancy glucose, insulin and HOMA-IR were associated with increased risks of a large-size-for-gestational-age infant, independent of maternal BMI (Odds Ratios: 1.16 (95% CI: 1.05, 1.27), 1.13 (95%CI: 1.02, 1.25), 1.14 (95%CI: 1.03, 1.25) per SDS increase in glucose, insulin, HOMA-IR, respectively). Effects were strongest among normal weight women. No associations with preterm birth or small-size-for-gestational-age at birth were present.

Conclusions – A suboptimal maternal glucose-insulin metabolism, already in early-pregnancy, is associated with higher third trimester fetal growth rates and an increased risk of delivering a large-size-for-gestational-age infant. These effects are only partly explained by maternal prepregnancy BMI.
P8 - Liver fat assessed by Magnetic Resonance Imaging and Cardio-metabolic Risk Factors in School-age Children

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Background – Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and is associated with cardiovascular disease in adulthood. It is unclear whether NAFLD is already associated with cardio-metabolic risk factors in children and whether the associations are restricted to NAFLD or also present across the full spectrum of liver fat accumulation.

Objective – To examine the associations of liver fat accumulation with cardio-metabolic risk factors in 10-year-old children.

Design – In 3,170 children with a mean age of 9.8 years (95% range: 9.4–10.8) participating in the Generation R Study, we measured liver fat fraction (in %) by Magnetic Resonance Imaging. At the same age, we measured body mass index (BMI), blood pressure and serum lipids, glucose, insulin and C-reactive protein blood concentrations. Childhood BMI was categorized into normal weight and overweight or obesity, using the International Obesity Task Force cutoffs.

Results – The median liver fat fraction in normal weight children was 2.0% (95% range: 1.2–4.1%) and in overweight children was 2.6% (95% range: 1.4–10.4%). In total, 2.8% of all children had NAFLD with more than ≥ 5% liver fat (95% range: 5.1–19.5%, median 6.5%). A higher liver fat fraction was associated with higher blood pressure and higher insulin, total cholesterol, LDL-cholesterol, triglycerides and C-reactive protein levels and with lower HDL-cholesterol levels (all adjusted p-values <0.01). The associations remained similar after adjustment for BMI and tended to be stronger in overweight children. Liver fat fraction was not associated with glucose concentrations.

Conclusions – Our results suggest that higher liver fat is associated with increased risk of cardio-metabolic risk factors at school-age, especially in overweight children. Further studies are needed to assess whether liver fat fraction in childhood is also associated with cardiovascular disease in later life.
Background – Four to five percent of children face parent’s death before reaching adulthood, which has been shown to increase the offspring’s risk to poor health outcomes and adverse social consequences.

Objective – We aimed to find out whether parent’s death abbreviated the time to a diagnosis of any psychiatric disorder in the offspring and to study the effect of the most common death causes on this association.

Design – The sample from the Northern Finland Birth Cohort 1986 includes 422 cohort members with parental death before the cohort member’s 18th birthday, and 6172 control subjects. Data on time and cause of parents’ deaths were obtained from the Cause of Death Register; and on time of the diagnoses of psychiatric disorders of the offspring up to 28 years of age through various healthcare registers. We compared the time to a diagnosis between the cohort members with and without parental death using Kaplan-Meier analysis and Cox regression.

Results – Of specified death causes, 334 (79.1%) were due to natural and 84 (19.9%) due to unnatural death causes. The cohort members with parental death were given a diagnosis of a psychiatric disorder earlier than their control subjects (10-year survival proportions: 88.6% vs. 93.1%, p<0.001). The corresponding survival proportions were 87.1% vs. 94.0% (p=0.068) for neoplasms and 88.9% vs. 95.6% (p=0.009) for endocrine, nutritional and metabolic diseases within natural death causes and 85.6% vs. 90.8% (p=0.052) for suicides within unnatural death causes.

Conclusions – This study provides a viewpoint for prevention of mental health problems among children and adolescents who lose their parent. Our study findings indicate that prevention of adversities should begin already when parent falls ill, especially with those chronic illnesses that are most common death causes in the population.
Objective – The aim was to assess whether loci associated with metabolic traits also have a significant role in BMI and mental traits/disorders.

Methods – We first assessed the number of single nucleotide polymorphisms (SNPs) with genome-wide significance for human metabolism (NHGRI-EBI Catalog). These 516 SNPs (216 independent loci) were looked-up in genome-wide association studies for association with body mass index (BMI) and the mental traits/disorders educational attainment, neuroticism, schizophrenia, well-being, anxiety, depressive symptoms, major depressive disorder, autism-spectrum disorder, attention-deficit/hyperactivity disorder, Alzheimer’s disease, bipolar disorder, aggressive behavior, and internalizing problems. A strict significance threshold of $p < 6.92 \times 10^{-6}$ was based on the correction for 516 SNPs and all 14 phenotypes, a second less conservative threshold ($p < 9.69 \times 10^{-5}$) on the correction for the 516 SNPs only.

Results – 19 SNPs located in nine independent loci revealed $p$-values $< 6.92 \times 10^{-6}$; the less strict criterion was met by 41 SNPs in 24 independent loci. BMI and schizophrenia showed the most pronounced genetic overlap with human metabolism with three loci each meeting the strict significance threshold. Overall, genetic variation associated with estimated glomerular filtration rate showed up frequently; single metabolite SNPs were associated with more than one phenotype. Replications in independent samples were obtained for BMI and educational attainment.

Conclusions – Approximately 5-10% of the regions involved in the regulation of blood/urine metabolite levels seem to also play a role in BMI and mental traits/disorders and related phenotypes. If validated in metabolomic studies of the respective phenotypes, the associated blood/urine metabolites may enable novel preventive and therapeutic strategies.
Background – Attention Deficit Hyperactivity Disorder (ADHD) is often accompanied by various psychiatric disorders during the life cycle. Previously we found that childhood emotional and behavioural symptoms predict adolescent ADHD with psychiatric comorbidity. Since comorbid ADHD is related to impairment in many domains of functioning, it is essential to identify other possible childhood factors predicting this severe form of ADHD.

Objective – We investigated whether childhood learning deficits and school success predict adolescent ADHD with and without psychiatric comorbidity.

Design – The study population was based on the non-selected Northern Finland Birth Cohort 1986 (N = 9,432). At the age of 8 years, children’s academic functioning was assessed by teachers. In adolescence, a subpopulation (n = 457) and their parents were interviewed with the Kiddie-SADS-PL and clinical psychiatric diagnoses were made. Adolescent ADHD was diagnosed in 105 individuals; among those, 49 had comorbid diagnoses of behavioural disorder, substance use disorder, or depressive disorder.

Results – Preliminary results suggest that childhood learning deficits may predict adolescent ADHD with comorbidity.

Conclusions – Teachers may have a key role in identifying children in need of pedagogical evaluation and subsequent support in learning due to increased risk of adolescent ADHD with comorbidity.
Background – To address the alarming reports of babies born with microcephaly due to Zika virus (ZIKV) infection in the mothers, large multicenter birth cohorts were funded across Latin America and the Caribbean, which are currently still recruiting pregnant women. Despite our growing understanding of the risk of ZIKV-related microcephaly, researchers are still working to understand regional variability in the risk of microcephaly and the clinical phenotypes beyond microcephaly. The possibility that ZIKV-related neurodevelopmental, auditory, or ocular abnormalities that go undetected at birth may manifest in infancy or early childhood if of particular concern. Also, given the hypothesis of potential interaction between Zika virus and other flaviviruses, the size of the cohorts needs to be large enough to allow stratification for background exposure to other flaviviruses, in particular dengue. Finally, with the decrease in transmission of Zika in many countries, the cohorts offer unique opportunities for research on other communicable and non-communicable diseases.

Objective – To map out a strategy for the integration of ongoing multicenter ZIKV-related birth cohorts into a (global) platform of birth cohorts and facilitate the exchange of scientific ideas and hypotheses. To open up the Zika birth cohorts for research on other communicable and non-communicable diseases. To discuss opportunities for protocol adaptation, data sharing, ethical issues, governance, and biobanking.

Design – The ongoing ZIKV birth cohorts in Latin America and the Caribbean were designed to estimate the risk of congenital and developmental abnormalities in infants born to mothers with confirmed ZIKV infection during pregnancy. Repeat blood samples are collected from mothers and infants. Across the EU-funded birth cohorts, the ages-and-stages and Bayleys ASQ3 instruments are used to measure developmental milestones. The protocols, case report forms, and data dictionaries were harmonized across the three EC-funded Zika birth cohorts. A joint statistical analysis plan is in preparation. In addition, a WHO-led effort aims at a harmonization with ongoing cohorts funded by Fiocruz and the US NIH and CDC, amongst other partners. Thus, a sizable multicenter birth cohort effort is currently under way in Latin America and the Caribbean.

Conclusions – The ZIKV birth cohorts in Latin America and the Caribbean offered the unique opportunity to generate harmonized protocols for birth cohorts in the region and possibly beyond. The investment in setting up the cohorts needs to be matched with a strategy for sustainability, taking into account opportunities for future research on other communicable and non-communicable diseases.
O8 - Prenatal cigarette smoke exposure and DNA methylation changes in adulthood

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Background – Maternal smoking during pregnancy alters DNA methylation in the exposed offspring. Many of these methylation changes appear to persist throughout childhood and into adolescence but whether they endure into adulthood is unclear.

Objective – To assess whether exposure to maternal smoking during pregnancy is associated with long-term changes in DNA methylation in the offspring.

Design – We assessed the association between maternal smoking in pregnancy and offspring blood DNA methylation at over 450,000 CpG sites by using the Illumina 450K BeadChip or Illumina EPIC 850 in 2,821 individuals (age between 16 and 48 years) from five prospective birth cohort studies.

Results – A meta-analysis of these studies showed evidence for 70 differentially methylated CpGs in 37 genomic regions (p-value < 1x10⁻⁷). All of these CpG sites showed similar direction of effects to that reported in previous studies with newborns (i.e. cord blood DNA methylation levels). We found a dose dependent effect on DNA methylation level in relation to smoking intensity during pregnancy, and longitudinal analysis indicated that the methylation changes observed at birth persisted largely into middle age; sensitivity analysis demonstrated that the associations were not mediated through offspring’s own smoking or paternal smoking behaviour, indicating intrauterine mechanisms.

Conclusions – Our findings provide evidence for the intra-uterine effects of maternal smoking on offspring methylome. Further studies are needed to identify potential implications of such epigenetic modifications for ill health later in life.
P12 - Cardiac autonomic function in adults born preterm; ESTER preterm birth study

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Background – Adults born preterm show several distinct risk factors for cardiovascular disease. However, whether preterm birth is associated with impaired cardiac autonomic function in adulthood is unclear.

Objective – We hypothesized that preterm birth is associated with impaired cardiac vagal modulation in young adults, measured by heart rate variability.

Design – We studied the association between preterm birth and cardiac autonomic function based on heart rate variability measurements in 600 adults with a mean age of 23.3 years. Participants were recruited through the Northern Finland Birth Cohort 1986 or Finnish Medical Birth Register. There were 117 participants born early preterm (< 34 wk), 207 born late preterm (34–36 full weeks), and 276 born term (controls). The autonomic function was assessed by calculating heart rate variability measures in time- and frequency domains and by analyzing the data with linear regression.

Results – Compared with the control group, the mean root mean square of successive differences, an indicator of cardiac vagal activity, was 12.0% (95% confidence interval [CI] 0.5% to 22.2%) lower in the early preterm group and 7.8% (95% CI -2.0% to 16.8%) lower in the late preterm group. The mean low frequency power, an additional indicator of cardiac vagal activity, was 13.6% (95% CI, 1.8% to 26.7%) lower in the early preterm group and 16.4% (95% CI 4.3% to 27.0%) lower in the late preterm group. The mean high frequency power, which quantifies cardiac vagal modulation in respiratory frequency, was 19.2% (95% CI -3.0 to 36.6%) lower in the early preterm group and 13.8% (95% CI -5.4% to 29.4%) lower in the late preterm group.

Conclusions – Preterm birth is associated with reduced cardiac vagal control in young adulthood. This association remains both in early and late preterms. Impaired autonomic control may be one mechanism underlying increased cardiovascular risk in adults born preterm.
**Background** – In Finland, guidelines for screening of gestational diabetes mellitus (GDM) were changed from the risk-based to comprehensive in 2008, which was expected to increase the prevalence of GDM. The significance for health of women and offspring is not yet known.

**Objective** – The Finnish Gestational Diabetes Study (FinnGeDi) was established to identify clinically relevant geno- and phenotypes of GDM diagnosed according to the new guidelines. Short- and long-term consequences of GDM on health of the mother and child, and across the generations, were objectives to follow.

**Design** – The FinnGeDi includes two cohorts founded and maintained by National Institute for Health and Welfare. The case-control cohort utilizes questionnaire, hospital and Medical Birth Register (MBR) data, and a DNA sample from the pregnant woman, her child and child’s father. (Epi) genomewide array has been analysed from a subset. In the register-based cohort all women, including those with GDM, delivered in 2009 were identified from MBR. Their children, children’s fathers and grandparents are included in the study and the data are compiled other national registers. The register-based follow-up will be performed regularly and continued for decades for both cohorts.

**Results** – In the case-control cohort, 1146 women with GDM and 1066 without GDM were recruited from seven delivery hospitals in 2009-2012. Women with GDM were older, more often obese and multiparous, had more often pre-eclampsia and their newborns had higher gestational-age adjusted birth weight as compared to controls. In the register-based cohort, 59918 women gave birth in 2009. Of them, 42.6% were screened and 8.9% diagnosed with GDM. Rates of labor induction and caesarean section were significantly higher in GDM group.

**Conclusions** – These results quantify the risks associated with GDM on a population level during comprehensive screening era. Both cohorts serve as comprehensive databases for future research.
P13 - Parental somatic illnesses and their association with subsequent externalizing and internalizing symptoms in children; Northern Finland Birth Cohort 1986 study

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Background – Parental illness can be a stressful event for children establishing a potential threat to mental and physical health of the children. However, the overall picture of the impact of parental somatic illnesses on behavioral problems in children is lacking.

Objective – To investigate whether parental somatic illnesses during childhood increase externalizing and internalizing problems in children at the age of 15-16. And if so, which specific parental illnesses are most relevant in this respect.

Design – The Northern Finland Birth Cohort 1986 covers all children (9432 in total) born alive in Northern Finland during one year. We compared children with and without each parental somatic illness. Analysis of variance was used to evaluate the impact of parental somatic illness on children’s problems measured by Youth Self Report (YSR) questionnaire (total, externalizing, internalizing symptom scores) at the age 16. Problems at age 8 evaluated by Rutter Children Behavior Questionnaire by the teachers were used as a covariate.

Results – There were several statistical significant associations. Most associations were found between maternal illness and males’ YSR externalizing scores, and maternal illness and females’ YSR internalizing scores. Paternal illness did not produce any statistically significant associations with YSR scores in females. Only one association was found between paternal illness and YSR scores in males. Mostly, if a parent had a specific somatic illness diagnosis, the child scored higher in YSR scores.

Conclusions – The impact of parental somatic illness on children’s behavioral problems is a complex issue. Our findings indicate that some of the maternal somatic illnesses may represent a potential threat to children’s mental health. Especially boys seem more vulnerable. More research is needed to understand the complex interface between the child, parental illness and other factors associated with children’s outcomes.
P14 - Early childhood BMI rise, the adiposity rebound, associates with PCOS diagnosis and obesity at ages 31 and 46 years - analysis of 46-year growth data from birth to adulthood in PCOS


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Background – The age at adiposity rebound (AR), at which BMI begins to rise after infancy around the age of 5 yrs, is associated with obesity and metabolic alteration in later life. Given that polycystic ovary syndrome (PCOS) has strong metabolic components, early growth patterns could reveal predisposition for PCOS.

Objective – We aimed to investigate the associations of growth trajectories from birth to puberty with PCOS diagnosis, body composition and hyperandrogenism later in adulthood.

Design – In this prospective, population-based longitudinal Norther Finland Birth Cohort 1966 study, women reporting isolated PCOS symptoms at age 31 (n=651), or PCOS diagnosis by age 46 (n=280) were compared with asymptomatic women (n=1573). Growth data from birth to 13 years, weight, height, serum testosterone levels at menarche, 14, 31 and/or 46 years were analyzed.

Results – Women with PCOS had lower birth weight (3·406 vs. 3·507g, p<0·001), earlier AR (5·19 vs 5·60 yrs, p<0·001) and higher BMI at menarche compared with controls. Early timing of AR associated with PCOS-diagnosis independently from BMI (OR:1·62, CI:1·37-1·92). Women with PCOS with early AR had an higher BMI at menarche and at age 31 and 46 compared with controls with early AR or PCOS with normal/late AR. Early AR was not associated with serum testosterone levels either at 31yrs or 46yrs.

Conclusions – Early AR associated with PCOS diagnosis later in life with additional risk for high BMI from menarche onwards in these women. Thus, adolescents with early AR and persisting high BMI at menarche should be screened for PCOS symptoms, such as persisting irregular cycles and hirsutism.
Background – Fetal growth restriction is associated with higher risks of impaired lung function and respiratory diseases in later life. Fetal blood flow redistribution might contribute to these associations.

Objective – We examined the associations of fetal body and pulmonary blood flow with wheezing patterns in early childhood, and lung function and asthma in later childhood.

Design – In a prospective cohort study among 903 pregnant women and their children we measured umbilical, cerebral and pulmonary fetal blood flow by pulsed-wave-Doppler at a median gestational age of 30.3 (95% range 28.8–32.3) weeks. A higher umbilical artery pulsatility index (PI)/cerebral artery PI (U/C) ratio indicates fetal blood flow redistribution in favor of the fetal brain at expense of the trunk. A higher pulmonary artery time velocity integral (TVI) indicates higher pulmonary vascular resistance. We measured wheezing patterns (early, late/persistent) until the age of 6 years by questionnaires. At the age of 10 years, lung function was measured by spirometry and information on current asthma was obtained by questionnaire.

Results – No associations of fetal blood flow redistribution with wheezing in early childhood were found. However we observed a tendency for a higher umbilical artery PI and U/C ratio to be associated with a higher risk of early wheezing. A higher pulmonary artery TVI was associated with a higher risk of late/persistent wheezing (OR (95%CI): 1.14(1.01-1.29) per unit increase in TVI)). A higher middle cerebral artery PI was associated with a higher FEV1/FVC (Z-score (95%CI): 0.21(0.01-0.42)). Results did not materially change after additionally adjustment for birth weight, gestational age at birth or childhood BMI. No further associations of fetal blood flow redistribution or pulmonary vascular resistance with lung function or current asthma were observed.

Conclusions – Fetal blood flow redistribution and higher pulmonary vascular resistance may have persistent consequences for lung development and for respiratory health.
Continuous tracking of BMI from birth to adolescence reveals BMI acceleration during preschool age as critical risk factor for developing sustained obesity

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Background - We assessed BMI dynamics of children from birth into adolescence to evaluate at what age obesity manifests and whether there is a vulnerable age for developing sustained obesity.

Design - We performed intra-individual prospective and retrospective analyses of continuous BMI courses on a population-based sample of 51,505 subjects with consecutive anthropometric data available during childhood (0-14 years) and adolescence (15-18 years). Additionally, we assessed the dynamics of annual BMI increments (ΔBMI-SDS) during childhood in 34,196 children.

Results - Retrospectively, the majority of normal-weight adolescents had always been normal-weight throughout childhood. The majority of adolescents being obese had been overweight or obese (53%) from 5 years onwards then further continuously increasing BMI with age. Prospectively, 87% of children who were obese at 3 years became overweight/obese in adolescence. In adolescents with overweight/obesity, the strongest acceleration in ΔBMI-SDS had occurred between age 2 to 6 years and remained positive thereafter indicating further continuous weight gain. A high ΔBMI-SDS acceleration particularly in preschool age imposed an 1.4fold increased risk of adolescent overweight/obesity compared to BMI acceleration in school age. Children born large for gestational age became more often overweight/obese (43.7%) compared to adequate (28.4%) or small (27.2%) newborns, resulting in an 1.5fold increased risk for adolescent obesity. Additional data from the LIFE Child cohort confirmed maternal obesity as a major risk factor for childhood obesity, but it did not affect the dynamics of the BMI development in the children.

Conclusions - In children with adolescent overweight/obesity, the strongest weight gain occurred between 2 and 6 years of age. The majority of children who are obese at that age will become obese in adolescence. Hence, this period at preschool age is the critical window for developing obesity.
Background - Schizophrenia has one of the highest heritability estimates in psychiatry. According to the diathesis-stress model of schizophrenia, environmental stressors including early adversity catalyze the association between genetic risk and psychosis onset. Furthermore, poor performance in judging different emotions from faces is a common feature in patients with schizophrenia and might be present in individuals with predisposition to schizophrenia.

Objective - Here we explore whether an individual’s polygenic risk score for schizophrenia (PRS) is associated with their degree of interregional similarities in BOLD signal and gray-matter volume of the face-processing network, and whether the exposure to early adversity moderates this association.

Design – A total of 90 individuals (mean age 22 years, both functional and structural data available) were used for discovery analyses and 211 individuals (mean age 26, only structural data available) were used for replication of the structural findings. Both samples were drawn from the Northern Finland Birth Cohort 1986. Questionnaire data were utilized to assess retrospectively the degree of early adversity.

Results - We found that the degree of interregional similarities in BOLD signal and gray- matter volume vary as a function of PRS; lowest interregional correlation (both measures) is observed in individuals with high PRS. We were also able to replicate the gray-matter volume finding. Using both the BOLD signal and gray- matter volume, we did not discover consistent early adversity by PRS on interregional correlation.

Conclusions - We suggest that our findings indicate that PRS for schizophrenia may lead to perturbations in the extraction of information relating to significance of faces.
Conclusions – Early social adversity increases the risk of adult obesity independent of BMI PRS, maternal BMI and sex. However, this risk may be modified through changing own exposure to social adversity in adulthood. Our findings can guide personalized obesity prevention targeting those exposed to high social adversity in early life.

Background – An individual’s risk of obesity begins at conception and is modified by environmental and biological factors throughout the lifecourse. Fetal exposure to social adversity has been linked to adult obesity. However, it is unclear whether this is due to programming effects or mediated by genetic or maternal risk factors.

Objective – Our aim was two-fold: i) to explore pathways in which fetal exposure to social adversity is associated with adulthood obesity; ii) to assess whether obesity risk can be influenced by changing own exposure to social adversity.

Design – Participants were from the Northern Finland Birth Cohort 1966 (n=5,861). Fetal social adversity was a composite variable including maternal and paternal occupation, maternal education and material wealth. Adult social adversity comprised education, occupation, employment status and home ownership at 46 years. Total factor scores were divided by interquartile range representing high (25%), intermediate (50%) and low (25%) exposure to social adversity. We used linear regression to assess the relationship with adult body mass index (BMI). Analyses were adjusted for BMI polygenic risk score (PRS), maternal pre-pregnancy BMI and sex.

Results – Early exposure to intermediate (β=0.45; 95%CI=0.06,0.84; P<0.05) and high social adversity (β=0.70; 95%CI=0.24,1.16; P<0.05) were associated with higher BMI at 46 years compared with low social adversity exposure, even following adjustment for BMI PRS, maternal BMI and sex. In adulthood, 25% of people had reduced their exposure to social adversity and this was associated with lower BMI than those who experienced increased exposure to social adversity (β=-0.51; 95%CI=-0.95,-0.07; P<0.05).
P18 - Northern Finland Birth Cohort 1986: study of extracellular nano vesicles exosomes in mental health

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Background – The exosomes are a group of secreted extracellular vesicles (EV) (30–100 nm) assembled in the multi-vesicular bodies. They are present widely in biological fluids such as breast milk, saliva, urine, blood and cerebrospinal fluid (Karla et al., 2016). The exosomes constitute a newly identified layer on homeostasis control since they cargo several types of molecular factors such as miRNAs, proteins, lipids and metabolites between cells (Krause et al., 2018, 2015). Exosomes can cross Blood-Brain-Barrier which is crucial for it’s function in addiction and neuropsychiatric disorders (Grabrucker et al., 2016). Neuropsychiatric implementation of nanomedicine via the secreted nano-vesicles provide a promising opening to develop novel diagnostics and therapeutics.

Objective –
1. Profiling of exosome derived biomarkers from blood of human subjects to find possible correlations with mental health and addictive behavior.
2. Detecting brain derived exosomes in the body fluids (Mustapic et al., 2017).
3. Detecting functionality and fate of labeled exosomes in the body fluid by hyperspectral camera.
4. Detecting functionality and fate of labeled exosomes in brain by MRI, PET.

Design – The exosomes have been extracted as pilot from 12 (3 males, 3 females of smoking mothers; 4 males, 2 females of non-smoking mothers) out of 426 serum samples (collected in 2001) from Northern Finland Birth Cohort (NFBC) 1986 by ExoSpin® (Qiagen, Hilden, Germany) and ExoEasy® (Qiagen, Hilden, Germany) Serum/Plasma kits. Nanoparticle Tracking Analysis, electron microscopy and qPCR data (Cq values) analysis of some potential miRNA biomarkers for addiction and psychiatry.

Results – Nanoparticle Tracking Analysis has detected concentration and intensity of nanoparticles of variable size in serum. It has also detected number of vesicles per ml of serum. Exosomes have been detected through electron microscopy of the serum samples. qPCR data (Cq values) of following 5 potential miRNA biomarkers were analyzed: miR-24a-3p (up-regulated in major depression and smoking), miR-99a-5p (up-regulated in schizophrenia), miR-320b (up-regulated in schizophrenia), miR-103a-3p (down-regulated in schizophrenia) and miR-193b-3p (down-regulated in schizophrenia). No significant differences in Extracellular Vesicles levels have been detected between females/males whose mothers either smoked or did not smoke during pregnancy.
Conclusions – Brain exosomes have some diagnostic, prognostic and therapeutic roles and would also have a function in the brain. miRNA biomarkers typical for addictions and psychiatric disorders could be detected in serum samples from NFBC1986. Identification of the brain derived exosomes and tracking of exosomes in brain by imaging could be done using mouse models and neural primary cell derived exosomes that have been engineered to contain the Cre-enzyme. When such exosomes being injected to floxed rosa26 reporter mice (lacz or GFP) perhaps could offer us ways for imaging exosomes.
Background – Lactase non-persistence (LNP) is the inability to digest lactose after weaning, the trait is heritable. The genotype frequency varies globally, with lowest frequencies of LNP in Nordic Countries (~10%). Previous European studies have found conflicting associations between LNP and obesity.

Objective – We aimed to investigate if the LNP genotype was associated with obesity at two adult time points and whether this could be attributed to differences in dietary/dairy intake.

Design – We analyse the participants from the Northern Finland Birth Cohort 1966 (N=4242), the genetic data was extracted during the clinical examination. The sample was categorised according to genotype (SNP: rs4988235), those with the homozygous recessive genotype were considered lactose intolerant (LI) whilst heterozygous and homozygous dominant were considered lactose tolerant. Dietary information was collected from postal questionnaires and BMI and waist circumference were measured during the 31 and 46 year clinical examinations. Linear regression was used to examine the relationships between diet, BMI and waist circumference with LI, analyses were sex adjusted.

Results – We found that 14.4% of participants were LI, slightly higher than the Nordic country average. At age 31, we observed an association between the LI phenotype and lower BMI (β=-0.37; 95%CI=-0.68,-0.05; P=0.03) and waist circumference. (β=-1.00; 95%CI=-1.87,-0.15; P=0.02). However, at 46 years, this relationship was no longer observed (P>0.05). At this time, only 30% of those with the LI genotype reported following a lactose free diet, however there was a significance between being LI and following a lactose free diet (P=<0.0001).

Conclusions – LI was associated with obesity at age 31 but not 46 years, suggesting that other factors such as diet differences are related to obesity as age increases. At the 46 year follow up in 2012 there were more lactose-free dairy products, compared to the 31 year-follow-up, possibly contributing to the decreased differences in diet.
P20 - Influence of maternal and fetal 25-hydroxyvitamin D levels on lung function and atopic disease development

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**Background** - Exposure to low levels of vitamin D in fetal life might be a risk factor for childhood asthma and allergy. We examined whether 25-hydroxyvitamin D levels in mid-gestation and at birth were associated with lung function, allergic sensitization, asthma and allergy at school-age.

**Methods** - We performed a population-based prospective cohort study among 2,809 Dutch mothers and their children. Maternal blood samples in mid-gestation and umbilical cord blood samples at birth were used to determine 25-hydroxyvitamin D levels. At age 10 years, lung function was measured by spirometry (forced expiratory volume in 1 second (FEV\textsubscript{1}), forced vital capacity (FVC), FEV\textsubscript{1}/FVC, forced expiratory flow at 25-75\% of FVC (FEF\textsubscript{25-75}) and forced expiratory flow (FEF\textsubscript{75})), inhalant allergen sensitization by skin prick tests, and physician-diagnosed asthma and inhalant allergy by postal questionnaire. For associations analyses, multivariate linear and logistic regression models were applied.

**Results** - Maternal levels of 25-hydroxyvitamin D in mid-gestation were not associated with lung function, asthma diagnosis, inhalant allergen sensitization or reported inhalant allergy. Compared with optimal 25-hydroxyvitamin D levels (> 75.0 nmol/L), deficient 25-hydroxyvitamin D levels at birth (< 50 nmol/L) were associated with a higher risk of inhalant allergic sensitization (adjusted odds ratio (95\% CI): 1.51 (1.11, 2.06)).

**Conclusion** - Our results suggest that deficient 25-hydroxyvitamin D levels at birth were associated with a higher risk of inhalant allergen sensitization in school-age children, but not with asthma.
P21 - Temporal changes in the incidence of treated psychiatric and neurodevelopmental disorders during adolescence; An analysis of two national Finnish Birth cohorts

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Background – Diagnoses of many adolescent mental health problems are proliferating. We address a lack of national time-trend studies on adolescent service use for a wide range of psychiatric outcomes.

Objective – We reviewed data from two national cohorts, 10 years apart, to establish the change in use of specialised services for psychiatric and neurodevelopmental diagnoses in Finland.

Design – We followed two population-based birth cohorts of all 59,472 and 58,802 individuals born in Finland in 1987 and 1997, respectively, from the 12th until the 18th birthday. The data were obtained retrospectively from Finnish nation-wide registers.

The primary outcome was time to incident specialized service use with a psychiatric or neurodevelopmental disorder diagnosis, treatment for self-harm, or suicide death (SSU). Additionally, we investigated 19 more specific classes of mental health outcomes.

Hazard ratios were estimated using Cox regression, adjusting for socio-economic factors: maternal smoking, maternal age, parents‘ education and social assistance benefits.

Results – The cumulative incidence of SSU was 15.0% (95% confidence interval (CI) 14.4%–15.6%) among females in the 1997 cohort, an increase of 5.2 percentage points (95% CI 4.8–5.6); among males, the increase was 2.7 percentage points into 8.9% (95% CIs 2.4–2.9, 8.5%–9.4%). Adjusted hazard ratios of SSU, contrasting the cohorts, were 1.61 (95% CI 1.50–1.72) and 1.47 (95% CI 1.35–1.60) for females and males respectively. With the exception of schizophrenia, increased incidence was observed for all outcomes: hazard ratio estimates ranged from 1.15 to 6.11.

Conclusions – An increasing proportion of young people are coming to contact with specialized mental health related services during adolescence. Regardless of gender, this increase is evident across the varied spectrum of psychiatric and neurodevelopmental disorders and self-harm.
Fatherless men have broken hearts as adults – The Helsinki Birth Cohort Study 1934–1944

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Background – Although marriage was normative when having children 80 years ago, 8 percent of babies were born out of wedlock. Unmarried mothers were usually women from lower socioeconomic groups and their children were overrepresented among poor relief recipients. Cardiovascular disease (CVD) originates in childhood and according to a large number of studies poor socioeconomic circumstances in early life increase the risk of CVD in later life.

Objective – We studied the association between maternal marital status at birth and parental occupation and CVD in adulthood in 13345 people born in 1934–1944 in Helsinki, Finland.

Design – We analyzed the data from the Helsinki Birth Cohort Study including birth, child welfare clinic and school healthcare records. Using the personal identification number we followed the subjects from 1971 to 2014 and identified deaths and hospital admissions from CVD.

Results – Being born to an unmarried mother was associated with increased CVD risk especially among those born before World War II (1934-1939), but not among those born during the war (1940–1944). The Hazard ratio for stroke among men born out of wedlock in the pre-war period was 1.85, 95% confidence interval 1.17, 2.92 and for CVD 1.49, 95% confidence interval 1.04, 2.13. For CVD the association was attenuated when adjusted for offspring adult educational attainment but for stroke remained statistically significant.

Conclusions – Being born out of wedlock 80 years ago is associated with health disadvantages throughout life especially among those born out of wedlock before World War II. Reduced socioeconomic differences due to food rationing, but also investments made in maternal and child welfare in the early 20th century and during the war, may have improved the position of unmarried mothers and their babies during the war as compared to pre-war period.
Background – Depression during pregnancy is common, but long follow-ups of the offspring of antenatally depressed mothers till middle adulthood are lacking.

Objective – The aim was to study whether offspring of antenatally depressed mothers have an elevated risk for several severe mental disorders till middle adulthood, taking account parental severe mental disorder.

Design – In the general population-based Northern Finland 1966 Birth Cohort with 12,058 children born alive, mothers were asked at mid-gestation if they felt depressed. The offspring were followed for over 40 years. Severe mental disorders were detected in the offspring till middle adulthood and also in the parents using the Finnish Hospital Discharge Register. Maternal smoking, perinatal risk, father’s social class and family type were considered as confounding factors.

Results – Adult offspring of antenatally depressed mothers had slightly, 1.5-foldly increased risk for severe depression and substance use when compared with the children of mothers without antenatal depression. The risk was not statistically significantly increased for bipolar disorder and schizophrenia.

The risks for severe depression (crude OR 3.6; 95%CI 2.0-6.4) and bipolar disorder (7.8; 2.6-23.1) and also for schizophrenia (4.3; 2.3-8.2) and substance use disorder (2.8; 1.7-4.7) were markedly higher in the offspring with both maternal antenatal depression and parental severe mental disorder, than in offspring with only one of these risk factors. The reference group was birth cohort members without maternal antenatal depression and without parental severe mental disorder. The risks remained statistically significant even after adjustment.

Conclusions – Maternal depression during pregnancy was associated with slightly increased risk for severe depression and substance use in the offspring when compared with the children of mothers without antenatal depression. Maternal antenatal depression combined with parental severe mental disorder was associated with increased risks for several severe mental disorders in the adult offspring.
To our knowledge, this is the first study of several severe mental disorders in the offspring of antenatally depressed mothers with long follow-up till middle age where familial vulnerability for severe mental disorders was taken into account in a general population-based sample.
Preterm birth and asthma according to age at diagnosis. The Finnish 1987-90 Birth Cohort

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Background – Preterm birth is associated with raised asthma risk in adults. Whether this risk is dose-dependent and changes during childhood and adolescence is unclear.

Objective – We examined the risk of asthma (based on Medical reimbursement) within gestational age (GA) groups: <28wks, 28-<32wks, 32-<34wks, 34-<37wks, 37-<39wks, (ref) 39-<42wks, ≥42wks during early life (birth-<2yrs and 2-<5yrs), in childhood (5-<10 years) and 10<15, and in adolescence (≥15 years- end of follow-up).

Design – Data on all births in Finland (1/1/1987-30/9/1990), from Medical Birth Registry (n=235624, GA: 98.7%) were linked with the Medical Reimbursement Register (birth-31/12/2013). In Finland, the entitlement for special medication reimbursement is based on physician’s statement following the criteria: need for continuous treatment (>6 months); reversible airflow obstruction. Association between GA and asthma was analysed by Cox regression, first-ever entitlement for medical reimbursement (asthma) as an outcome (adjs. sex, birth weight SD score, maternal smoking, age and parity, parental education and asthma history).

Results – 5.2% were born preterm. Entitlement for asthma medication reimbursement was granted to 6.1%. Dose-dependent relationship between preterm birth (GA<37wks) and asthma was identified: shorter gestation indicated higher asthma risk. This was highly significant in all preterm groups for the first 2 years of life, persisting up to 5 years of age. Those born during 28-<34wks and 34-<37wks had stable raised asthma risk at 5-10 years (HR: 1.2, 95% CI: 1.1-1.4), and for 32-<34wks (1.6, 1.1-2.5) and 37-<39wks (1.1, 1.0-1.3) asthma risk at ≥15 years of age persisted. Female sex, higher birth weight and older motherhood were protective whereas parental asthma history posed a stable asthma risk throughout.

Conclusions – Preterm birth and early-term births are associated with asthma (based of medical reimbursement). This association is strongest for asthma diagnosed in early years. Our results underscore the importance of careful respiratory follow-up of children/adolescents born preterm and early term.
P25 - Low vitamin D does not mediate the association between body mass index and chronic inflammation - Study from the Northern Finland Birth Cohort 1966

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Background – Obesity, vitamin D insufficiency and pro-inflammatory patterns often co-occur suggesting that intervention aiming to improve the vitamin D status can help to reduce the conversion of obesity into chronic co-morbid patterns. We have yet to study in greater detail if low vitamin D aggravate the inflammatory condition associated with obesity.

Objective – The objectives were to i) examine the associations of BMI and vitamin D [indicated by 25-hydroxyvitamin D, 25(OH)D] with a panel of inflammatory biomarkers and, ii) investigate whether the association of BMI with inflammatory markers could be mediated/influenced by 25(OH)D.

Design – We measured BMI, serum 25(OH)D, inflammatory biomarkers using data collected on 3,586 participants from the Northern Finland Birth Cohort 1966 at 31 years. Multiple linear regression analyses were used to evaluate the association of both BMI and 25(OH)D with inflammatory biomarkers. We performed Baron and Kenny mediation analyses to assess whether the association of BMI with inflammatory biomarkers was mediated through reduced 25(OH)D. To determine causality, Mendelian Randomisation (MR) was performed using SNP-estimates of 25(OH)D and CRP, AGP, sICAM-1 obtained from summarised data on genetic associations.

Results – Plasma inflammatory biomarkers correlated with each other forming four molecular clusters: interleukins, adhesion molecules, acute phase proteins and chemokines. BMI was positively associated with 10 inflammatory biomarkers in all four molecular clusters [(FDR)<0.05]. 25(OH)D was inversely associated with IL-8, sICAM-1, CRP and AGP (FDR<0.05). The associations between BMI and both AGP and sICAM-1 were modestly mediated through reduced 25(OH)D. However, Mendelian Randomisation using summarised data did not establish a causal relationship.

Conclusions – This evidence-based analysis based on prospective data, a large panel of inflammatory biomarkers as well a two-sample MR brings insufficient evidence to support a role for vitamin D in reducing the inflammatory load associated with obesity.
P26 - Cat ownership in childhood and development of schizophrenia

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Background – Studies indicate that having cat in the household during childhood might have a connection to development of schizophrenia. This connection can be explained by toxoplasma gondii which the cat carries. Higher levels of antibodies for toxoplasma gondii have been found in patients with schizophrenia.

Objective – We were able to study cat ownership at childhood and later development of schizophrenia and schizotypal traits in a birth cohort with the possibility to take into account a number of confounders.

Design – Participants were members of the Northern Finland birth cohort 1966 (NFBC 1966). In a survey, they were asked if they had had a cat in the household before the age of 7 years. Nationwide registers were used to detect participants with schizophrenia until the age 49 years. A questionnaire including Physical Anhedonia Scale (PAS), Social Anhedonia Scale (SAS), Perceptual Aberration Scale (PER) and Schizoidia Scale (SCHD) was completed at age of 31 years. In the analysis, potential confounders were sex, birth weight, urban/rural, maternal education, marital status of the mother, wantedness of pregnancy, maternal depression during pregnancy, and maternal smoking during pregnancy.

Results – The cumulative incidence of schizophrenia was 0.9 % in those who had cat in their household during childhood. Respective figure was 1.0 % (p=0.80) in those who had not cat in their household. Of the schizotypal scales SAS, PER and SCHD associated positively with cat ownership. After confounding Social Anhedonia Scale (SAS) associated positively with cat ownership in childhood (t=2.2 , p= 0.026).

Conclusions – Our study supported only partially earlier findings of the connection between cat ownership in childhood and later development of schizophrenia. There was no association between cat ownership and development of schizophrenia in the present study. On the other hand, cat ownership associated slightly with vulnerability to schizophrenia.
P27 - Meta-analysis of maternal smoking GFI1-CpGs and cardio-metabolic phenotypes in adults

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Background – Downstream impact of in-utero exposure to maternal smoking likely pervades through substantially modulated epigenetic patterns, leading to changes in gene expression, and in broader context development of cardio-metabolic diseases in later life.

Objective – To explore whether changes to GFI1-DNA methylation induced through maternal smoking during pregnancy associate with cardio-metabolic disorders in adults.

Design – Seventeen studies participated with a total sample size of 17,505. Majority of the studies included European ethnicity and two had mixed ethnicity. We analysed methylation in whole blood at eight GFI1-CpGs, cg04535902, cg09662411, cg09935388, cg10399789, cg12876356, cg18146737, cg14179389 and cg18316974. Seven cardio-metabolic phenotypes were included as primary outcomes; body mass index (BMI), waist circumference (WC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting glucose (FG), diastolic blood pressure (DBP) and systolic blood pressure (SBP). Linear regression analyses were conducted by participating studies and results were meta-analysed.

Results – The study had a total sample size of 17,505. In the meta-analysis, cg14179389 hypomethylation showed inverse association with BMI, WC, DBP and SBP, which became stronger when adjusted for sex, age and participant smoking. cg14179389 consistently showed the lowest heterogeneity and was robust for Bonferroni correction (p<7.14 x 10^-3). In contrast, positive association was observed between cg09935388, cg12876356, cg018316974 and cg09662411 hypomethylation with decreased BMI, WC and BP and increased HDL-C and TG (p<0.05). No change in effect observed when adjusted. Similarly, hypomethylation at cg04535902 and cg18146737 was observed to be associated with decreased BMI and WC and adjustments revealed stronger associations (p<0.05).

Conclusions – Our study has provided insight into the potential role of GFI1 on cardio-metabolic phenotypes and identified an epigenetic marker cg14179389, which may be of potential therapeutic relevance. It provides a proof of concept for the early life epigenetic programming of adult cardio-metabolic health.
Background – Tobacco smoking is one of the biggest challenges for global public health. People with psychosis are known to smoke more cigarettes and more intensively compared to general population. Smoking cessation in psychotic disorders includes specific issues to be considered.

Objective – This study aims to synthesize the evidence of effectiveness and safety of smoking cessation interventions in people with schizophrenia. The main objective was to systematically assess and review current evidence of the efficacy of smoking cessation interventions. Secondary objective was to assess the efficacy of psychosocial interventions.

Design – Systematic review and meta-analysis.

Results – 27 original studies of 23 original trials were included in qualitative synthesis and 11 trials were included in meta-analysis. Bupropion was most commonly studied intervention. Motivational interviewing was mostly studied psychosocial intervention. Bupropion was effective intervention in smoking cessation at the dose 300 mg/day measured by point prevalence abstinence (RR=3.33 95% CI 1.40-7.95) and continuous abstinence (RR=5.55 95% CI 1.33-23.16). Motivational interviewing combined with co-interventions was effective after few months in continuous abstinence (RR=1.93 95% CI 1.16-3.20). Varenicline was effective at the end of intervention measured by smoking reduction (RR=2.51 95% CI 1.01-6.19). In the long-term (at least 6 months after the end of intervention) there was no evidence of the effectiveness of interventions.

Conclusions – There are interventions for smoking cessation that are effective and relatively safety to use at least at clinically stable phases of psychotic disorders. The long-term effectiveness of these interventions is unclear and combination of different interventions and support may be needed to maintain abstinence from smoking in people with psychosis.
P29 – Childhood growth patterns associate with cardiovascular autonomic function in midlife; a prospective cohort study

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Background – Postnatal growth patterns, specifically, later peak of body mass index (BMI) during infancy (BMIP) and earlier BMI rebound in childhood (BMIR) are related to adverse cardiometabolic outcomes in adulthood. However, it is unclear if they associate with later cardiovascular autonomic function, an important risk factor associated with future cardiac events.

Objective – We tested the hypothesis that these growth patterns would associate with poorer cardiovascular autonomic function in midlife.

Design – At the age of 46, the subjects of the Northern Finland Birth Cohort 1966 participated in clinical examinations including measurement of vagally mediated heart rate variability (rMSSD) from R-R intervals (RRi) and cross-spectral baroreflex sensitivity (BRS) based on low frequency (LF) oscillations in RRi and systolic blood pressure (SBP) during sympathetic stimulus by standing position. LF power of SBP oscillations (LF_{SBP}) was used to describe peripheral sympathetic modulation of blood pressure. BMI at various ages was calculated from frequent anthropometric measurements collected from child welfare clinical records. Age at BMIP and BMIR were derived from random effect models fitted at 0-1.5 years and >1.5-13 years. Linear regressions included 895 subjects without cardiorespiratory diseases and diabetes for age at BMIP and 1,100 subjects for age at BMIR and were adjusted for birth, maternal and adult variables potentially confounding the relationship between early growth and autonomic function.

Results – Age at BMIR correlated negatively with LF_{SBP} (r=-0.084, p=0.005). This association remained significant after adjustments (p<0.01). Age at BMIR was not associated with BRS or rMSSD. Unexpectedly, age at BMIP correlated positively with BRS (r=0.087, p=0.009). This association diminished to nonsignificant after adjustments.
P30 – Pilot phases of CELSPAC: TNG

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Background – The Next Generation (TNG) study is longitudinal prospective birth cohort study. TNG is designed to identify important exposome factors and their effects on the child health. TNG is part of CELSPAC (Central European Longitudinal Studies of Parents and Children) infrastructure. This infrastructure also consists of Czech and Slovak ELSPAC and Ageing cohort of ELSPAC parents.

Objective – The main aim of this study is to introduce the pilot phases of TNG

Design – TNG study has been initiated in April 2015. The pilot phase was split into four independent sub-studies. The first sub-study had three aims; a) evaluate feasibility of a protocol for collection, processing and storing of biological samples (cord blood; venous blood, urine and buccal smear from mothers; stool, dry blood spot and buccal smear; b) estimate future study response rates; willingness to participate in the study. The aim of the second sub-study was to introduce information systems for online data processing and management of biological samples and on-line management software for administration of TNG study. The aim of the third sub-study was to evaluate on-line distribution and respond rate of questionnaires. The last step will be set up automated processing and storing of biological samples.

Results – Based on the samples quality assessment the protocol for all biological samples was prepared. It seems feasible to collect process and store in a freezer all types of samples within 180 minutes 24 hours per day 7 days per week. Majority of approached mothers were willing to participate in the study - 70 % of them donate cord blood, provide health data and fill basic questionnaire; 90 % of mothers were willing to donate venous blood in 38th week of pregnancy. Short questionnaires about baby development are more popular than others.

Conclusions – Based on the results of the pilot phase the full scale TNG study is scheduled to start in January 2018
P31 – Mortality in offspring of subjects with severe psychiatric disorders

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Background – The lifespan of people with Severe Mental Illness (SMI) is shorter compared to the general population, and this is mainly due to physical illness. There is only sparse literature of the mortality of offspring of people with SMI. Existing studies have reported that offspring of psychiatric inpatients are at higher risk of death from all causes; and further, that offspring of mothers with psychotic disorders have an almost two-fold higher mortality risk from birth until early adulthood.

Objective – We were able to study long-term the mortality and causes of deaths in the offspring of people with SMI.

Design – Participants were members of the Northern Finland Birth Cohort 1966 (NFBC 1966; N=12,231). The data of cause of deaths of the members of the NFBC 1966 was obtained from the Population Register Center until year 2015. Causes of deaths were divided into two categories: natural deaths and unnatural deaths. Alcohol related deaths were considered as unnatural deaths. The data of hospital treated psychiatric disorders in the parents was obtained from nationwide Care Register for Health Care. Cumulative incidences by age were calculated separately for natural and unnatural deaths in NFBC 1966 members having parent with SMI and those who did not have.

Results – Six percent (N=771) of the NFBC 1966 members had died during the follow-up. This number included 173 stillborn children. There were 465 (3,8 %) cases of natural deaths and 301 (2,5 %) cases of unnatural deaths. There were five cases whose the cause of death was unclear.

Conclusions – In the presentation, we will be able to compare causes of deaths in NFBC 1966 members with and without a parent with Severe Mental Illness. We aim to replicate the results in the Northern Finland Birth Cohort 1986 and in the National Birth Cohort 1987.
P32 – Cerebellar white matter in young adults with a familial risk for psychosis

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\textbf{Background} – Structural abnormalities of the cerebellum have been connected to psychotic disorders. However, the role of cerebellar white matter in development of psychosis is unknown.

\textbf{Objective} – Our objective was to find out if there are differences in fractional anisotropy and mean diffusivity between a control group and a group with familial risk for psychosis.

\textbf{Design} – We explored six cerebellar peduncles in patients with familial risk for psychosis. Participants were members of the Northern Finland Birth Cohort 1986, aged between 20 and 24 years. Participants in familial risk group had a parent with psychotic disorder (\textit{n}=47). Control participants were drawn randomly from the same birth cohort (\textit{n}=51). Diffusion tensor imaging and tractography were used to obtain fractional anisotropy and mean diffusivity values of the superior, middle and inferior cerebellar peduncle in both hemispheres. We also compared fractional anisotropy and mean diffusivity in the subgroup with familial risk for schizophrenia (\textit{n}=13) to 13 gender-matched controls.

\textbf{Results} – No significant differences in fractional anisotropy or mean diffusivity values were found between the familial risk and control groups.

\textbf{Conclusions} – Our findings suggest that the risk for psychosis may not manifest as structural changes in cerebellar white matter.
O11 – Investigating the impact of second-hand tobacco smoke exposure on DNA methylation and related health risks; the Avon Longitudinal Study of Parents and Children

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Background – Second-hand tobacco smoke (SHS) is associated with numerous health risks and with smoking initiation. DNA methylation is strongly associated with own and prenatal smoke exposure and may be a mechanism by which smoking impacts health. Evidence on methylation changes in relation to postnatal SHS is scarce.

Objective – To investigate associations between cotinine levels (an objective marker of SHS) and DNA methylation at 2,622 smoking-responsive CpG sites in a cohort of non-smoking children and adolescents.

Design – The Avon Longitudinal Study of Parents and Children with plasma cotinine and DNA methylation measured at age 7y and 15-17y.

Results – In linear regression analyses adjusted for age, sex, batch and cell count, plasma cotinine (ng/ml) at 7y was associated with methylation at 2 CpG sites at 7y (n=942) and methylation at 1 CpG site among non-smokers at 15-17y (n=781), with Bonferroni correction (p<1.9x10^-5). These sites were: cg12803068 (MYO1G; b=0.016, p=3.1x10^-7), cg04180046 (MYO1G; b=0.011, p=9.0x10^-7) and cg25464840 (FRMD4A; b=0.006, p=1.5x10^-5). Cotinine at 15-17y was less associated with methylation at the same time point (n=649). With adjustment for prenatal smoke exposure, associations attenuated at cg12803068 (MYO1G) and cg04180046 (MYO1G) (b=0.003, p=0.42 and b=0.003, p=0.30, respectively) although the association at cg25464840 (FRMD4A) persisted (b=0.006, p=0.001). Examining a cis-SNP associated with methylation at cg25464840 in two-sample Mendelian randomization analyses of UK Biobank data (n=336,067) suggested a causal effect of methylation at cg25464840 on ever-smoking status (OR 1.02 (95% CI 1.01,1.03; p=0.004) per SD-increase in methylation).

Conclusions – In a cohort of non-smoking children and adolescents, we identified differential methylation at several CpGs in relation to cotinine levels as a measure of SHS exposure. Associations at CpG sites in MYO1G are likely confounded by prenatal smoking, but methylation in FRMD4A may be independently associated with postnatal SHS. Mendelian randomization estimates suggest a causal role of methylation at this site on smoking initiation. Further methods are required to confirm causality.
P33 - Antenatal corticosteroid therapy (ACT) and size at birth

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BACKGROUND - Whether Antenatal Corticosteroid Therapy (ACT) is associated with birth size is debated.

METHODS - We used data from the Finnish Medical Birth Register covering all births in Finland during a 5-year period to assess whether ACT exposure is associated with birth size adjusted for background and medical characteristics. Propensity score approach was used to mimic a randomized controlled trial through matching. All analyses were stratified by gestational age at birth.

RESULTS - A total of 278,508 live-born singleton births were analyzed. Of these, 11,896 (4.27%) infants were born preterm and 4887 women were treated with ACT (1.75%). More than one-third, 37.34% of the exposed infants (n=1825) were born at term. As compared to unexposed, infants exposed to ACT weighed less at birth: -220.18g (±SE 21.43, P<.0001), -140.68g ±SE (±SE 23.09, P<.0001), and -89.38g (±SE 14.16, P<.0001), for preterm, near-term, and term infants. Significant reductions in birth length and head circumference were also observed. There were no differences among very preterm or post-term infants. Sensitivity analyses showed that ACT was associated with significantly smaller birth size among infants born at term and likely to be healthy (birthweight: -79.60g ±SE 17.97; birth length: -0.30cm ±SE 0.08; head circumference: -0.21cm ±SE 0.05, all P<.0001).

CONCLUSIONS - ACT was consistently associated with reduction in birth size for infants born preterm, near-term, or at term. Poor gestational condition, potentially precipitating treatment, is likely to contribute to overall birth size reduction, but does not account for it fully. Reduced growth should be considered when making early care decisions.
P34 – Oral iron supplementation during first year of life and diphtheria, tetanus pertussis and polio vaccination reduce the risk of inflammatory bowel disease; a follow-up of the Northern Finland Birth Cohort

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Background – The pathogenesis of inflammatory bowel disease (IBD) is unclear. Environmental factors in combination with genetic predisposition may play a role.

Objective – Our aim was to analyze prenatal, pregnancy period and infancy period risk factors for IBD.

Design – The Northern Finland Birth Cohort 1966 is a longitudinal research program to promote health. Data from mothers living in the two northernmost provinces of Finland with expected dates of delivery between Jan 1st - Dec 31st, 1966 (96.3% of all births during 1966) was collected from antenatal clinics, hospital registers and by postal questionnaires. Data from infants was collected from child health center visits. IBD patients were identified using Social Insurance Institution of Finland reimbursement data for IBD drugs (from 1966 – to 2016) and hospital registers (from 1966 – to 2015). Data were analyzed by chi square test and logistic regression.

Results – 7077 individuals gave informed consent. For those 157 (2.2 %) had IBD, 113 (1.6 %) had ulcerative colitis (UC) and 44 (0.6 %) had Crohn’s disease (CD). Smoking during pregnancy increased the risk for IBD [OR 1.6 (1.03-2.33), p=0.034]. Consumption of antibiotics during pregnancy increased the risk for CD [OR 2.9 (1.36-6.08), p=0.006. Vitamin D supplementation or antibiotics during first year of life were not associated with IBD. However, oral iron supplementation [OR 0.55 (0.40-0.77), p<0.001], diphtheria, tetanus and pertussis vaccination (DTP) ≥ 3 times [OR 0.56 (0.37-0.86), p=0.008] and polio vaccination ≥ 2 times [OR=0.67 (0.46-0.93), p=0.03] reduced the risk for IBD and breastfeeding the risk for CD [13/3018 vs. 9/451, p<0.001].

Conclusions – Smoking during pregnancy increased the risk for IBD and antibiotics during pregnancy increased the risk of Crohn’s disease. Oral iron supplementation at infancy and DTP and polio vaccination reduced the risk for IBD and breastfeeding the risk for CD later in life.
P35 – Maternal hemoglobin and pregnancy outcomes in Northern Finland Birth Cohorts

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Background – Decreasing maternal hemoglobin (mHb) concentration during pregnancy is a natural phenomenon, which results mainly from the increase of maternal blood volume. However, extreme changes in mHb during pregnancy may indicate a distress in the developing child with long-lasting consequences.

Objective – This study aims to understand the association between mHb during pregnancy and adverse pregnancy outcomes.

Design – Northern Finland Birth Cohorts 1966 and 1986 are longitudinal, population-based cohorts together comprising over 21,700 mothers and their children. Concentrations of mHb at first and last antenatal visits were categorized as medium (reference), low and high (lowest and highest 10%). Odds ratios for mHb categories and pregnancy outcomes such as prematurity, small for gestational age (SGA) and large for gestational age (LGA) were assessed using multinomial logistic regression analyses with adjustments for maternal cofactors.

Results – At late pregnancy, low mHb associated with increased risk of prematurity and LGA whereas high mHb associated with increased risk of SGA. Low mHb at early pregnancy associated with decreased risk of SGA and increased risk of LGA.

Conclusions – Current results indicate that both low and high mHb associate with adverse pregnancy outcomes. Most of the studies on mHb are located in low-income countries with poor antenatal care and nutritional status of the mother. In these populations, abnormal mHb may be accompanied by other maternal deficiencies detrimental to the developing child. Our study shows that mHb should be studied also in high-income countries to reveal its association with adverse pregnancy outcomes without the nutritional and socioeconomic confounders.
Background – Heart-rate variability provides an insight into cardiac autonomic activity and is a crucial marker of cardiovascular health. The longitudinal associations of psychosocial risk factors in childhood with heart-rate variability in adulthood have remained unclear.

Objective – This study investigated whether psychosocial risk factors in childhood predict heart-rate variability in adulthood.

Design – The participants (N=956) were from the Cardiovascular Risk in Young Finns study. Psychosocial risk factors were evaluated in 1980 (when participants were aged 3–18 years) and included health behaviors in family, parental socioeconomic factors, stressful life events, and emotional family environment. Heart-rate variability was measured in 2001 with five indicators: heart rate; the square root of mean squared differences of successive RR intervals (RMSSD); the percentage of RR intervals with >50 ms variation (PNN50); the high-frequency component (HF); and the ratio of high-frequency component with low-frequency component (HF:LF ratio).

Results – When adjusted for age and gender, adverse health behaviors in family predicted a lower HF:LF ratio (β=.065, p<.05). Unfavorable parental socioeconomic factors predicted higher heart rate (β=.064, p<.05). Frequent stressful life events predicted higher heart rate (β=.069, p<.05), a lower RMSSD (β=.072, p<.05), a lower PNN50 (β=.078, p<.05), and a lower HF (β=.073, p<.05). Emotional family environment did not predict heart-rate variability. The total score of psychosocial risk factors in childhood predicted higher heart rate (β=.063, p<.05). When adjusted for participants’ educational level, perceived social support, triglycerides, cholesterol, blood pressure, body-mass index, smoking, alcohol use, coffee consumption, and physical activity, all the associations became non-significant, except for the association of stressful life events with a lower RMSSD.

Conclusions – Psychosocial risk factors in childhood, especially frequent stressful life events, predict lower heart-rate variability in adulthood. The associations may be mostly indirect via health behaviors and other qualities of cardiovascular health.
Background – Traumatic experiences early in life causing early life stress (ELS) may lead to an increased risk of adverse health outcomes across the life span. ELS is a risk factor for mental and physiological health. An acceleration in the biological age-related changes can be induced by ELS and thus may have an impact on work career.

Objective – We examined whether early exit from the workforce in terms of disability pension, unemployment pension, part-time pension and death before retirement differed between those who were separated from their family due to evacuations during World War II (WWII) and those who were not.

Design – The HBCS comprises 13345 individuals born in Helsinki, Finland, between the years 1934-1944. A unique identification number was used to link data from national registers until the year 2013. From the original cohort, 1781 (13.3 %) individuals were identified as being separated temporarily from their parents. Age of overall retirement according to separation status was estimated by the Kaplan-Meier method. Multinomial regression analyses were used to calculate the odds for the four types of early exit from the workforce the old age pension being the reference group.

Results – Compared to non-exposed, those who were exposed to ELS were more likely to have transitioned into disability pension (OR 1.20; 95% CI: 1.10-1.37) or unemployment pension (OR 1.25; 95% CI: 1.10-1.48). Men with separation status were less likely part-time pensioners (OR 0.66; 95% CI: 0.49-0.90). Age of overall retirement was similar in both groups.

Conclusions – The work career in later life may be influenced by ELS. Early interventions in order to prevent ELS or mitigate its negative effects may prolong future work careers along with healthier aging across the life-span.
Background – Maternal obesity and excessive gestational weight gain are associated with an increased risk of obesity in the offspring. It remains unclear whether maternal adiposity also affects organ fat measures, which have important adverse cardiometabolic health consequences.

Objective – We aimed to examine the associations of maternal pre-pregnancy body mass index (BMI) and gestational weight gain with general, abdominal, pericardial and liver fat measures in 10-year-old children.

Design – In a population-based prospective cohort study among 2,354 mothers and their children, we obtained maternal pre-pregnancy BMI and gestational weight gain and offspring BMI, fat mass index (total fat mass/height^4), subcutaneous fat index (subcutaneous fat mass/height^4), visceral fat index (visceral fat mass/height^3), pericardial fat index (pericardial fat mass/height^3) and liver fat fraction by Magnetic Resonance Imaging (MRI) at 10 years.

Results – A 1-standard deviation score (SDS) higher maternal BMI was associated with higher childhood BMI (difference 0.32 (95% CI 0.28, 0.36) SDS), fat mass index (difference 0.28 (95% CI 0.24, 0.31) SDS), subcutaneous fat index (difference 0.26 (95% CI 0.22, 0.30) SDS), visceral fat index (difference 0.24 (95% CI 0.20, 0.28) SDS), pericardial fat index (difference 0.12 (95% CI 0.08, 0.16) SDS) and liver fat fraction (difference 0.15 (95% CI 0.11, 0.19) SDS). After conditioning each MRI adiposity measure on BMI at 10 years, higher maternal BMI remained associated with higher childhood subcutaneous and visceral fat indices. Maximum gestational weight gain was not consistently associated with organ fat.

Conclusions – Higher maternal BMI, but not gestational weight gain, was associated with higher abdominal, pericardial and liver fat. The associations with subcutaneous and visceral fat were independent of BMI. Promoting a healthy BMI in women of reproductive age may be of greater importance for childhood organ fat than influencing gestational weight gain.
P39 – Frequent intoxication and alcohol tolerance in adolescence: associations with subsequent psychiatric disorders

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Background – Large longitudinal studies on the relation of adolescent alcohol drinking patterns and psychiatric disorders later in life are scarce.

Objective – To prospectively study the associations between frequency of intoxication and number of drinks needed to become intoxicated in mid-adolescence and psychiatric disorders in early adulthood.

Design – In the Northern Finland Birth Cohort 1986, data on alcohol use were collected using questionnaires at age 15 – 16 years (N = 6,548 subjects including 69.4% of the original sample). Outcomes were psychiatric disorders in early adulthood gathered from nationwide health care, pension and insurance registers by the age of 30 years. Number of drinks needed to become intoxicated was categorized into three classes: (1) No alcohol use or intoxication, and (2) low and (3) high alcohol tolerance (more than 7/9 drinks for females/males) groups. Similarly, intoxication frequency was divided into three classes: (1) never, (2) 1 – 2 times and (3) 3 or more times during the past 30 days. Information regarding gender, family type, other drug use, psychopathology using Youth Self-Report total score, and parental psychiatric disorders were considered as confounding variables.

Results – Number of drinks needed to become intoxicated was associated with the risk of substance use disorder [odds ratio (OR) 5.9, 95% CI 2.7 – 13.0 for high and OR 3.1, 95% CI 1.5 – 6.4 for low alcohol tolerance group]. More frequent intoxication was associated with increased frequency of mood disorder [OR 1.6, 95% CI 1.1 – 2.3] and substance use disorder [OR 1.6, 95% CI 1.1 – 2.3] in the high alcohol tolerance group.

Conclusions – Intoxication frequency, but not alcohol tolerance, in adolescence appears to be associated with increased risk of mood disorder in adulthood. In addition, both frequent intoxication in mid-adolescence and high alcohol tolerance was associated with increased risk of substance use disorder in early adulthood.
P40 – Prenatal maternal smoking may modify the maternal and child genetic influence on childhood obesity; a study within the Danish National Birth Cohort (DNBC)

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Background – Maternal smoking during pregnancy and a genetic predisposition are well-established risk factors for childhood obesity.

Objective – We aimed to investigate whether the effect of genetic predisposition to BMI of 1) the mother and 2) the child interact with maternal smoking during pregnancy on the risk of child overweight at age 7 years.

Design – Within the DNBC (n=100,418), we have selected mother-child pairs with genome-wide genetic information:

1. randomly selected mothers and their children (Sample 1, n=510)
2. obese mothers and their children (Sample 2, n=431)

A maternal genetic risk score (GRSm) based on 77 BMI associated genetic variants identified in adults and a child genetic risk score (GRSc) based on 15 childhood BMI associated genetic variants were created and divided into respective tertiles (low, medium, high). Genetic risk scores were weighted by summing the number of BMI-increasing alleles weighted by the effect sizes of the variants estimated in the respective GWAS discovery studies. Logistic regression analyses were applied to assess the risk of child overweight according to the interactions of GRSm × maternal smoking (defined as yes or no current smoking) and GRSc × maternal smoking.

Results – Compared to nonsmoking mothers and low GRSc/GRSm, the OR for overweight for a child with a high GRSc and a smoking mother was 7.37 (95% CI: 2.86-19.01), and for a child with a mother with a high GRSm who had been smoking during pregnancy 2.02 (95% CI: 0.87-4.66). There was a significant GRSc × maternal smoking interaction on childhood overweight (pinteraction=0.006) but not for GRSm × maternal smoking (pinteraction=0.8).

Conclusions – Maternal smoking and child genetic predisposition to obesity affect the risk of childhood overweight while maternal genetic predisposition has a weaker effect. This study suggest that there is an interaction between the child genetic risk score and maternal smoking on child overweight.
Genome-wide meta-analysis identifies genetic locus in chromosome 9 associated with Modic Changes

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Background – Low back pain (LBP) is a common disabling condition and the leading cause for workplace absenteeism. Lumbar disc degeneration (LDD) is one of the contributing factors behind LBP. Modic change (MC), is a distinct phenotype of LDD, presented as a pathological bone marrow signal change adjacent to vertebral endplate on magnetic resonance imaging (MRI). It is strongly associated with LBP and its heritability is estimated to be around 30%.

Objective – Our aim was to identify genetic loci associating with MC using genome-wide association study.

Design – Presence of MC was evaluated from lumbar MRI in Northern Finland Birth Cohort 1966 (NFBC1966, N=1182) and TwinsUK (N=647). The genome-wide association analyses were carried out using GEMMA v0.9 in TwinsUK and SNPTEST v.2.5.2 in NFBC1966. A linear regression model was fit to test for additive effects of SNPs adjusting for age, sex, and BMI. In TwinsUK family relatedness was adjusted for via a kinship matrix and population stratification in NFBC1966 using principal components. A meta-analysis of the two studies was carried out in METAL using inverse-variance weighting approach.

Results – A locus associated with MC with a genome-wide significance (p<5e-8) was found on chromosome nine with the lead SNP in intron of the \(PTPRD\) gene. According to RegulomeDB, the SNP is located in the region of binding for several transcription factors including SPI1 that is involved in differentiation of osteoclasts. PTPRD is a member of the protein tyrosine phosphatase (PTP) family containing signaling molecules controlling variety of cellular processes. It is important for neural system development and acts as a tumor suppressor and it is also expressed in cartilage. Another PTP family member (\(PTPN11\)) is involved in cartilage development and homeostasis.

Conclusions – We identified a novel gene locus in chromosome 9 associated with MC which will shed further light on their pathogenesis and potentially the role of MC in back pain.
Background – Low back pain (LBP) is a common disabling condition and the leading cause for workplace absenteeism. Lumbar disc degeneration (LDD) is one of the contributing factors behind LBP. Modic change (MC), is a distinct phenotype of LDD, presented as a pathological bone marrow signal change adjacent to vertebral endplate on magnetic resonance imaging (MRI). It is strongly associated with LBP and its heritability is estimated to be around 30%.

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Results – A locus associated with MC with a genome-wide significance (p<5e-8) was found on chromosome nine with the lead SNP in intron of the PTSPRD gene. According to RegulomeDB, the SNP is located in the region of binding for several transcription factors including SPI1 that is involved in differentiation of osteoclasts. PTSPRD is a member of the protein tyrosine phosphatase (PTP) family containing signaling molecules controlling variety of cellular processes. It is important for neural system development and acts as a tumor suppressor and it is also expressed in cartilage. Another PTP family member (PTPN11) is involved in cartilage development and homeostasis.

Conclusions – We identified a novel gene locus in chromosome 9 associated with MC which will shed further light on their pathogenesis and potentially the role of MC in back pain.
P43 - Metabolomic consequences of genetic inhibition of PCSK9 compared with statin treatment

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Background - Both statins and PCSK9 inhibitors lower blood low-density lipoprotein cholesterol (LDL-C) levels to reduce risk of cardiovascular events. To assess potential differences between metabolic effects of these two lipid-lowering therapies, we performed detailed lipid and metabolite profiling of a large randomized statin trial and compared the results with the effects of genetic inhibition of PCSK9, acting as a naturally occurring trial.

Objective - To compare metabolic effects of statins in a randomized trial versus metabolic effects of PCSK9 inhibition approximated using a genetic proxy.

Design - 228 circulating metabolic measures were quantified by nuclear magnetic resonance spectroscopy, including lipoprotein subclass concentrations and their lipid composition, fatty acids, and amino acids, for 5,359 individuals (2,659 on treatment) in the PROspective Study of Pravastatin in the Elderly at Risk (PROSPER) trial at 6-months post-randomization. The
corresponding metabolic measures were analyzed in eight population cohorts (N=72,185) using PCSK9 rs11591147-T as a proxy for the effects of PCSK9 inhibitors.

**Results** - Scaled to an equivalent lowering of LDL-C, the metabolic effects of genetic inhibition of PCSK9 were generally consistent with those of statin therapy (R²=0.88). Alterations in lipoprotein lipid composition and fatty acid balance were similar. Discrepancies were observed for very-low-density lipoprotein (VLDL) measures: for instance, genetic inhibition of PCSK9 showed weaker effect on lowering of VLDL-cholesterol compared with statin therapy (54% vs. 77% reduction, relative to the lowering effect on LDL-C; P=2x10⁻⁷ for heterogeneity). Genetic inhibition of PCSK9 showed no robust effects on amino acids, ketones, and a marker of inflammation (GlycA); in contrast, statin treatment lowered GlycA levels.

**Conclusions** - Genetic inhibition of PCSK9 results in similar metabolic effects as statin therapy across a detailed metabolic profile. However, for the same lowering of LDL-C, PCSK9 inhibitors are predicted to be less efficacious than statins at lowering VLDL lipids, which could potentially translate into subtle differences in cardiovascular risk reduction.
P44 - Reaction times, learning and executive functioning in adults born preterm; ESTER preterm birth study

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Background - Neurocognitive difficulties among children and adults born extremely or very preterm (<32 gestational weeks), have been well established, and are characterized by deficits in executive functioning.

Objective - Our aim was to examine if those born <34 gestational weeks, which we refer to as early preterm, perform worse than controls at computerized neurocognitive testing in adulthood, and whether these differences extend to those born late preterm (34+0 to 36+6 gestational weeks).

Design - This study is part of the ESTER Preterm Birth Study. 722 participants (133 early preterm, 241 late preterm, and 348 full-term controls) without severe disability performed Cogstate test (computer-based test battery measuring associate learning, psychomotor function, executive function, memory, attention, visual learning, working memory, and emotional cognition). Mean testing age was 23.1 (SD, 1.4) years. Main statistical method was linear regression and full models were adjusted with multiple pre- and postnatal characteristics and childhood socioeconomic position.

Results - Those born early preterm performed worse than full-term controls at Groton maze learning test measuring executive function, problem solving and reasoning. Mean results were 8.74 (SD, 1.94)/ 8.46 (1.76)/ 8.06 (1.79) moves/ 10 s for controls/ late preterm/ early preterm adults (higher value is better). Those born early preterm made 0.59 less correct moves/ 10 s (95% CI: -1.00; -0.17) in fully adjusted model. For those born late preterm, there was a smaller difference in model adjusted for sex and age. In the fully adjusted model it remained significant only for those born late preterm and small for gestational age. Performance was similar in all three groups regarding most tested abilities; paired associate learning, psychomotor function, attention, visual learning, working memory, and emotional cognition.

Conclusions - Young adults born early preterm and also those born both late preterm and small for gestational age did not reach the level of full-term controls at test measuring executive function.
Background - Depression has long been known to affect memory. Studies have shown evidence for cognitive deficits in different neurocognitive domains, varying from small to large in scale. Population-based studies about depression as a predictor for cognitive deficits has mainly focused on older age groups.

Objective - The objective of this longitudinal cohort study was to examine the association between depressiveness at age 31 years and visual memory at the age of 46 years. We investigated the following hypotheses: 1) Baseline depressiveness at the age of 31 years predict visual memory deficits at the follow-up at the age of 46 years. 2) The change in depressiveness between 31 and 46 years predict visual memory deficits at the follow-up.

Design - The participants of the study were members of the Northern Finland Birth Cohort 1966 (NFBC 1966) study. They filled in Symptom Checklist -25 (SCL-25) both at the baseline and at the follow-up. SCL-25 includes 13 items of depressive symptoms during last week. Visual memory was assessed using Paired Associative Learning (PAL) test at the follow-up. Of the PAL measures, first trial memory score and total errors adjusted were used as outcomes in the present study. Basic educational level, marital status, physical activity and diet at the baseline were considered as confounding factors. Linear regression analysis was used to analyze the data.

Results - A total of 5029 (57 % females) participants were included in the main analysis. No associations were found between depressiveness or change in depressiveness and visual memory scores.

Conclusions - Contrary to our hypothesis, neither baseline depressiveness nor chance in depressiveness predicted visual memory 15 years later. Sub-clinical symptoms of depression might not affect cognition in population.
O12 - Antisocial and borderline personality disorders in the adult offspring of antenatally depressed mothers in the Northern Finland 1966 Birth Cohort: Relationship to parental severe mental disorder

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Background - Maternal antenatal depression is common. In previous studies, offspring of antenatally depressed mothers have had an elevated risk for borderline personality features in childhood, and for antisocial, criminal and violent behaviour in adolescence, but very long-term outcomes are unknown.

Objective - We examined whether the adult offspring of antenatally depressed mothers have an elevated risk for severe antisocial and borderline disorder, taking account of parental severe mental disorder.

Design - In the general population based Northern Finland 1966 Birth Cohort, mothers of 12,058 children were asked during mid-gestation if they felt depressed. The offspring were followed over 30 years. Their hospital-treated personality disorders were detected using the Finnish Hospital Discharge Register (FHDR) and validated against DSM-III-R criteria. Parental severe mental disorders were also detected using the FHDR.

Results - The risk for both antisocial (OR 3.8; 95% CI 1.5-9.6) and borderline (OR 9.0; 95% CI 2.9-28.6) personality disorders was elevated among male offspring of antenatally depressed mothers. The male offspring with both maternal antenatal depression and parental severe mental disorder had a markedly higher risk for antisocial personality disorder (OR 16.9; 5.2-55.0), than male offspring of antenatally depressed mothers without one or both these risk factors. The results remained statistically significant even after adjustments. Maternal antenatal depression was not associated with elevated risk for personality disorders in female offspring.

Conclusions - Maternal antenatal depression was associated with increased risk for both antisocial and borderline personality disorder in male offspring. The joined effect of maternal antenatal depression and parental severe mental disorder resulted in especially high risk for antisocial personality disorder in male offspring. Patients with personality disorders do not often respond to treatment. Early detection and treatment of antenatal depression and parental mental disorders may present an opportunity in prevention of severe personality disorders, at least in the male offspring.
O13 - Longitudinal trajectories of physical activity from childhood to adulthood and their determinants: the Cardiovascular Risk in Young Finns Study

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Background - Determining the trajectories of lifelong physical activity (PA) and their determinants is essential in order to promote a physically active lifestyle throughout the life-course.

Objective - We aimed to identify PA trajectories from childhood to midlife and their determinants in a longitudinal population-based cohort.

Design - This study is a part of the Cardiovascular Risk in Young Finns Study (YFS). From 1980, a population-based cohort (N = 3596; 1764 boys/1832 girls, age 3-18 years) has been followed up for 31 years. PA indices were formed based on self-reported data (between age 9-49 years) on frequency, duration, and intensity of leisure (during childhood) or high-intensity (at later age) PA and on sports club participation/competitions. PA trajectories were analyzed using group-based trajectory modeling. Childhood (age 12 years), young adulthood (age 24 years), and early midlife (age 37 years) determinants were analyzed.

Results - Five PA trajectories were identified: persistently active (6.6%), decreasingly active (13.9%), increasingly active (13.5%), persistently low active (51.4%, reference group), persistently inactive (14.6%). In childhood, rural residential area (OR 0.45, 95% CI 0.21-0.96) and high academic performance (OR 2.18; 95% CI 1.58-3.00) associated with persistently active group. In early midlife, smoking (OR 1.66; 95% CI 1.07-2.58) associated with persistently inactive group, regular alcohol drinking (OR 2.91; 95% CI 1.12-7.55) with persistently active group and having children (OR 2.07; 95% CI 1.27-3.38) with decreasingly active group. High adulthood education associated with both decreasingly (OR 1.87; 95% CI 1.05-3.35) and increasingly (OR 2.09; 95% CI 1.19-3.68) active groups.

Conclusions - We identified five PA trajectories from childhood into midlife. Most prominent determinants were academic achievement, education, having children and health habits (i.e. smoking/alcohol use).
Background - Individuals born preterm at <32 weeks or <1500 g report less physical activity and have lower cardiorespiratory and muscular fitness than term-born peers. Whether this phenomenon extends to the much larger groups of adults born moderately or late preterm has been less studied.

Objective - To study cardiorespiratory and muscular fitness in young adults born preterm.

Design - We identified all men born in Finland between Jan 1987 and Sep 1990 through the National Medical Birth Register including data on gestational age at birth. We linked these data with Finnish Defence Forces’ fitness tests: 12 min run (cardiorespiratory fitness), standing long jump (explosive leg power), and number of sit-ups (abdominal dynamic endurance) and push-ups (upper extremity power/dynamic endurance and trunk static endurance) in 60 s. We analysed data with linear regression.

Results - Fewer adults born preterm had fitness data (37.3% (<32 wks); 58.8% (32-33 wks); 67.6% (34-36 wks); 69.6% (37-38 wks, early term); 70.8% (39-41 wks). For 12 min run, those born at <32 weeks performed poorer (-66 m (95% CI -103 to -31). We found a dose-response relationship between each week shorter gestational length and poorer performance for standing long jump (-0.43 cm (95% CI -0.53 to -0.33) and sit-ups (-0.09 (95% CI -0.14 to -0.05); even those born early term had lower performance than controls. Push-ups were not related to gestational age. When adjusting for maternal smoking, age, primiparity, and birth weight SD score, the associations remained unchanged.

Conclusions - Adults born preterm or early term have poorer muscular fitness, at least for leg and abdominal muscles. Cardiorespiratory fitness was poorer among those born at <32 weeks. Lesser availability of fitness data among preterm-born adults probably indicates exemptions because of health conditions. Therefore, our results represent a conservative estimate generalisable for apparently healthy young men.
P46 - Associations of maternal *Chlamydia trachomatis* infection with wheezing, lung function and asthma in children; the Generation R Study

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**Background** - Maternal *Chlamydia trachomatis* infection during pregnancy might induce inflammatory changes and increased airway hyperreactivity, and subsequent adverse respiratory health in childhood.

**Objective** - To study the associations of maternal *Chlamydia trachomatis* during pregnancy with early childhood wheezing, and school-age lung function and asthma.

**Design** - This study among 2,294 children was embedded in a population-based cohort study. Maternal *Chlamydia trachomatis* was tested in a urine sample provided at enrollment during pregnancy. Information on wheezing was obtained by multiple questionnaires between birth and age 6 years. At the age of 10 years, Forced Expiratory Volume in the first second (FEV\(_1\)), Forced Vital Capacity (FVC), FEV\(_1)/FVC\) and Forced Expiratory Flow after exhaling 75\% of the FVC (FEF\(_{75}\) were measured at our research center, and information on physician-diagnosed current asthma was obtained by questionnaire. Regression models and generalized estimating equations models were used, and adjusted for socio-economic, growth and lifestyle factors.

**Results** - The prevalence of maternal *Chlamydia trachomatis* during pregnancy was 3.1\%. Maternal *Chlamydia trachomatis* infection during pregnancy was associated with an increased risk of wheezing at the child’s age of 6 years only (OR (95\% CI): 2.66 (1.05, 6.22)). Additionally, maternal *Chlamydia trachomatis* infection during pregnancy was associated with an increased risk of current asthma (OR (95\% CI): 2.28 (1.01, 5.20)), but not with lung function measures of children at age 10 years.

**Conclusions** - Maternal *Chlamydia trachomatis* infection during pregnancy is associated with early childhood wheezing and school-age asthma. Further studies are needed to assess potential underlying mechanisms and clinical implications.
O15 - Metabolic changes in response to an oral glucose tolerance test in 4,620 middle-aged individuals; 46y follow-up of the Northern Finland Birth Cohort 1966

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Background - Glucose ingestion after overnight fasting triggers a rapid release of insulin and subsequently various metabolic changes occur to restore glucose homeostasis. Though the dynamics of insulin and glucose during this process are well studied, much less is known for other circulating nutrients.

Objective - We aim to characterise systemic metabolic changes in response to an oral glucose tolerance test (OGTT) and study how impaired insulin sensitivity would affect these changes.

Design - Serum samples from 4620 individuals from the Northern Finland Birth Cohort 1966 at fasting baseline, 60, 90 and 120 min during an OGTT were profiled by NMR spectroscopy. Over 200 lipid, lipoprotein, fatty acid and metabolite measures, representing multiple metabolic pathways, were analysed. Metabolic changes were examined in all individuals and were compared between those at the first and fourth quartile of insulin resistance (IR). For those changes associated with IR, we further compared their metabolic trajectories in subjects with normal glucose tolerance (NGT), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and newly-diagnosed type 2 diabetes (NDDM).

Results - After glucose ingestion, glycolysis-related metabolites were increased whereas amino acids, ketone bodies, triglycerides in VLDL and HDL, and circulating fatty acids were suppressed. Compared to individuals at the first quartile of IR, most of these metabolic changes were blunted for those at the fourth quartile, including reduced increase in glycolysis metabolites and reduced decrease in ketone bodies, branched-chain amino acids and VLDL and HDL triglycerides. These individuals had also a larger decrease in large HDL subclasses and a larger increase in docosahexaenoic acid. Similarly, compared to NGT, these changes were increasingly blunted in IFG, IGT and NDDM.
**Conclusions** - Insulin resistance is associated with a wide range of postprandial metabolic abnormalities and such metabolic dysregulations are already apparent in prediabetic individuals, particularly for those with IGT.
P47 - Influence of maternal psychological distress during pregnancy on childhood general and organ fat mass measures; the Generation R Study

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Background – Observational studies suggest that psychological distress during pregnancy may have persistent effects on growth and adiposity development in the offspring. We hypothesized that psychological distress during pregnancy also affects organ fat measures, which have important cardiometabolic consequences.

Objective – To examine the associations of maternal psychological distress, depression and anxiety during pregnancy with general and organ fat measures assessed by Magnetic Resonance Imaging (MRI) in children aged 10 years.

Design – In a population-based prospective cohort study among 4,161 mothers and their children, we obtained self-reported information about maternal psychological distress, depression and anxiety in the second trimester. We measured child body mass index (BMI) (weight/height^2) and fat mass index (total fat mass/height^4) by dual-energy X-ray absorptiometry, and visceral fat index (visceral fat mass/height^3), pericardial fat index (pericardial fat mass/height^3) and liver fat fraction (%) by Magnetic Resonance Imaging (MRI) at a mean age of 9.8 years.

Results – Overall, 8 to 9% of all women experienced psychological distress, depression, or anxiety during pregnancy. Maternal overall psychological distress was only associated with higher fat mass index (difference 0.14 (95% Confidence Interval (CI) 0.04, 0.24) standard deviation scores (SDS)) in their offspring. Maternal anxiety was associated with higher BMI (difference 0.16 (95% CI 0.05, 0.26) SDS) and fat mass index (difference 0.19 (95% CI 0.10, 0.28) SDS) in children. Maternal scales were not associated with childhood abdominal, liver and pericardial fat measures.

Conclusions – Psychological distress and anxiety during pregnancy were associated with higher general fat measures in the offspring, but were not associated with organ fat measures. Our results suggest that a healthy mental state during pregnancy may be a target in the prevention of child adiposity.
P48 - Associations of genetic variants for birth weight with fetal growth measures in different periods of pregnancy; the Generation R Study

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Background - Recent large genome-wide association studies (GWAS) have identified 60 common genetic variants (single nucleotide polymorphisms, SNPs) associated with birth weight. It is unknown how these SNPs relate to fetal growth patterns throughout pregnancy.

Objective - To determine the associations of a genetic risk score based on these birth weight related SNPs with longitudinal fetal growth patterns.

Design - In a population-based prospective cohort study, GWAS data and repeated fetal ultrasound growth measures were collected among 5374 singleton live-born children. A genetic risk score was calculated for each child, based on the number of birth weight increasing alleles for each of the 59 available SNPs, weighted by their reported effect sizes. Main outcome measures were standard deviation scores (SDS) of fetal weight, (femur) length and head circumference at 20 and 30 weeks and at birth. Linear mixed models and multivariable linear regression were used to study the association of the risk score with longitudinal and cross-sectional fetal growth, adjusted for sex and genetic ancestry.

Results - Longitudinal analyses showed that the effect of the genetic risk score on fetal growth measures increased throughout pregnancy (p<0.001). At 20 weeks of gestation, the genetic risk score was not associated with any fetal growth measure, whereas at 30 weeks it was associated with all fetal size measures. The strongest effect estimates were observed at birth: a 0.15 SDS (0.13-0.18) higher birth weight, 0.12 SDS (0.08-0.19) larger birth length and 0.08 SDS (0.05-0.12) larger head circumference per SD increase in the genetic risk score.

Conclusions - Our results suggest that genetic variants related to birth weight exert their effect on fetal growth most strongly in second half of pregnancy.
Background - Maternal cow’s milk intake during pregnancy stimulates fetal growth, resulting in higher birth weights. We hypothesized that maternal milk intake during pregnancy also influences long-term offspring adiposity and glucose metabolism.

Objective - We aimed to assess the associations of maternal milk intake during pregnancy with childhood adiposity and glucose metabolism.

Design - In a population-based cohort from early pregnancy onwards among 2,841 Dutch mothers and children, we assessed maternal first trimester milk intake by food frequency questionnaire (FFQ). At 6 and 10 years, we assessed overall and abdominal adiposity by body mass index (BMI), Dual-Energy X-ray absorptiometry (DXA), ultrasound and Magnetic Resonance Imaging (MRI), and insulin and glucose levels.

Results - The median maternal milk intake was 1.6 glasses/day (95% range: 0, 5.4). As compared to mothers with low milk intake, those with higher milk intakes were lower educated, smoked more often, and had a higher BMI and total energy intake. After adjustment for lifestyle-related confounders, children whose mothers consumed ≥5 glasses of milk/day had a higher BMI, fat mass index (FMI) and abdominal subcutaneous fat mass at 6 and 10 years, as compared to those whose mothers consumed 0-1 glass/day (differences for BMI: 0.27 (95% CI: 0.10, 0.44) and 0.22 SDS (95% CI: 0.02, 0.42), respectively). These children also had a higher android-gynoid fat mass ratio and abdominal visceral fat mass at 10 years (all p-values<0.05). These effects were not present for lower milk intakes. No associations were observed for insulin and glucose levels.

Conclusions - Our results suggest that high maternal milk intake during pregnancy is related to higher overall and abdominal adiposity in childhood, but not to glucose metabolism.
Background – Genome-wide association studies (GWAS) have revealed many genetic variants (single nucleotide polymorphisms, SNPs) associated with adult body mass index (BMI). To date, only two GWAS have been performed on childhood BMI and obesity. Although a large genetic overlap has been found between childhood and adult BMI, the genetic background between these two stages of life may differ in terms of specific loci and effect sizes.

Objective – We aimed to identify genetic variants influencing childhood BMI using a genome-wide association approach based on data imputed the 1000 Genomes imputation panel.

Design – The discovery phase included 26 studies with a total sample size of 39,618 children between the ages of 2 and 10 years. Childhood BMI was converted into sex- and age-adjusted standard deviation scores. Genome-wide association analyses were performed in all studies individually and results were then combined in fixed-effects inverse-variance weighted meta-analysis. We performed conditional analyses to select independently associated SNPs. All genome-wide significant or suggestive SNPs (P values < 5 × 10^{-8} and < 5 × 10^{-6}, respectively) were taken forward for replication in 14 replication cohorts with a total sample size of 23,805.

Results - 25 independent SNPs reached genome-wide significance in the combined discovery and replication analyses. Of these, 22 SNPs mapped to loci known for their association with adult or childhood BMI or obesity. One locus was previously associated with adult height and two loci were novel.

Conclusions - This study supports a large overlap in genetic background between childhood and adult BMI. Furthermore, we identified two novel loci, suggesting that the genetic background of BMI may show some variation with age.
P50 - Sociodemographic and health-related determinants of change in television viewing during adulthood: The Cardiovascular Risk in Young Finns Study

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Background - There is growing concern about sedentary behavior in adults. However, determinants of change in television viewing from young adulthood to early midlife have not been clarified.

Objective - We aimed to investigate possible factors contributing to change in television viewing in young adults over 10 years.

Design - Participants (N=2929) of the longitudinal Cardiovascular Risk in Young Finns Study had self-reported their television viewing in 2001 (aged 24-39), 2007 and 2011 and answered to repeated questionnaires to provide additional other information, as well as the required medical examination. The determinants of initial levels and slopes of television viewing were examined by using a linear growth curve model.

Results - Among men, inverse associations with initial levels of television viewing were observed for students becoming employed (p=0.002) and having children (p=0.016), and direct associations were observed for both those who stayed a smoker (p=0.031) and stayed overweight/obese (p=0.001). Increasing attention to health habits (p=0.022) was inversely associated with decrease in television viewing, whereas age (p<0.001) and becoming unemployed (p=0.038) were associated with increase in television viewing. For women, inverse associations with the levels of television viewing were found for age (p<0.001), staying in non-manual work (p=0.012), and paying consistently high and increasing attention to health habits (p=0.001 and p=0.008), and direct associations were found for staying unemployed (p=0.017), smoking (p=0.009) and overweight/obese (p<0.001), and becoming employed (p=0.002), single (p=0.018) and non-smoking (p=0.001). Increasing physical activity (p=0.03), becoming employed (p=0.013), motherhood (p<0.001) and normal weight (p=0.032) were decrease in associated with television viewing, whereas age (p<0.001) and staying in non-manual work (p=0.013) were associated with increase in television viewing.

Conclusions - Increasing and maintaining a healthy and active lifestyle are potential targets for interventions and action to reduce overall sedentary time during adulthood.