Welcome Greetings

Dear Colleagues,

On behalf of the organizing committee, it is my pleasure to welcome you to Oulu to participate in the Conference on Epidemiological Birth Cohort Studies, 2nd Paula Rantakallio Symposium organized jointly with the 6th Conference on Epidemiological Longitudinal Studies in Europe, CELSE. 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 in the Dinner on Thursday 16th of June 2016 in Hotel Lasaretti. Let’s have fruitful discussions during the conference and during the dinner! 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 Männikkö
Sylvain Sebert
Juha Veijola
Tuula Ylitalo
Programme

Day 1: June 15, 2016

Session I
Chair, Juha Veijola, University of Oulu, Finland

09.00 – 10.00 Welcome coffee and registration
10.00 – 10.15 Opening remarks
Kyösti Oikarinen, Dean of the Medical Faculty, University of Oulu, Finland
10.15 – 10.45 Long term consequences of maternal obesity on offspring health
Johan Eriksson, University of Helsinki, Finland
10.45 – 11.15 Has time come to limit the use of paracetamol during pregnancy? Results from the Danish National Birth Cohort
Jørn Olsen, Aarhus University, Denmark
11.15 – 11.30 Maternal BMI before pregnancy as a risk factor for ADHD and autism in children; a follow-up study in the Danish National Birth Cohort
Sanne Lemcke, Aarhus University, Denmark
11.30 – 13.00 Lunch, Posters, exhibition

Session II
Chair, Marjo-Riitta Järvelin, University of Oulu, Finland, Imperial College London, UK

13.00 – 13.30 Population Neuroscience: Observing to Change
Tomas Paus, University of Toronto, Canada
13.30 – 13.45 A life-course approach to premature aging associated with pre-diabetes; a pilot study in Northern Finland Birth Cohort 1966 by the DynaHEALTH EU-action
Estelle Lowry, University of Oulu, Finland
13.45 – 14.00 Childhood adversity, prodromal symptoms and brain response to faces in young adulthood
Johannes Pulkkinen, University of Oulu, Finland
14.00 – 14.30 Population Neuroscience: The Generation R cohort
Henning Tiemeier, Erasmus Medical Center, Rotterdam, Netherlands
14.30 – 15.00 Coffee
15.00 – 15.30 Molecular mechanisms behind disease biomarkers - a systems medicine approach
Johannes Kettunen, University of Oulu, Finland
15.30 – 15.45  Genome-wide multi-phenotype and eQTL analyses provide novel insights into omega fatty acid metabolism  
**Marika Kaakinen**, Imperial College London, UK

15.45 – 16.00  Causal relationship between high milk consumption and cardio-metabolic traits - a Mendelian Randomization approach; the 1958 British Birth Cohort  
**Vimal Karani**, University of Reading, UK

16.00 – 16.15  Early nutrition interrupts the risk association of Caesarean section and obesity: secondary analysis of a randomized clinical trial  
**Martina Weber**, University of Munich Medical Center, Germany

16.15 – 16.30  Using web-based questionnaires to assess medication use during pregnancy: a validation study in pREGnant and the PRIDE Study  
**Nel Roeleveld**, Radboud university medical center, Netherlands

19.00 – 20.30  City of Oulu reception (City Hall, Kirkkokatu 2A)

---

**Day 2: June 16, 2016**

**Session I**
**Chair, Minna Männikkö**, University of Oulu, Finland

09.00 – 09.30  Coffee

09.30 – 10.00  Genome-wide association studies on social-scientific variables lead to new insights about health outcomes  
**Philipp Koellinger**, VU University of Amsterdam, Netherlands

10.00 – 10.15  Risk aversion and framing among the Northern Finland Birth Cohort 1966 participants  
**Mikko Vaaramo**, University of Oulu, Finland

10.15 – 10.30  Migration history sequence analysis of young adults living in the largest cities of Finland; results from the 1987 Finnish Birth Cohort study  
**Liisa Törmäkangas**, National Public Health Institute, Oulu, Finland

10.30 – 11.00  Making the most of it: Collaboration between birth cohorts  
**Anne-Marie Nybo Andersen**, University of Copenhagen, Denmark

11.00 – 12.30  Lunch, Posters exhibition

**Session II**
**Chair, Sylvain Sebert**, University of Oulu, Finland

12.30 – 13.00  DNA methylation signatures of novel biomarkers of health risk factors  
**Zdenka Pausova**, University of Toronto, Canada

13.00 – 13.15  Childhood height and body mass index at 7 years of age and incidence of adult type 2 diabetes  
**Lise G Bjerregaard**, Institute of Preventive Medicine, Denmark

13.15 – 13.30  The association of multiple melanocytic nevi with education, gender and skin type; a Northern Finland Birth Cohort 1966 Study with 46 years’
Suvi-Päivikki Sinikumpu, University of Oulu and Oulu University Hospital, Finland

13.30 – 14.00
Physical activity, body composition and metabolic health - lessons from the Calex family study spanning three generations
Shulin Cheng, University of Jyväskylä, Finland

14.00 – 14.30
Coffee

14.30 – 15.00
The role of changes in early life exposures in the obesity epidemic
Thorkild I.A Sørensen, Institute of Preventive Medicine, Copenhagen, Denmark

15.00 – 15.15
Educational differences in accelerometer-based physical activity and sedentary time in young adults during weekdays and weekend days
Marko Kantomaa, Imperial College London, UK

15.15 – 15.30
Association between vitamin D status and inflammation: stratification by body mass index-findings from the Northern Finland Birth Cohort 1966
Saranya Palaniswamy, University of Oulu, Finland

15.30 – 16.00
The psychological life course consequences of being born preterm
Dieter Wolke, University of Warwick, UK

19.00 -
Dinner, at the restaurant Lasaretti

Day 3: June 17, 2016

Session I
Chair, Juha Veijola, University of Oulu, Finland

09.30 – 10.00
Coffee

10.00 – 10.30
Longitudinal views of risks in psychiatry and immunology
Peter B. Jones, University of Cambridge, UK

10.30 – 10.45
Premorbid temperament as a predictor for remission in depression
Jouko Miettunen, University of Oulu, Finland

10.45 – 11.15
Adverse adult consequences of adolescent alcohol exposure: Longitudinal results from the Northern Finland Birth Cohort, 1966
Richard J Rose, Indiana University, USA

11.15 – 11.45
The genomics of metabolic health from an early growth perspective
Inga Prokopenko, Imperial College London, UK

11.45 - 12.00
Closing remarks
Marjo-Riitta Järvelin, University of Oulu, Finland, Imperial College London, UK
Keynote speakers
Johan G. Eriksson graduated from medical school in 1986 and defended his doctoral thesis in 1988, focusing upon psychosomatic aspects of coronary artery bypass surgery. He became professor in General Practice at the University of Helsinki in 2006 and holds specialties in general practice and internal medicine. He is also chief physician at Helsinki University Hospital and Director for the Program of Public Health Research at Folkhälsan Research Centre. He also has an adjunct professorship in experimental endocrinology at University of Helsinki.

He has published over 500 articles in internationally peer-reviewed journals primarily around the pathogenesis of type 2 diabetes, prevention of type 2 diabetes and programming of health and disease. His h-index is 84.

He has initiated the Helsinki Birth Cohort Study and is the PI of that study and he is also the PI of the GDM prevention study RADIEL. The Finnish DPS-study was the first randomized lifestyle intervention study showing that prevention of Type 2 diabetes is possible while the RADIEL study was the first randomized study showing that prevention of GDM by lifestyle intervention is possible. He has been closely involved in both studies. He works clinically mainly in the field of diabetes and gastric bypass surgery and is the chairperson for the Finnish Diabetes Association’s Doctors Board.
Long term consequences of maternal obesity on offspring health

Email address: johan.eriksson@helsinki.fi

The Developmental Origins of Health and Disease (DOHaD) hypothesis proposes that several non-communicable diseases – including coronary heart disease and type 2 diabetes (T2D) - have their origins in prenatal life and in early childhood. The intrauterine milieu which is influenced by a large number of factors - including maternal characteristics - affects the developing fetus via a number of pathways resulting in the programming of future health outcomes.

Early life programming has mostly been studied in relation to long-term health outcomes in relation to being born with a small body size. Maternal obesity is associated with immediate adverse neonatal outcomes including an increased risk of congenital defects and miscarriage. However, recent studies have been reporting associations between maternal obesity and long-term health outcomes in the offspring. Maternal obesity in pregnancy has been associated with an increased risk of premature death in adult offspring. Further based upon findings from the Helsinki Birth Cohort Study it has been shown that higher maternal pregnancy BMI is associated with an increased risk of cancer, cardiovascular disease, and T2D among the adult offspring. The association with T2D is stronger in women, consistent with the transmission of T2D from the mother to her daughters being stronger than transmission to her sons. One plausible explanation for the association between maternal adiposity during pregnancy and later offspring health is in utero programming. This may work through environmental, metabolic, genetic, and epigenetic mechanisms.
Jørn Olsen is senior consultant at Department of Clinical Epidemiology and professor at Aarhus University, University of Southern Denmark and University of California, LA (UCLA) in the US. Jørn has previously been employed at Section of Epidemiology at Institute of Public Health, Aarhus University and was head of center for fundamental epidemiologic research during 1994-2004. He was chair at Department of Epidemiology from 2005 to 2011. Besides, Jørn has been chairman of the International Association for the Evaluation of Educational Achievement (IEA) and the Danish Society of Epidemiology. He is currently chairman of the Working Environment Research Foundation. He has also been a member of the Danish Research Council.

The majority of Jørn’s research activities lie within the field of reproduction epidemiology and he is the head of the Danish National Birth Cohort. He is editor of International Journal of Epidemiology and associate editor of several other scientific journals. His scientific production includes publications in scientific journals and books published by OUP and Springer.
Has time come to limit the use of paracetamol during pregnancy?

Email: jo@ph.au.dk

Background
In the talk, an updated status of the Danish National Birth Cohort (DNBC) will be given and the use of paracetamol while pregnant will be used as an example of recent use of the cohort. Paracetamol is used by half of pregnant women in many countries. It is considered safe (without proper documentation) and it is often sold ‘over-the-counter’ even in supermarkets. Therefore, it escapes most registration systems. Animal studies show it has hormonal disrupting effects and may for that reason cause mental disorders post-partum.

Objective
To examine if prenatal exposure to paracetamol increases offspring risks of Attention Deficit Hyperactivity Disorder (ADGD), Autism Spectrum Disorder (ASD) and lower IQ at age 5. Such as study requires a large scale cohort with prospectively collected exposure data.

Design
Two cohort studies within the DNBC and a crossover sectional study at age 5 with a series of psychological tests applied to about 1500 children in the cohort.

Conclusion
Prenatal exposure to paracetamol was associated with both ADHD and ASD, especially the syndrome with hyperkinetic disorders. A small decrease in IQ was detected but paracetamol may also prevent an IQ lowering effect of fever.
Dr. Paus is the Tanenbaum Chair in Population Neuroscience at Baycrest, Professor of Psychology and Psychiatry at the University of Toronto, and the Dr. John and Consuela Phelan Scholar at Child Mind Institute in New York. His work integrates epidemiology, neuroscience and genetics – through a new discipline of population neuroscience - in the pursuit of knowledge relevant for child and youth mental health.

The work published by Dr. Paus and his colleagues have been well received by peers, being cited in over 30,000 publications. In 2013, Springer published his book “Population Neuroscience”. Dr. Paus received the Royal Society Wolfson Merit Award, Gold Medal of the Masaryk University, is an elected member of the International Neuropsychology Symposium and an elected fellow of the Association for Psychological Science, serves as Associate Editor of the Human Brain Mapping and Social Neuroscience, and as a member of several Scientific Advisory Boards in Europe and North America.
Population neuroscience endeavors to identify environmental and genetic factors that shape the function and structure of the human brain; it uses the tools and knowledge of genetics (and the “omics” sciences), epidemiology, and neuroscience. By understanding the processes driving variations in brain function and structure across individuals, we will also be able to predict an individual’s risk of (or resilience against) developing a brain disorder. In the long term, the hope is that population neuroscience will lay the foundation for personalized preventive medicine and, in turn, reduce the burden associated with complex, chronic disorders of brain and body.

In this talk, I will introduce the basic concepts of population neuroscience and illustrate this approach using data collected in the Saguenay Youth Study, the IMAGEN Study and ALSPAC. I will close by outlining possible strategies for translating knowledge obtained by such observational sciences into stratified preventive strategies aimed at changing health behaviors and, in turn, preventing common disorders of the brain and body.

Henning Tiemeier is Professor of Psychiatric Epidemiology at the Erasmus Medical Center, Rotterdam and Adjunct Faculty at the Harvard School of Public Health, Boston, where he teaches Child Psychiatric Epidemiology. He received a medical and a sociological degree from the University of Bonn, Germany. He obtained a Dr. med. for sleep deprivation studies in Bonn and his PhD in epidemiology from the Erasmus University in 2003 for work on vascular depression in the Rotterdam Study. Since May 2002 he has a joint-appointment in the Departments of Epidemiology and Child- and Adolescent Psychiatry and is a Principal Investigator of the Rotterdam Study and the Generation R Study. In 2011 he was appointed tenured Professor in Rotterdam.

Dr. Tiemeier’s research interest is the aetiology of common psychiatric disorders, his work in the elderly takes a neurodegenerative and his work in children a neurodevelopmental approach. Most of his research is longitudinal and conducted in large population-based studies. In the Rotterdam Study he has been working on risk factors for sleep problems, depression and complicated grief. Also, he supervises the child psychiatric and cognitive research the Generation R birth cohort of nearly 10,000 children and their mothers in Rotterdam. Together with several external partners, he examines how social, psychological and biological risk factors during foetal or early postnatal life contribute to the onset of problem behaviour. His work focuses on intra-uterine influences, neurodevelopment and genetics. Currently, much of his work involves brain imaging. Within Generation R more than 4500 pre-adolescents underwent structural and functional imaging.

His research group currently comprises 14 PhD students and 3 post docs from 9 countries. He has published over 350 peer-reviewed publications. His H-index is 41. He (co)-leads several working groups in national and international epidemiological consortia, including CHARGE-sleep, CORNET, EAGLE-behaviour group and participates in the PGC consortium.
Population Neuroscience. Research findings from the Generation R Study

Email: h.tiemeier@erasusmc.nl

Background
Birth cohort studies showed that early life adversities underlie the vulnerability for childhood psychopathology. These studies relied on psychiatric assessments whereas our knowledge whether neurodevelopmental changes underlie the effect of early life adversities on psychopathology is limited.

Objective
To report results from a large-scale imaging study designed to evaluate the role of multiple environmental on brain development

Design
The Generation R Study is a large, prospective, prenatal-cohort of nearly 10,000 children that began in 2002 in Rotterdam, the Netherlands.

Methods
Maternal thyroid hormones were assessed in early pregnancy, organophosphates were repeatedly measured in all trimesters of pregnancy and parenting was observed at home and at the research center. From September of 2009, 6–11 year old children from the Generation R Study were invited to participate in a magnetic resonance imaging component of the study. I will provide an overview of the study design and results for the first 4050 children recruited for the neuroimaging component of the study.

Results
The focus of my presentation will be on how prenatal exposure to maternal thyroid deficiency and organophosphates (pesticides) shapes global brain development; moreover, the effects of selected maternal nutritional deficiencies during pregnancy on child development will be discussed. In particular, hypothyroxinemia, i.e., low maternal thyroid function, was related to autistic symptoms, a lower IQ and less cerebral white matter in children. Also, the specific effects of insensitive parenting on cognitive and cerebral gray matter development are presented. Also, I will discuss methodological challenges.

Conclusions
Birth cohorts with their prospective ascertainment of modifiable risk factors are ideally suited to study neurodevelopmental problems. Research in Generation R shows that many early life risk factors have very unspecific effects, in particular prenatal risk factors often have a more global impact on the brain than later adverse exposures such as poor parenting.
Dr Johannes Kettunen is the Head of Genetics at the Computational Medicine Research Group, Center for Life Course Health Research, University of Oulu, Finland. He has a doctorate and a docentship in genetics. He started his career in the field of genetics and has been spearheading genome-wide association studies, particularly in combination with metabolomics. His field of expertise has expanded from genetics research to epidemiology and biomarker discovery, causal inference in epidemiology as well as systems medicine. The unifying theme in his current research is combining omics data to elucidate mechanisms underlying common complex traits and all-cause mortality. One of his current hot topics is trying to understand the pathophysiological mechanisms behind systemic biomarkers that predict short-term mortality and he has pioneered in systems medicine where he used gene expression data and electronic health records to unravel molecular mechanisms underlying the short-term mortality risk.
Molecular mechanisms behind disease biomarkers - a systems medicine approach

Email. Johannes.kettunen@computationalmedicine.fi

Background
Metabolomics is producing new biomarkers for adverse outcomes where often the underlying mechanism is unknown. The combination of metabolomics, genomics, transcriptomics and electronic health records is a way to elucidate these mechanisms and understand processes that lead to for example heart disease or early demise.

Objective
Our objective was to understand the molecular mechanisms underlying the strongest predictor of all-cause mortality, acetylation of glycoproteins (GlycA).

Design
Population based cohorts with biomarker measurements, circulating cytokines, electronic health records and whole blood expression available totaling over 10 000 individuals.

Results
We linked the GlycA biomarker with a new mechanism that is associated with increased risk for mortality. We were also able to show that high GlycA predisposes to higher risk for severe infections.

Conclusions
The combination of different omics and electronic health records is a useful approach to understand molecular mechanisms behind new biomarkers
"Trained as an economist at Humboldt-University Berlin, Koellinger started as assistant professor at the Erasmus School of Economics in Rotterdam in 2006 and became full professor at the University of Amsterdam in 2014. As one of the pioneers in the emerging field of genoeconomics, he is one of the co-founders and principal investigators (PI) of the Social Science Genetic Association Consortium (SSGAC - www.ssgac.org). With more than 90 participating cohorts, the SSGAC is the largest international collaboration of scientists to conduct statistically well-powered association analyses on social scientific outcomes. As a PI of the SSGAC, Koellinger has led projects that were published in Science, Nature, Nature Genetics, PNAS, Psychological Science, and many other journals. Koellinger won several awards and grants, including a ERC Consolidator Grant. In 2015, he accepted a full professorship in genoeconomics at the Vrije Universiteit Amsterdam. His current work investigates how genes influence economic behavior, and how insights into the genetic architecture of behavioral outcomes can inform social and medical research."
Genome-wide association studies on social-scientific variables lead to new insights about brain anatomy and health outcomes

Email: p.d.koellinger@vu.nl

Background
The success of genome-wide association studies (GWAS) on genetically complex traits crucially depends on available sample sizes. In contrast to many health outcomes, some moderately heritable social-scientific phenotypes can be cheaply and easily collected in very large samples.

Objective
We exploit the very large sample sizes that are available for educational attainment and subjective well-being to gain novel genetic insights into brain anatomy and health.

Design
We conducted GWASs on educational attainment and subjective well-being including ≈300,000 Europeans. Genetic correlation among traits was estimated using LD score regression. We investigate associations between genome-wide significant loci identified by our primary GWASs with brain anatomy and health outcomes using GWAS meta-analysis results from independent samples.

Results
We identify novel genetic associations for intracranial and hippocampal volume, schizophrenia, depression, and neuroticism.

Conclusions
Educational attainment and subjective well-being are primarily determined by environmental factors and the explanatory power of individual SNPs on these traits is small. Yet, the large GWAS sample sizes available for these outcomes affords insights into their genetic architecture and allows to use them as proxy-phenotypes for brain anatomy and health outcomes.
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 is currently Professor of Social Epidemiology at 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 working conditions, 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. Collaboration between birth cohorts is a key issue and Anne-Marie is founder and web administrator of www.birthcohorts.net.

Anne-Marie has been a board member of Danish Epidemiology Society and European Councillor for International Epidemiological Association. Among other tasks, she is currently in the Danish National Birth Cohort’s Board of Directors and member of the Scientific Advisory Committee for several European birth cohorts.

Email: amny@sund.ku.dk
Professor, Department of Physiology (primary) and Department of Nutritional Sciences (secondary), University of Toronto, Toronto, Canada

Dr. Pausova is a co-director on the Saguenay Youth Study, which is a CIHR- and HSFC-funded program investigating cardiometabolic and brain health (and genetic, epigenetic and lipidomic biomarkers) in 2,000 Canadian adolescents and their parents (http://www.saguenay-youth-study.org). In this research, her group focuses on early stages and trans-generational trajectories of common cardio-metabolic and brain diseases. This research is guided by the following biomedical considerations: (1) many common cardio-metabolic and brain disease originate in utero; (2) they involve interactions between adverse environments and vulnerability genes; (3) many of these diseases emerge during adolescence and become established during middle-aged adulthood; and (4) most of them are multi-systemic, affecting both the brain and body.

The main research interests are:
- Intra-abdominal obesity and its links to cardiometabolic health, brain structure and cognition
- Eating behavior, addiction and the adolescent brain
- Genetic and environmental factors modulating DNA methylation
Obesity, systemic inflammation and brain health in adolescence

Email: zdenka.pausova@sickkids.ca

The basis of my presentation will be our recent findings from the Saguenay Youth Study (SYS) on the role of obesity in brain health during adolescence. The SYS is a two-generational study of 2,000 adolescents and their parents aimed at investigating the etiology, early stages and trans-generational trajectories of common cardio-metabolic and brain diseases. The cohort was recruited from the genetic founder population of the Saguenay Lac St. Jean region of Quebec, Canada.

Mid-life obesity is a well-established risk factor for cognitive impairment and dementia in older individuals, but the underlying mechanisms and initial stages are not well understood; thus, the early identification of individuals at risk is difficult. Greater brain reserve, defined as a biological capacity of the brain to resist age- and disease-related influences, is protective from cognitive impairment and dementia. Obesity may diminish this brain-reserve capacity. Excess body-fat promotes systemic inflammation that, in turn, may promote neuroinflammation and associated changes in brain-tissue properties leading ultimately to neurodegeneration, cognitive impairment and dementia. Current technological advances in mass spectrometry (MS) have enabled large-scale identification of novel bioactive molecules. These molecules include glycerophosphocholine (GPC) metabolites, which are potent modulators of systemic inflammation. Recently, specific GPC metabolites were identified as predictors of Alzheimer’s disease and stroke recurrence. Using advanced MS (LC-ESI-MS), we have identified novel GPC metabolites and some of them showed particularly strong associations with obesity-related systemic inflammation and brain-tissue properties in the adolescents.
Sulin Cheng is a professor in the Sport and Health Sciences faculty at the University of Jyväskylä, Finland. She is also a Chair professor at Shanghai Jiao Tong University. Dr. Cheng’s research spans a wide range of disciplines including body composition, physical activity, nutrition, public health, endocrinology, physiology and genetics. Dr. Cheng has conducted several well-funded (from government agencies, foundation, and industrial companies) multidisciplinary and multi-center projects in Finland, USA, and China as Principal Investigator (PI) and co-PI in the field of body composition related health and technology issues spanning childhood to old age. Her over 15-year longitudinal study of growing children and their families (the Calex and Calex-family-study) yielded very significant scientific findings with great social impact. She has over 140 international peer reviewed publications in scientific journals. She has received 8 international awards and 6 national awards.
Physical activity, body composition and metabolic health - lessons from the Calex family study spanning three generations

Email: shulin.cheng@jyu.fi

During past 10 years, our research group has focused on investigating development of body composition and cardio-metabolic status from early childhood to old age in a longitudinal family study spanning 3 generations. With this extensive data and state-of-art tools including metabolomics and new analytical approaches such as constructive models, we attempt to identify the underlying factors and possible mechanisms associated with the change of body composition and cardio-metabolic status throughout women’s lifespan. In this talk, I will share some of our experiences in conducting the Calex longitudinal family study. Particularly, I will discuss our findings related to the effects of hormones (IGF-1 and sex steroids), biomarkers (osteocalcin and glucose), metabolic profile (amino acids and lipids) and physical activity on the body composition development and cardio-metabolic risks.
Thorkild IA Sørensen, MD in 1971, Dr Med Sci in 1983, was originally trained as clinician, but switched to full time research in 1989. He is currently professor of metabolic epidemiology at the Novo Nordisk Foundation Center for Basic Metabolic Research, and professor of clinical epidemiology at the Department of Public Health at the Faculty of Health and Medical Sciences at the University of Copenhagen. He is Director of the Institute of Preventive Medicine at the Bispebjerg-Frederiksberg University Hospital in Copenhagen, and he is affiliated with Bristol University, UK, as honorary visiting professor in public health and with Aarhus University as adjunct professor of public health. The main focus of his research has for decades been on general, clinical, and genetic epidemiology of obesity and related disorder, covering genetic and environmental causes, development, epidemic occurrence, physiological and psychosocial aspects, health consequences, including mortality. He has been heavily involved in research supported by the EU framework programs, and has through many years had inspiring and productive research collaborations with several Finnish colleagues.
The role of changes in early life exposures in the obesity epidemic

Email: TSOE0005@Regionh.dk

The prevailing understanding of the obesity epidemic is that it is driven by an increasing obesogenic conversion of the environment of the populations, making more energy-dense food and less demands of physical activity available. When obesity is developed, it requires more energy supplies to the increased lean body mass, which is satisfied by increased food intake, and any physical activity requires more energy to move the greater body mass, which is compensated for by reduced activity. The observation that obese people eat more and move less than non-obese people is an obvious consequence of the obese state. If these needs cannot be met, it reduces the risk of development of obesity. Thus, the obesogenic environment plays a permissive role for development of obesity, i.e. the obesity epidemic would be less likely to develop in non-obesogenic environments. However, a critical question is whether increased food intake and reduced physical activity are also drivers of the development of the obesity epidemic in populations with obesogenic environments or whether there are other essential drivers of the epidemic. A common idea is that the segments of the population that are genetically predisposed to obesity and therefore susceptible to the obesogenic environmental influences explain the distributions of obesity within the populations. However, various studies in the Danish population suggest that some environmental changes very early in life, either before conception, during gestation or during infancy, with persisting effects may be crucial drivers. This opens up for possible targeted preventive activities in a narrow age window, where such activities are presumably easier to implement than by changing the general obesogenic character of the societies. However, it is still an open question what these changes in early life environmental exposures are and whether they are carried through by parental obesity.
My research entails an interdisciplinary approach to identify mechanisms of how early biological and social experiences work together to lead to long term adverse or adaptive outcome. This requires the use of prospective longitudinal studies and I have worked over the last 33 years on initiating, running and funding large longitudinal studies. My particular expertise is in Developmental Psychopathology and how biological factors work themselves out of the skin ¹ (e.g. experience of prematurity, altered brain development) or how experiences work themselves under the skin (e.g., abuse or being bullied by peers: e.g. changing inflammation, altered stress responses, altered cognitive processing and biased perception) ². I developed an interest in the interface of biology and psychology by working in medical settings (e.g. King’s College Hospital, the Hospital for Sick Children) working alongside medical specialists and assessing effects of medical risk factors and their psychological sequelae. Our research in the field of early regulatory problems, the effects of preterm birth or peer/sibling social influences and parenting has paved new ground. Our research was one of the first to establish that early regulatory behavior (e.g., excessive crying) has long term adverse consequences ³. Our longitudinal research on bullying established that bullying has at least as adverse effects as maltreatment by caretakers into adulthood for victims ⁴. We described a characteristic phenotype of consequences of preterm birth on psychological functioning (e.g. multiple cognitive problems, attention, social problems and autistic features). Whether regulatory problems, preterm birth or bullying experiences, comparison across cohorts in different studies is important to establish whether universal mechanisms are at work ⁵ and thus we work across borders and collaborate with a number researchers worldwide.


The psychological life course consequences of being born preterm

Email: D.Wolke@warwick.ac.uk

Background
11% of children worldwide are born before term (<37 weeks gestation) and 15 - 20% of these in Europe (approx. 60,000) are born very or extremely preterm (VP; < 32 weeks GA). Up to a third of VP have significant cognitive, psychological and educational difficulties in childhood.

Objective
Do VP outgrow these their psychological or cognitive problems into adulthood?

Design
The Bavarian Longitudinal Study (BLS) is a geographically defined prospective study of children born in Germany in 1985/86. Of 682 born VP/VLBW, 411 were eligible for re-assessment in adulthood (26 years) and 260 (63.3%) participated. Of 308 term controls eligible 229 (74.4%) participated in adulthood.

Results
VP/VLBW still had IQ scores in adulthood approx. 1 SD below controls. They more often had multiple cognitive problems than specific executive function problems. While IQ in adulthood was poorly predicted by 20 months developmental assessments in term children (r=.25), correlations were highly significant in VP/VLBW (r=.74). IQ differences in VP/VLBW were associated with brain structural and network alterations compared to controls. While ADHD problems reduced from childhood to adulthood in both VP/VLBW and controls, VP/VLBW had significantly more often still ADHD. VP/VLBW could be characterized as more often socially withdrawn in their personality (autistic features, introverted, risk averse and anxious) compared to controls. Quality of life was significantly poorer in VP/VLBW than controls. VP/VLBW had less income, lived more often at home, had fewer or no friends, were less likely to have had sexual relations or had found a partner. The quality of parenting and peer relationships were significantly related to academic achievement and parents own quality of life.

Conclusions
A significant minority of VP/VLBW do not outgrow their childhood psychological problems. VP/VLBW children are more sensitive to parenting and poor peer relationships and social interventions are likely to improve their life chances and quality of life.
Professor of Psychiatry & Deputy Head, School of Clinical Medicine, University of Cambridge

Director, NIHR CLAHRC East of England

Honorary Consultant Psychiatrist, Cambridge & Peterborough Foundation Trust (CPFT)

Peter qualified in medicine at Westminster Medical School following a first degree in neurobiology at KCL. Having first work as a physician at The Whittington Hospital and KCH, he trained in psychiatry at the Maudsley Hospital and epidemiology at the London School of Hygiene. He has been Professor of Psychiatry at Cambridge since 2000 and in October 2014 stepped down as Head of Department to become Deputy Head of the School of Clinical Medicine. He is a NIHR Senior Investigator.

Peter’s research interests are in the epidemiology of mental illness, particularly early life determinants, and in evaluation of effective interventions at the individual and system level. Clinically, with Ed Bullmore, he led the award-winning CAMEO.nhs.uk early intervention service until taking on his NIHR responsibilities in the Collaboration for Leadership in Applied Health Research & Care East of England, a partnership between researchers and health services to accelerate the generation and application of evidence from applied health research in policy and practice.
Longitudinal views of risks in psychiatry and immunology

Email: pbj21@cam.ac.uk

Background
There is current interest in the prospect of identifying at an early, clinical stage people who will go on to develop schizophrenia. The at-risk mental state is a description of partial states of psychosis that may form part of a predictive test. However, epidemiological studies who that, not only are psychotic experiences that comprise the at-risk mental state rather common, but are also associated with more severe symptomatology in what conventional diagnostic classifications would call mild to moderate depression and anxiety.

Objective
Our objective was to explore the practical implications of these inconsistent proposals for people with psychosis. Few people with at-risk mental states at the population level ever develop a psychotic illness, but the majority of people have depression and anxiety. Thus, if only a few people with at-risk mental states are taken into care because they are in a sub-group at high risk of transition to schizophrenia, the vast majority of ill people with depression, anxiety and psychotic experiences are ignored. This is not useful at the personal, clinical or population levels. Current diagnostic systems simply do not accommodate reality.

Design
The evidence for these propositions will be reviewed using population-based data, largely from birth cohorts, particularly the Northern Finland 1966 and 1986 cohorts, and the Avon Longitudinal Study of Parents and Children (ALSPAC). Observational data from clinical settings regarding autoimmunity will also be presented.

Results
Population-based evidence of potentially causal or mechanistic inflammatory mechanisms for these mental state transcend unsatisfactory, traditional diagnostic boundaries. Evidence for autoimmune mechanisms in first episode psychosis will be presented together with the protocol for a recently funded trial in the UK comparing immunological with standard antipsychotic therapies.

Conclusions
Our ideas on diagnosis and the distinction between the mind, the brain and the immune system require an inflammatory reformulation.
Richard J. Rose is Emeritus Professor of Psychological & Brain Sciences at Indiana University, Bloomington, and of Medical & Molecular Genetics at the Indiana University School of Medicine, Indianapolis; he is also Visiting Professor in the Faculty of Medicine at the University of Helsinki. Born and raised in Minnesota, he earned a Ph.D. in Clinical Psychology from the University of Minnesota; with support from the National Science Foundation, he completed post-doctoral training at McGill University with Donald Hebb, before assuming his initial academic position at the University of Illinois. He was a founding member of the Behavior Genetics Association, and for thirty years, he has collaborated with Finnish investigators in Helsinki, Jyväskylä, and Oulu, directing longitudinal “FinnTwin” studies in behavioral and medical genetics, with a major focus on substance use and abuse. He has received the James Shields Memorial Award for twin research, the Dobzhansky Memorial Award for lifetime scholarship in behavioral genetics, a MERIT award and a Research Scientist Award from the National Institutes of Health. He has been a NATO traveling Scholar and a Senior International Fellow with the Fogarty Center of the NIH. He is a Fellow of the American Association for Advancement of Science, the Association for Psychological Science, and the Society of Behavioral Medicine. His current research interests include follow-up studies of Finnish twin pairs discordant for their adolescent alcohol exposure and tests of the generalizability of discordant twin results with the 1966 Northern Finland Birth Cohort.
Adverse adult consequences of adolescent alcohol exposure: Are associations causal?

Email: rose@indiana.edu

Background
Adolescent alcohol exposure is associated with adverse adult outcomes. But whether these associations are causal or arise from shared third-factor familial confounds remains uncertain, and persistence of associations over long-term follow-up awaits confirmation.

Objective
To confirm predictive associations of heavier drinking during early adolescence with adverse adult outcomes in paired comparisons of drinking-discordant monozygotic (MZ) twin pairs, controlling for both shared genes and family environments. And to test for generalizability of results from (highly selected) discordant co-twins in an extended follow-up of a population-based cohort, tracking drinking and intoxicating at age 14 to adult outcomes assessed at age 46.

Design
Finnish MZ twin pairs born 1975-79, discordant for drinking patterns at ages 16-18, and pairs born 1950-57, drinking-discordant at 18-25, have been followed into mid- and late adulthood. A follow-up of the Northern Finland Birth Cohort (NFBC1966) from age 14 to 46 complements discordant twin comparisons and tests their generalizability. NFBC data compare adult outcomes in ‘cases’, who reported frequent drinking and intoxicating at age 14, with ‘controls’ reporting infrequent drinking without intoxicating; controls match cases on gender, familial structure/status, and urban residency. Outcomes of interest include continuity of substance use and its abuse, symptom reports, truncated educational attainment, occupational instability, life dissatisfaction, and self-rated health.

Results
In both data sets, alcohol exposure was significantly associated with adverse adult outcomes at follow-up. Heavier drinking co-twins and NFBC cases were more likely unmarried, less satisfied with life, reported more physical and psychiatric symptoms, and lower education attainment. But associations are modest in magnitude and sample attrition constrains power.

Conclusions
These analyses encourage more detailed paired comparisons, including structured psychiatric interviews of drinking-discordant MZ twin pairs; linkages of population records for NFBC cases and controls, and exploring gender differences in associations of early alcohol exposure within both population samples.
Dr Inga Prokopenko

Dr Inga Prokopenko is a Senior Lecturer in Human Genomics at the Faculty of Medicine, School of Public Health, Imperial College London.

Dr Prokopenko has received a Rising Star Award from EASD (European Association for the Study of Diabetes), European Association for the Study of Diabetes in 2011, and she is a member in several professional bodies: the European Association for the Study of Diabetes (EASD), 2007; the European Society of Human Genetics (ESHG), 2013; Diabetes UK, 2008; and the American Society of Human Genetics (ASHG), 2007.

She has more than 130 publications with research interest in understanding the genetic architecture underlying susceptibility to complex disorders and in dissecting the genetic background of quantitative phenotypes in healthy individuals. She has previously participated in the research investigating genetics of Depression and Schizophrenia, Multiple Sclerosis, studies on population isolates, epidemiology of birth defects and congenital malformations. Her current research interest focuses on dissecting the multi-phenotype effects on cardiometabolic traits in highly dimensional whole genome and metabolomics data through usage of multivariate analytical methods.

Email: i.prokopenko@imperial.ac.uk
ABSTRACTS (in alphabetical order)
Contents

P1   Testing change over time with latent variable modeling: An Illustration .......................... 40

P2   Cost-effective quantitative serum NMR metabolomics platform for large-scale epidemiology – a practical molecular tool to reveal genetic pleiotropy and assist Mendelian randomization analyses ................................................................. 41

P3   Influence of intrinsic factors on erosive tooth wear in a large scale cohort study ........... 42

P4   The impact of preterm, early term and post term birth on child protection actions in early childhood – a follow-up register linkage study ............................................................. 43

O1   Childhood height and body mass index at 7 years of age and incidence of adult type 2 diabetes 44

P5   Structural properties of the human corpus callosum: Multimodal assessment and sex differences .................................................................................................................................. 45

P6   Exploring the developmental overnutrition hypothesis using polygenic risk scoring (PRS) in the Northern Finland Birth Cohort 1966 ...................................................................... 46

P7   Web-based testing for cognitive epidemiology ..................................................................... 47

P8   Motor development milestones and schizophrenia: meta-analysis .................................. 48

P9   Long-term antipsychotic use and brain volume changes in schizophrenia: The Northern Finland Birth Cohort 1966 study .................................................................................. 49

P10  The accumulation and interaction of factors related to deficits in health and risk of marginalisation in young adults in the Northern Finland ................................................................... 50

P11  Cerebellar activity in young people with familial risk for psychosis – The Oulu Brain and Mind Study ................................................................................................................................. 51

P12  Prevalence of TMD in Northern Finland Birth Cohort 1966 .............................................. 52

P13  What has birth cohort revealed on prognosis of schizophrenia? – The Northern Finland Birth Cohort 1966 ......................................................................................................................... 53

O2   Genome-wide multi-phenotype and eQTL analyses provide novel insights into omega fatty acid metabolism .......................................................................................................................... 54

O3   Educational differences in accelerometer-based physical activity and sedentary time in young adults during weekdays and weekend days ........................................................................... 55

P14  Interarch relationship measurement using digital 3-D models in transversal view .......... 56

P15  Somatic comorbidity in schizophrenia and other psychoses: a 46 year follow-up of the Northern Finland Birth Cohort 1966 ............................................................................................................. 57

P16  Longitudinal Evidence of the Association Between Physical Activity and the Built Environment – A Systematic Review ........................................................................................................... 58
O4 Maternal BMI before pregnancy as a risk factor for ADHD and autism in children; a follow-up study in the Danish National Birth Cohort

O5 A life-course approach to premature aging associated with pre-diabetes; a pilot study in Northern Finland Birth Cohort 1966 by the DynaHEALTH EU-action

P17 Protein intake during the first three weeks after birth predicts caloric intake 20 years later; Helsinki Study of Very Low Birth Weight Adults

P18 Pulse wave velocity in elderly of the Oulu45 cohort - effects of type 2 diabetes, physical activity and cholesterol

O6 Premorbid temperament as a predictor for remission in depression

P19 Birth size, childhood growth and hip fractures in old age; a follow-up of the Helsinki Birth Cohort Study

P20 A follow-up of twins in the two Northern Finland Birth Cohorts 1966 and 1986

P21 Adolescent smoking as a risk factor for psychosis after adjusting with prodromal symptoms

P22 Early traumas in young adults with Clinical and Familial Risk for psychosis; a follow-up of the Northern Finland Birth Cohort 1986

P23 Is adiposity rebound a predictor of metabolically healthy obesity?

P24 Effect of preterm birth and intrauterine life on adulthood lung function; a clinical follow-up of births (1985-89) in Finland

P25 Overweight and Obese but not Normal Weight Women with PCOS Are at Increased risk of Type 2 Diabetes Mellitus - a Prospective, Population-Based Cohort Study

O7 Association between vitamin D status and inflammation: stratification by body mass index-findings from the Northern Finland Birth Cohort 1966

P26 Duration of untreated psychosis and the use of antipsychotic medication during the course of illness in the Northern Finland 1966 Birth Cohort

P27 Impact of phthalate exposure on pregnancy outcomes, children’s health and neurodevelopment –REPRO_PL Cohort

O8 Childhood adversity, prodromal symptoms and brain response to faces in young adulthood

P28 Adolescent metabolic markers and cognitive deficits in young adults: association and interaction with psychosis in the Oulu Brain and Mind samples

P29 Pathway from perinatal circumstances to mortality at midlife in psychoses; a 45-year follow-up study of the Northern Finland Birth Cohort 1966

P30 Long-term unemployment is related to impaired glucose metabolism in middle-aged men; a follow-up of the Northern Finland Birth Cohort
P31 Validity of a web-based questionnaire to assess perinatal outcomes in the PRIDE Study.... 78
O9 Using web-based questionnaires to assess medication use during pregnancy: a validation study in pREGnant and the PRIDE Study........................................................................................................................................ 79
P32 Genome-wide association studies and meta-analyses of gastroesophageal reflux disease in 24766 Northern Europeans .................................................................................................................................................. 79
O10 Adverse adult consequences of adolescent alcohol exposure: Longitudinal results from the Northern Finland Birth Cohort, 1966............................................................................................................................................... 80
P33 Effects of preterm birth on bone health and fracture risk; observations on the Finnish birth cohort 1987-1990 .................................................................................................................................................. 82
O11 The association of multiple melanocytic nevi with education, gender and skin type; a Northern Finland Birth Cohort 1966 Study with 46 years’ follow-up................................. 83
P34 Non-alcoholic fatty liver disease does not appear to cause changes in circulating metabolites: A Mendelian randomization study............................................................ 84
P35 Early life stress, FKBPS polymorphisms, and insulin............................................................................... 85
P36 Mood disorders and schizophrenia in the offspring of antenatally depressed mothers - Relationship to parental history of severe mental disorder; a follow up of the Northern Finland 1966 Birth Cohort.............................................................................................................. 86
P37 Leisure-time physical activity in young adults born preterm – The ESTER Study..................... 87
O12 Migration history sequence analysis of young adults living in the largest cities of Finland; results from the 1987 Finnish Birth Cohort study.............................................................. 88
P38 Uterine Fibroids and Cardiovascular Risk; a population based Northern Finland Birth Cohort 1966 Study .................................................................................................................................................. 89
O13 Risk aversion and framing among the Northern Finland Birth Cohort 1966 participants..... 90
O14 Early nutrition interrupts the risk association of Caesarean section and obesity: secondary analysis of a randomized clinical trial .......................................................................................... 91
P39 The association between height and knee and hip osteoarthritis; the Northern Finland Birth Cohort 1966 study...................................................................................................................... 92
O15 Causal relationship between high milk consumption and cardio-metabolic traits - a Mendelian Randomization approach; the 1958 British Birth Cohort ................................................. 93
P40 Cloninger’s temperament dimensions and longitudinal alcohol use in early midlife; a Northern Finland Birth Cohort 1966 study ......................................................................................... 94
P41 Effect of maternal smoking during pregnancy on incidence of asthma among offspring between the ages of 31 and 46 years .................................................................................................................. 95
P1 - Testing change over time with latent variable modeling: An Illustration

Anthony O. Ahmed, PhD

Email: aoa9001@med.cornell.edu

Department of Psychiatry, Weill Cornell Medical College, 21 Bloomingdale Road, White Plains, New York, USA 10605

**Background**: Latent variable modeling allows researchers to test for individual differences in developmental trajectories that may underlie psychiatric data. Latent growth curve (LGC) modeling and growth mixture models (GMM) are particularly informative for investigating rate of change in longitudinal data.

**Objective**: The goal of the presentation is to illustrate the use of latent variable modeling to investigate change data.

**Design**: Participants were 2,898 drawn from the CATIE trial that completed measures of psychosis, cognition, and psychosocial functioning. Participants were administered the Positive and Negative Syndrome Scale (PANSS), neurocognitive measures, and the Quality of Life Interview at baseline and several follow-up periods. We submitted participant scores to LGC to examine changes in psychotic symptoms, neurocognition, and functioning during the study from baseline to each follow-up period. GMM served to investigate the presence of sub-populations within the data that may differ in their change trajectory. We will test models with predictors including age, sex, and treatment.

**Results**: We will present the hypothesized LCG model with intercept and slope parameters. The model was evaluated with the Comparative Fit Index (CFI), Tucker Lewis Fit Index (TLI), Root Mean Square Error of Approximation (RMSEA), and the Standardized Root Mean Square Residual (SRMR). The LGC model was successfully fit to the PANSS and neurocognition data with adequate fit demonstrating the validity of the hypothesized model. The GMMs fitted to the data were evaluated with Bayesian Information Criteria (BIC), Akaike Information Criteria (AIC), and Adjusted BIC and likelihood ratio-based tests—Vuong-Lo-Mendell-Rubin test (VLMR-LRT) and Adjusted Lo-Mendell-Rubin (Adjusted LRT). Only with negative symptoms drawn from the PANSS was there evidence of a subgroup of individuals with a disparate negative symptoms trajectory.

**Conclusion**: Latent trajectories are apparent in schizophrenia patients going through antipsychotic treatment. LGC and GMM are adaptable to investigating the heterogeneity of growth trajectories in longitudinal data.
P2 - Cost-effective quantitative serum NMR metabolomics platform for large-scale epidemiology – a practical molecular tool to reveal genetic pleiotropy and assist Mendelian randomization analyses

Mika Ala-Korpela$^{1,2,3,4}$, Peter Würtz$^1$, Antti J Kangas$^1$, Pasi Soininen$^{1,2}$, and George Davey Smith$^{3,4}$

Email: mika.ala-korpela@computationalmedicine.fi

$^1$University of Oulu & Biocenter Oulu, Computational Medicine, Oulu, Finland, $^2$University of Eastern Finland, School of Pharmacy, NMR Metabolomics Laboratory, Kuopio, Finland, $^3$University of Bristol, MRC Integrative Epidemiology Unit, Bristol, UK, $^4$University of Bristol, School of Social and Community Medicine, Bristol, UK

**Background:** Causality assessment is a fundamental challenge in epidemiology and is currently increasingly tackled via Mendelian randomization (MR) analyses.

**Objective:** Inference of causal pathways via MR entails a specific genetic instrument and necessitates extensive data.

**Design:** We have developed a cost-effective high-throughput serum nuclear magnetic resonance metabolomics platform, optimised for large-scale epidemiology that is assisting MR studies with respect to both of these difficult tasks.

**Results:** Extensive data on 14 lipoprotein subclasses, fatty acids, amino acids, glycolysis-related metabolites, and many other circulating molecules are available. The outcome is a set of absolute concentrations that can be analysed with standard statistical methods and combined with other ‘omics and clinical data. The platform has been used in >100 epidemiological and clinical studies with some 400,000 samples being analysed. In the assessment of the validity of a genetic instrument, e.g., if a single-nucleotide polymorphism (SNP) is pleiotropic, the comprehensive metabolic coverage offered by the platform is extending the evaluation of the gene-metabolite associations to a lot more refined situation than possible with only a few conventional markers. We have illustrated that many SNPs in various lipid genes, thought to be good genetic instruments, are actually highly pleiotropic. Genome-wide association studies are also suggesting that pleiotropic effects on human complex traits are widespread. Nevertheless, MR analyses have remarkable scientific value in systems epidemiology and also as a substitute for randomised controlled trials.

**Conclusions:** The ability to assess the validity of genetic instruments via detailed metabolic profiling is a prominent addition to MR studies. The presentation will introduce the metabolomics platform and give illustrative examples of genetic pleiotropy and MR analyses.
**P3 - Influence of intrinsic factors on erosive tooth wear in a large scale cohort study**

Viivi Alaraudanjoki1,2, Marja-Liisa Laitala1, Leo Tjäderhane1,2,3, Paula Pesonen2,4, Adrian Lussi5, Jukka Ronkainen6,7, Vuokko Anttonen1

Email: viivi.alaraudanjoki@oulu.fi

1University of Oulu, Research Unit of Oral Health Sciences, 2Oulu University Hospital and University of Oulu, Medical Research Center Oulu, 3University of Helsinki and Helsinki University Hospital, Department of Oral and Maxillofacial Diseases, Helsinki, Finland, 4University of Oulu, Center for Life Course Health Research, Oulu, Finland, 5University of Bern, Department of Preventive, Restorative and Pediatric Dentistry, Bern, Switzerland, 6Primary Health Care Center Tornio, Finland, 7University of Oulu, Center for Life Course Health Research, Oulu, Finland

**Background:** Erosive tooth wear is defined as a chemical dissolution of tooth surface caused by intrinsic or extrinsic acids, enhanced by mechanical forces such as tooth grinding. Interplay of causative and protective factors on erosive wear is complex and little is known about the long-term effects of them.

**Objective:** The main aim of this study was to assess the long-term influence of self-reported intrinsic factors (gastroesophageal reflux disease (GERD), alcoholism, heavy use of alcohol, multiple pregnancies and eating disorders) on erosive tooth wear in a middle-aged cohort sample.

**Design:** Of the total Northern Finland Birth Cohort (NFBC 1966), a convenience sample (n=3,181) was invited for an oral health examination in 2012-2013, of which 1,962 participated, comprising the final study group. Erosive tooth wear was assessed by sextants using the Basic Erosive Wear Examination Index (BEWE, 0–18). Clinical data was supplemented by questionnaires conducted in 1997/1998 and 2012/2013. The participants were divided into severe (BEWE sum≥9) and no to moderate (BEWE sum=0-8) erosive wear groups and logistic regression model was applied.

**Results:** Selected intrinsic factors were quite rare in this cohort sample and explained only 5.9% of the difference in the prevalence and severity of erosive wear. Daily symptoms of GERD (OR 3.8, CI 1.2-12.0) and hyposalivation (OR 3.8 CI 1.2-11.8) were the strongest risk indicators for severe erosive wear. Additionally, variables associated with elevated risk for severe erosive wear were diagnosed alcoholism at any point (OR 2.5, CI 0.7-9.7) and self-reported heavy use of alcohol in both questionnaires (OR 2.0, CI 0.6-6.2). Even low-dose long-term consumption of alcohol was associated with erosive wear.

**Conclusions:** In this cohort sample, intrinsic factors such as GERD or alcoholism alone are relatively uncommon causes of erosive tooth wear. The role of long-term use of alcohol in erosion process may be bigger than presumed.
P4 - The impact of preterm, early term and post term birth on child protection actions in early childhood – a follow-up register linkage study

Suvi Alenius¹, Eero Kajantie ¹, ², Pieta Näsänen-Gilmore¹, Marja Vääräsmäki³, ⁴, Mika Gissler¹, Petteri Hovi ¹, ²

Email: suvi.alenius@thl.fi

¹National Institute for Health and Welfare, Helsinki, Finland; ²Children’s Hospital, Helsinki University Hospital and University of Helsinki, Helsinki, Finland, ³National Institute for Health and Welfare, Oulu, Finland, ⁴Department of Obstetrics and Gynecology, MRC, Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland

Background: Several studies investigate how a child's background characteristics affects his/her placement risk, but only few studies include prematurity as a covariate when assessing this phenomenon. Fewer studies take into account the whole range of gestational age in analyses.

Objective: To assess how gestational age (GA) at birth predicts the rate of children ever placed outside home and affects child's age at first placement.

Design: We used data from the Finnish Medical Birth Register to identify singleton born infants (n=223672) of five gestational age -categories born between Jan 1st 1987 and Sep 30th 1990. Register of Child Welfare provided follow-up data (7679 first placements outside home, 3.4%) until 18th birthday. We analyzed the effect of gestational age by Cox regression. All the analyses were stratified by index child's birth year.

Results: We compared hazard ratios (HR) for ever been placed outside home, as well as for placement before 13th birthday, to those born at full term (39-41 gestational weeks) first with a model adjusted for IC’s sex and maternal age. Hazard ratios for placement before 13th birthday were 2.58 for early preterm (<34weeks), 1.90 for late preterm (34-<37), 1.38 for early term (37-<38) and 1.31 for post term (>=42). When further adjusted for maternal smoking in pregnancy, her highest attained education and number of previous live born children, the <34-wk hazard ratio attenuated to 2.00 with other hazard ratios unchanged.

Conclusions: Early environmental conditions may have life-long consequences for individual, family and society: As compared to full term children, preterm, early term and post term children are predisposed to placement outside home especially in early childhood.
**O1 - Childhood height and body mass index at 7 years of age and incidence of adult type 2 diabetes**

Lise G Bjerregaard¹, Michael Gamborg¹, Jennifer L Baker¹

Email: lise.geisler.bjerregaard@regionh.dk

¹Institute of Preventive Medicine, Bispebjerg and Frederiksberg Hospital, The Capital Region, Denmark

**Background:** Fast height growth in childhood has in a few small studies been associated with development of adult type 2 diabetes (T2D). The impact of sex and BMI on the association between childhood height and T2D, however, remains largely unknown.

**Objective:** We investigated associations between childhood height and T2D throughout adulthood, taking the influence of BMI during childhood into account.

**Design:** We included 148,037 men and 144,790 women born 1930-1983 with weights and heights measured at age 7 years in the Copenhagen School Health Records Register followed in national registers from 1977-2013 for information on T2D (11,548 men and 7,472 women). Hazard ratios (HR; 95% confidence intervals [CI]) of T2D (age ≥30 years) were estimated for height z-scores at age 7 years with adjustment for BMI.

**Results:** Among men, the influence of height varied by BMI levels (p=0.01). Among men with a below-average height (z-score<0) and a below-average BMI at 7 years (z-score<0), being short was associated with an increased risk of T2D (HR=0.88 per height z-score [0.84-0.93]) whereas a below-average height at 7 years had less influence on T2D if the BMI was above-average (z-score>0) (HR=0.95 [0.90-1.00]). Among men with an above-average height (z-score>0) at 7 years and below-average BMI, height was not associated with T2D (HR=1.03 [0.97-1.09]), whereas men who also had an above-average BMI had a slightly decreased risk of T2D (HR=0.95 [0.90-1.00]). Among women, the influence of height did not vary by BMI levels. In models adjusting for BMI among women, inverse associations between below-average height (HR=0.94 [0.90-0.99]) and above-average height (HR=0.93 [0.89-0.98]) and T2D were found.

**Conclusions:** Regardless of BMI, short childhood height was positively associated with T2D suggesting that compromised linear growth during childhood may contribute to the origins of T2D.
P5 - Structural properties of the human corpus callosum: Multimodal assessment and sex differences

Lassi Björnholm¹, Juha Nikkinen², Vesa Kiviniemi³, Tanja Nordström⁴, Mark Drakesmith⁵, C. J. Evans⁵, Juha Veijola¹, Tomáš Paus⁶ -⁸

Email: lassi.bjornholm@oulu.fi

¹University of Oulu and Oulu University Hospital, Department of Psychiatry, Oulu, Finland, ²Oulu University Hospital, Department of Radiotherapy, Oulu, Finland, ³Oulu University Hospital, Department of Diagnostic Radiology, Oulu, Finland, ⁴University of Oulu, Center for Life Course Health Research, Oulu, Finland, ⁵Cardiff University, School of Psychology, Cardiff, United Kingdom, ⁶Rotman Research Institute, Baycrest, Toronto, Canada, ⁷Departments of Psychology and Psychiatry, University of Toronto, Toronto, Canada, ⁸Child Mind Institute, New York, USA

Background: Corpus callosum (CC) is the main interhemispheric fiber tract in the human brain, consisting of about 200 million axons. The microstructure of CC, as of all white matter (WM), can be characterized in vivo by combining quantitative MRI (qMRI) data with knowledge of the underlying histology and the biophysical description of the MR contrast-generating parameters.

Objective: 1) Characterize MRI contrast-generating parameters in human brain WM, 2) study sex differences in WM.

Design: In Part 1, we combine information from six qMRI-based measures from the Avon Longitudinal Study of Parents and Children (450 males, age 18-21 years) with earlier literature on CC histology. In Part 2, we use this knowledge to interpret sex differences in three different qMRI measures of 451 men and women, from the Northern Finland Birth Cohort 1986, NFBC86 (age 25-27 years). Mean intensities from 10 midsagittal segments of the CC were extracted from images of each MRI measure. Part 1: Similarities of cross-CC profiles of MRI- and histology-based measures were estimated. Part 2: Sex differences in MRI measures were tested using linear mixed effects analyses and post-hoc t-tests. Both parts included hierarchical clustering of MRI data.

Results: Part 1: The cross-CC profiles of MRI measures were either similar to “large-fiber” or “small-fiber” profile. Part 2: A Sex * Segment interaction was found for one and a main effect of Sex for another MRI measure.

Conclusions: The same division of the six MRI measures being similar to either small or large fiber profile was also observed in hierarchical clustering of the MRI measures, suggesting that fiber diameter is a prominent MRI contrast-generating parameter. The sex difference found in the NFBC86 is different to observations in adolescents, suggesting changes in WM microstructure until early adulthood.
P6 - Exploring the developmental overnutrition hypothesis using polygenic risk scoring (PRS) in the Northern Finland Birth Cohort 1966

Tom Bond¹, Adam Socrates², Dylan Williams³, Juha Auvinen⁴, Minna Männikkö⁴, Sirkka Keinänen-Kiukaanniemi⁴, Sylvain Sebert⁴,⁵, Marc Gunter⁶, Paul O’Reilly⁴, Marjo-Riitta Jarvelin¹,⁴,⁵

Email: tb1614@ic.ac.uk

¹Imperial College London, London, UK; ²King’s College London, London, UK, ³Karolinska Institutet, Stockholm, Sweden, ⁴Center for Life Course Health Research, University of Oulu, Finland, ⁵Biocenter Oulu, Oulu, Finland, ⁶IARC, Lyon, France

Background: The developmental overnutrition hypothesis proposes that maternal adiposity during pregnancy causes increased offspring adiposity via intrauterine mechanisms. We aimed to test the extent to which this association is driven by genetic factors, using polygenic risk scoring (PRS).

Methods: We analysed prospective data from 4459 singleton offspring from the Northern Finland Birth Cohort 1966. Associations of maternal pre-pregnancy BMI with offspring ponderal index (PI) at birth and BMI at 31 years were examined using multiple linear regression, adjusting for potential confounding by maternal and offspring factors. Models were adjusted for the genetic determinants of adult BMI using a PRS derived from offspring genome-wide SNP data (8672 genetic variants included) and effect estimates for adult BMI provided by the GIANT consortium.

Preliminary results: The BMI PRS explained 5.6% of variance in 31 year BMI but only 0.1% of variance in ponderal index at birth. Maternal pre-pregnancy BMI was positively associated with offspring PI at birth (0.11 SD increase in offspring PI per maternal BMI SD, 95% CI=0.07, 0.14, P<0.001) and at 31 years (0.28 SD, 95% CI=0.24, 0.31, P<0.001). On adjustment for the BMI PRS these associations were attenuated by 2.6% and 9.3% respectively.

Conclusions: A PRS for adult BMI appears to partially mediate the association between maternal pre-pregnancy BMI and young adult BMI. Inference about the extent to which fetal programming underlies this association is complicated by uncertainty about the heritability of BMI. Further work will seek to quantify the proportion of the covariance of maternal and offspring BMI attributable to genetic and non-genetic factors.
**P7 - Web-based testing for cognitive epidemiology**

Francesca Cormack¹, Nick Taptiklis¹, Charlotte Housden¹², Jennifer H. Barnett¹²

Email: Francesca.cormack@camcog.com

¹Cambridge Cognition, ²Department of Psychiatry, University of Cambridge

**Background:** Neurological and mental health problems are major contributors to the global burden of disability. Understanding the environmental and genetic factors underpinning these conditions requires epidemiological studies. Web-based cognitive testing has the potential to allow large-scale and high-frequency data collection in a cost-and time effective manner. There is, however, legitimate concern regarding reliability and validity of unsupervised testing, particularly in those with a history of mental health issues or substance abuse.

**Objective:** 1) Identifying markers of inattention in online testing 2) comparing participants with and without a self-reported history of mental health issues (depression/ anxiety/substance abuse) on these metrics.

**Design:** 400 participants completed an on-line assessment of spatial working memory (SWM), a Cantab test known to be affected in psychiatric disorders. Participants were asked to report whether they had a history of depression, anxiety or other neurological or psychiatric condition, and 200 participants completed the PHQ8 rating scale of depression symptoms. In addition to measures of errors and strategy we extracted trial-by-trial data related to timing, and browser information (whether the participant stayed on task or not). We compared performance of the online groups that of a benchmark sample of 94 participants tested in laboratory conditions. Repeatability data was collected in both samples.

**Results:** Results indicated comparable levels of performance in online and laboratory based testing. Within web-based testing participants with a self-reported history of mental health problems were equally likely to display off-task behaviour, showed equivalent reaction times, variability in reaction time and task performance.

**Conclusions:** Participants with a self-reported history of mental health issues perform just as consistently as those with no such history in online testing, suggesting that this method of cognitive assessment can be reliably for screening into clinical trials or remote monitoring of cognitive performance.
**Background:** Neurodevelopment theories of schizophrenia suggest that abnormalities in developing nervous system and exposure to early risk factors in childhood betray vulnerability to the illness. Motor milestones, such as learning to walk or standing unsupported, are predictors of later schizophrenia but studies have not been systematically reviewed.

**Objective:** The aim of present systematic review and meta-analysis was to explore the association between motor development milestones in early childhood and adult schizophrenia.

**Design:** Articles reporting original research were searched from PubMed, PsycINFO and Scopus databases in July 2015. The following keywords were used: infant, child*, early, schizophrenia, psychosis, schizoaff*, psychotic, impairment, delay, skill, ability, function, deficit, coordination, performance, problem, milestone*, complication*, risk*, functioning, precursor*, predictor*, motor movement, neuromuscular, psychomotor, neuromotor and development*. Inclusion criteria required a standardized and reliable assessment of schizophrenia (e.g. registers, clinical diagnoses, interview diagnoses, validated diagnoses by physician, no self-reports). Studies with only childhood onset cases (age of onset of psychosis/schizophrenia <12 years old) were excluded from the analyses. Milestones were required to have been assessed during the period from 0 to 13 years old for inclusion. Neither publication date nor language restrictions were applied. Hedges’ g was used to estimate effect size.

**Results:** 69 full text articles were accessed for eligibility and 5 included in meta-analyses. Three to five studies were included in meta-analysis of each milestone. Three milestones were significantly associated with schizophrenia: walking unsupported (g=0.46, 95% CI 0.27-0.64; p<0.001), standing unsupported (g=0.28, 0.16-0.4; p<0.001) and sitting unsupported (g=0.18, 0.05-0.31; p=0.007). Results for the milestones ‘holding head up’ and ‘grabbing object’ were not significant.

**Conclusions:** Walking, sitting and standing unsupported had a significant small effect. The findings support the neurodevelopment theory of schizophrenia.
**P9 - Long-term antipsychotic use and brain volume changes in schizophrenia: The Northern Finland Birth Cohort 1966 study**

Sanna Huhtaniska\textsuperscript{1,2,3}, Tuomas Heikka\textsuperscript{3}, Erika Jääskeläinen\textsuperscript{1,2,3}, Jani Moilanen\textsuperscript{2,3,4}, Tanja Nordström\textsuperscript{1,2}, Jussi Tohka\textsuperscript{5}, José V. Manjón\textsuperscript{6}, Pierrick Coupe\textsuperscript{7}, Lassi Björnholm\textsuperscript{2,3}, Juha Veijola\textsuperscript{2,3,4}, Matti Isohanni\textsuperscript{3,4}, Vesa Kiviniemi\textsuperscript{7}, Graham Murray\textsuperscript{9,10}, Jouko Miettunen\textsuperscript{1,2,3}

Email: sanna.huhtaniska@oulu.fi

\textsuperscript{1}Center for Life Course Health Research, University of Oulu, Finland; \textsuperscript{2}Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Finland; \textsuperscript{3}Research Unit of Clinical Neurosciences, Department of Psychiatry, University of Oulu, Finland; \textsuperscript{4}Department of Psychiatry, Oulu University Hospital, Finland; \textsuperscript{5}Department of Bioengineering and Aerospace Engineering, Universidad Carlos III de Madrid, Leganes, Spain; \textsuperscript{6}Instituto de Aplicaciones de las Tecnologías de la Información y de las Comunicaciones Avanzadas (ITACA), Universitat Politècnica de València, Spain; \textsuperscript{7}Laboratoire Bordelais de Recherche en Informatique, Unité Mixte de Recherche CNRS (UMR 5800), PICTURA Research Group, France; \textsuperscript{8}Department of Diagnostic Radiology, Oulu University Hospital, Finland; \textsuperscript{9}Department of Psychiatry, University of Cambridge, UK; \textsuperscript{10}Behavioural and Clinical Neuroscience Institute, University of Cambridge, UK

**Background:** The effects of long-term antipsychotic medication use on structural brain changes in schizophrenia are still unknown. Higher cumulative antipsychotic exposure has been found to associate with gray matter volume decrease without effects of illness duration or severity.

**Objective:** The objective was to analyze whether scan interval antipsychotic dose would have an effect on brain structural changes during a 9-year follow-up in a population based sample of schizophrenia cases with illness duration on average 10 years at baseline.

**Design:** The Northern Finland Birth Cohort 1966 (NFBC 1966) is an unselected, general population birth cohort identified during mid-pregnancy. Data of 32 individuals with schizophrenia from the NFBC 1966 were collected by interview and from medical records. The participants had an average illness duration of 10.4 years at baseline. Data on antipsychotic medication was collected using all available medical records and an interview, and transformed to cumulative dose of antipsychotics expressed as dose-years of a daily dose of 100 mg chlorpromazine. Structural MRI data at ages of 34 and 43 were acquired on 1.5 GE Signa scanner and brain structures were extracted using volBrain automated volumetry system (http://volbrain.upv.es). The data were analyzed with linear regression with intracranial volume as a covariate.

**Results:** Higher scan interval antipsychotic dose associated with increase in both right and left lateral ventricles (standardized beta, b=0.45, \(p=0.006\); and b=0.43, \(p=0.010\); respectively) and with decrease in left caudate (b=-0.38, \(p=0.023\)), right accumbens (b=-0.38, \(p=0.036\)), and total gray matter (b=-0.38, \(p=0.035\)).

**Conclusions:** This is one of the first studies being able to study long-term effects of antipsychotics on brain structure in schizophrenia cases in their midlife. Even after ten years of illness onset it is possible to detect structural brain changes that antipsychotic medication may contribute to. These structural alterations should be considered when adjusting antipsychotic doses in clinical practice.
P10 - The accumulation and interaction of factors related to deficits in health and risk of marginalisation in young adults in the Northern Finland

Tuula M. Hurtig¹,², Hanna E. Ebeling², Anja M. Taanila³, Pirjo Mäki¹, Pentti Kuronen³, Kai Parkkola⁴, Heli Koivumaa-Honkanen⁵

Email: Tuula.hurtig@oulu.fi

¹University of Oulu, Department of Psychiatry, Oulu, Finland, ²University and University Hospital of Oulu, Clinic of Child Psychiatry, Oulu, Finland, ³University of Oulu, Center for Life Course Research, Oulu, Finland, ⁴University of Tampere, Faculty of Medicine, Tampere, Finland, ⁵University of Eastern Finland, Department of Psychiatry, Kuopio, Finland

Background: Marginalisation due to deficits in individual resources is a health problem in many western societies, especially among young people.

Objective: This research investigates the accumulation and interaction of individual deficits in mental health and wellbeing as potential risk factors of marginalisation in young adults. It is hypothesized that especially depression, neuropsychiatric symptoms and social and communication deficits are related to the risk of marginalisation through failure in social or academic achievements.

Design: The multidisciplinary study utilizes two large community-based samples in the provinces of Oulu and Lapland in Finland. First one is a one-year military call-up sample including 4500 men born in 1996. The call-up sample comprises all men in our target area attending obligatory military call-up examination in the year 2014 before entering military service the next year. The other one is the Northern Finland Birth Cohort 1986 sample including 4872 men born in 1985/1986. Internationally validated questionnaires measuring health, wellbeing, and educational and occupational achievements were completed in both study populations. In addition, information from national health registers are used. Both cross-sectional and longitudinal designs are obtained as well as time-trend comparisons between the samples.

Results: Preliminary results show that the symptoms or diagnosis of depression were common and were related to rejection from military service. The data collection in the birth cohort sample is still ongoing.

Conclusions: The research provides new information in identifying individuals and groups at risk of marginalisation because of unfavorable conditions, health deficits or insufficient personal resources. The information can be used to plan interventions on multiple levels, and to develop social and health care services and professional education to meet current and future needs in the North.
P11 - Cerebellar activity in young people with familial risk for psychosis – The Oulu Brain and Mind Study

Tuomas Jukuri¹,²,³, Vesa Kiviniemi⁴,⁵, Juha Nikkinen⁵,⁶, Jouko Miettunen¹,²,⁵,⁶, Pirjo Mäki¹,²,⁵, Sari Mukkala¹,², Jenni Koivukangas¹,³, Tanja Nordström⁵,⁷, Irma Moilanen³,⁸, Jennifer H. Barnett⁹,¹⁰, Peter B. Jones⁹, Graham K. Murray⁹, Juha Veijola¹,²,³,⁵

Email: tuomas.jukuri@oulu.fi

¹University of Oulu, Department of Psychiatry, ²Oulu University Hospital, Department of Psychiatry, ³University of Oulu, Thule Doctoral Programme, ⁴Oulu University Hospital, Department of Diagnostic Radiology, MIPT, ⁵Oulu University Hospital and University of Oulu, Medical Research Center, ⁶Oulu University Hospital, Department of Oncology and Radiotherapy, ⁷University of Oulu, Center for Life Course Health Research, ⁸Oulu University Hospital and University of Oulu, Department of Child Psychiatry, ⁹Oulu, Finland, ¹⁰University of Cambridge, Department of Psychiatry, Cambridgeshire, UK

Background: The study aim was to compare the R-fMRI activity of the cerebellum in two groups of people without psychosis: one with a history of psychotic disorder in one or both parents (the FR group), the other without any such family risk of psychosis (the control group).

Objective: The cerebellum plays a critical role in cognition and behavior. Altered function of the cerebellum has been related to schizophrenia and psychosis but it is not known how this applies to spontaneous resting state activity in young people with familial risk for psychosis.

Design: We conducted resting-state functional MRI (R-fMRI) in 72 (29 male) young adults with a history of psychosis in one or both parents (FR) but without their own psychosis, and 72 (29 male) similarly healthy control subjects without parental psychosis. Both groups in the Oulu Brain and Mind Study were drawn from the Northern Finland Birth Cohort 1986. Participants were 20–25 years old. Parental psychosis was established using the Care Register for Health Care. R-fMRI data pre-processing was conducted using independent component analysis with 30 and 70 components. A dual regression technique was used to detect between-group differences in the cerebellum with p< 0.05 threshold corrected for multiple comparisons.

Results: FR participants demonstrated statistically significantly increased activity compared to control subjects in the anterior lobe of the right cerebellum in the analysis with 70 components. The volume of the increased activity was 73 mm³. There was no difference between the groups in the analysis with 30 components.

Conclusions: The finding suggests that increased activity of the anterior lobe of the right cerebellum may be associated with increased vulnerability to psychosis. The finding is novel, and needs replication to be confirmed.
Background: Temporomandibular disorders (TMD) have shown to be among the most common pain conditions of the craniofacial area. Prevalence of TMD among adult population varies greatly depending on the examination methods as well as on the subjects participating in them. Studies in adult populations have shown symptoms of TMD manifesting in approximately 25-50% of subjects, while clinical findings in 40-90% of subjects are even more usual.

Objective: The follow-up study concerning the Northern Finland Birth Cohort 1966 (NFBC 1966) subjects was performed during 2012-2013 including questionnaires and clinical examinations. The aim of the study was to investigate the prevalence of TMD symptoms and signs in 45-46-year-old cohort subjects.

Design: Altogether 1964 individuals (912 men and 1052 women) participated in oral health investigation, including medical and dental clinical examination and additional questionnaires. The stomatognathic examination was performed by the modified protocol of DC/TMD presented in Symposium at IADR Conference in 2010 (Barcelona, Spain) (Shiffman et al. 2014).

Results: Most common clinical signs of TMD were clicking in temporomandibular joints (26.2%) and pain in masticatory muscles (11.2%). Women had clinical signs of TMD more often than men, especially pain in masticatory muscles (odds ratio [OR] = 2.59; 95% confidence interval [CI]=1.89-3.54) and limited mouth opening (OR=2.5; 95% CI=1.47-4.25). Most common diagnosis was disk displacement with reduction (7.0%). Myalgia, arthralgia and disc displacement with reduction were statistically significantly more common in women than in men (p < 0.05).

Conclusions: The prevalence of TMD was higher in women than in men. Most common clinical sign was clicking in temporomandibular joints and most common diagnosis was disk displacement with reduction. The results were comparable with other similar population studies.
Background: Schizophrenia is prevalent and important public health problem.

Objective: The aim of this study was to explore the prognosis and predictors of outcomes in schizophrenia in a birth cohort sample.

Design: The sample included subjects with schizophrenia (n=29-161, depending on the analyzed topic) from the Northern Finland Birth Cohort 1966. Outcomes and their predictors were analyzed by utilizing national registers, questionnaires and personal examinations made on several time points (e.g. during pregnancy, at age 1 year, 14-years, 34- and 43- years). Occupational and social functioning, amount of psychiatric symptoms, utilization of treatments, and cognition were used as measures of outcomes. Several plausible factors associating to outcomes were studied, e.g. gender, family history of psychosis, development and childhood related factors, school performance, and illness related factors around the onset of psychosis, brain morphology and cognitive functioning, and lifetime antipsychotic medication.

Results: Around the age of 34-years recovery was possible though quite uncommon (3.4%), some persons achieved symptomatic remission (21%), and many were on disability pension (54%). Around the age of 43-45 years only 11.2% were employed, and 19% were in remission. Earlier age of illness onset, longer duration of untreated psychosis, suicidal ideation and poorer functioning around illness onset, brain morphological changes and poorer cognition, and higher lifetime doses of antipsychotics associated to poor outcomes. Cognition did not markedly decline from 34 to 43 years of age, but poorer premorbid school performance and higher lifetime doses of antipsychotics predicted more decline of cognition.

Conclusions: Our results indicate heterogeneous and still relatively unsatisfactory prognosis of schizophrenia in this sample. Several predictors of outcomes have been found, and especially factors related to illness onset and high lifetime cumulative dose of antipsychotics are of interest. Birth cohort setting offers unique possibility to study long-term prognosis of schizophrenia.
O2 - Genome-wide multi-phenotype and eQTL analyses provide novel insights into omega fatty acid metabolism

Marika Kaakinen¹, Annique Claringboud¹,², Fiona Hagenbeek¹,³,⁴, Reedik Mägi⁵, Pasi Soininen⁶,⁷, Marjo-Riitta Järvelin⁸,⁹,¹⁰,¹¹, BIOS Consortium, Andrew P. Morris¹², Inga Prokopenko¹

Email: m.kaakinen@imperial.ac.uk

²Imperial College London, Department of Genomics of Common Disease, London, UK; ¹University Medical Centre Groningen, Department of Genetics, Groningen, The Netherlands; ³VU University Amsterdam, Department of Biological Psychology, Amsterdam, The Netherlands; ⁴EMGO+ Institute for Health and Care Research, Amsterdam, The Netherlands; ⁵University of Tartu, Estonian Genome Center, Tartu, Estonia; ⁶University of Eastern Finland, NMR Metabolomics Laboratory, Kuopio, Finland; ⁷University of Oulu, Computational Medicine, Oulu, Finland; ⁸Imperial College London, Department of Epidemiology and Biostatistics, London, UK; ⁹University of Oulu, Center for Life Cycle Health Research; ¹⁰University of Oulu, Biocenter Oulu; ¹¹Oulu University Hospital, Unit of Primary Care, Oulu, Finland; ¹²University of Liverpool, Department of Biostatistics, Liverpool, UK

Background: There is evidence for favourable effects of diets rich in omega-3 fatty acids (FAs) on cardiovascular disease. However, little is known on the genetic contribution to FA levels, since most studies have focused on serum lipid concentrations typically used in clinical practice.

Objective: The aim of this study was to dissect the genetic architecture of FA levels.

Design: We undertook common and rare variant genome-wide multi-phenotype analyses (MPA) of FA levels using nuclear magnetic resonance-based measures of FAs and 1000 Genomes imputed data from the Northern Finland Birth Cohorts 1966 (N=4949) and 1986 (N=3055). To avoid multicollinearity issues, we selected four FAs out of the available data for MPA: omega-3, -6, -7/9 and other polyunsaturated FAs. Expression quantitative locus (eQTL) analysis was performed on the Dutch BIOS consortium RNA-seq data (N=2116).

Results: The common variant meta-analysis detected 10 signals associated with FAs (P<5x10⁻⁸), including a novel FA locus at MACROD1 (rs1006207). Variation in the other identified loci PCSK9, GCKR, FADS1, ZNF259, LIPC, PDXDC1, PBX4, APOE and ADAMTS3 has previously been associated with triglycerides and cholesterol levels, but not specifically with FAs. FADS1 was also identified in the rare variant MPA. The eQTL analysis indicated eight out of 10 MPA-identified signals with significant cis-eQTL effects on gene expression levels. The novel MACROD1 variant was a cis-eQTL for PRDX5 expression, suggesting a role in protection against oxidative stress.

Conclusions: With a combination of refined lipid measures, MPA and eQTL analysis we have identified genetic loci and differentially expressed genes involved in FA metabolism, providing novel clues for the complex relationship between lipids and cardiovascular disease.
O3 - Educational differences in accelerometer-based physical activity and sedentary time in young adults during weekdays and weekend days

Marko T. Kantomaa¹,², Marjaana Tikanmäki³,⁴, Anna Kankaanpää¹, Marja Vääräsmäki⁵,⁶, Marika Sipola-Leppänen³,⁴,⁷, Ulf Ekelund⁸,⁹, Hårt Hakonen¹, Marjo-Riitta Järvelin²,⁶,¹⁰,¹¹, Eero Kajantie⁵,¹²,¹³, Tuija H. Tammelin¹

Email: m.kantomaa@imperial.ac.uk

¹LIKES – Research Center for Sport and Health Sciences, Jyväskylä, Finland; ²Imperial College London, School of Public Health, Department of Epidemiology and Biostatistics, MRC Health Protection Agency (HPA) Centre for Environment and Health, London, UK; ³National Institute for Health and Welfare Oulu, Chronic Disease Prevention Unit, Oulu, Finland; ⁴University of Oulu, Institute of Health Sciences, Oulu, Finland; ⁵Oulu University Hospital and University of Oulu, Medical Research Center Oulu, Department of Obstetrics and Gynaecology, Oulu, Finland; ⁶National Institute for Health and Welfare Oulu, Department of Children and Young People and Families, Oulu, Finland; ⁷Oulu University hospital and University of Oulu, Medical Research Center Oulu, Research Unit for Pediatrics, Dermatology, Clinical Genetics, Obstetrics and Gynecology, Oulu, Finland; ⁸Norwegian School of Sport Sciences, Department of Sport Medicine, Oslo, Norway; ⁹University of Cambridge, Medical Research Council Epidemiology Unit, Cambridge, UK; ¹⁰University of Oulu, Biocenter Oulu, Oulu, Finland ¹¹Oulu University Hospital, Unit of Primary Care, Oulu, Finland; ¹²National Institute for Health and Welfare, Diabetes Prevention Unit, Helsinki and Oulu, Finland; ¹³Helsinki University Central Hospital and University of Helsinki, Children’s Hospital, Helsinki, Finland

Background: Educational variation in physical activity and sedentary behavior is important as it may represent a causal pathway by which social inequalities lead to poor health.

Objective: This study examined educational differences in objectively measured physical activity (PA) and sedentary time (ST) in young adults.

Design: Data from the ESTER study (2009–2011) from Finland (n=538) was used to examine associations between educational attainment (primary, vocational, upper secondary, college, polytechnic, university) and different subcomponents of PA and ST measured by hip-worn accelerometer (ActiGraph GT1M) for seven consecutive days. Overall PA, moderate-to-vigorous PA, light-intensity PA, and ST were calculated separately for weekdays and weekend days. The associations were examined with a linear regression analysis, stratified by sex and the days of the week (weekdays vs. weekend days). The analyses were adjusted for preterm birth, maternal gestational diabetes and hypertension, employment status, and self-assessment of the economic situation. Latent profile analysis was conducted in order to identify different profiles of ST and subcomponents of PA.

Results: Educational differences in PA and ST varied according to subcomponents of PA, and between weekdays and weekend days. High education level was associated with high moderate-to-vigorous PA during weekdays (males: B=1.631, P=0.001; females: B=1.824, P=0.001) and weekend days (males: B=2.409, P=0.003; females: B=1.490, P=0.011), with high ST during weekdays (males: B=3.045% of wearing time/day, P<0.001; females: B=1.294% of wearing time/day, P=0.001), and with low amount of light-intensity PA during weekdays in males (B=–31.063, P<0.001) and during weekdays (B=–17.301, P<0.001) and weekend days (B=–7.587, P=0.047) in females.

Conclusions: Results indicate different challenges related to unhealthy behavior for young adults with low and high education: low education is associated with lack of moderate-to-vigorous PA, whereas high education is associated with lack of light-intensity PA and with high ST especially during weekdays.
P14 - Interarch relationship measurement using digital 3-D models in transversal view

Heikki Kiviahde¹, Lea Bukovac¹, Päivi Jussila¹, Ritva Nääpänkangas¹, Kirsi Sipilä², Pertti Pirittiniemi¹ and Aune Raustia¹

Email: Heikki.kiviahde@oulu.fi

¹Research Unit of Oral Health Sciences, Faculty of Medicine, University of Oulu, Oulu, Finland; Medical Research Center Oulu (MRC Oulu); Oulu University Hospital and University of Oulu, Finland; ²Institute of Dentistry, University of Eastern Finland, Kuopio, Finland.

Background: Only few studies are available related to inter-arch relationship measurements performed on digital models. 3D models have made it possible to develop new view to measure interarch relationship.

Objective: The aim of the study was to evaluate the method for measuring dental interarch relationship in transversal view using 3D models.

Design: The sample comprised 30 sets of study models of subjects randomly selected from Northern Finland 1966 Birth Cohort (Sipilä et al, 2006). Dental casts were placed in intercuspal position and scanned by 3Shape® 3D Scanner. Measurements were done on 3D digital models using 3Shape Ortho Analyser® software. In transversal view and marked points in both dental arches were projected to the occlusal plane. Occlusal characteristics measured included bilateral first-molar relationship, bilateral canine relationship, transversal inter-molar asymmetry and midline asymmetry. All the measurements were repeated in two weeks.

Results: Intra-examiner error in measurements of bilateral first-molar relationship varied from 0.00 to 0.39 mm, canine relationship from 0.01 to 0.8 mm, transversal asymmetry from 0.00 to 0.42 mm and midline asymmetry from 0.00 to 0.24 mm.

Conclusion: The study showed that the use of digital 3-D models is a valid, accurate and repeatable method in interarch relationship measurements.
P15 - Somatic comorbidity in schizophrenia and other psychoses: a 46 year follow-up of the Northern Finland Birth Cohort 1966

Hanna Korpela, Jouko Miettunen, Nina Rautio, Matti Isohanni, Marjo-Riitta Järvelin, Erika Jääskeläinen, Juha Auvinen, Sirkka Keinänen-Kiukaanniemi, Tanja Nordström and Jussi Seppälä

Email: hanna.korpela@student.oulu.fi

1Center for Life Course Health Research, University of Oulu, Oulu, Finland; 2Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland; 3Research Unit of Clinical Neuroscience, University of Oulu, Oulu, Finland; 4Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland; 5Department of Epidemiology and Biostatistics, MRC–PHE Centre for Environment & Health, School of Public Health, Imperial College London, UK; 6Biocenter Oulu, University of Oulu, Oulu, Finland; 7Department of Psychiatry, South-Savo Hospital District, Mikkeli, Finland

Background: Studies have well documented that individuals with psychoses, and especially with schizophrenia have increased rates of physical illnesses compared with the general population. Objective: We studied the cumulative incidence of physical illnesses in schizophrenia (SCZ) or in other psychoses and among people without psychoses until age of 46 years.

Design: The sample consisted of 10,933 members of the Northern Finland Birth Cohort 1966 (NFBC 1966) of which 411 were diagnosed with psychosis. In the psychotic population 212 had SCZ while 199 subjects were diagnosed with other psychoses. Diagnoses concerning physical illnesses were based on nationwide registers followed until end of 2013, and coded according to the ICD-8, ICD-9 or ICD-10. Psychoses were classified as SCZ and other psychoses.

Results: Diseases of the blood and blood forming organs (prevalence in SCZ was 11 % versus 6 % in controls, p 0.003) and endocrine, nutritional and metabolic diseases (18 % vs. 11 %, p 0.002) were more common among individuals with SCZ compared with controls. Diseases of musculoskeletal system and connective tissue were less common in SCZ than among controls (30 % vs. 42 %, p<0.001) and this association was found especially in men with SCZ (prevalence in men with SCZ was 29 % vs. 42 % of men in controls, p=0.004). People with other psychoses than SCZ had significantly more all somatic diagnoses, except neoplasms, diseases of the eye and adnexa, musculoskeletal system and connective tissue, than controls.

Conclusions: A new finding is that especially people with other psychoses than SCZ show a greater occurrence of somatic diseases compared with those without psychosis. The increased occurrence of somatic comorbidity in psychoses should be noted by medical professional, and further longitudinal studies are warranted to study its possible risk factors during lifespan.
Background: In order to develop better communities and effective interventions it is important to gain robust knowledge of the most essential modifiable factors related to the built environment that make people active. The cross-sectional evidence of the association between built environment (BE) and physical activity (PA) is strong but causality has been recognized as a major lack in the existing literature.

Objective: The objective of this systematic review is to examine evidence from the latest studies utilizing advanced longitudinal research design in order to identify the environmental determinants and not merely associations of physical activity. This review will systematically evaluate the evidence specifically from the natural experiments, interventions and prospective longitudinal studies regarding the connection between BE and PA that are expected to provide the highest level of evidence. The review seeks answers to the following questions: What are the key environmental determinants of physical activity identified in longitudinal studies? How changes in the built environment affect physical activity? The review will provide valuable information of the most recent robust evidence between community planning and active living which can be utilized by decision makers and other researchers. It will follow the PRISMA statement for conducting systematic reviews.

Design: Systematic Review

Results: Not applicable yet

Conclusions: Not applicable yet
O4 - Maternal BMI before pregnancy as a risk factor for ADHD and autism in children; a follow-up study in the Danish National Birth Cohort

Christina H. Andersen¹, Per H. Thomsen¹, Ellen A. Nøhr², Sanne Lemcke¹

Email: sanne.lemcke@ps.rm.dk

¹Aarhus University Hospital, Centre for Child and Adolescent Psychiatry, Aarhus, Denmark; ²University of Southern Denmark, Institute of Clinical Research, Odense, Denmark

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD) are neurodevelopmental disorders which are caused by both genetic and environmental factors. Previous studies have investigated maternal obesity before pregnancy as an environmental factor, and the results are divergent.

Objective: To investigate a possible association between maternal weight before pregnancy and the occurrence of ADHD and ASD in children in a large birth-cohort. We hypothesized that mothers with a BMI>25 would have an increased risk of having a child with ADHD or ASD.

Design: This study is based on the Danish National Birth Cohort in which more than 92,000 Danish women were enrolled between 1996 and 2002. The women were interviewed about lifestyle factors, including (pre-pregnancy) weight and height, in week 12 of gestation. They were divided into groups based on Body Mass Index (BMI) according to the World Health Organization. Children with a clinical diagnosis of ADHD and/or ASD were identified in the Danish health registries using their personal identification number as linkage. Hazard ratios for ADHD and/or ASD in children were estimated using Cox proportional hazards regression analysis.

Results: The results showed that overweight and obese mothers had an elevated risk of having a child with ADHD compared to normal weight mothers. The higher the BMI the higher the risk of having a child with ADHD. The association was not as clear for ASD.

Conclusions: Maternal pre-pregnancy overweight is a risk factor for having a child with ADHD, but no clear association was found with ASD. Despite these results we cannot say that maternal BMI is a causal risk, but needs more studies to conclude about the causation.
O5 - A life-course approach to premature aging associated with pre-diabetes; a pilot study in Northern Finland Birth Cohort 1966 by the DynaHEALTH EU-action

Estelle Lowry1,2, Nina Rautio1,3, Ville Karhunen1, Sirkka Keinänen-Kiukaanniemi1,3, Leena Alam-Mursula1, Inga Prokopenko5, Alex Lewin4,5, Jouko Miettunen1,6, Sylvain Sebert1,2,5 and Marjo-Riitta Järvelin1,2,5

Email: estelle.lowry@oulu.fi

1Center for Life Course Health Research, University of Oulu, Finland; 2Biocenter Oulu, University of Oulu, Finland; 3Unit of Primary Health Care, Oulu University Hospital, Finland; 4Brunel University of London, UK; 5School of Public Health departments of Epidemiology and Public Health and Genomics of Complex diseases, Imperial College London, UK; 6Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Finland

Background: There is increased awareness that the process of premature aging starts in early life via psycho-social adversities acting on human physiology. It is therefore highly relevant to study the life-course trajectories leading to pre-diabetic states and its impact on the risk of premature aging.

Objective: We hypothesize that a composite score of biological and psycho-social factors can be created to predict premature aging associated with Type 2 diabetes.

Design: The prototype study is based on data prospectively collected from the Northern Finland Birth Cohort 1966 aged 31 and 46 years. 2,046 males and 1,888 females had complete data on glycemic, psychological and social traits including longitudinal outcomes. Factor analyses were performed to derive latent factors comprising the Gluco-Psycho-Social Axis (GPA), which may be used to predict decline of metabolic function from ages 31 to 46 years.

Results: Exploratory factor analysis and subsequent confirmatory factor analysis indicated a three factor solution to best fit the data. Examination of factor loadings and variable content suggest factors are representative of the hypothesized construct areas: Glycemic; Psychological; Social. Sex stratified analysis suggested measurement variance across gender and therefore separate male and female models may be best.

Conclusions: Evidence from this pilot analysis supports an interplay of gluco- and psycho-social factors in establishing risk of premature aging associated with pre-diabetic states. The current prototype is designed as part of the DynaHEALTH European action (www.dynahealth.eu). Structural equation models will be employed to look at life-course modelling of the GPA upon healthy aging.
P17 - Protein intake during the first three weeks after birth predicts caloric intake 20 years later; Helsinki Study of Very Low Birth Weight Adults

Hanna-Maria Matinolli¹,², Petteri Hovi¹,³, Esko Levälahti¹, Katri Hemiö¹, Anna-Liisa Järvenpää³, Johan G Eriksson¹,⁴,⁵, Sture Andersson³, Jaana Lindström¹, Eero Kajantie¹,³,⁶

Email: hanna-maria.matinolli@thl.fi

¹National Institute for Health and Welfare, Department of Health, Helsinki, Finland; ²University of Oulu, Center for Life Course Health Research, Oulu, Finland; ³University of Helsinki and Helsinki University Hospital, Children’s Hospital, Helsinki, Finland; ⁴University of Helsinki and Helsinki University Hospital, Department of General Practice and Primary Health Care, Helsinki, Finland; ⁵Folkhälsan Research Center, Helsinki, Finland; ⁶Oulu University Hospital and University of Oulu, PEDEGO Research Unit, MRC Oulu, Oulu, Finland

Background: Epidemiological studies and animal models have shown that early postnatal nutrition and growth can influence the future health of an individual. However, the role of nutrition vs growth remains controversial.

Objective: We studied how the intake of protein plus growth during the first weeks of life predict the total energy intake in young adults born with very low birth weight (VLBW, birthweight<1500g) who after birth undergo a period of immaturity-associated illness and poor nutrition.

Design: We collected the daily nutritional intake and weight measurements during the initial hospital stay from hospital records for 109 VLBW participants. The participants attended a clinical examination at the mean age of 22.5 years during which their body composition was measured by DXA. They filled in a 3-day food record. We used path analysis (CFI=1.000, TLI=1.031, RMSEA=0.000), to investigate the association between neonatal protein intake, early growth and energy intake in relation to lean body mass (LBM) in young adult age.

Results: When adjusted for age, sex, neonatal illnesses and pregnancy complications the mean protein intake during the first three weeks of life had both, a direct effect (-5.9(95% CI -12.4,-0.6)) and indirect effects (sum of indirect effects: -2.0 (-4.9,-0.1)) on caloric intake in relation to LBM in young adult age. Indirect effects of mean protein intake (postnatal weeks 0-2 and postnatal weeks 3-5) were mediated through weights at 3, 6 and 9 weeks of age. A total effect was -7.8 kcal/kg of LBM (-13.8,-2.1).

Conclusions: These results indicate that higher early protein intake during first three weeks of life of VLBW infants predicts lower caloric intake in relation to lean body mass in adult age. This association is only partly mediated through early postnatal growth.
**P18 - Pulse wave velocity in elderly of the Oulu45 cohort - effects of type 2 diabetes, physical activity and cholesterol**

**Erja T Metsämänttila**¹, Sauli Herrala², Juhani Leppäluoto¹, Enrique Rodilla-Sala³, Sirkka M Keinänen-Kiukaanniemi²,⁴, Karl-Heinz Herzig¹,⁵,⁶

Email: erja.metsamarttila@oulu.fi

¹University of Oulu, Research Unit of Biomedicine and Biocenter of Oulu, Oulu, Finland; ²University of Oulu, Center for Life Course Health Research, Oulu, Finland; ³Cardenal Herrera University, Department of Medicine and Surgery, Valencia, Spain; ⁴Oulu University Hospital, Unit of General Practice, and Health Center of Oulu, Finland; ⁵Poznan University of Medical Sciences, Department of Gastroenterology and Metabolism, Poznan, Poland; ⁶University of Oulu, Medical Research Center (MRC), Oulu, Finland

**Background:** Pulse wave velocity (PWV) is a measure of arterial stiffness and associated with age and blood pressure. Higher PWV have been found in type 2 diabetes (T2D) patients compared with healthy peers, indicating that T2D may worsen the vascular structure.

**Objective:** We wanted to examine, how T2D and impaired glucose metabolism (IGM) effect PWV in relation to physical activity in subjects in the City of Oulu, Finland born in 1945 (Oulu45 cohort).

**Design:** The study population consisted of the participants of Oulu45- cohort with specific exclusion criteria (BMI over 40, irregular heart rate). Physical activity of the participants was measured objectively with a wrist-worn acceleration meter (Polar Electro, Finland). PWV was determined by a non-invasive applanation tonometry (AtCor Medical, Australia). Oral glucose tolerance test was performed and cholesterol and triglycerides analyzed. All participants gave their written informed consent to the study. The ethics committee of the Northern Ostrobothnia Hospital District approved the study.

**Results:** Data from 572 subjects was available. Significance was determined as p < 0.05. Fasting and 2 h glucose and HbA1C correlated significantly and positively with PWV. PWV values in IGM and T2D subjects were significantly higher than in normal glycemic subjects. There were no associations between PWV and total and LDL cholesterol, but there was a negative correlation between PWV and HDL cholesterol. PWV and number of daily steps were significantly inversely correlated.

**Conclusions:** T2D significantly accelerates arterial aging. Interestingly, in this cohort lipids did not have an additional effect on vascular aging in T2D subjects. In contrast, high physical activity (over 10 000 steps per day) has a beneficial effect on PWV.
O6 - Premorbid temperament as a predictor for remission in depression

Jouko Miettunen\textsuperscript{1,2}, Riikka Marttila\textsuperscript{1,2}, Nina Rautio\textsuperscript{1,2,3}, Eka Roivainen\textsuperscript{4}, Sirkka Keinänen-Kiukaanniemi\textsuperscript{1,2,3}, Leena Ala-Mursula\textsuperscript{1}, Juha Auvinen\textsuperscript{1,3}, Markku Timonen\textsuperscript{1,2}

Email: jouko.miettunen@oulu.fi

\textsuperscript{1}Center for Life Course Health Research, University of Oulu, Oulu, Finland; \textsuperscript{2}Medical Research Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland; \textsuperscript{3}Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland; \textsuperscript{4}Verve Rehabilitation, P.O. Box 404, 90101 Oulu

Background: Temperament traits have been associated with risk for depressive disorders. Studies with premorbid measures on temperament are uncommon.

Objective: The objective was to estimate effect of premorbid personality as a predictor for remission in depressive disorders.

Design: The sample is based on the large Northern Finland Birth Cohort 1966. Temperament traits were measured at age 31 years using the Temperament and Character Inventory. At the age of 46 years depressive symptoms were measured using the Beck Depression Inventory – II (BDI). The sample included those with self-reported life-time depression history at age 46 years but not yet at age 31 years (n=298). Temperament at age 31 years was used to predict remission (BDI\leq13) at age 46 years using logistic regression analysis, with gender and educational level as confounders. Cohen’s $d$ was used as effect size measure.

Results: In total, 201 (67.4\%) of individuals with self-reported depression were on remission at the follow-up. Low harm avoidance (total scale, and subscales anticipatory worry, shyness, and fatigability), low impulsiveness and high exploratory excitability (subscales of novelty seeking), and low sentimentality (subscale of reward dependence) predicted significantly remission with effect sizes between 0.28 and 0.45, highest effect being in harm avoidance.

Conclusions: Premorbid temperament traits predicted remission status in depression with small to moderate effect sizes. Temperament may associate with treatment response in depression or natural course of depression.
P19 - Birth size, childhood growth and hip fractures in old age; a follow-up of the Helsinki Birth Cohort Study

Tuija M Mikkola¹,², Mikaela von Bonsdorff¹,², Johan Eriksson¹,³,⁴

Email: tuija.m.mikkola@jyu.fi

¹Folkhälsan Research Center, Helsinki, Finland; ²University of Jyväskylä, Gerontology Research Center and Department of Health Sciences, Jyväskylä, Finland; ³University of Helsinki and Helsinki University Hospital, Helsinki, Finland; ⁴National Institute for Health and Welfare, Department of Health, Helsinki, Finland

**Background:** There is evidence that childhood growth is associated with bone density and structure in adulthood. However, little is known about the contribution of childhood growth to bone fracture risk.

**Objective:** The objective was to investigate the association between childhood growth and hip fractures in older age.

**Design:** Men and women (n=7866) from the Helsinki Birth Cohort Study were followed until 2013 (age 69-79 years). Height and weight from birth to 11 years was obtained from health care records and information on hip fractures from the national hospital discharge register. Conditional growth variables, which were independent of earlier size/growth, were created. Cox proportional hazards models were adjusted for age, length of gestation, childhood socioeconomic status, and mother’s body size.

**Results:** Altogether, 140 subjects sustained a hip fracture during the follow-up. In women, greater birth length and weight reduced the risk of hip fracture in old age (HR per 1 SD increase in length 0.71, 95% CI 0.53-0.94; HR for weight 0.72, 95%CI 0.53-0.97). Further, greater weight gain between ages 7 and 11 years reduced the risk of hip fracture (HR=0.77, 95%CI 0.60-0.98). In men, high birth BMI reduced the risk of hip fracture in a non-linear manner (quadratic term HR=0.65, 95%CI 0.47-0.91). Low and high gain in height between 2 and 7 years increased the risk of hip fractures (quadratic term HR=1.18, 95%CI 1.09-1.27). Further, low and high gain in BMI between 7 and 11 years increased the risk of hip fractures (quadratic term HR=1.12, 95%CI 1.00-1.25).

**Conclusions:** Body size at birth and growth during childhood may contribute to the risk of hip fracture in older age, but the pattern differs by sex. These results help in determining critical time windows for interventions aiming at prevention of fractures in older age.
P20 - A follow-up of twins in the two Northern Finland Birth Cohorts 1966 and 1986

Irma K Moilanen¹, Leena Joskitt¹, Tuula M Hurtig¹², Hanna E Ebeling¹, Anja M Taanila⁴, Marjo-R Järvelin³⁴

Email: irma.moilanen@oulu.fi

¹University of Oulu, PEDEGO research center, Child Psychiatry, Oulu, Finland; ²University of Oulu, Neuroscience Research Unit, Psychiatry, Oulu, Finland; ³Imperial College London, Department of Epidemiology and Biostatistics, London, UK; ⁴University of Oulu, Center for Life Course Health Research, Faculty of Medicine, Oulu, Finland

**Background:** Twins’ environment and well-being are changing

**Objective:** Follow-up of twins and singletons in 1966 and 1986 NFBC’s from pregnancy to adolescence.

**Design:** In NFBC-66 12068 mothers gave birth to 12231 newborns, and in 1986 NFBC 9362 mothers to 9478 newborns. Differences between twins and singletons are given as such and after adjusting (1) by sex and maternal factors (age, parity and place of residence at birth) and (2) in addition also perinatal factors (birth weight and gestational age).

**Results:** The share of twin pregnancies in 1966 was 1.4% and 1.2% in 1985/86. While in 1966 the twins were often born as last children to multiparous women in rural area, in 1986 they were more often first born children to elderly mothers in urban area; share of multiparous women had fallen from 24.5% to 4.4%. In 1966 mean gestational weeks: 37.0 (twins) and 39.1 (singletons), 1986: 36.2 and 39.4, correspondingly. Mean birth weights 1966: 2701g and 3508g, 1986: 2544g and 3567g, correspondingly. NFBC1966 and 1986 twins began to walk later than singletons, even after controlling by (1). Speech development was slower in 1966 twins, and the difference stayed after adjusting with (1). In adolescence, NFBC1966 twins exercised sports more and drunk less alcohol, and the difference stayed significant even after adjusting by (1) and (2). In NFBC-86 no difference was found in exercising sports, smoking, use of alcohol, but the twins were less often drunken, and this difference stayed even after adjusting by (1) and (2). Adolescent NFBC1986 twins reported less internalizing and externalizing symptoms, and the difference stayed in externalizing symptoms even after adjusting by (1) and (2).

**Conclusions:** In spite of difficulties at birth, twins’ outcome in terms of living habits and psychological well-being in adolescence seem favorable.
P21 - Adolescent smoking as a risk factor for psychosis after adjusting with prodromal symptoms

Antti Mustonen\textsuperscript{1,2}, Solja Niemelä\textsuperscript{3,4}, Tanja Nordström\textsuperscript{2}, Graham K. Murray\textsuperscript{5}, Pirjo Mäki\textsuperscript{2,3,6}, Juha Veijola\textsuperscript{2,3,6}, Erika Jääskeläinen\textsuperscript{1,2,3}, Jouko Miettunen\textsuperscript{1,2,3}

Email: antti.mustonen@student.oulu.fi

\textsuperscript{1}Center for Life Course Health Research, University of Oulu, Oulu, Finland; \textsuperscript{2}Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland; \textsuperscript{3}Research Unit of Clinical Neuroscience, Department of Psychiatry, University of Oulu, Oulu, Finland; \textsuperscript{4}Department of Psychiatry, Lapland Hospital District, Rovaniemi, Finland; \textsuperscript{5}Department of Psychiatry, University of Cambridge, Cambridge, UK; \textsuperscript{6}Clinic of Psychiatry, Oulu University Hospital, Oulu, Finland

Background: The role of smoking as a risk factor for psychosis has been controversial. Recent meta-analysis stated that daily smoking is associated with greater risk and earlier onset of psychosis. The authors conclude that future studies, with larger sample sizes, should investigate the relation between daily smoking and development of psychosis with adequate adjustment for potential covariates.

Objectives: Our objective is to examine associations between adolescent smoking and the risk of psychosis in 12 years follow-up while taking into account the prodromal symptoms of psychosis in a prospective general population sample.

Design: The sample (N=6040) composed of a prospective Northern Finland Birth Cohort 1986. Questionnaire on prodromal symptoms for psychosis (PROD-screen) and on drug use was conducted when the cohort members were 15-16 years old. The participants were asked if the smoke tobacco daily. Information on psychoses was gathered from different national registers until age 28 years.

Results: Altogether 109 psychoses emerged. The hazard ratio (HR) for risk of psychosis in daily smokers was 2.2 (95% CI 1.4-3.3) compared to non-smokers. When adjusted for prodromal symptoms the association remained at the same level and statistically significant (HR = 2.3; 95% CI 1.5-3.6). The association remained significant also when gender, history of cannabis use and parental psychosis were adjusted with (HR = 2.1; 95% CI 1.3-3.4).

Conclusions: Smoking in adolescence is independently associated with higher risk for psychosis after adjustment for several other known risk factors.
P22 - Early traumas in young adults with Clinical and Familial Risk for psychosis; a follow-up of the Northern Finland Birth Cohort 1986

Pirjo Mäki1,2,3,4, Tuija Mähönen1, Tanja Nordström5, Juha Veijola1,2,3

1University of Oulu, Research Unit of Clinical Neuroscience, Department of Psychiatry, Oulu, Finland; 2Oulu University Hospital, Department of Psychiatry, Oulu, Finland; 3Oulu University Hospital and University of Oulu, Medical Research Centre Oulu, Finland; 4Länsi-Pohja Healthcare District, Department of Psychiatry, Keropudas; the Middle Ostrobothnia Central Hospital, Department of Psychiatry, Kiuru, Kokkola; Joint Municipal Authority of Wellbeing in Raahe District, Mental Health Services, Raahe; Basic Health Care District of Kallio, Mental Health Services, Ylivieska and the Northern Ostrobothnia Hospital District, Visala Hospital, Ylivieska, Finland; 5University of Oulu, Center for Life Course Health Research, Oulu, Finland

Background: Childhood trauma increases the risk for later psychosis and prodromal symptoms, too. Anyhow, early trauma in subjects with Familial Risk for psychosis is less studied.

Objective: Aim was to study childhood traumas in young adult offspring with parental history of psychosis. In addition, objective was to replicate the previous findings of the connection between childhood trauma and prodromal symptoms for psychosis and psychoses in a birth cohort sample.

Design: A field study for a subsample of the general population based Northern Finland 1986 Birth Cohort (NFBC 1986) was conducted in 2007-2010. According to the Structured Interview for Prodromal Syndromes (SIPS) and the national Care Register for Health Care (previously the Finnish Hospital Discharge Register FHDR) and other register data four groups were created: psychosis (N = 30), Clinical Risk CR (N = 47) and Familial Risk FR (N = 61) of psychosis and controls (N = 74). The Trauma and Distress Scale (TADS) – questionnaire was used to measure five types of traumatic childhood and adolescence experiences: emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect.

Results: After adjusting with gender, family socio-economic status SES and family type, birth cohort members with FR did not have increased risk for any of the five trauma types compared to controls. Subjects with CR had statistically significantly increased risk for emotional abuse (p<0.01), physical abuse (p<0.05) and emotional neglect (p<0.01) compared to controls. Young participants with psychosis had increased risk having had experienced emotional abuse (p<0.05), physical abuse (p<0.05) and sexual abuse (p<0.01) in childhood compared to controls.

Conclusions: Surprisingly, parental psychosis did not increase the risk for childhood trauma in this study. As expected, childhood traumas were connected to psychoses and prodromal syndromes for psychosis.

Reference: Veijola J et al. 2013 Early Interv Psychiatry
P23 - Is adiposity rebound a predictor of metabolically healthy obesity?

Rozenn Nédélec$^{1,2}$, Jari Jokelainen$^{1,3}$, Sylvain Sébert$^{1,2}$, Karl-Heinz Herzig$^{2,4,5}$, Jouko Miettunen$^{1,6}$, Minna Männikkö$^1$ and Marjo-Riitta Järvelin$^{1,2,3,7,8}$

Email: rozenn.nedelec@oulu.fi

Background: A subset of obese individuals appears to be protected from cardio-metabolic disorders associated with obesity. They are known as metabolically healthy obese (MHO).

Objective: As early adiposity rebound has been recognized as an important predictor of adult obesity, we hypothesized that the distinction between metabolically healthy and unhealthy obese categories finds its origin in early growth.

Design: In order to identify early origins of adult MHO, we studied 4,378 members of the Northern Finland Birth Cohort 1966 (NFBC1966). At 31 years, they were categorized according to their BMI as obese, overweight or normal weight and, in each group, defined as metabolically healthy if they fulfilled 0 or 1 of the adverse cardio-metabolic criteria related to blood pressure, triglycerides, high density lipoprotein cholesterol, glucose, C-reactive protein and HOMA-IR and metabolically unhealthy if they fulfilled more than 1 criteria. We obtained six different groups. We used data from Child Health and Welfare Clinics to model their growth.

Results: In our study, 22.9% of the obese men and 37.3% of the obese women were MHO. At adiposity rebound, MHO men had a greater BMI (16.6±1.1 kg/m$^2$) and were younger (4.8±0.9 years) than the other metabolic groups. The differences with the other groups were significant except with metabolically unhealthy obese (MUO). In women, the MHO group had also the greatest BMI at adiposity rebound (16.4±1.2 kg/m$^2$), but was not the youngest group (4.6±0.9 years), the MUO group being almost four months younger. The differences with the other groups were significant, the difference in age at adiposity rebound between MHO and MUO becoming significant only after adjustment.

Conclusions: These findings support evidence that early adiposity rebound predicts adult obesity. To our knowledge, this is the first study to show that a very early adiposity rebound might predict MHO in men but not in women.
P24 - Effect of preterm birth and intrauterine life on adulthood lung function; a clinical follow-up of births (1985-89) in Finland

Pieta Näsänen-Gilmore¹, Marika Sipola-Leppänen¹-⁵, Marjaana Tikanmäki¹,², Hanna-Maria Matinolli¹,², Johan G Eriksson¹,⁶-⁹ Marjo-Riitta Järvelin¹,²,¹⁰, Marja Väärsämäki¹,¹³, Petteri Hovi¹,¹⁴, Eero Kajantie¹,⁴,¹³-¹⁴

Email: pieta.nasanen-gilmore@thl.fi

¹National Institute for Health and Welfare, Helsinki and Oulu, Finland; Center for Life Course Health Research, University of Oulu; ²PEDEGO Research Unit; ³Medical Research Centre Oulu; ⁴Oulu University Hospital and University of Oulu, Finland; ⁵Folkhälsan Research Center, Helsinki; ⁶Department of General Practice and Primary Health Care, University of Helsinki, Helsinki; ⁷Unit of General Practice, Helsinki University Central Hospital, Helsinki, Finland; ⁸Vaasa Central Hospital, Vaasa, Finland; ⁹MRC Health Protection Agency (HPA) Centre for Environment and Health, School of Public Health, Imperial College London, UK; ¹⁰Biocenter Oulu, University of Oulu, ¹¹Unit of Primary Care, Oulu University Hospital; ¹²Department of Obstetrics and Gynaecology, MRC Oulu, Oulu University Hospital and University of Oulu, Finland; ¹³Children’s Hospital, Helsinki University Central Hospital, Helsinki, Finland

Background: Foetal origins of lung function and obstructive lung disorders have been proposed. To what extent the adulthood lung function is related to preterm birth (whole range) or underlying pregnancy conditions remains unsolved.

Objective: To examine the effect of preterm birth, intrauterine environment (maternal pregnancy disorders e.g. hypertension and gestational diabetes) on adulthood lung function.

Design: Participants came from the preterm birth study ‘ESTER’, a cohort of individuals born in Northern Finland in 1985-89, which examines association between gestational age, intrauterine exposures, and adulthood health. Participants were by gestational age at birth: early preterm (<34wks) (n=139), late preterm (34<37wks) (n=239), ≥37wks (n=341). At mean age of 23yrs they underwent spirometry (Forced vital capacity (FVC), Forced Expiratory volume in 1 second (FEV1), FEV/FVC as z-scores) and provided details of pulmonary health history.

Results: Preterm-born had poorer adulthood lung function compared to full-term (Early preterm: Forced vital capacity: -0.44 (95% CI: -0.64, -0.25), ratio of forced vital capacity /forced vital capacity: -0.29 (95% CI: -0.47, -0.10), late preterm: ratio of forced vital capacity /forced vital capacity: -0.13 (95% CI: -0.28, 0.02). Multivariate regression modelling suggested preterm birth as the strongest determinant of adulthood lung function, with clear positive dose-dependent relationship. Very little effect of maternal pregnancy conditions (gestational diabetes, hypertension, asthma, smoking), or subject’s smoking habit and physical activity was observed.

Conclusions: Early preterm birth is associated with obstructive airflow in young adult life with dose-dependent association relation observed in late preterm birth. Preterm birth may increase the risk of and cause an earlier development of chronic obstructive pulmonary disease later in life, beyond the normal lung function decline due to age. Obstructive airways disease in those born preterm may contribute to heterogeneity of asthma.
**P25 - Overweight and Obese but not Normal Weight Women with PCOS Are at Increased risk of Type 2 Diabetes Mellitus - a Prospective, Population-Based Cohort Study**


Email: meri-maija.ollila@student.oulu.fi

1University of Oulu and Oulu University Hospital, Department of Obstetrics and Gynecology, Medical Research Center Oulu and PEDEGO Research Unit, Oulu, Finland; 2University of Oulu, Center for Life Course Health Research, Oulu, Finland; 3Oulu University Hospital, Unit of Primary Health Care, Oulu, Finland; 4National Institute for Health and Welfare, Department of Children, Young People and Families, Oulu, Finland; 5Imperial College London, Department of Epidemiology and Biostatistics, MRC–PHE Centre for Environment & Health, School of Public Health, London, UK; 6University of Helsinki and Helsinki University Hospital, Department of Obstetrics and Gynecology, Helsinki, Finland; 7Imperial College London, Institute of Reproductive and Developmental Biology, London, UK

**Background:** Polycystic ovary syndrome (PCOS), the most common endocrine disorder in fertile aged women, is associated with an increased risk of type 2 diabetes (T2DM). However, the respective roles of PCOS *per se*, body mass index (BMI) and long-term weight gain on the development of pre-diabetes and/or T2DM in women with PCOS remains unclear.

**Objective:** To determine the respective roles of PCOS, weight gain and/or obesity for the development of pre-diabetes or T2DM by the end of reproductive life.

**Design:** In the prospective follow-up Northern Finland Birth Cohort 1966 questions on oligo-amenorrhea (OA) and hirsutism (H) were asked at 31 years (81% answered) and diagnosis of PCOS at 46 years (72% answered). Women reporting both OA+H and/or with a formal diagnosis of PCOS were considered as having PCOS (n=279).

Clinical examinations were performed at 31 and 46 years and 2-hour oral glucose tolerance test (n=2780) was performed at 46 years. T2DM diagnosis was completed and verified from the postal questionnaires and from the national drug and hospital discharge registers.

**Results:** The PCOS *per se* increased the risk of T2DM by three-fold (OR=2.51 (95%CI[1.38-4.56]) and the risk remained significantly increased when comparing overweight/obese PCOS and overweight/obese control women (OR=2.45 95%CI[1.28-4.67]). Normal-weight PCOS women did not present with an increased risk of pre-diabetes or T2DM. The increase in BMI between all three time-points (14, 31 and 46 years) was significantly greater in women with PCOS developing pre-diabetes or T2DM than in women with PCOS and normal glucose tolerance.

**Conclusions:** These results emphasize the role of weight management during adolescence and early adulthood to prevent the development of T2DM in women with PCOS. Furthermore, our results support the view that, particularly in the present times of limited resources for healthcare, OGTT-screening should be targeted to overweight and obese women with PCOS rather than to all women with PCOS.
O7 - Association between vitamin D status and inflammation: stratification by body mass index-findings from the Northern Finland Birth Cohort 1966

Saranya Palaniswamy1,2, Jari Jokelainen2,8, Toni Karhu1,3, Sirkka-Keinänen Kiukaanniemi2,8, Karl-Heinz Herzig1,3,4,5, Marjo-Riitta Järvelin1,2,6,7,8 and Sylvain Sebert1,2,9

Email: saranya.palaniswamy@oulu.fi

1Biocenter Oulu, University of Oulu, Oulu, Finland, 2Center for Life-Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland; 3Institute of Biomedicine, Department of Physiology, University of Oulu, Oulu, Finland; 4Department of Gastroenterology and Metabolism, Poznan University of Medical Sciences, Poznan, Poland; 5CEU Cardenal Herrera University, Valencia, Spain; 6Department of Epidemiology and Biostatistics, School of Public health, Imperial College, London, United Kingdom; 7MRC-PHE Centre for Environment and Health, School of Public health, Imperial College, London, United Kingdom; 8MRC and Unit of Primary Care, Oulu University Hospital, Oulu, Finland; 9Department of genomics, School of Public Health, Imperial College, London, United Kingdom

Background: There is evidence for a link between the vitamin D status and inflammation suggesting that vitamin D can be a safe tool to moderate the metabolic risk in obesity. However, the influence played by BMI in modulating the aforementioned association is unclear.

Objective: To determine the extent to which serum 25-hydroxyvitamin D [25(OH)D] and BMI are associated with inflammatory biomarkers and to assess whether BMI modifies the relationship between 25(OH)D and inflammation in young adults.

Design: We performed an association study for vitamin D with multiple inflammatory markers in an unselected sample of 3,983 individuals from the Northern Finland Birth Cohort 1966 at 31y. We then stratified for BMI to explore interplay with the risk of obesity. Briefly, the molecular markers measured in the fasted state were vitamin D and 17 inflammatory biomarkers: among others interleukin (IL)-1 receptor antagonist, interferon gamma-induced protein (IP)-10, monocyte chemoattractant protein (MCP)-1, soluble CD40 ligand (sCD40L) and tumor necrosis factor alpha (TNF)-α. The analysis was adjusted for environmental, lifestyle and social cofactors.

Results: In normal weight and overweight subjects, serum concentration of vitamin D was correlated with TNF-α and MCP-1 (p<0.05, FDR corrected). However, the strength of the associations, but not its orientation was lost in obese and morbidly obese subjects. The observation seen in obese could not be simply explained by a smaller size and warrants further investigation.

Conclusions: We speculate that normal vitamin D status is insufficient to modulate chronic inflammation frequently linked to obesity. It also supports evidence that a tailored vitamin D supplementation, based on BMI, shall be defined to combat inflammation in obesity.
P26 - Duration of untreated psychosis and the use of antipsychotic medication during the course of illness in the Northern Finland 1966 Birth Cohort

Matti Penttilä1,2, Jani Moilanen1, Marianne Haapea1, Matti Isohanni1, Hannu Koponen3, Jouko Miettunen1,2,4,5, Erika Jääskeläinen1,4,5

Email: matti.penttila@oulu.fi

1University of Oulu, Research Unit of Clinical Neuroscience, Department of Psychiatry, Oulu, Finland; 2Oulu University Hospital, Department of Psychiatry, Oulu, Finland; 3University of Helsinki, Department of Psychiatry, Helsinki, Finland; 4University of Oulu, Center for Life Course Health Research, Oulu, Finland; 5Oulu University Hospital and University of Oulu, Medical Research Center, Oulu, Finland

Background: Long duration of untreated psychosis (DUP) predicts poor short- and long-term outcome in schizophrenia. It may also be a marker of resilience and associate with lower doses or shorter periods of using antipsychotic medication which may or may not be correlated with the association between DUP and outcome.

Objective: To study the association between DUP and the use of antipsychotic medication in long-term follow-up and to find out whether the delayed treatment in first-episode psychosis associates with using less antipsychotic medication during the course of illness.

Design: In the prospective Northern Finland 1966 Birth Cohort length of DUP and information on lifetime use of antipsychotic medication for 60 individuals with schizophrenia was assessed from medical records from the first episode until age 34 years. Association between length of DUP and cumulative dose-years of antipsychotics was analysed using linear regression analysis. Logarithmic transformations of DUP and dose years were used.

Results: Mean DUP was 227 days (SD 359) and mean of cumulative dose years was 2.41 (SD 1.29). Symptoms measured using PANSS ranged from 30 to 122, mean 53 (SD 21). Duration of untreated psychosis did not associate with the use of antipsychotic medication (beta = -0.124, p = 0.343).

Conclusions: There was no evidence of an association between DUP and the use of antipsychotic medication. Although long DUP has long-term association with poor outcome, it does not have an association with the use of antipsychotic medication based on the population-based long-term follow-up.
P27 - Impact of phthalate exposure on pregnancy outcomes, children’s health and neurodevelopment –REPRO_PL Cohort

Kinga Polanska¹, Danuta Ligocka², Wojciech Sobala¹, Wojciech Hanke¹

Email: kinga@imp.lodz.pl

¹Nofer Institute of Occupational Medicine, Department of Environmental Epidemiology, Lodz, Poland; ²Nofer Institute of Occupational Medicine, Bureau of Quality Assurance, Lodz, Poland

**Background:** Widespread phthalate exposure has prompted investigations concerning their potential adverse health effects.

**Objective:** The objective of this study was to evaluate the impact of phthalate exposure on pregnancy outcomes and children’s health.

**Design:** The study was based on the data from the Polish Mother and Child Cohort (REPRO_PL) - a multicenter prospective cohort study established in 2007 with the aim to evaluate a variety of environmental factors contributing to the pregnancy outcomes, children’s health and neurodevelopment. Phthalate exposure was determined by measuring 11 phthalate metabolites (MEP, MiBP, MnBP, 3OH-MnBP, MBzP, MEHP, 5OH-MEHP, 5oxo-MEHP, OH-MiNP, oxo-MiNP, and MnOP) in the urine from third trimester of pregnancy (prenatal exposure) and from their children at the 24th month of age (postnatal exposure). The analysis was performed by the HPLC–MS/MS method. The following outcome measures were considered: gestational age, birth outcomes, children’s health and neurodevelopment. Child psychomotor development was assessed by the Bayley Scales of Infant and Toddler Development.

**Results:** Pregnancy duration was inversely associated with MEP ($\beta$=-0.2; $p=0.04$), head circumference with MOiNP ($\beta$=-0.1; $p=0.05$) and child motor development with 3OH-MnBP ($\beta$=-2.3; $p<0.05$), 5OH-MEHP ($\beta$=-1.2; $p<0.05$), and oxo-MEHP ($\beta$=-1.8; $p<0.05$). Postnatal child exposure to phthalates was not associated with any of the measured scores of child psychomotor development. We showed that higher urine concentrations of MBzP increased the risk of child food allergy (OR=4.2; $p<0.05$).

**Conclusions:** The study findings underscore the importance of policies and public health interventions aiming at reduction of phthalate exposure.
O8 - Childhood adversity, prodromal symptoms and brain response to faces in young adulthood

Johannes Pulkkinen¹, Vesa Kiviniemi², Juha Nikkinen², Pirjo Mäki³, Jouko Miettunen³, Jennifer H. Barnett⁴, Peter B. Jones⁴, Graham K. Murray⁴, IMAGEN, Tomas Paus⁵,⁶,⁷, Juha Veijola¹

Email: johannes.pulkkinen@oulu.fi

¹Department of Psychiatry, Research Unit of Clinical Neuroscience, University of Oulu, Oulu, Finland; ²Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland; ³Center for Life Course Health Research, University of Oulu, Oulu, Finland; ⁴Department of Psychiatry, University of Cambridge, Cambridge, UK; ⁵Rotman Research Institute, Baycrest, Toronto, Ontario, Canada; ⁶Departments of Psychology and Psychiatry, University of Toronto, Toronto, Ontario, Canada; ⁷Child Mind Institute, New York, New York, USA

Background: Early traumatic experiences in social interactions play a key role in shaping interindividual differences in vulnerability to psychosis.

Objective: The aim of the present study was to investigate the association between childhood adversities and prodromal symptoms of psychosis with brain response to faces in young adults.

Design: 176 individuals drawn from the Northern Finland 1986 Birth Cohort participated in face-task functional magnetic resonance imaging (fMRI). We extracted blood oxygen level-dependent (BOLD) response to happy and fearful faces from 25 regions of interests (ROI) shown previously to be engaged in a robust manner by faces. We then reduced the 25 ROIs into smaller set of functional entities based on factor loadings acquired from a principal component analyses of BOLD responses measured across the same 25 ROIs in a large independent dataset (N=1739). MANCOVA followed by post-hoc regressions were conducted to explore relationships between childhood adversities and prodromal symptoms with brain response to faces.

Results: We observed independent relationships between factors representing brain response to fearful faces and childhood adversities (P = 0.008) and positive prodromal symptoms of psychosis (P = 0.036). No associations between negative or disorganization symptoms of psychosis with brain response to faces were found.

Conclusions: Our results suggest that face processing, including early visual attention and further perception, might be modulated by childhood adversities and positive (but neither negative nor disorganization) prodromal symptoms of psychosis. We speculate that childhood adversities and positive prodromal symptoms of psychosis modulate face processing via early visual attention.
P28 - Adolescent metabolic markers and cognitive deficits in young adults: association and interaction with psychosis in the Oulu Brain and Mind samples

Hugh Ramsay¹, Jennifer Barnett², Jouko Miettunen¹,³, Anti J Kangas³, Pasi Soininen⁴, Mika Ala-Korpela³, Juha Veijola¹

Email: drhughramsay@gmail.com

¹University of Oulu, Department of Psychiatry, Oulu, Finland; ²University of Cambridge, Department of Psychiatry, Cambridge, United Kingdom, ³University of Oulu, Center for Life Course Health Research, Oulu, Finland, ⁴University of Eastern Finland, School of Pharmacy, Kuopio, Finland

Background: Psychotic disorders are a major international public health problem and are associated with cognitive deficits in early adulthood. Metabolic markers have shown increasing promise in predicting poorer cognitive outcomes in older adults. It remains to be seen if metabolic markers may also be significant in predicting cognition in younger individuals, particularly those at high-risk for cognitive difficulties such as those with psychotic disorders or at risk for psychotic disorders.

Objective: We aimed to measure if metabolic markers in adolescence are associated with cognition in early adulthood and whether these associations are especially significant for those who develop psychosis or high risk for psychosis.

Design: Two subsamples, the Oulu Brain and Mind 1 and 2 samples (n=713), were recruited from the Northern Finland Birth Cohort 1986 (NFBC 1986). Principal components factor analysis was defined five factors from 21 metabolic markers and we examined the association between these five factors (expressed as categorical quartiles) and five cognitive tests. Following this, we examined if observed associations were especially significant among those with later psychosis or psychosis risk.

Results: Five metabolic factors were identified: membrane factor, HDL factor, omega-3 factor, omega-6 ratio factor and amino acid factor. The omega-6 ratio factor was associated with better performance in verbal fluency (beta=0.31 at the middle two quartiles (P=0.007 and P=0.006 respectively) and with a linear decrease in errors on Paired Associates Learning (PAL) (beta=-0.30, P=0.010). These findings did not interact with psychosis/psychosis risk.

Conclusions: Middle omega-6 ratios to total fatty acids were associated with better executive function while higher ratios were associated with better performance on visual memory in young adulthood. The reasons are unclear but appear to operate independently of the development of cognitive deficits associated with psychosis in young adults.
P29 - Pathway from perinatal circumstances to mortality at midlife in psychoses; a 45-year follow-up study of the Northern Finland Birth Cohort 1966

Nina A. Rautio¹,², Erika Jääskeläinen¹,³,⁴, Tanja M. Nordström¹,⁴, Jouko A. Miettunen¹,³,⁴, Matti K. Isohanni¹,³,⁴, Jussi K.M. Seppälä¹,⁵

E-mail: nina.rautio@oulu.fi

¹Center for Life Course Health Research, University of Oulu, Oulu, Finland, ²Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland, ³Research Unit of Clinical Neuroscience, University of Oulu, Oulu, Finland, ⁴Medical Research Center Oulu, Oulu University Hospital and University of Oulu, University of Oulu, Finland, ⁵Department of Psychiatry, South-Savo Hospital District, Finland

Background: Increased mortality in schizophrenia has been reported widely. Less is known about other psychoses and perinatal factors as its predictors.

Objective: To examine mortality and causes of death in schizophrenia and other psychosis compared to individuals without psychosis, and whether perinatal factors predict mortality.

Design: Within the Northern Finland Birth Cohort 1966 (n=10 933), mortality and causes of death were followed until end 2011 by national registers. Altogether, 203 individuals had schizophrenia and 178 other psychoses. Mother’s antenatal depression, wantedness of pregnancy, mother’s age at birth, smoking during pregnancy, parity, paternal socio-economic status and family type at birth were examined as predictors of mortality in persons with and without psychoses.

Results: Altogether, 11.8% (n=24) in schizophrenia, 12.9% (n=23) with other psychosis and 3.2% (n=339) without psychosis had died. Compared to persons without psychosis, mortality was higher in schizophrenia (HR 3.60; 95% CI 2.38-5.45) and other psychoses (4.05;2.65-6.17) after adjustment for gender. The hazard ratio for natural death was 2.01 (0.82-4.91) in schizophrenia and 4.63 (2.43-8.80) in other psychoses compared to those without psychoses after adjustment for gender. Corresponding figures for unnatural deaths were 4.71 (2.94-7.54) and 2.94 (1.56-5.55), respectively. Among all psychoses, those whose father was a farmer had lower risk for mortality (HR 0.19; 0.05-0.82) than those belonged to high socio-economic class after adjustment for gender and parental psychoses. Among cohort members without psychoses, mother’s depression and smoking and father’s low socio-economic status predicted mortality after adjustments.

Discussion: In over 40 years follow-up data, the risk of natural death was 2-fold in schizophrenia and nearly 5-fold in other psychoses and in unnatural deaths it was almost contrarily. Perinatal factors seem to be more important predictors of mortality in individuals without psychoses than with psychoses. It is important to diagnose high-risk groups and provide effective somatic and psychiatric treatment.
Long-term unemployment is related to impaired glucose metabolism in middle-aged men; a follow-up of the Northern Finland Birth Cohort 1966


E-mail: nina.rautio@oulu.fi

1 Center for Life Course Health Research, University of Oulu, Oulu, Finland, 2 Unit of Primary Health Care, Oulu University Hospital, Oulu, Finland, 3 Kallio Primary Health Care Unit, Ylivieska, Finland, 4 Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland, 5 Finnish Institute of Occupational Health, Oulu, Finland, 6 MRC-PHE Centre for Environment and Health, Imperial College London, London, United Kingdom, 7 Biocenter Oulu, University of Oulu, Oulu, Finland, 8 Department of Genomics, Imperial College London, London, United Kingdom

Background: Stressors related to working life have been suggested to predispose to type 2 diabetes, typically occurring in the working age. However, unemployment has been scarcely studied in relation to the development of type 2 diabetes.

Objective: We explored whether registered unemployment is associated with impaired glucose metabolism in the general population.

Design: As a part of the 46-year follow-up study of the Northern Finland Birth Cohort 1966, we analyzed the oral glucose tolerance tests of 1970 men and 2544 women in relation to their individual three-year employment histories collected from national registers and classified into three categories: employed, short-term (≤ 1-year) and long-term (> 1-year) unemployed.

Results: Among men, pre-diabetes was found in 19.2% of employed, 23.0% of short-term unemployed and 27.0% of long-term unemployed individuals, and the corresponding figures for screen-detected type 2 diabetes were 3.8%, 3.8% and 9.2%, respectively (p<0.01). Among women, the corresponding figures for pre-diabetes were 10.0%, 12.6% and 16.2% and for screen-detected type 2 diabetes 1.7%, 3.4% and 3.6%, respectively (p<0.01). Among long-term unemployed men, 4.1% of the risk of pre-diabetes could be attributed to unemployment, and the corresponding figure for women was 6.0%. In addition, among long-term unemployed men, 13.1% of the risk of screen-detected type 2 diabetes was attributable to unemployment, and the corresponding attributable risk was 10.3% for the long-term unemployed women. Long-term unemployed men had a higher risk for pre-diabetes (OR 1.59, CI 95% 1.01-2.50) and screen-detected type 2 diabetes (OR 2.38, CI 95% 1.08-5.27) than employed men, after adjustment for education, smoking, alcohol intake, physical activity and body mass index (BMI). Among women, these associations were diluted by the adjustments.

Conclusions: Long-term unemployment may be a risk for type 2 diabetes in middle-aged men. For clinicians, awareness of the patient’s unemployment status may be helpful in recognizing undiagnosed cases.
P31 - Validity of a web-based questionnaire to assess perinatal outcomes in the PRIDE Study

Marleen MHJ van Gelder1,2, Saskia Vorstenbosch3, Lineke Derks1, Bernke te Winkel3, Eugene P van Puijenbroek3, Nel Roeleveld4,4

Email: Nel.Roeleveld@radboudumc.nl

1Radboud university medical center, Radboud Institute for Health Sciences, Nijmegen, The Netherlands; 2Radboud university medical center, Radboud REshape Innovation Center, Nijmegen, The Netherlands; 3Netherlands Pharmacovigilance Centre Lareb, 's Hertogenbosch, The Netherlands; 4Radboud university medical center Amalia Children's Hospital, Dept of Paediatrics, Nijmegen, The Netherlands

Background: Previous validation studies showed that maternal recall of perinatal outcomes, including infant birth weight and gestational age, is generally excellent when using interviews or paper-based questionnaires. However, knowledge on the validity of data on perinatal outcomes collected with web-based questionnaires is limited.

Objective: The aim of this study was to validate a web-based questionnaire on perinatal outcomes in a prospective birth cohort study.

Design: We included 1,124 women with an estimated date of delivery between February 2012 and February 2015, who have been participating in the nationwide PRegnancy and Infant DEvelopment (PRIDE) Study in the Netherlands. Data on pregnancy outcome, including mode of delivery, plurality, gestational age, birth weight and length, head circumference, birth defects, and infant sex were collected by means of a web-based questionnaire completed 2 months after birth. These data were compared with data from obstetrical records as the reference standard. For the continuous outcome variables, intraclass correlation coefficients (ICC) with 95% confidence intervals (CI) were calculated, while sensitivity and specificity were determined for categorical variables.

Results: We observed only very small differences between the two methods of data collection for gestational age (ICC 0.85; 95% CI 0.83-0.88), birth weight (ICC 0.98; 95% CI 0.98-0.98), birth length (ICC 0.89; 95% CI 0.86-0.92), and head circumference (ICC 0.85; 95% CI 0.73-0.95). Agreement between the web-based questionnaire and the obstetrical records was high as well, with sensitivity ranging between 0.90 (post-term birth) and 1.00 (multiple outcomes) and specificity between 0.95 (emergency caesarean section) and 1.00 (multiple outcomes).

Conclusions: The validity of the web-based questionnaire for perinatal outcomes in the PRIDE Study was similar or higher compared to the traditional modes of data collection. Therefore, web-based questionnaires should be considered as a complimentary or alternative method of data collection in reproductive and perinatal epidemiology.
O9 - Using web-based questionnaires to assess medication use during pregnancy: a validation study in pREGnant and the PRIDE Study

Marleen MHJ van Gelder¹,², Saskia Vorstenbosch³, Bernke te Winkel³, Eugene P van Puijenbroek³, Nel Roeleveld¹,⁴

Email: Nel.Roeleveld@radboudumc.nl

¹Radboud university medical center, Radboud Institute for Health Sciences, Nijmegen, The Netherlands; ²Radboud university medical center, Radboud REShape Innovation Center, Nijmegen, The Netherlands; ³Netherlands Pharmacovigilance Centre Lareb, 's Hertogenbosch, The Netherlands; ⁴Radboud university medical center Amalia Children's Hospital, Dept of Paediatrics, Nijmegen, The Netherlands

**Background:** Collecting valid self-reported data on medication use during pregnancy is challenging and medication use is likely to be underreported when using paper-based questionnaires or interviews.

**Objective:** The aim of this validation study was to validate two comparable web-based questionnaires with indication-oriented questions to assess prescription and over-the-counter medication use during pregnancy in two prospective birth cohort studies.

**Design:** Participants in the nationwide PRegnancy and Infant DEvelopment (PRIDE) Study (n=387) and the Pregnancy Drug Registry pREGnant (n=166) in the Netherlands completed a six-week paper-based diary on medication use in gestational weeks 19-24 or 26-31. In week 34, they completed a web-based questionnaire, which included questions on the exact name of the medication, time period and frequency of use, and quantity taken. To assess the degree of underreporting, the questionnaire’s sensitivity (Se) with 95% confidence interval (CI) was calculated with the medication diary as reference standard.

**Results:** Among the women who completed a diary, 65.7% used at least one medication in the six-week diary period. Sensitivity of the questionnaire was high for many medication groups, including topical corticosteroids (Se 0.89; 95% CI 0.74-1.00), levothyroxine (0.76; 0.56-0.97), antiepileptics (0.88; 0.75-1.00), antacids (0.77; 0.69-0.85), and ferrous fumarate (0.77; 0.54-1.00). Sensitivity was lower for medication for short-time use, with sensitivities of 0.50 (95% CI 0.22-0.78) for systemic antibiotics, 0.50 (0.38-0.62) for ear, eye, nose and throat preparations, 0.59 (0.52-0.67) for analgesics, and 0.56 (0.49-0.64) for acetaminophen specifically. No differences in sensitivity were observed between the PRIDE Study and pREGnant questionnaires.

**Conclusions:** For a large number of medication groups, underreporting is limited in an indication-oriented web-based questionnaire. For some medications, however, a substantial number of exposures will be missed with this method of data collection, but the degree of underreporting is much lower compared to paper-based questionnaires.
P32 - Genome-wide association studies and meta-analyses of gastroesophageal reflux disease in 24766 Northern Europeans

Jukka Ronkainen1,2,3, Ferdinando Bonfiglio4, Pirro G. Hysi5, Weronica Ek4,6, Ville Karhunen1,15, Natalia V. Rivera4, Minna Männikkö1, Helena Nordenstedt7, Marco Zucchelli8, Francesca Bresso4,8,9, Frances Williams11, Hans Tornblom12, Patrik Magnusson13, Nancy L. Pedersen13, Peter Thelin Schmidt10, Mauro D'Amato8,15

Email: minna.mannikko@oulu.fi

1University of Oulu, Center for Life Course Health Research, Finland; 2Primary Health Care Centre, Tornio, Finland; 3Centre for Family Medicine, Karolinska Institutet, Stockholm, Sweden; 4Department of Biosciences and Nutrition, Karolinska Institutet; 5Department of Ophthalmology, King’s College London, St Thomas’ Hospital Campus, London, UK; 6Department of Immunology, Genetics and Pathology, Science for Life Laboratory Uppsala, Uppsala University, Sweden; 7Department of Public Health Sciences, Karolinska Institutet, Sweden; 8Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden; 9Gastrocentrum, Karolinska University Hospital, Stockholm, Sweden; 10Center for Digestive Diseases, Karolinska University Hospital, Karolinska Institutet; 11Department of Twin Research & Genetic Epidemiology, King’s College London, UK; 12Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden; 13Department of Medical Epidemiology and Biostatistics, Karolinska Institutet; 14BioCruces Health Research Institute and Ikerbasque, Basque Foundation for Science, Bilbao, Spain; 15Oulu University Hospital, Oulu, Finland.

Background: Gastroesophageal reflux disease (GERD), the regurgitation of gastric acids leading to troublesome heartburn symptoms and/or complications like erosive esophagitis, Barrett’s esophagus and esophageal adenocarcinoma, affects up to 20% of the general population. Genetic predisposition is suspected from twin and family studies, but gene-hunting efforts have so far been scarce and no large-scale genome-wide association study (GWAS) has ever been reported.

Objective: We exploited data available from three large general population samples, and studied self-reported reflux symptoms in relation genetic variants.

Design: We included 24766 individuals from three independent population-based cohorts from Sweden (SALT), Finland (NFBC1966) and UK (TwinsUK). GERD cases and asymptomatic controls were identified using questionnaire-derived symptom data. Upon stringent quality controls (QC), genotype and HapMap imputed data for > 2.5 million markers were used for association testing with logistic regression and meta-analysis of individual GWA studies. Bioinformatic characterization of genomic regions associated with GERD included gene-set enrichment analysis (GSEA), in silico prediction of genetic risk effects on regulatory mechanisms and gene expression, and gene-based computational drug-target enrichment analysis using Connectivity Map (cMap) data.

Results: GWAS and meta-analysis identified 30 GERD suggestive risk loci (P ≤ 5×10⁻⁵), with concordant risk effects in all cohorts, and predicted functional/regulatory effects on gene expression in relevant tissues. GSEA revealed functional involvement of GERD risk genes in biological processes associated with the regulation of ion channel, ion transport and cell adhesion. From the cMap analysis, omeprazole had significant effects on GERD risk gene expression, while anti-tuberculosis, corticosteroids and other anti-inflammatory drugs scored highest among the repurposed compounds.

Conclusions: We report the first large-scale genetic study of GERD, and highlight genes and pathways that contribute to further our understanding of its pathogenesis and therapeutic opportunities.
O10 - Adverse adult consequences of adolescent alcohol exposure: 
Longitudinal results from the Northern Finland Birth Cohort, 1966

Richard J. Rose¹, Juha Veijola², Richard J. Viken¹, Anja Taanila³, Irma Moilanen²

Email: rose@indiana.edu

¹Indiana University, Department of Psychological & Brain Sciences, Bloomington, Indiana, USA; ²University of Oulu, Department of Psychiatry, Oulu, Finland; ³University of Oulu, Center for Life Course Health Research, Oulu, Finland

Background: Adolescent alcohol exposure is associated with adverse adult outcomes. But whether these associations are causal or consequent to shared third-factor familial confounds remains uncertain, and the persistence of these associations over long-term follow-up awaits confirmation. We aimed to confirm drinking-outcome associations from individual differences in alcohol exposure assessed at age 14 over a 32 year follow-up, using case-control comparisons within a well-defined Finnish population cohort.

Objective: To confirm associations of heavier alcohol exposure during early adolescence with adverse adult outcomes over three decades of longitudinal follow-up of a population-based cohort of Finns born in 1966, tracking self-reported drinking habits at age 14 through a follow-up conducted during 2012.

Design: Data are from three waves of follow-up of the Northern Finland Birth Cohort 1966, with questionnaire data from ages 14, 31 and 46. We compared 320 cases reporting frequent drinking and intoxicating at age 14 with 1320 controls reporting infrequent drinking and without intoxicating; four controls were matched with each case for gender, familial structure and status, and urban residency. Outcomes of interest included continuity of substance use, the 25-item Hopkins symptom check list, educational attainment, marital status and occupational stability, life satisfaction and self-rated health.

Results: Cases were significantly more likely to report adverse adult outcomes at both 31 and 46 years: more likely unmarried, less satisfied with life, more psychiatric symptoms and lower education attainment. All associations were of modest magnitude, and sample attrition constrains power.

Conclusions: These initial analyses create a context for more detailed paired comparisons of cases and controls matched for frequency of drinking at age 14 but differing in intoxication experience, and in tracking trajectories of alcohol use and abuse among males and females within this population sample from a defined and homogenous geographic area.
Background: Within the DOHaD paradigm the effects of preterm birth on bone growth can be explicated as various quantitative models which predict certain growth patterns. Registers provide an important source of evidence for vindicating such models.

Objective: A between-groups comparison is made in order to analyse the hypothesized differences between the fracture profiles of preterm/full term children and young adults. Prima facie, the group of individuals born preterm is thought to experience a relatively greater amount of fracture events due to lower bone mineral density.

Design: Retrospectively collected data from Finnish health registries are linked to identify full term and preterm births among the class of newborn infants (n= 235 622) in the cohort 1987-1990. The available time series data is studied with the methods of survival analysis, linking KM diagrams with Cox-regression. We use both Poisson and negative binomial regression to model the count data, and take the necessary precautions related to the problem of overdispersion.

Results: While the survival times of experiencing a fracture do not exhibit clinically significant differences between the two groups, the duration of the treatment episode is seen to depend on gestational age. The count data exhibit similar regularities.

Conclusions: Preterm birth does not seem to expose an individual to fracture events in early adulthood.
O11 - The association of multiple melanocytic nevi with education, gender and skin type; a Northern Finland Birth Cohort 1966 Study with 46 years’ follow-up

Suvi-Päivikki Sinikumpu¹, Laura Huilaja¹, Jari Jokelainen², Juha Auvinen²,³, Markku Timonen²,³, Kaisa Tasanen¹

Email: suvi-paivikki.sinikumpu@oulu.fi

¹University of Oulu and Oulu University Hospital, Department of Dermatology, Medical Research Center, PEDEGO Research Group, Oulu, Finland; ²University of Oulu, Faculty of Medicine, Center for Life Course Health Research, Oulu, Finland; ³Oulu University Hospital, Unit of General Practice, Oulu, Finland

Background: Multiple melanocytic nevi (> 50 nevi) are one of the strongest risk factors of melanoma. There are both genetic and environmental factors, that contribute to the development of pigmented nevi but their epidemiology in adults is partly unclear.

Objective: The purpose of the study was to analyze the prevalence of multiple pigmented nevi and the associated risk factors.

Design: Comprehensive dermatologic status was performed for 1,932 birth cohort study cases during the 46-year follow-up study. This study population belongs to the 1966 Northern Finland Birth Cohort. The association of socioeconomic status (education) in childhood and adulthood, skin type, sunbathing habits (the number of sunburns, sun vacations and the use of sunscreens), inflammatory skin diseases and gender, with multiple pigmented nevi were analyzed in multinomial logistic regression analysis.

Results: The prevalence of multiple melanocytic nevi in this study population was 11.6% (223/1,930). Higher education (OR 2.11, 95% CI 1.51–2.96), male gender (OR 1.48, 95% CI 1.07–2.06), sun-sensitive skin type (OR 2.09, 95% CI 1.34–3.27) and regular use of sunscreens (OR 2.03, 95% CI 1.23–3.37) were associated with increased risk of multiple nevi. Inflammatory skin diseases decreased (OR 0.49, 95 CI% 0.33–0.72) the risk of multiple nevi.

Conclusions: High education level, male gender, and fair skin type increased the risk of multiple nevi, and therefore, the risk of melanoma. Preventive information about the risks of UV exposure and more healthy sunbathing habits should be highlighted especially in these risk groups.
Non-alcoholic fatty liver disease does not appear to cause changes in circulating metabolites: A Mendelian randomization study

Eeva Sliz1,2,3, Sylvain Sebert1,2,4, Peter Würtz5, Antti J Kangas5, Pasi Soininen5,6, Terho Lehtimäki7, Mika Kähönen8, Jorma Viikari9, Minna Männikkö1,2,3, Mika Ala-korpela1,2,5,6,10,11, Olli Raitakari12,13 and Johannes Kettunen1,2,5,6

Email: eeva.sliz@oulu.fi

1Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland, 2Biocenter Oulu, University of Oulu, Oulu, Finland, 3Faculty of Biochemistry and Molecular Medicine, University of Oulu, Oulu, Finland, 4Department of Genomics of complex diseases, School of Public Health, Imperial College London, UK, 5Computational Medicine, Faculty of Medicine, University of Oulu, Oulu, Finland, 6NMR Metabolomics Laboratory, School of Pharmacy, University of Eastern Finland, Kuopio, Finland, 7Department of Clinical Chemistry, Fimlab Laboratories, University of Tampere School of Medicine, Tampere University, Tampere, Finland, 8Department of Clinical Physiology, University of Tampere and Tampere University Hospital, Tampere, Finland, 9Department of Medicine, University of Turku and Turku University Hospital, Turku, Finland, 10Computational Medicine, School of Social and Community Medicine and Medical Research Council Integrative Epidemiology Unit, University of Bristol, Bristol, UK, 11Medical Research Council Integrative Epidemiology Unit at the University of Bristol, Bristol, UK, 12Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland, 13Department of Clinical Physiology, Turku University Hospital, Turku, Finland

Background: Non-alcoholic fatty liver disease (NAFLD) is a common liver disorder characterized by deposition of excess fat in the liver in the absence of excessive alcohol intake. NAFLD has been associated with a plethora of metabolic changes in circulation; however, the causality between NAFLD and metabolite aberrations remains unclear.

Objective: The aim of this study is to evaluate causal effects of NAFLD on circulating metabolites using two-sample Mendelian randomization.

Design: Observational estimates for association between NAFLD and metabolites were determined in The Cardiovascular risk in Young Finns Study (YFS) population (N=2042). Genetic variants on Patatin-like phospholipase domain containing 3 (PNPLA3), Neurocan (NCAN), Lysophospholipase-like 1 (LYPLAL1) and Glucokinase regulator (GCKR) were used as instruments in Mendelian randomization, and their effect sizes on NAFLD were obtained from a published GWAS. Associations of the genetic variants to metabolites were obtained from a GWAS including up to 24,925 European individuals.

Results: NAFLD displayed cross-sectional association with 87 metabolites. Mendelian randomization resulted in heterogeneous causal effects on the metabolites. The strongest genetic contributor to NAFLD, PNPLA3 rs738409, displayed no effects on circulating metabolites. The remaining instruments resulted in one profile matching the NAFLD metabolic associations (GCKR) and another profile that indicated opposite effects than the NAFLD associated changes (NCAN).

Conclusions: The present study informs on the causal effects of NAFLD on deviations in circulating metabolites and indicates that NAFLD does not appear to cause the metabolic deviations associated with it. The divergence in the direction of the obtained causal effect estimates suggest that NAFLD is a mechanistically heterogeneous condition and that there are at least three distinct metabolic pathways leading to liver fat accumulation. Nevertheless, the association of NAFLD and circulating metabolites is strong, which implies that there are confounding factors that are causal to both NAFLD and metabolite alterations.
P35 - Early life stress, FKB5 polymorphisms, and insulin

Anna Suarez1, Jari Lahti1,2,3, Eero Kajantie4,5,6, Johan G. Eriksson2,4,7 & Katri Räikkönen1

Email: anna.suarez@helsinki.fi

1University of Helsinki, Institute of Behavioural Sciences, Helsinki, Finland, 2Folkhälsan Research Center, Helsinki, Finland, 3University of Helsinki, Helsinki Collegium for Advanced Studies, Helsinki, Finland, 4National Institute for Health and Welfare, Helsinki, Finland, 5Helsinki University Hospital and University of Helsinki, Hospital for Children and Adolescents, Helsinki, Finland, 6Oulu University Hospital and University of Oulu, PEDEGO Research Unit, Oulu, Finland, 7University of Helsinki and Helsinki University Hospital, Department of General Practice and Primary Health Care, Helsinki, Finland

Background: Early life stress (ELS) has been shown to influence health later in life. Functioning of the hypothalamic–pituitary–adrenal (HPA) axis, regulated partly by FKB5 gene, may moderate these effects.

Objective: We examined whether FKB5 single nucleotide polymorphisms (SNPs) interact with ELS on insulin secretion, insulin sensitivity, and insulin resistance.

Design: 1,728 Helsinki Birth Cohort Study participants born 1934-44 were genotyped for FKB5 SNPs (rs1360780, rs9394309, rs9470080), administered a 2-h (75 g) oral glucose tolerance test and a questionnaire on physician-diagnosed and medication use for chronic diseases at a mean age of 61.5 years. Of them 273 were exposed to ELS, namely were separated from their parents at a mean age of 4.7 years due to evacuations during WWII. Other participants constituted the control group.

Results: ELS interacted with FKB5 SNPs in the analyses of fasting (rs1360780, p=.015), 30-min (rs1360780, p=.031; rs9394309, p=.041) and incremental insulin (rs1360780, p=.032; rs9394309, p=.028; rs9470080, p=.043), and insulin area under the curve (rs1360780, p=.044); among carriers of at least one copy of minor allele, but not among major allele homozygotes, insulin values were higher if they were separated compared to if they were not. Corresponding associations were found with a haplotype formed by minor alleles in all three SNPs for fasting, 30-min, and incremental insulin (p<.05).

Conclusions: FKB5 polymorphisms in combination with ELS exposure predict higher insulin values in midlife. Our findings support the role for HPA axis dysregulation in health-related metabolic outcomes.
P36 - Mood disorders and schizophrenia in the offspring of antenatally depressed mothers - Relationship to parental history of severe mental disorder; a follow up of the Northern Finland 1966 Birth Cohort

Tiina Taka-Eilola¹, Sarianna Mykkälä¹, Merja Kyllönen², Juha Veijola¹,³,⁴ and Pirjo Mäki¹,³,⁴,⁵

Email: Tiina.A.Riekki@student.oulu.fi

¹University of Oulu, Research Unit of Clinical Neuroscience, Department of Psychiatry, Oulu, Finland, ²University of Oulu, Center for Life Course Health Research, Oulu, Finland, ³Oulu University Hospital, Department of Psychiatry, Oulu, Finland, ⁴Oulu University Hospital and University of Oulu, Medical Research Center Oulu, Finland, ⁵Länsi-Pohja Healthcare District, Department of Psychiatry, Keropudas; the Middle Ostrobothnia Central Hospital, Department of Psychiatry, Kiuru, Kokkola; Joint Municipal Authority of Wellbeing in Raasepori District, Mental Health Services, Raasepori; Basic Health Care District of Kallio, Mental Health Services, Ylivieska and the Northern Ostrobothnia Hospital District, Visala Hospital, Ylivieska, Finland

Background: Follow-up studies of the association between maternal antenatal depression and severe mental disorders in the adult offspring are lacking.

Objective: Our aim was to determine whether maternal antenatal depression (AD) increases the risk for mood disorders and schizophrenia in the offspring when taking account parental severe mental disorder (PMD).

Design: The Northern Finland 1966 Birth Cohort includes 12,058 children, whose mothers were asked at mid-gestation if they felt depressed. Mood disorders and schizophrenia in the offspring, and severe mental disorders in the parents were detected using the Care Register for Health Care. The reference group was birth cohort members without AD and without PMD.

Results: Of the mothers, 14% had rated themselves as depressed during pregnancy. Of the parents, 10% had suffered from a severe, hospital-treated mental disorder. Maternal depression during pregnancy increased slightly the risk for mood disorders in the offspring (OR 1.6; 95%CI 1.2-2.2) but not for schizophrenia, when compared with the children of mothers without depression. The risks for both depression (OR 3.6; 95%CI 2.0-6.4) and bipolar disorder (7.8; 2.6-23.1) and also schizophrenia (4.3; 2.3-8.2) were higher in the offspring with both AD and PMD than in those with AD but without PMD (for depression 1.4; 0.9-2.1; for bipolar disorder 1.7; 0.6-4.5 and for schizophrenia 0.9; 0.5-1.6) or those without AD and with PMD (for depression 1.5; 0.9-2.3; for bipolar disorder 5.1; 2.4-11.0 and for schizophrenia 1.2; 0.7-2.3). The statistically significant associations remained significant even after adjustments.

Conclusions: Antenatal depression increased the risk for mood disorders in the offspring slightly but not for schizophrenia when compared with the children of mothers without AD. The risks for mood disorders and also schizophrenia were higher in the offspring with both AD and PMD than in those with AD but without PMD or those without AD and with PMD.
Leisure-time physical activity in young adults born preterm – The ESTER Study

Marjaana Tikanmäki1,2, Nina Kaseva1, Tuija Tammelin3, Marika Sipola-Leppänen1,2,4, Hanna-Maria Matinolli1,2, Satu Miettola1,2, Johan G Eriksson1,5,6, Marjo-Riitta Järvelin6,7,8,9, Marja Vääräsmäki4,11 and Eero Kajantie1,4,12

Email: marjaana.tikanmaki@thl.fi

Background: Young adults born preterm have higher levels of cardiometabolic risk factors than their term-born peers. Physical activity (PA) has important cardiometabolic and other health benefits. Adults born preterm with very low birth weight (<1500g) report less PA and are less fit than their term-born peers.

Objective: We studied self-reported leisure time physical activity (LTPA) among early (<34 weeks) and late (34 to 36 weeks) preterm born young adults. We hypothesized that physical activity levels among preterm born individuals decrease along with the degree of prematurity.

Design – The 779 participants of ESTER Preterm Birth Study “Preterm birth and early life programming of adult health and disease” were recruited among the participants of Northern Finland Birth Cohort 1986 and among all children born 1987-1989 in the same geographical area, identified via the Finnish Medical Birth Register. At the age of 23.1 (SD 1.4) years 656 non-pregnant, unimpaired participants completed a modified Kuopio Ischemic Heart Disease Risk Factor Study-questionnaire on 12-month PA. Yearly volume and energy expenditure of conditioning and non-conditioning LTPA were calculated among 123 adults born early preterm, 215 late preterm and 318 controls born at term. Group differences were examined by linear regression.

Results: As compared with controls, early preterm group reported 30.1% (95%CI 14.2-43.1) lower volume of leisure-time PA (MET/year), to which both lower conditioning and non-conditioning PA contributed. This resulted in 29.0% (13.4-41.7) lower energy expenditure (kcal/year). Also the level of vigorous PA (MET≥6) was lower among early preterm group. Differences in late preterm group compared with controls were not statistically significant. Adjustments for potential early life confounders or current mediating health characteristics did not change the results.

Conclusions: Young adults born early preterm report engaging in less LTPA compared with term-born controls which may predispose them to cardiometabolic and other chronic diseases.
O12 - Migration history sequence analysis of young adults living in the largest cities of Finland; results from the 1987 Finnish Birth Cohort study

Liisa Törmäkangas¹, Pasi Haapakorva¹, Tiina Ristikari¹, Mika Gissler²

Email: liisa.tormakangas@thl.fi

¹National Public Health Institute, Department of Welfare, Oulu, Finland, ²National Public Health Institute, Department of Information Services, Helsinki, Finland

Background: Indicators of health and welfare of young adults show marked differences between six of the largest cities in Finland. At the same time these cities are also experiencing positive net migration of the same age groups.

Objective: Considering the migration history of the young adults living in six of the largest cities at the age of 25, we aimed to analyze who were those having problems with their welfare.

Design: The 1987 Finnish Birth Cohort (FBC) data contains a complete migration history of the cohort members and several indicators of welfare obtained from different Finnish registers. History of residence cities of the 1987 FBC members living in Helsinki, Espoo, Vantaa, Turku, Tampere or Oulu at the end of year 2012 were processed by sequence analysis method using R package TraMineR. Optimal matching of the sequences produced four different clusters: 1. those who had lived in the city for most of their lives, 2. those who moved in from other Finnish cities earlier (2005-2008) or 3. those who moved in from other cities later (2009-) and 4. those who moved in from the neighboring cities. Different cluster groups for each city were analyzed for the percentage of the FBC members having short education, social assistance or criminality.

Results: Shortest education and social assistance were most often associated with cluster 1 and criminality with clusters 1 and 4. Cluster 3 was associated with longest education and cluster 2 with long education and least criminality.

Conclusions: Cities with universities are attracting young people having fewer problems with their welfare compared to those FBC members who had lived in these cities for the whole of their lives. Vantaa appeared as an exception to this and attracted people having more welfare problems especially from the neighboring cities.
Background: Uterine fibroids are the most common tumour in females with incidence of nearly 70% by age 50 years. Recent studies suggest similarities in biological disease mechanisms for fibroid and atherosclerosis. Similar risk factors have been associated with both conditions: obesity, hypertension, and abnormal lipids.

Objective: To evaluate the association between uterine fibroids and adverse cardiovascular and metabolic profiles.

Design: The Northern Finland Birth Cohort (NFBC1966) is a prospective population-based study including all children with expected birth date in 1966 in the area. The data were collected from national registries, postal questionnaires and health examinations. Cases and controls were identified among all females in the NFBC1966 who underwent extensive clinical health examinations at age 46 years (n=3,268).

Results: A total of 729 fibroid cases were identified. With logistic regression analysis, the odds ratio of risk of fibroids (all cases, and ICD-code identified cases) according to serum lipid profile, metabolic syndrome by the International Diabetes Federation (IDF) definition and body composition was estimated. With adjustment for parity, education and BMI, the risk of fibroids rose significantly for every 1 mmol/l increase in LDL and triglycerides, (OR=1.14 95%CI 1.02,1.26 vs. OR=1.27 95%CI 1.09, 1.48). With the same adjustment model, IDF-defined metabolic syndrome raised the risk of ICD-code fibroid diagnosis significantly (OR=1.50 95%CI 1.10, 2.03).
Additionally every 1 cm increase in waist circumference increased the risk of fibroids (all fibroids: OR=1.02 95%CI 1.00, 1.04; ICD-code fibroid diagnosis: OR=1.03 95%CI 1.01, 1.06).

Conclusions: In this study a large number of known cardiovascular risk factors were tested within a single cohort. Increased lipids and metabolic syndrome are associated with increased risk of uterine fibroids. Along with central obesity these findings add to an increased risk for cardiovascular disease among women with fibroids. These observations might also suggest that metabolic factors could have roles in underlying biological mechanism in fibroid development.
O13 - Risk aversion and framing among the Northern Finland Birth Cohort 1966 participants

Mikko Vaaramo

Email: mikko.vaaramo@oulu.fi

University of Oulu, Oulu Business School, Department of Economics, Oulu, Finland

Background: Arrow-Pratt measurements of risk aversion are important measurements to analyze individual’s attitude towards risks. Outcomes of choice alone cannot explain individual’s decision but also a frame of choice have effect.

Objective: My goal is to find out the frame that gives rational and consistent values risk aversion in case of small lottery and investment choices. I also examine characteristics of data, for example differences in risk aversion between income groups and correlation between self-evaluation and real risk aversion.

Design: Relative risk aversion relates measurement of risk aversion to wealth. I calculate those measurements for cohort participants and examine values given by different wealth variable. I try to find out values that are consistent with other studies and theory. Data is from Northern Finland Birth Cohort 1966’s 46-years follow-up study and includes two questions about games, a lottery and an investment. As a wealth variable I use individual’s year 2012 income from Tax Administration. Characteristics I examine by looking differences between groups and correlation between answers.

Results: People with higher income have smaller absolute risk aversion and there is no correlation between self-evaluation and calculated risk aversion. I observed that people relate lottery gambles to an amount of money that is approximately an amount they earn per week. In the investment case individuals were less willing to participate but participants were more risk tolerant. In an investment question individuals got 10 000€ before choice. That is a logical choice for wealth variable and gives rational relative risk aversion values. Lower risk aversion values in the investment question can be caused by house money-effect.

Conclusions: Individuals relate risks to an amount of money depending on frame. In a lottery case frame individuals relate risk to an amount they probably have easy access. In the investment case frame is given in the question.
O14 - Early nutrition interrupts the risk association of Caesarean section and obesity: secondary analysis of a randomized clinical trial

Martina Weber¹, Veronica Luque², Annick Xhonneux³, Fiammetta Vecchi⁴, Dariusz Gruszfeld⁵, Berthold Koletzko¹ and Veit Grote¹ for the European Childhood obesity trial study group

Email: martina.weber@med.uni-muenchen.de

¹Dr. von Hauner Children’s Hospital University of Munich Medical Center, Div. of metabolic and nutritional medicine, Munich, Germany, ²Universitat Rovira I Virgili, Unitat de Recerca en Pediatria, Nutrició i Desenvolupament Humà, Reus, Spain, ³CHC St. Vincent, Liège-Rocourt, Belgium, ⁴San Paolo Hospital University of Milan, Department of Paediatrics, Milan, Italy, ⁵Children’s Memorial Health Institute, Neonatal Intensive Care Unit, Warsaw, Poland

Background: Early life factors affecting early growth and metabolism are of growing interest to face the obesity epidemic. Beside infant nutrition, delivery mode causing different gut colonization is shown to be associated to early weight gain and obesity risk.

Objective: To examine whether infant feeding and delivery mode have interactive long-term programming effects on weight gain and body-mass-index.

Design: The CHOP study is a multicenter randomized European intervention trial. Healthy infants who could not be breastfed were randomized within the first two months of life to receive infant and follow-on formula with different protein content (higher protein (HP: 1.6 and 3.2 g/dl): N=550 (Caesarean section 116); lower protein (LP: 1.25 and 2.05 g/dl): N=540 (129)), predominantly breastfed (BF) infants (N=588 (118)) were included as a reference. Regular weight and height measurements were performed from 3 months to 11 years of age. Information on delivery was assessed by questionnaire at inclusion.

Results: Twenty-two percent of the cohort were delivered by Caesarean section and 583 (Caesarean section: 163) children could be followed to 11 years of age. Weight gain in the first year (as z-score difference according to WHO growth standards) was significantly different between feeding groups (P<0.001) and significantly increased by Caesarean section. Interaction was not significant but stratified by feeding group the effect of caesarean section was the smallest in BF: 0.11 (n.s.), LP 0.27 (P=0.020) and HP 0.36 (P=0.004). In longitudinal analysis stratified by feeding group, BMI tracks of children delivered by Caesarean section are significantly increased in the HP group at 6 and 8 years, in the LP group at 11 years and not at all in the breastfed group.

Conclusions: Caesarean section is an early risk factor for later obesity. Early nutrition might offer strategies to interrupt this risk relation since breastfeeding acts protective and LP formula retarding.
P39 - The association between height and knee and hip osteoarthritis; the Northern Finland Birth Cohort 1966 study

Maiju Welling1,2,3, Juha Auvinen1,4, Petri Lehenkari5, Minna Männikkö1, Jaro Karppinen1,2,6, Pasi J. Eskola1

Email: maiju.welling@oulu.fi

1University of Oulu, Center for Life Course Health Research, Oulu, Finland, 2Oulu University Hospital and University of Oulu, Department of Physical and Rehabilitation Medicine, Medical Research Center Oulu, Oulu, Finland, 3University of Oulu, Faculty of Biochemistry and Molecular Medicine, Oulu, Finland, 4Oulu University Hospital, Unit of Primary Care, Oulu, Finland, 5University of Oulu and Oulu University Hospital, Department of Anatomy and Cell biology and Surgery Clinic, Medical Research Center, Oulu, Finland, 6Finnish Institute of Occupational Health, Oulu, Finland

Background: Osteoarthritis (OA) is the most common joint disease and causes serious medical, social and economic problems worldwide. However, the pathomechanisms behind OA are still poorly understood.

Objective: The aim of this study was to investigate the association of height at the age of 31 with the incidence of knee and hip OA at following 15 years.

Design: The participants of The Northern Finland Birth Cohort 1966 (NFBC1966) who were diagnosed with knee OA or hip OA between the ages of 31 and 46 were used as OA cases. Study subjects without knee and hip OA were used as controls. Height and weight were measured in a clinical examination at the age of 31. Mean heights between OA cases and controls were compared. Cox regression analysis was performed to calculate the risk for OA in different height quartiles. The results were adjusted for body mass index (BMI), education, smoking and leisure-time physical activity at baseline.

Results: 98 men and 104 women diagnosed with knee OA, and 22 men and 18 women diagnosed with hip OA were used as OA cases. The number of controls was 3,764 for men and 4,216 for women. Men with knee OA were 2.6 cm ($P < 0.001$) and women with knee OA 1.2 cm taller ($P = 0.048$) than controls. The adjusted hazard ratio (HR) for knee OA in the highest quartile was 2.5 (95% CI 1.4-4.5) for men and 1.8 (95% CI 1.0-3.1) for women. Hip OA was found to be equally frequent in different height quartiles among both men and women.

Conclusions: Height at the age of 31 was associated with incident, early knee OA diagnosed prior to age of 46 years. The low incidence of hip OA makes our results on hip OA inconclusive.
O15 - Causal relationship between high milk consumption and cardio-metabolic traits - a Mendelian Randomization approach; the 1958 British Birth Cohort

Vimal Karani S,1,2, Alana Cavadino A2,3, Zhou,4 Elina Hyppönen E2,4

Email: v.karani@reading.ac.uk

1Hugh Sinclair Unit of Human Nutrition, University of Reading, UK, 2Population, Policy and Practice, UCL Institute of Child Health, UK, 3Wolfson Institute of Preventive Medicine, Queen Mary University of London, UK, 4Centre for Population Health Research, University of South Australia, Adelaide, Australia

Background: Studies have shown associations between high milk intake and cardio-metabolic traits. However, the direction of possible causality is uncertain.

Objective: We explored the causal direction of the relationship between milk consumption and cardio-metabolic traits using a gene variant as an instrumental variable in a Mendelian Randomization analysis.

Design: We tested the association of lactase persistence (LCT-13910 C>T, rs4988234) genotype with milk consumption (for validation) and with cardio-metabolic traits such as body mass index (BMI), fasting glucose and insulin, HOMA-IR and lipids (for a possible causal association) in up to 5,680 individuals from the 1958 British Birth Cohort (1958BC). The findings from the 1958BC were further confirmed using the summary statistics from the following consortia: Genetic Investigation of Anthropometric Traits (GIANT, N up to 131,916), Global Lipids Consortium (N up to 188,577), the Meta-Analyses of Glucose and Insulin-related traits Consortium (MAGIC, N up to 22,293) and International consortium for Blood Pressure (ICBP, N up to 146,581).

Results: The LCT variant showed a strong association with milk consumption (P<0.0001) suggesting that the variant is a good instrument for high milk intake. Under a recessive model, the variant, rs4988234, showed a significant association with increased LDL (P=0.007) and total cholesterol (P=0.002) levels in the 1958BC. None of the other genetic associations were statistically significant (P>0.05) in the 1958BC. The association of the variant, rs4988234, with LDL cholesterol (P=7.03x10^-6) and total cholesterol (P=1.24x10^-7) was confirmed in the Global Lipids consortium. In addition, there was an association of the variant with decreased HDL cholesterol (P=0.001) [Global Lipids], increased body mass index (P=0.001) [GIANT] and increased fasting insulin (P=0.014) and HOMA-IR (P=0.035) [MAGIC] suggesting the effect of the variant on metabolic and cardiovascular disease-related phenotypes.

Conclusions: Our study provides genetic evidence for the association of high milk consumption with cardio-metabolic disease-related traits.
P40 - Cloninger’s temperament dimensions and longitudinal alcohol use in early midlife; a Northern Finland Birth Cohort 1966 study

Daniel Vladimirov1,2, Solja Niemelä3,4, Juha Auvinen1,5, Markku Timonen1, Leena Ala-Mursula1, Sirkka Keinanen-Kiukaanniemi1,5, Jouko Miettunen1,2,3,6

Email: daniel.vladimirov@student.oulu.fi

1Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Finland, 2Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Finland, 3Department of Psychiatry, Research Unit of Clinical Neurosciences, Finland, 4Department of Psychiatry, Lapland Hospital District, Finland, 5Unit of Primary Care, Oulu University Hospital, Finland, 6Department of Psychiatry, Oulu University Hospital, Finland

Background: Temperament is suggested to contribute to the development of substance use disorder, but longitudinal studies on how temperament is related to alcohol use are scarce.

Objective: To examine how the different dimensions of temperament predict changes in alcohol use in adulthood.

Design: In the Northern Finland Birth Cohort 1966 (N=5,247), alcohol use and Cloninger’s TCI (Temperament and Character Inventory) were surveyed at ages 31 and 46. Based on median splits of the TCI-scores, the participants were categorized into low and high groups at both time points. Proportions of binge and heavy drinkers and mean alcohol consumption was calculated for each group. Multinomial regression analysis was conducted with TCI-scores as factors influencing the change in alcohol consumption. Cross-lagged structural equation model was conducted for novelty seeking and mean alcohol consumption.

Results: High novelty seeking was associated with increased consumption, binging and heavy drinking among both sexes at both time points (P<0.01). Low persistence was associated with increased consumption at both time points among men and among women at age 46. In the adjusted model baseline novelty seeking predicted increasing consumption (OR 1.03; 95% CI: 1.01-1.05) for men. In the cross-lagged model baseline novelty seeking predicted higher alcohol consumption at 46 years, but baseline alcohol consumption did not predict changes in novelty seeking.

Conclusions: High novelty seeking and low persistence were cross-sectionally associated with problematic alcohol use among middle-aged Finns of northern origin. High alcohol consumption and novelty seeking are rather stable longitudinally, high novelty seeking modestly predicts increasing alcohol use, but high alcohol use does not predict changes in novelty seeking. Gender differences in predictors exist as high novelty seeking predicted more strongly increasing consumption for men in the cross-lagged model. Overall, temperament scores do not seem to affect strongly changes in alcohol use.
P41 - Effect of maternal smoking during pregnancy on incidence of asthma among offspring between the ages of 31 and 46 years

Baizhuang Xu¹, Jussi Lampi¹, Juha Auvinen², Juha Pekkanen¹,³

Email: Baizhuang.xu@oulu.fi

¹Department of Environmental Epidemiology, Institute for Health and Welfare, Finland; ²Center for Life Course Health Research, University of Oulu, Oulu, Finland; ³Department of Public Health, University of Helsinki, Finland

Background: Many studies show that children exposed to maternal smoking during pregnancy and in early life have a higher risk of developing asthma in childhood. However few studies have studied the association with risk of asthma in middle age.

Objective: The current paper examines the effect of maternal smoking during pregnancy on the incidence of asthma among offspring between the ages 31 and 46 years.

Design: The study was based on 5500 subjects from Northern Finland Birth Cohort 1966 with complete information on doctor diagnosed asthma both at age 31 and 46 years. All subjects were non-asthmatics at 31 years.

Results: The incidence rate of doctor diagnosed asthma between the ages of 31 and 46 years was 7.6%, 5.5% among males and 9.2% among females. Risk of developing asthma between 31 and 46 years for offspring whose mothers smoked during the last three months of pregnancy was 1.52 (95% CI 1.17-1.96) as compared to offspring with non-smoking mothers. In multivariate analysis adjusting for gender, maternal education, parity, maternal BMI, ponderal index, parental asthma as well as education, BMI and smoking status at 31 years, the risk did not appear to change, being 1.55 (95% CI 1.09-2.21). However, the multivariate adjusted effect was stronger and statistically significant only among females (RR 1.82, 95% CI 1.19-2.77), but not among males (RR 1.04, 95% CI 0.53-2.02).

Conclusions: The results suggest that the effect of maternal smoking during pregnancy on risk of developing asthma lasts up to adulthood among females.