

# Longitudinal and Life Course Studies: International Journal

Supplement: CELSE2010 Abstracts



Published by **Longview**

Company No. 5496119 Reg Charity No 1114094  
[www.longviewuk.com](http://www.longviewuk.com)

VOLUME 1 | ISSUE 3 | 2010

# Longitudinal and Life Course Studies: International Journal

## Supplement: CELSE2010 Abstracts

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The Editors are most grateful to the Nuffield Foundation for supporting the journal through its development phase.

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# Introduction

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This Supplement to the International Journal, *"Longitudinal and Life Course Studies"*, comprises abstracts of papers presented at the 5<sup>th</sup> Conference of Epidemiological Longitudinal Studies in Europe (CELSE2010), held in Paphos, Cyprus, 13-15<sup>th</sup> October 2010. The abstracts reflect the growing importance of longitudinal studies to a variety of disciplines and focus on the latest longitudinal research advances and contributions to science and society. In this context, CELSE acts as a global forum for stimulating interdisciplinary interactions, hence fostering the exchange of ideas and the building of collaborative ties between researchers using longitudinal methods.

This biennial conference started as a smaller-scale European-based initiative. Thanks to the efforts of a small group of longitudinal scientists over the past decade it has now grown to have a strong global presence, attracting research teams using longitudinal cohorts from all corners of the globe. Longitudinal scientists who attend have the opportunity to showcase their scientific contributions on a wide range of themes from the fields of medicine, psychology, sociology, biology, genetics, statistics, education and economics. To cover the latest research trends in longitudinal science, the abstracts presented in CELSE2010 also encompass individual papers and symposia on topics such as lifecourse epigenetic influences, genome-wide association studies, and the use of non-human data in longitudinal studies.

**Demetris Pillas**

Chair of CELSE2010 Organising and Scientific Committee

## **S1.1.0**

### **Symposium: Intergenerational influences on children's development: Who, how, when and what**

**Amanda Sacker<sup>1\*</sup>, Yvonne Kelly<sup>2</sup>, Anne McMunn<sup>2</sup> and Lidia Panico<sup>2</sup>**

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#### **Abstract**

The theme of this symposium is the way that parental behaviours and attributes (family structure, paid and unpaid labour, conflict and anthropometric characteristics) affect children's development. It brings together four papers with common outcomes: childhood socio-emotional behaviour, cognitive development, growth and health. The sample for all papers is the UK Millennium Cohort Study of over 18,000 children born in socioeconomically and ethnically diverse circumstances. Data from interviews when the children were 9 months, 3 years and 5 years of age are used throughout. Outcomes at age 5 include socio-emotional behaviour measured using the Strengths and Difficulties Questionnaire (SDQ); cognition measured by the BAS verbal ability sub-scale; height and obesity measures taken by trained interviewers; and respiratory illness and unintentional accidents reported by the primary caregiver.

The first paper by Amanda Sacker will examine ethnic differences in growth in early childhood, asking who is developing better or worse than the majority White British population. Differences in height between ethnic groups do not mirror patterns for birth weight. The results are interpreted in the light of intrauterine insufficiency and parental height potential hypotheses.

In the second paper, Yvonne Kelly will examine how family conflict affects children's development. Socioeconomic and psychosocial confounders and mediators are analysed to ascertain their role in the adverse relationship between family conflict and child development.

What happens when families separate or are reconstituted is one theme of the work by Lidia Panico. While the relationship between family structure and socio-emotional health has been studied in detail, less is known about family structure during the first five years and physical health outcomes.

The final paper by Anne McMunn explores what forms of sharing of paid employment and unpaid domestic labour impact on children's socio-emotional development. Together these papers provide a unique insight into the relationship between characteristics and behaviour of one generation and the well-being and healthy development of the next generation.

## S1.1.1

### Ethnic differences in growth in early childhood

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#### **Abstract**

*Objectives:* Ethnic minority status is associated with a greater risk of low birth weight and of obesity in childhood, but whether these disparities are replicated in other markers of physical development is unknown. This study examines ethnic disparities in children's height at 5 years.

*Methods:* Data are from the UK Millennium Cohort Study, constructed to over-represent ethnic minority children, giving reasonable sample sizes for Indian, Pakistani, Bangladeshi, Black African and Black Caribbean groups. Parental and child height was measured at the age 5 interview. Birth weight was reported by the main respondent (usually the mother) at the 9 month interview.

*Results:* Mean birth weight of ethnic minority children was lower than that of the ethnic majority (3.06 – 3.34 kg versus 3.41 kg), but ethnic minority children were not shorter at 5 years. Indian, Pakistani, Black Caribbean and Black African children were actually taller on average (by 0.6cm, 0.5 cm, 1.4 cm. and 3.5 cm). Controlling for parental height and birth weight did not affect height differentials. Two mechanisms were hypothesised: (a) a cramped intrauterine environment given the short stature of some minority children's mothers resulted in catch-up growth and (b) conditions during the parents' childhood led to a reduced capacity to reach their height potential. A reparameterization of parent heights showed that mother's height contributed more to predicting child height than joint parental height alone. Birth weight was positively related to height and attenuated the extra contribution from mothers' heights. Decomposing the effects into their constituent parts found some support for both hypotheses. There was some evidence that parents of ethnic minority children had failed to reach their growth potential with stronger evidence for Pakistani parents. There was also some evidence of catch-up growth in low birth weight minority children.

*Conclusions:* These results suggest that children from ethnic minority backgrounds are not disadvantaged with respect to height growth compared with the ethnic majority. However, if adiposity is more likely when children are tall for their age, then ethnic inequalities in adult health could increase as the current generation of children mature.

## S1.1.2

### **Do mum and dad get along? Family conflict and health and development in early childhood: findings from the UK Millennium cohort Study**

**Yvonne Kelly<sup>1\*</sup>, Anne McMunn<sup>1</sup>, Mel Bartley<sup>1</sup>, Noriko Cable<sup>1</sup>, Amanda Sacker<sup>2</sup> and Scott Montgomery<sup>3</sup>**

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#### **Abstract**

*Objectives:* Previous work suggests that family conflict impacts adversely on child development. But it is not clear to what extent these relationships might hold in a contemporary population setting. This study examines 1. the extent to which markers of parental conflict are associated with child development 2. the influence of socioeconomic and psychosocial factors in the observed relationships.

*Methods:* Data from the UK Millennium cohort study were used (N=9144). Questions on parental conflict – whether they felt they were on the brink of separation and on the experience of physical force/violence in the relationship were answered by both parents when cohort members were age 9 months, 3 and 5 years. Markers of child development at age 5 were height, socioemotional difficulties, and verbal ability.

*Results:* Girls and boys whose mothers felt they were on the brink of separation from their partner were shorter (girls 109.0 vs 110.3, boys 110.9 vs 111.3cm), more likely to have socioemotional difficulties (girls 9.7 vs 4.1, boys 15.7 vs 6.4%) and lower verbal test scores (girls 55.5 vs 57.1, boys 52.9 vs 56.5) compared with children where this was not the case. For girls height differences remain statistically different on adjustment for socioeconomic and psychosocial factors, whilst differences in socioemotional difficulties and verbal ability were rendered statistically non-significant on adjustment for psychosocial factors. For boys differences in the likelihood of socioemotional difficulties and verbal ability were reduced on adjustment for socioeconomic and psychosocial factors but remained statistically significant.

*Conclusions:* Children living in homes in which there was likely family conflict had poorer developmental outcomes compared with children living in more favourable circumstances. Gender differences in factors that explained observed patterns were apparent.



### **S1.1.3**

## **Family structure and child health: a longitudinal model using the Millennium Cohort Study**

**Lidia Panico<sup>1\*</sup>, Mel Bartley<sup>1</sup>, Yvonne Kelly<sup>1</sup>, Anne McMunn<sup>1</sup> and Amanda Sacker<sup>2</sup>**

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#### **Abstract**

*Objectives:* An increasing number of children are born to unmarried parents due to an increase in lone parenthood and unmarried cohabitation. A number of studies, particularly in the US, have shown that children growing with two continuously married parents do better on a range of cognitive, emotional and developmental outcomes, both in childhood and adulthood. Less literature is available from the UK, and we do not know if there is also a link with child's physical health.

*Methods:* The Millennium Cohort Study, a nationally representative study, follows about 18,000 children born in the UK between 2000 and 2001. This paper will look at a range of physical health outcomes including respiratory illnesses, BMI and waist circumference, and unintentional accidents, over the first 5 years of life. A longitudinal model will explore the relative importance of socio-economic disadvantage, parental mental health and parenting behaviours in producing these outcomes. The paper will also explore how to capture longitudinal change in these types of variables.

*Results:* I will show that children living with continuously married parents do best, followed by those living with continuously cohabiting parents, while those living with a lone parent do worst (for example, 11.8% of children living with continuously married parents had asthma by age 5, compared to 22.2% of those always living with a lone parent and 14.4% of those living with continuously cohabiting parents). Those who experience changes in family structure are a heterogeneous group with diverse experiences. Of this group, households that experience both lone parenthood and cohabitation do worst (20.8% of children report asthma) while lone parents who marry do best (12.1%). I will argue that socio-economic disadvantage is the most important factor driving these results.

*Conclusions:* Children living with married parents, both looked at cross-sectionally and longitudinally, have the best physical health outcomes. Children living with lone parents appear to do worst and those living with cohabiting parents are in between. Those who experience a change in family structure in the first 5 years of life are a diverse group and do not have uniformly poor outcomes. Socio-economic factors are important drivers of these effects.

## **S1.1.4**

### **Effects of parental divisions in paid employment and unpaid domestic labour on child socio-emotional behaviour: Longitudinal evidence from the United Kingdom**

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#### **Abstract**

*Objectives:* This study examines the effects of parental participation in paid employment and non-paid domestic labour in the early years on child socio-emotional behaviour at age 5 in the United Kingdom.

*Methods:* Participants of the Millennium Cohort Study were born between September 2000 and January 2002 (n=18,819). Data on parental employment and domestic labour across three sweeps of data collection (infancy, age 3 and age 5) were used to investigate: (i) the extent to which the current generation of British fathers are equally involved in domestic responsibilities, (ii) whether equally shared parenting in the early years influences child socio-emotional behaviour at age 5, (iii) the effects of different types of parental paid work arrangements on child socio-emotional behaviour at age 5, and (iv) whether these relationships vary by the gender of the child. Child socio-emotional behaviour was measured using the Strengths and Difficulties Questionnaire.

*Results:* There were significant gender differences in the effects of parental paid work arrangements on behavioural outcomes. Girls whose mothers were not in paid work at all during their first five years were 77% (95% CI=1.21-2.57) more likely to have behavioural difficulties at age 5 than girls whose mothers were in paid work throughout their early years, independent of maternal characteristics and household income. For boys this was not the case, but boys in households in which their father was not in paid work for at least one period during their first five years were at an increased risk for behavioural problems at age 5. The most beneficial working arrangement for both girls and boys was that in which both mothers and fathers were present in the household and in paid work. Parents were more likely to share childcare responsibilities than other forms of domestic labour. Traditional gender divisions of labour in relation to cooking, cleaning, and doing laundry were common.

*Conclusions:* Maternal employment in the early years is not detrimental to children's socio-emotional development. Gendered divisions of labour appear to be less common in relation to paid employment and childcare, but more common for non-childcare domestic labour among the current generation of British parents.

## S1.2.0

### Symposium: Statistical methods for life course investigations of growth and health

Darren Dahly<sup>1\*</sup>, Kate Tilling<sup>2</sup>, Yu-Kang Tu<sup>1</sup>, Mark Gilthorpe<sup>1</sup> and Robert West<sup>1</sup>

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#### Abstract

The goal of this symposium is to introduce and demonstrate statistical methods that can be used to study anthropometric change across the life course (i.e. *growth*). Researchers have long recognized the utility of infant and childhood anthropometric measures such as height and body mass as key indicators of human health and development. However, the modern life course perspective on chronic disease epidemiology has further emphasized the importance of understanding human growth.

Small birth size, an indicator of poor foetal growth and development, has been linked to chronic disease later in adulthood. However, in many studies an inverse relationship between birth size and adult outcomes was only apparent upon adjustment for adult body size. This has led some to posit that there are critical periods in infancy and childhood in which an individual's growth rate will determine later health outcomes. Further evidence suggests that risk of some chronic diseases later in life may be highest in individuals who were born small, but become relatively large adults, suggesting that it is the overall pattern of postnatal growth that is most important. The importance of early growth is also highlighted by the alarming increases in childhood obesity seen around the world.

These observations could critically impact policy, as growth promotion is a cornerstone of public health practice. The ideas that growth can be over-promoted, and that there may be *ideal* growth patterns that promote long term health, need much more investigation. While the birth cohort data needed to test these ideas are becoming more widely available, there is still too little advice on the application of statistical methods to analyze these data in a life course framework. To help fill this gap, this symposium was put together to introduce and demonstrate to an audience of applied health researchers (with or without formal training in statistics) a variety of longitudinal methods (multi-level models; latent growth curve models; growth mixtures; functional data analysis; compositional analysis) and to highlight a number of important issues for this rapidly developing field (e.g. autocorrelation; missing data; the relative importance of critical periods versus overall patterns).

## S1.2.1

### Developing multilevel linear spline models for summarising individual growth

Kate Tilling<sup>1\*</sup>, Neil M Davies<sup>2,3</sup>, Frank Windmeijer<sup>3</sup>, George Davey Smith<sup>2</sup>, Yoav Ben-Shlomo<sup>1</sup>, Michael S Kramer<sup>4</sup> and Richard M Martin<sup>1</sup>

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#### Abstract

*Objectives:* It is hypothesised that there are critical periods in childhood and infancy in which an individual's growth rate will determine later health outcomes. Examining such hypotheses requires analysis of repeated measures of growth, which can be affected by missing data, autocorrelation and measurement error (which may change over time). Our objective was to use multilevel models to develop parsimonious summary measures of individual growth trajectories between birth and 5 years of age to use as exposures in relation to later outcomes.

*Methods:* We modelled weight gain in 10,494 children from Belarus who participated in a cluster randomised trial of a breastfeeding promotion intervention. Each child had up to 13 measures of weight from birth to age 6.5 years. We used multilevel models with fractional polynomials to derive the best-fitting curve for weight change with age. Linear spline random-effects models were then used to approximate this curve, with various methods of selecting the optimal knot points compared. The best-fitting model (according to our final criteria) had 2 knots (thus dividing follow-up into 3 time periods, each with its own trajectory). This spline model was used to estimate 4 random effects for each individual: birth weight; early infant weight velocity (birth – 3 mo); late infant weight velocity (3 mo – 1 yr) and childhood weight velocity (1 yr – 5 yrs). Together, these coefficients summarise each child's growth curve from birth to 5 years. We used linear regression and path analysis to relate these growth measures to blood pressure at 6.5 years

*Results:* Birth weight and weight velocity at all 3 time-periods were positively associated with blood pressure. There was no evidence of a particularly important effect of early growth, as had been hypothesised.

*Conclusions:* Multilevel linear spline models provide an efficient way to reduce the dimensionality (and thus some of the autocorrelation) of multiple measures of growth. Such methods can be used to relate patterns of growth to later outcomes in a relatively simple, easily-interpretable way. These methods make optimal use of the data, allow for subjects to have some missing growth measures, and allow for measurement error.

## S1.2.2

### Compositional data analysis for life course research – a partial least squares regression approach

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#### **Abstract**

*Objectives:* We propose a new approach to analyse the association between body size during life course and health outcomes in later life by transforming body size measurements as compositional data. Current body size can be considered the sum of growth in body size at different phases during life course. Therefore, body size measurements can be re-parameterised as compositional data, i.e. the growth in body size as the percentage of current body size.

*Methods:* Data are from the 960 males enrolled on the Cebu Longitudinal Health and Nutrition Survey, a community based study of birth cohort living in Metropolitan Cebu, Philippines with body weights measured at birth, age 1 yr, 2 yr, 8 yr, 15 yr and 19yr. As compositional data is not full-rank, we use partial least squares (PLS) regression to estimate the association between percentage growth across life course and blood pressure at age 19 yr.

*Results:* In models with the first PLS component, birth weight (Wt0) and weight change up to yr 2 have negative associations with systolic blood pressure (SBP) (Wt0: -2.14 mmHg per 1% change; Wt1-0: -0.90; Wt2-1: -0.41), whilst weight changes between yr 8 and 19 have positive associations with SBP (Wt15-8: 0.08; Wt19-15: 0.04). Birth weight (Wt0) and weight change up to yr 2 have negative associations with diastolic blood pressure (DBP) (Wt0: -1.67 mmHg per 1 percent change; Wt1-0: -0.41; Wt2-1: -0.25), whilst weight changes between yr 2 and 15 have positive associations with SBP (Wt8-2: 0.11; Wt15-8: 0.07). There are only small changes in the regression coefficients when more PLS components are retained.

*Conclusions:* Analysing life course data as compositional data evaluates the impact of relative growth rates in different phases of life course. Our results suggest rapid early growth is associated with lower blood pressure whilst growth in adolescence is associated with higher blood pressure.

## **S1.2.3**

### **Investigating body mass index trajectories using growth mixture models**

**Darren Dahly\***

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#### **Abstract**

*Objective:* Some evidence suggests that rapid weight gain very early in life is associated with later obesity. Our goal was to test this hypothesis using growth mixture modelling to investigate life course trajectories of body mass in a birth cohort of young adult Filipinos.

*Methods:* Data are from the 1620 males enrolled on the Cebu Longitudinal Health and Nutrition Survey (CLHNS), a community based study of a one-year birth cohort living in Metropolitan Cebu (pop 1.9 million), Philippines. We estimated a freed-loading latent growth curve of body mass index (BMI) measures collected bimonthly from birth to age 2, then at ages 9, 12, 18 and 22 years. The model was then extended to a mixture model, which was used to test the hypothesis that the sample is better characterized as a mixture of subpopulations with different BMI trajectories.

*Results:* Based on a variety of criteria (model fit, classification quality, subjective interpretation) a 5 class model was selected to interpret. The 5 classes were characterized by distinctly different early (0-2 years) BMI trajectories that frequently crossed over, and parallel trajectories after the age of 8 years. Four of the classes had very similar BMI values at age 22 (mean 21.04; 80<sup>th</sup> percentile 22.95), whereas the 5<sup>th</sup> group was characterised by substantially elevated BMI (mean 25.80; 80<sup>th</sup> percentile 29.9). The early pattern of BMI in the group with higher mean BMI was not consistent with previous observations.

*Conclusions:* The patterns of BMI we observed were not consistent with the hypothesis that rapid early gains in body mass are associated with increased risk of obesity in young adulthood.

## S1.2.4

### The importance of accommodating autocorrelation in latent class growth curve models of cohort data

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#### Abstract

*Objective:* Researchers increasingly explore longitudinal data using growth mixture models. A feature of such data often overlooked is autocorrelation. The impact of autocorrelation on model structure and interpretation remains unclear. We contrast the impact of ignoring autocorrelation vs. modelling it explicitly for growth mixture models of a cohort study of weight change in adolescents from Cincinnati, OH, USA.

*Methods:* The outcome comprises repeated measures of body mass index (BMI). In seeking latent class growth trajectories to describe the cohort, we examine models with and without an AR(1) structure to establish to what degree this affects: (i) likelihood-based model-fit and the 'optimum' number of classes as determined by these criteria; (ii) class sizes; and (iii) class variance structure.

*Results:* Models that account for autocorrelation consistently score better according to both AIC and BIC. AIC fails to attain a minimum for up to eleven classes, though it ceases to improve significantly after ten classes for models with autocorrelation. BIC attains a minimum at five classes with autocorrelation and at ten classes without. The proportion of individuals in models with and without autocorrelation, but with the same number of classes, increases as class number increases. For a given number of classes, there is a tendency for smaller classes to contain a larger proportion of individuals if autocorrelation is modelled than if not. The mean variance of random intercepts amongst latent class trajectories with autocorrelation is four times that amongst latent class trajectories without. In contrast, the mean variance of random slopes amongst latent class trajectories with autocorrelation is half that amongst latent class trajectories without.

*Conclusion:* For growth mixture models, adoption of an autocorrelation structure makes a difference to which model is determined as 'optimum'. Modelling autocorrelation differentiates membership of smaller classes more clearly and ensures that features of interest in growth trajectories (i.e. means and slopes) are estimated with appropriate consideration given to how the data were generated. Failure to recognise the importance of modelling autocorrelation could give rise to misleading models and hence erroneous inferences.

## S1.2.5

### The use of functional data analysis for longitudinal studies

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#### **Abstract**

*Objective:* To illustrate the use of functional data analysis for life course data, and in particular to show the advantages of considering covariates as functions of time.

*Methods:* Data from the Cebu Longitudinal Health and Nutrition Survey were used to illustrate the approach. Systolic blood pressure (SBP) at age 22 was used in two regressions: first on weight considered as a function of time, and then regressed upon the functional principal components of weight. It is useful to note that the first approach provides the best estimate of SBP but that due to the reversal paradox, the time-varying coefficient cannot be interpreted. However, for the second regression the principal components are orthogonal and so the reversal paradox is avoided. This approach identifies features and assigns relative importance to them, thus fulfilling the aims of life course analysis, potentially identifying critical periods of growth for later disease risk.

*Results:* The functional regression indicates that the contribution of weight to SBP is greatest for recent measurements (Figure 1). The principal component regression shows that there is also a contribution from the early life course pre- puberty, identifying catch-up growth, when excess weight above the average is associated with increased SBP later in life.

*Conclusions:* This is a novel application of functional data analysis that provides a means to identify aspects of growth that contribute to the development of systolic blood pressure over the life course. The relative contributions of these features associated with the development of health and disease can be quantified bypassing the issues of the reversal paradox. Thus this approach provides an appropriate methodology for life course analysis.



## **S1.3.0**

### **Symposium: Epigenetics and longitudinal cohort studies**

**Caroline Relton<sup>1\*</sup>, Bas Heijmans<sup>2</sup>, Jonathan Mill<sup>3</sup> and Vardhman Rakyan<sup>3</sup>**

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#### **Abstract**

There is intense interest in the possible role of epigenetic mechanisms in mediating health outcomes across the life course. This symposium will present recent evidence that epigenetic variation is altered in response to early life exposures and that it is associated with phenotypic variation. The symposium will highlight important issues in conducting epigenetic epidemiological studies including the tissue specificity and temporal stability of epigenetic patterns and the assessment of causality when interpreting associations between epigenetic variation and phenotype.

## **S1.3.1**

### **The epigenome: linking early development and adulthood disease**

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#### **Abstract**

Our aim is to identify epigenomic marks that are susceptible to the (prenatal) environment and to establish their contribution to human disease. We recently reported differences in the methylation of various candidate loci including *IGF2* and *LEP* among individuals who were prenatally exposed to the Dutch Famine 6 decades ago. To systematically characterize the epigenomic changes associated with prenatal famine, we are performing genome-scale studies employing reduced-representation bisulfite sequencing. Uncovering such persistent epigenomic changes is a crucial step towards explaining the long-term consequences of the prenatal environment. To assess their role in disease, however, a framework for epigenetic epidemiology is required within which studies can be designed capitalizing on biobanks that comprise large numbers of patients and controls. We explored key elements of such a framework including the prospects of 'methylation-tagging', the temporal stability of DNA methylation and the usefulness of blood as a marker tissue. Furthermore, initial data suggested the presence of DNA methylation differences between incident myocardial infarction cases and controls at loci sensitive to the prenatal environment. Studies that integrate epigenomic and genetic data may eventually reveal genomic risk factors that are more powerful than those solely based on DNA sequence variation.

## **S1.3.2**

### **Epigenetic trajectories in the risk for mental illness**

**Jonathan Mill\***

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#### **Abstract**

Psychiatric disorders make a substantial contribution to the global burden of disease. As with other complex disease phenotypes, traditional etiological approaches have focussed primarily on the role of genetic factors in mediating susceptibility. Sequencing the genome, however, was only the first step in our quest to understand how genes are expressed and regulated. Sitting above the DNA sequence is a second layer of information that regulates several genomic functions, including when and where genes are turned-on or -off. 'Epigenetics' refers to the reversible regulation of gene expression mediated principally through changes in DNA methylation and chromatin structure. Epigenetic processes are essential for normal cellular development and differentiation, and allow the regulation of gene function through non-mutagenic mechanisms. Unlike the DNA sequence, which is stable and strongly conserved, epigenetic processes are tissue-specific, developmentally-regulated and relatively dynamic. Epigenetic dysfunction can explain numerous epidemiological, clinical, and molecular peculiarities associated with psychiatric disorders that are difficult to rectify using traditional gene- and environment-based approaches. These include the incomplete concordance between monozygotic twins for psychiatric phenotypes, a fluctuating disease course with periods of remission and relapse, sexual dimorphism, peaks of susceptibility to disease coinciding with major hormonal rearrangements, and parent-of-origin effects. In this talk I will present data highlighting the role of developmental epigenetic changes in mediating neurobiological processes in the brain. Using genome-wide methylomic profiling approaches and a unique collection of post-mortem brain tissue, disease-discordant monozygotic twins and longitudinal population cohorts, our studies provide strong evidence for the role of epigenetic factors in mediating susceptibility to a number of psychiatric conditions including schizophrenia, bipolar disorder, major depression, and autism.

### **S1.3.3**

## **Epigenetic variation and type 1 diabetes – lessons from twin studies**

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### **Abstract**

Discordance for multi-factorial human diseases is often observed in monozygotic (MZ) twin pairs e.g. in childhood-onset Type 1 Diabetes, an autoimmune disease, MZ twin discordance is ~50%, suggesting a role for environmental and/or epigenetic factors in disease pathogenesis. To obtain evidence for an epigenetic component of T1D, we performed genome-wide DNA methylation analysis of CD14+ monocytes from 15 T1D-discordant MZ twin pairs. At  $P < 0.01$ , we identified 58 T1D-associated methylation variable positions (T1D-MVPs) hypermethylated (hyperT1D-MVPs), and 74 T1D-MVPs hypomethylated (hypoT1D-MVPs) in the T1D-affected co-twins. Then, we analyzed DNA methylation profiles of CD14+ cells obtained from 7 singletons before and immediately after they presented with clinical T1D and found that in both pre- and post-T1D samples relative to controls, the same T1D-MVPs display methylation differences in the expected direction ( $P < 0.015$ ). These results provide independent replication of T1D-MVPs, and, notably, demonstrate that T1D-MVPs precede clinical diagnosis, can be identified in the context of normoglycaemia, and are not due to physiological conditions after diagnosis, metabolic dysfunction, pharmacological or insulin treatment, or the twinning event (since the replication was performed in singletons). T1D-MVP-associated genes include several known to be associated with T1D or immune responses. Overall, we demonstrate that T1D-associated epigenetic variation antedates clinical type 1 diabetes and is unlikely to be due to genetic heterogeneity, metabolic dysfunction, insulin or other pharmacological treatment, clinical disease, or twinning. Rather, we propose that T1D-MVPs arise at an early stage of the process that leads to clinical disease, and thus could contribute to T1D pathogenesis.

## **S1.3.4**

### **Epigenetic patterns at birth predict body composition in childhood**

**Caroline Relton\***

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#### **Abstract**

Epigenetic markings acquired in early life may have phenotypic consequences later in development through their role in transcriptional regulation and such mechanisms are relevant to the developmental origins of diseases including obesity. The goal of this study was to investigate whether DNA methylation levels at birth predict body composition phenotype later in childhood. We used a study design involving two childhood cohorts to conduct transcription profiling followed by DNA methylation analysis in peripheral blood. Transcription profiling was undertaken in a total of 14 individuals with had a mean body mass index (BMI) difference of 9.93 (2.37) kg/m<sup>2</sup>. DNA methylation analysis in cord blood DNA in 178 individuals with body composition data prospectively collected at a mean age of 7.45 (0.13) years and 11.75 (0.22) years was then undertaken. Twenty-nine of the differentially expressed genes supplemented with a further 22 genes known to be associated with body composition through recent genome wide association studies were analysed to determine DNA methylation levels at 1-3 sites per gene. DNA methylation in 18 of the 43 (42%) genes studied were associated with BMI at 7 years, 9 years and/or 11 years of age, displaying a mean change of 0.76 kg/m<sup>2</sup> of BMI with each SD shift in DNA methylation at birth. Change in BMI was largely explained by altered fat mass. In the majority of cases a decrease in BMI was associated with increased promoter region DNA methylation and decreased gene expression. These observations support the hypothesis that DNA methylation patterns at birth are associated with the regulation of genes involved in the determination of body composition in childhood.

## **S1.4.0**

### **Symposium: Aetiology of inattention and hyperactivity problems in the life course: Potential for prenatal and genetic Interplay**

**Alina Rodriguez<sup>1,2,3\*</sup>, Claudia Buss<sup>4</sup>, Philip Asherson<sup>3</sup> and Mary L Schneider<sup>5</sup>**

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#### **Abstract**

Attention Deficit Hyperactivity Disorder (ADHD) is the most common disorder in child and adolescent psychiatry. ADHD is a neurodevelopmental disorder with early childhood onset and is characterized by levels of inattentive, hyperactive and impulsive behaviours that are inappropriate for the developmental stage. Even when symptoms of inattention and hyperactivity are not severe enough to fulfill psychiatric criteria, the symptoms may nonetheless be associated with profound disruption to the individual, family, and society. The causes of inattention and hyperactivity are largely unknown, but both environmental, particularly during prenatal period, and genetic factors have been implicated. The objective of this symposium is to present the latest research to understand both prenatal environmental and genetic factors in the etiology of ADHD symptoms.

The research presented in this symposium features multi-method approaches to explore genetic and environmental factors for the aetiology of inattention and hyperactivity.

The first presentation describes Nordic epidemiological studies using genetically informed designs to investigate the impact of the prenatal environment.

A series of in-depth studies from the United States are covered in the second presentation which examine whether exposure to maternal stress during pregnancy is related to delayed infant mental development and child brain morphology.

Twin data from the UK, Australia and Sweden are presented by the third speaker to estimate familial (genetic and environmental) risks on ADHD symptoms in adults.

Lastly, the fourth presentation highlights the use of a primate model for the understanding the gene x environment interplay in the development of neurodevelopmental disturbances.

## **S1.4.1**

### **Prenatal programming of Attention Deficit Hyperactivity Disorder (ADHD) symptoms**

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#### **Abstract**

*Objective:* This research is based on the concept that various exposures primarily related to maternal lifestyle during pregnancy perturb fetal brain development. Thus, the origins of child mental health may lie in part during prenatal development when genes interact for the first time with the environment in utero. Current research suggests that exposure to maternal stress during prenatal development can permanently place the offspring on a negative developmental trajectory often manifested as early behavioural problems, poor scholastic performance, and a higher risk of psychopathology later in life, all which have an enormous impact on families and society. This talk critically explores biologically plausible mechanisms and presents epidemiological studies examining evidence for in utero programming of symptoms related to Attention Deficit Hyperactivity Disorder (ADHD) while using a genetically informed design.

*Method:* We are conducting a range of studies focused on identifying and understanding factors in the prenatal environment that are associated with negative developmental outcomes in children, particularly those related to ADHD. This talk presents data from prospective pregnancy cohorts from Sweden as well as other Nordic countries to elucidate etiological underpinnings of ADHD. Data were consecutively gathered during pregnancy via self-report and medical records. Children have been followed from birth until childhood or adolescence. Genetic analyses are underway and focus on the potential interplay between genes and environment. Candidate genes will be examined in relation to prenatal exposure to maternal stress and ADHD symptoms in childhood and adolescence. Moreover family studies are used to control for familial confounding and to inform on potential heritable associations.

*Results:* These studies suggest that prenatal exposures, particularly maternal stress, during pregnancy are associated with neurobehavioral alterations in children related ADHD.

*Conclusions:* These findings provide evidence linking exposure to maternal stress during pregnancy and ADHD symptoms in childhood as well as adolescence. Further, the genetic analyses will inform to what extent candidate genotypes moderate children's liability to exposure to prenatal stress and potential risk of behaviour problems across development.

## **S1.4.2**

### **The impact of maternal prenatal pregnancy-specific anxiety on infant and child neurodevelopmental outcomes**

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#### **Abstract**

*Objective:* The origins of susceptibility for many neurodevelopmental and neuropsychiatric disorders can be traced back to the intrauterine period of life. The unfolding of all developmental processes from genotype to phenotype is context-dependent, wherein the developing embryo/ foetus responds to, or is acted upon by, conditions in the internal or external environment during sensitive periods of cellular proliferation, differentiation and maturation, resulting in structural and functional changes in cells, tissues and organ systems. Due to the rapid developmental changes the brain is undergoing during the prenatal period, it is especially vulnerable to environmental insults during this early phase of development.

*Methods:* Over the past several years our studies at the UC Irvine Development, Health and Disease Research Program have addressed the interface between biological, behavioural and social processes in human pregnancy, with a focus on the impact of maternal psychosocial stress and stress biology on foetal development, birth outcomes, and subsequent newborn, infant, and child developmental and health outcomes. In the context of this presentation, findings from our ongoing longitudinal studies will be presented with a focus on the impact of prenatal maternal pregnancy-specific anxiety, assessed repeatedly over the course of gestation, on infant mental development, infant and child temperament and child brain morphology and cognitive performance.

*Results:* Our studies suggest that high levels of maternal pregnancy-specific anxiety are associated with delayed infant mental development, more difficult infant and child temperament, localized reductions in brain gray matter volume and impairment in executive function.

*Conclusions:* It is well-established that alterations of brain morphology and function are associated with several neuropsychiatric, neurodevelopmental and behavioural disorders. Foetal programming of the brain might affect an individual's susceptibility for these disorders across the lifespan. Pregnancy specific worries during gestation may therefore be a target for interventions that could improve neurodevelopmental outcome in the offspring.

(This research was supported by National Institute of Health grants NS-41298, HD-51852 and HD28413).



### S1.4.3

## Family and twin studies of ADHD in adulthood

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#### Abstract

*Objective:* Attention Deficit Hyperactivity Disorder (ADHD) is a childhood onset disorder that frequently persists into adulthood. Family and twin studies delineate a disorder with strong genetic influences in children and adolescents yet the continuity of the aetiological influences on ADHD symptoms in adults has yet to be so well studied. We therefore investigate the role of genetic and environmental influences underlying inattentive and hyperactive-impulsive symptoms in adults.

*Method:* Family and twin methods were applied to self and informant reported assessments of ADHD using clinical and population samples from the UK, Australia and Sweden, to evaluate the familial (genetic and environmental) risks on ADHD symptoms in adults.

*Results:* The results of the various studies all concur that familial effects on self-rated ADHD symptoms in adults are moderate, with estimated heritability for self-rated inattentive and hyperactive-impulsive symptoms of 35% and (37%) respectively. The genetic correlation between the inattentive and hyperactive-impulsive dimensions (from the Swedish twin sample) was estimated at 0.63 which is similar to that seen in younger cohorts using informant ratings. Estimates of familial risk for ADHD symptoms are sensitive to rating (self versus informant) and age of onset effects. A preliminary family study further found that evoked response potentials during a cued CPT task were particularly sensitive to the familial liability of ADHD in adults.

*Conclusions:* Overall our findings are consistent with previous literature on self-rated ADHD symptoms in older children and adolescents and retrospective reports of self-rated childhood ADHD by adults. Heritability estimates were further confounded by adult onset ADHD symptoms that showed no familial association with ADHD in children. The discrepancy in heritability estimates between self and informant ratings could indicate a true developmental change in the heritability of ADHD, or could be related to various sources of measurement error. We conclude that ADHD is a heritable phenotype; longitudinal studies of ADHD need to use comparable measures across the lifespan; age of onset of ADHD symptoms is likely to be an important variable related to aetiology; and intermediate electrophysiological phenotypes may help to delineate the aetiological influences and underlying processes involved.

## S1.4.4

### **Prospective longitudinal primate study of prenatal stress and alcohol exposure: Brain, behavior, stress reactivity, and genes**

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#### **Abstract**

*Objective:* Evidence from human and animal studies indicates that the foetal environment can have long-lasting effects on health and development. Because foetal alcohol-exposed individuals are often conceived within a stressful environment, interactions between prenatal stress and alcohol exposure reflect a common yet understudied condition.

*Methods:* We have been following a unique cohort of 45 monkeys to study the effects of mild prenatal stress, moderate prenatal alcohol exposure, or the combination of conditions compared to controls in an experimental study. We adapted the Brazelton Newborn Assessment Scale to assess neonatal neurobehaviour. We assessed hypothalamic-pituitary-adrenal (HPA) axis function and biogenic amines in CSF after social separations. In adulthood, we used high-resolution positron emission tomography (PET) to assess measures of dopamine (DA) and serotonin (5-HT) function in striatum and frontal cortex. We assessed DA D1 and D2 receptor and DA transporter binding as well as 5-HT1A binding in the brain using the radiotracers [11C]SCH23390, [18F]Fallypride, [18F]FECNT and [18F]Mefway, respectively. All monkeys were genotyped for variation in the serotonin transporter (rh5-HTTLPR) polymorphism.

*Results:* We described developmental impairments from prenatal treatments that include impaired infant attention and motor maturity. Infant temperament, HPA axis reactivity, and concentrations of DA and 5-HT metabolites in CSF were altered in PN alcohol exposed monkeys carrying the short version of the 5-HT transporter allele. On PET measures, PN stressed monkeys showed higher DA D2 receptor and DA transporter binding in striatum. Females from the PN stress condition showed higher D1R binding in prefrontal cortex as well as other cortical regions. Interestingly, children with ADHD have 40-50% increase in DAT binding.

*Conclusion:* Our results suggest a link between PN stress, reduced attention, disrupted habituation and abnormalities of the DA system in monkeys, possibly reflecting disruption in some aspects of frontostriatal circuitry. Fronto-striatal DA circuits play a role in integrative functions in the brain, such as motor control, attention, working memory, and inhibitory control. Foetal brain organization can be altered by the environment by yielding long-term functional changes.

(Supported by AA10079 and AA12277)

## S2.1.0

### **Symposium: Early life origins of health and disease: Novel approaches and new directions**

**Demetris Pillas<sup>1\*</sup>, Gabriella Conti<sup>2</sup>, Sarah Finer<sup>3</sup>, Ronny Geva<sup>4</sup>**

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#### **Abstract**

Examining the latent, pathway and cumulative effects of early life factors on adult health is one of the most popular research themes in longitudinal epidemiology. It is now acknowledged that health and disease can be fully understood and explained only if a life course perspective is followed – one that starts from the day of conception. However, since the prediction power for many diseases remains weak, in order to fully reach the potential that the life course approach offers, it is fundamental that research scientists aim to: i) utilise novel methodological approaches, and ii) explore new directions and explanatory mechanisms.

This symposium will highlight how the early life origins of health and disease can be examined through a number of different approaches. The aim is to showcase the potential of utilising genetic and non-genetic, intra- and intergenerational, human and non-human data, study approaches and strategies to enhance our understanding of how early life affects the rest of the life course.

*Study 1* uses data from rhesus monkeys to examine the effects of early rearing conditions on health. Gene and environment interactions are examined as well as intergenerational effects.

*Study 2* uses a mouse model of gestational diabetes to explore potential causal effects of the pregnancy environment on the health of the offspring. Inferences are made relevant to early life epigenetic modifications.

*Study 3* uses data on neonates with intrauterine growth restriction to evaluate the effect of time-dependent early life growth processes on later neuropsychological development.

*Study 4* uses data on locomotor development in infancy and blood pressure levels in adulthood to highlight the importance of further exploring developmental, non-growth-related, effects of early life on later disease.

Together, these studies: i) highlight the potential of using a diverse set of approaches when aiming to make causal and non-causal inferences on the effects of early life on later health and disease, and ii) provide insights into the potential of new research avenues for future studies in this area.

## S2.1.1

### Early life and later health: new evidence from rhesus monkeys

**Gabriella Conti<sup>1\*</sup>, Christopher Hansman<sup>1</sup>, James Heckman<sup>1,2</sup>, Matthew Novak<sup>3</sup>,  
Angela Ruggiero<sup>3</sup> and Stephen Suomi<sup>3</sup>**

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#### **Abstract**

*Objective:* We seek to understand the effects of early rearing conditions on physical and mental health in a sample of Rhesus Macaques, and to test for the presence of gene-environment interactions and intergenerational transmission mechanisms.

*Methods:* We retroactively analyze the records of a sample of 248 Rhesus Macaques, all part of an ongoing randomized experiment on early rearing conditions. Outcomes are obtained from quarterly physical examinations and biannual behavioural observations. We compare a variety of outcomes (health and body conditions, presence of abnormal behaviours and alopecia) across Mother Reared, Peer Reared, and Surrogate Peer Reared monkeys, and allow for both gene (HTTLPR and MAOA) x environment interactions and intergenerational effects.

*Results:* We find evidence of negative effects of adverse early rearing conditions on physical health, stronger for males than for females. While the negative effects of early rearing conditions dissipate over time for Peer Reared monkeys, they are long-lasting for Surrogate Peer Reared monkeys. Early rearing conditions have long-lasting effects on the mental health of both Peer and Surrogate Peer Reared monkeys. We find significant evidence of HTTLPR-by-rearing interaction on health, with effects which vary by gender. We also find that male monkeys carrying the low-activity variant of the MAOA gene are more likely to experience health issues or alopecia if raised in an adverse environment. Finally, we find evidence of strong intergenerational effects, especially on physical health for males and mental health for females, with the majority of effects operating through Surrogate Peer Reared mothers.

*Conclusions:* We have exploited a unique experiment in a colony of rhesus monkeys to study the effects of early rearing conditions on health. We have found long-lasting effects of early maternal and social deprivation on physical and mental health, especially for males. We have also discovered the presence of significant HTTLPR- and MAOA-by-rearing interactions. Finally, we have shown that the effects of early maternal and social deprivation carry out through the next generation.

## S2.1.2

### A model of intrauterine hyperglycaemia provides evidence for fetal programming of glucose tolerance and a platform for epigenomic studies in mouse and human

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#### Abstract

*Objectives:* Exposure to hyperglycaemia in utero has been shown to programme adult cardiometabolic diseases offspring in a range of human cohorts and animal models. However, the mechanisms underlying these programming effects are not understood. The study of epigenetic modifications is providing insight into the combined role of genetic and environmental influences that mediate programming.

*Methods:* An inbred mouse model of gestational diabetes has been used to characterise the phenotypic and epigenomic changes in exposed vs. unexposed offspring. 24 Female *Lepr<sup>db/+</sup>* (*db/+*) and 23 *Lepr<sup>+/+</sup>* (*+/+*) mice (C57BL/6 background strain, Jackson lab) were crossed with C57BL/6 males. 10 litters from each group were culled at 17.5 days post-coitus (dpc). The remaining offspring were housed under normal conditions in mixed cages until 6 months of age, when detailed phenotypic testing was performed prior to cull.

*Results:* At 17.5 dpc Female *db/+* mice were more hyperglycaemic than wildtypes, as determined by intraperitoneal glucose tolerance testing (AUC *+/+* 572, *db/+* 726, 95% confidence interval 65-242,  $p = 0.001$ ). Male wildtype offspring born to *db/+* mothers were more glucose intolerant at 6 months of age than those born to *+/+* mothers (AUC wildtype offspring born to *+/+* mothers 2777, *db/+* mothers 3365, 95% CI 157-1019,  $p = 0.008$ ). Greater body weight, liver weight and fat mass (determined by gonadal and retroperitoneal fat pad weights) were also seen in offspring born to *db/+* mothers at this age.

*Conclusions:* Phenotypic testing confirms programming in offspring exposed to the adverse environmental conditions of pregnancy conferred by *db/+* mothers. In comparing isogenic mice from an inbred mouse strain, genetic factors are eliminated and it can be expected that the pregnancy environment (hyperglycaemia and leptin resistance) has induced epigenetic modifications leading to glucose intolerance and increased fat deposition in aged offspring. Epigenomic studies using Medip-seq are currently being performed on foetal liver to identify aetiological DNA methylation differences. This discovery-based approach will identify differentially-methylated regions that will direct additional study of developmental changes, tissue- and sex-specificity. Furthermore, the results of this study will focus hypothesis-testing in a related human cohort of gestational diabetes currently taking place.

### **S2.1.3**

## **Time-locked growth processes and neuropsychological development: The case of intrauterine growth restriction**

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### **Abstract**

*Objectives:* Recent volumetric brain size studies on normally developing and clinical populations motivated the current study. Foetuses whose growths in uteri are restricted are subject to time-locked foetal programming processes that trigger circulatory changes and neural adaptive modifications aimed at conserving the developing brain. Nevertheless, children born with intrauterine growth restriction (IUGR) frequently have subtle, long-term, cognitive impairments, soft neurological symptoms, and learning difficulties in school. The relationships among rate of pre- and postnatal head growth and neuropsychological outcome is not clear. This study was conducted to evaluate the effect of rate and timing of head volume catch-up growth on cognitive competence and neuropsychological profile of 9-year-old children born with IUGR, using a large-scale prospective longitudinal paradigm.

*Methods:* 163 neonates diagnosed with asymmetric IUGR (birth weight percentile < 10<sup>th</sup> percentile for gestation age) were followed-up for 9 years. Anthropometric measurements of head circumference (HC), weight and height and intelligence quotients (IQ) were collected annually. At 9 years of age, participants were evaluated with an extensive neuropsychological battery to assess IQ, learning and memory, visuo-motor skills, visuo-spatial integration, attention, language, and executive functions. The control group comprised an additional appropriate-for-gestational-age group (N=64) matched for gestation, familial and socioeconomic factors. Standardized and normalized scores were used as outcome measures.

*Results:* Longitudinal time dependent trends of global cognitive competence were found, such that normalized IQ and HC scores of children born with IUGR stabilized early at a period when significant standardized changes were still in progress in the control group. Furthermore, discrete functions were sensitive to growth catch up rates, such that executive functions were significantly affected by neonatal HC, and were not modulated by postnatal catch-up growth rate. Postnatal HC growth, body weight and length measurements, affected visuo-motor functioning.

*Conclusions:* The data support a long-term foetal programming hypothesis, whereby prenatal growth restriction compromises macro decade long growth patterns and selectively affects discrete developmental spurts.

## S2.1.4

### Exploring the neurodevelopmental origins of adult disease: the case of infant locomotion and adult blood pressure

**Demetris Pillas<sup>1,2\*</sup>, Marika Kaakinen<sup>3,4</sup>, Ioanna Tzoulaki<sup>2</sup>, Gopalakrishnan Netuveli<sup>1,5</sup>, Erik Fung<sup>6</sup>, Tuija H. Tammelin<sup>7</sup>, David Blane<sup>1,5</sup>, Iona Y. Millwood<sup>2,8</sup>, Rebecca Hardy<sup>9</sup>, Alina Rodriguez<sup>2,10,11</sup>, Ulla Sovio<sup>2</sup>, Laila Arnesdatter Hopstock<sup>12</sup>, Sarianna Vaara<sup>13</sup>, Anokhi Ali Khan<sup>2</sup>, Diana Kuh<sup>9</sup> and Marjo-Riitta Jarvelin<sup>2,3,4,13</sup>**

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#### Abstract

**Objective:** Evidence from animal models suggests that locomotion and blood pressure share common neurophysiological regulatory systems. As a result of this common regulation, we hypothesized that the development of locomotion in human infants would be associated with blood pressure levels in adulthood.

**Methods:** For 4347 individuals, the achievement times of three key stages of locomotive and one stage of non-locomotive neuromotor development were recorded at monthly intervals throughout infancy. Systolic and diastolic blood pressure levels were measured at 31 years.

**Results:** A linear association was found between later achievement of neuromotor milestones related to locomotion and higher blood pressure. Within the three locomotive milestones examined, later developers had, on average, 3.2 mm Hg higher systolic blood pressure and 2.2 mm Hg higher diastolic blood pressure compared to earlier developers. For every month of later achievement of walking without support, systolic blood pressure was higher by 0.36 mm Hg (95 percent confidence interval, 0.10 to 0.63;  $P=0.008$ ) and diastolic blood pressure by 0.43 mm Hg (95 percent confidence interval, 0.19 to 0.66;  $P<0.001$ ). The magnitude and significance of this association did not change after adjusting for measures of intra-uterine and post-natal growth, indicating that this process runs separately and complementary to intra-uterine and post-natal growth effects. Standardized coefficients showed this association to be stronger than the birthweight-adult blood pressure association. This association did not occur for milestones relating to non-locomotive neuromotor development.

**Conclusion:** These results highlight the positive sequelae of advanced locomotive development during infancy and also suggest the period of infant locomotive development as a sensitive neurodevelopmental period for the development of hypertension.

## **S2.2.0**

### **Symposium: Risk and resilience among children and adolescents**

**Ingrid Schoon\***

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#### **Abstract**

In this symposium we examine risk and protective factors associated with psychological health and behaviour adjustment of children and adolescents.

Four studies from three different countries use longitudinal data to investigate the role of socio-economic circumstances threatening the wellbeing of children, and individual variation in response to these risks. Each of the studies will address questions about what enables some children to succeed against the odds, and to maintain positive functioning in the face of adversity.

*Study 1* examines the influences of poverty and family instability on behaviour adjustment of 5 year olds, using data collected for the UK Millennium Cohort.

*Study 2* investigates factors and processes enabling young people aged 10 to 18 who were orphaned by AIDS to maintain positive mental health, using data from low income settlements in Cape Town, South Africa.

*Study 3* assesses the mental health outcomes associated with chronic exposure to bullying victimisation during primary and secondary school, drawing on data collected for the UK Environmental Risk study.

*Study 4* examines the reciprocal interactions between being bullied at school and school adjustment in a Finnish longitudinal study.

Together these studies provide insights into the multiple sources of risk exposure experienced by young people in different socio-cultural contexts and at different life stages. Moreover, accumulation of risk over time is examined, as well as interactions between risk exposure and adaptive responses to this risk.



## S2.2.1

### Family poverty, family instability, and behavioural adjustment among 5-year olds

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#### Abstract

*Objective:* Associations between characteristics of the family environment, in particular poverty and family structure and child adjustment are well established, yet little is known on the role of timing and accumulation of risk in early childhood. The aim of this paper is to assess the associations between income poverty, family instability and behavioural adjustment during the first five years of life, and to examine the protective factors and processes enabling children to strive against the odds.

*Methods:* Using data from the UK Millennium birth cohort (n=12517), this paper assesses the interlinked effects of poverty and family instability on children's development and examines the factors and processes enabling some children to do well despite the experience of adversity. In particular we assess the role of mother-child interactions as possible mediators of the associations between family adversity and the child's adjustment. We define resilience in terms children exposed to family poverty and instability who show no behaviour problems (assessed via maternal report on the Strength and Difficulties Questionnaire).

*Results:* The findings suggest that cumulative family hardship and family instability were significantly associated with behaviour adjustment. The impact of family adversity on behavioural adjustment is partially mediated by the level of maternal distress, which in turn shapes the quality of parent-child interactions. Children growing up with parents who were able to maintain a warm and supportive relationship within a structured family environment were more likely to withstand the negative influences of socio-economic adversity. Findings are discussed in terms of family stress processes and the family investment model.

*Conclusion:* The study confirms the devastating negative effect of poverty, which affects families economically, socially, as well as on an emotional level. Despite the fact that some children maintain positive adjustment in the face of adversity, targeting family poverty should be a major objective of social policy aiming to improve life chances and the health of the nation.

## S2.2.2

### Resilience in young people orphaned by AIDS and other causes: predictors and mechanisms

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#### Abstract

*Objective:* This study investigates longitudinal predictors of resilience in young people orphaned by AIDS, living in informal settlements in Cape Town, South Africa. Children in these communities live under high levels of poverty and community violence; in addition, some children are affected by death of a parent due to AIDS or other causes. Despite this very high level of background risk, orphanhood due to AIDS greatly raises the risk of mental health problems in these young people, doubling the risk for example of depression and PTSD, compared to non-orphans from the same impoverished communities. However, there is considerable variation in outcome, leading us to investigate factors predicting resilience in the face of such difficult lives. We focus on risk and protective factors found to be important in prior studies of this population, especially factors that are potentially amenable to intervention, in order to enhance policy relevance.

*Methods:* We examine predictors of resilience in a sample of young people aged 10-18 (n=944) at time 1, living in very low income settlements in Cape Town, including young people orphaned by AIDS, and two comparison groups: those orphaned by other causes, and non-orphans. The young people were followed up 4 years later, with 74% of the sample traced at follow up. Of those traced, 99% agreed to be interviewed. We defined resilience as absence of any scores above standard cut offs on mental health screening instruments (depression, anxiety, PTSD, conduct problems and delinquency) at both time points. Analyses will i) examine longitudinally factors hindering and promoting resilience at the level of the young person, family and community, and ii) test in moderator analyses which risk and promotive factors have specific relevance for AIDS orphans, and which apply more generally to young people in this context.

*Results:* Preliminary descriptive analyses, prior to the main resilience analyses, show that 71% of non-orphans vs. 48% of AIDS orphans were 'resilient' to mental health problems, by the above definition. At 4 year follow up these figures had reduced to 60% and 43% respectively. Figures for young people orphaned by other causes were intermediate between the two.

## S2.2.3

### **Chronic bullying victimization: Investigating the role of genes and environment**

**Lucy Bowes<sup>1\*</sup>, Barbara Maughan<sup>1</sup>, Sania Shakoor<sup>1</sup>, Harriet Ball<sup>1</sup>, Avshalom Caspi<sup>1,2</sup>, Terrie E Moffitt<sup>1,2</sup> and Louise Arseneault<sup>1</sup>**

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#### **Abstract**

*Objectives:* The cumulative risk associated with chronic exposure to stressors such as bullying victimization can have devastating consequences for children's development. We examined mental health outcomes of chronically victimized children compared to situational victims of bullying. The aetiology of chronic victimization was investigated using a genetically sensitive design. Identifying the relative genetic and environmental influences on persistent victimization from middle to late childhood will enhance understanding of the type of factors that represent targets for intervention work aimed at preventing chronic victimization.

*Methods:* Data were from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally representative 1994-1995 birth cohort of 1,116 families with twins. We used mother and child reports of bullying victimization during primary school (5-10 years) and secondary school (11-12 years). Regression analyses were used to examine age 12 outcomes of chronic versus situational victimization (limited to primary school or secondary school only). A longitudinal behavioural genetic design was used to examine the relative contribution of genetic and environmental influences contributing to stability in victimization status from primary school to secondary school.

*Results:* Compared to children who experienced situational victimization, chronic victims of bullying were found to have an increased risk of mental health difficulties at age 12, including internalizing and externalizing problems. A greater proportion of the chronic victims also exceeded clinical cut-offs for depression and showed at least one definite symptom of psychoses. Using a genetically sensitive design, we found that children's heritable characteristics influence their risk of being chronically victimized. However environmental factors were equally important: factors shared between children in the same family also influenced their risk of chronic victimization. Children who escaped chronic victimization received higher levels of maternal warmth and had more structured and stable home environments.

*Conclusions:* Shared environmental factors together with heritable characteristics help to explain why some children are chronically victimized during childhood. Conversely, children who receive higher levels of maternal warmth and who have positive, well-structured home environments are more likely to escape chronic bullying victimization. Such family factors represent key targets for early intervention work aiming to prevent children from becoming chronically victimized.

## S2.2.4

### School burnout and engagement: Antecedents and consequences

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#### **Abstract**

*Objective:* This study has three objectives: To examine 1. the role of study demands and resources for school burnout and engagement; 2. the cross-lagged paths between school burnout and engagement; and 3. the role of burnout and engagement to later well- and ill-being in the context of school transitions. According to the demands-resources model high study demands would be related to study burnout, while the availability of study resources would be related to study engagement. Study burnout, in turn, is assumed to be related to later ill-health, such as depressive symptoms, while engagement would be related to later commitment and well-being.

*Methods:* The study draws on the FinEdu Longitudinal Study, following 700 students from their last year in comprehensive school with further three annual assessments after the transition to upper secondary education. Study demands and resources as well as personal resources were examined in comprehensive school, while school burnout and engagement were examined twice during secondary education. Finally, depressive symptoms, life satisfaction and later educational tracts were examined two years later.

*Results:* The findings suggest that study demands were related to students later school burnout, while study as well as personal resources were positively related to later school engagement and negatively to burnout. Moreover, both school burnout and engagement showed stability and school burnout predicted negatively school engagement one year later. Finally, school burnout predicted later depressive symptoms, while engagement predicted later life satisfaction.

*Conclusion:* The demand-resources model has been used in the work context but based on our results it seems to fit well also to the school context.

## **S2.3.0**

### **Symposium: Mental health over the life course in the Northern Finland Birth Cohort (NFBC)**

**Alina Rodriguez<sup>1,2,3\*</sup>, Marjo-Riitta Järvelin<sup>2,4,5</sup>, Anja Taanila<sup>5,6</sup> and Irma Moilanen<sup>7</sup>**

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#### **Abstract**

This symposium will introduce the audience to a series of studies on mental health within the framework of the Northern Finland Birth Cohorts, NFBC launched in 1966 and in 1986. A unique design feature is that data were gathered during early pregnancy and nearly 20,000 individuals in total have been followed from birth to adulthood. Data are available from a variety of sources including objective clinical assessments (including biological samples), official records, as well as participant reports. These prospective data are essential to understand the developmental course of mental health across the lifespan.

The first presentation provides an historical overview of the purpose of the cohorts and describes the design and methods of the studies. Some recent findings from various studies including schizophrenia will be highlighted.

The second presentation describes a series of studies examining exposure to early life risk and the development of poor mental health outcomes in children and adolescents.

Developmental difficulties for children showing early signs of language impairments are the focus of the third presentation.

The last presentation examines Attention Deficit Hyperactivity Disorder (ADHD) across the lifespan and highlights factors related to continuity and discontinuity in fulfillment of diagnostic criteria across development.

The symposium concludes by integrating findings and discussing the potential to identify early life risks that can be treated and ultimately be used to prevent poor mental health outcomes in childhood and adulthood.

## S2.3.1

### Overview of the Northern Finland Birth Cohort (NFBC) programme with emphasis on mental health issues

**Marjo-Riitta Järvelin<sup>1,2,3\*</sup>, Anneli Pouta<sup>4</sup>, Anna-Liisa Hartikainen<sup>5</sup>, Anja Taanila<sup>3</sup>, Alina Rodriguez<sup>1,6,7</sup>, Matti Isohanni<sup>5</sup> and Juha Veijola<sup>5</sup>**

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#### **Abstract**

*Objective:* The NFBC programme is the product of a project initiated in the 1960s to examine risk factors for pre-term birth and intrauterine growth retardation, and the consequences of these early adverse outcomes on subsequent morbidity, including mental health disabilities and mortality.

*Methods:* The two cohorts of women and newborns were collected at a 20-year interval from the provinces of Oulu and Lapland. The younger cohort set with an expected date of birth between 1.7.1985 and 30.6.1986 (9362 mothers, 9479 children, NFBC1986), and the older with an expected date of birth in 1966 (12068 mothers, 12231 children, NFBC1966). Pregnancies were followed prospectively from the first antenatal contact (10-16th wk). The children were followed-up at the ages of 6-12 m, 7-8y (NFBC 1986), 14-16y (NFBC 1966, 1986) and at the age of 31y (NFBC 1966). At these time points, a wide range of phenotypic, lifestyle (smoking, drinking, drugs), demographic and other data were gathered using questionnaires and clinical examination. This includes an extensive prospective growth data from birth until adult age, mental health assessments (e.g. sub-studies on ADHD, schizophrenia), blood pressure, pulse, physical fitness measures, anthropometry, skin prick tests, lung function, and blood samples (DNA/genome wide genotypes, metabonomic and other metabolic measures of function). Subjects with mental/behavioural disorders and their controls have gone through brain MRI scans. Linkage to national registries (hospitalizations, deaths, education, medication, pensions) provide extensive resource.

*Results:* Many of the avoidable prenatal risk factors such as smoking and drinking have adverse effects on child's later health and behaviour. In the NFBC 1966, we reported a strong association between poor intrauterine growth and schizophrenia and an interaction of genetic risk for schizophrenia with an environmental risk. Maternal depression during pregnancy significantly increases the risk of schizophrenia in offspring if one of the parents has a psychotic disorder.

*Conclusions:* NFBCs provide extensive dataset for intermediate and disease phenotypes with established relevance to psychiatric and many other chronic diseases, and provide possibly the world's largest data on early pregnancy measures with follow up until age 45y, with in-depth measures of metabolic and mental health/disabilities, and temperament.

## S2.3.2

### The prenatal environment in relation to mental health in childhood and adolescence

**Alina Rodriguez<sup>1,2,3\*</sup>, Marjo-Riitta Järvelin<sup>2,4,5</sup>, Aini Bloigu<sup>6</sup>, Tuija Mannisto<sup>7</sup>, Marika Kaakinen<sup>5</sup> and Irma Moilanen<sup>8</sup>**

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#### Abstract

*Objective:* This presentation reports on a series of studies that investigate whether mental health disturbances in children can be programmed in utero via exposure to maternal obesity or impaired growth in the child. We were first to report an association between exposure to maternal overweight/obesity and increased risk of inattention and hyperactivity in children within the framework of the Nordic Network on Attention Deficit Hyperactivity Disorder, ADHD. In light of the obesity epidemic, the public health significance of these findings is huge if the association is causal. Therefore, ongoing work is conducted to identify possible mechanisms underlying the association. Thyroid hormone plays a key role in growth and weight regulation as well as with other metabolic functions. We test whether maternal plasma thyroid dysfunction, which is often associated with maternal obesity, accounts for the association with mental health and cognitive impairments in children. We also examine whether altered growth pattern at birth, childhood, and adolescence is associated with inattention and hyperactivity.

*Methods:* Prospective data come from the Northern Finland Birth Cohort 1986 (NFBC 1986). Data on maternal body mass index (BMI) were extracted from the prenatal medical record and maternal serum was collected during the first-trimester of pregnancy and frozen. We analyzed thyroid hormones [TSH, free T(3) and T(4), (fT3, fT4)] and antibodies [thyroid-peroxidase antibody (TPO-Ab) and thyroglobulin antibody (TG-Ab)]. Birth size was recorded in the medical record and child growth was assessed at 7 and 16 years.

*Results:* Overall, the results showed significant associations between maternal thyroid dysfunction in pregnancy and later behavioural and cognitive impairments in the child. However, the amount of explained variance was not large and did not fully account for the association between maternal obesity and child behaviour problems. Growth was also found to be impaired in children and adolescents who had elevated inattention/hyperactivity symptoms.

*Conclusion:* These studies show that maternal thyroid dysfunction may play a role in child mental health and cognitive impairments and that altered growth is seen in children and adolescents who have elevated inattention and hyperactivity symptoms. Thus these are biologically plausible pathways that can be targeted for surveillance and treatment within health care to improve child mental health.

### S2.3.3

## Behavioural and psychiatric problems in children and adolescents with speech and language disabilities: A follow-up study of the Northern Finland Birth Cohort 1986

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#### Abstract

*Objectives:* There are not very many studies where speech and language disabilities (SLDs) have been studied longitudinally in connection with behavioural and psychiatric problems. In the Northern Finland Birth Cohort 1986 (N=9432) we wanted to find out whether there is an association between SLDs at the age of 8 and behavioural and psychiatric problems at the age of 16. In addition, we studied some potential risk factors related to SLDs, such as socio-economic status, family structure and parents' education.

*Methods:* At the age of 8 (n=9357) parents assessed children's speech and language skills and teachers their behaviour using Rutter-Scale. At the age of 16 (n=9340) parents assessed adolescents' behavioural problems (ADHD symptoms) using Swan-scale and adolescents themselves their behavioural and psychiatric problems by using Youth Self Report (YSR).

*Results:* At the age of 8, 13.1% of the children with SLDs (speech production 13.6%, reception 6% and both 2%) had behavioural and psychiatric problems compared to those without (8.9%)(p=.001). According to parents' and adolescents' assessments, having SLDs at the age of 8 predicted behavioural and psychiatric problems at the age of 16. Boys who had a lot of problems in speech production and reception lived more often in divorced or reconstructed family. Additionally, families many times belonged to the second social class. For the girls the family structure and social status did not affect statistically significantly SLDs.

*Conclusion:* Our study showed that SLDs at 8 years are associated with behavioural and psychiatric problems at 16 years. Further research is necessary to find out the effects of the SLDs at early school years on behaviour in adolescence.



## S2.3.4

### Continuation of ADHD-symptoms from childhood to young adulthood

**Irma Moilanen<sup>1\*</sup>, Päivi Lindholm<sup>1</sup>, Hanna Ebeling<sup>1</sup>, Anja Taanila<sup>2</sup>, Tuula Hurtig<sup>1,2</sup>, Juha Veijola<sup>3</sup> and Marjo-Riitta Järvelin<sup>2,4,5</sup>**

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#### **Abstract**

*Objective:* To study, if childhood hyperactivity-impulsivity (HI) and inattention (IA) symptoms continue up to adulthood.

*Methods:* In the prospective Northern Finland Birth Cohort 1986, approved by the Ethical Committee of the Northern Ostrobothnia Hospital District, the children's ADHD symptoms were evaluated at three ages: childhood, adolescence and young adulthood. At the child's age of 8, teachers of 8525 children filled in the Child Behavioural Questionnaire by Rutter, including two items on HI and one on IA. At the age of 15, parents provided information on HI and IA symptoms in 6985 adolescents using Strengths and Weaknesses of ADHD symptoms and Normal Behaviors questionnaire (SWAN), and the psychiatric diagnoses of 457 selected adolescents were defined with the Schedule for Affective Disorders and Schizophrenia for School-AGE Children, Present and Lifetime Version (Kiddie-SADS PL), including 9 items of HI and 9 on IA. At the age of 22 years, the young adults having diagnosed as ADHD in adolescence, were invited to the diagnostic interview on ADHD.

*Results:* When following the symptom profile of the 457 individuals having evaluated by teachers in childhood and participated Kiddie-SADS in adolescence, the HI scores decreased from childhood to adolescence, while IA scores showed a mild increase. When following the symptom profile of those 30 having participated both in adolescence and in young adulthood, both HI and IA symptoms were decreasing

*Conclusion:* HI symptoms are decreasing along with age from childhood to adulthood, while IA symptoms show a transient increase in adolescence, possibly because of adolescent turmoil.

## **S2.4.0**

### **Symposium: Health inequalities at older ages: the English Longitudinal Study of Ageing**

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#### **Abstract**

Baseline adult socioeconomic position (SEP) is inversely associated with incident type 2 diabetes and elevated depressive symptoms in the English Longitudinal Study of Ageing. Childhood SEP is also inversely associated with these outcomes but these associations are explained by elevated depressive symptoms, body mass index, health behaviours, comorbidities and physical limitations. Age modifies to some extent the association between SEP and elevated depressive symptoms with the effect of SEP on depressive symptoms being weaker and less clearly graded in older ages.

SEP is also associated with biomarkers such as CRP, fibrinogen, total cholesterol, waist circumference, body mass index, IGF-1 and DHEAS but the pattern of these associations is not always clear and in the same direction.

## S2.4.1

### Childhood and adult socioeconomic position and elevated depressive symptoms in the English Longitudinal Study of Ageing. Exploring the modifying effect of age

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#### Abstract

*Background:* It is well-known that socioeconomic position (SEP) is strongly related to depression. However, it is less clear whether this association persists in older ages and whether age modifies this association. Moreover, little research has focused on the exploration of the pathways of socioeconomic inequalities in depression in older ages.

*Methods:* We examined the longitudinal associations between childhood (paternal occupation at 14 years of age) and adult SEP (tertiles of total net non-pension household wealth, categories of educational attainment, occupational class (NS-SEC) and subjective social status) and elevated depressive symptoms (dichotomized score of the summary score of the eight-item Centre for Epidemiological Studies-Depression scale) using 2-year lagged Generalized Estimating Equations (GEE) models. The sample comprised 6,153 men and women aged 50 and over from the English Longitudinal Study of Ageing.

*Results:* We found a strong inverse graded association between baseline SEP and depressive symptoms that was not explained by the following time-varying covariates: comorbidities, physical limitations, cognitive functioning, health behaviours, pain, sense of control and social support and baseline BMI and waist. Additional analyses showed that neither lipids nor inflammatory markers explained the association. The only exception was the association between childhood SEP and depressive symptoms that was explained by time-varying comorbidities, physical limitations and health behaviours. Age was a significant modifier of the associations between some of the SEP markers (i.e. wealth, subjective social status and childhood SEP) and depressive symptoms. The effect of SES on depressive symptoms became weaker and less clearly graded with increasing age but overall remained significant.

*Conclusions:* Baseline adult SEP was inversely associated with the risk of elevated depressive symptoms and no covariate fully explained this association. Childhood SEP was also inversely associated with the risk of elevated depressive symptoms through comorbidities, physical limitations and health behaviours. The association between SEP and depressive symptoms became weaker with increasing age but overall remained significant.

## S2.4.2

### **Social inequalities in biomarkers: findings from the English Longitudinal Study of Ageing (ELSA)**

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#### **Abstract**

*Objectives:* Although social inequalities in health are widely recognized and reducing health disparities is an important public health priority, the process by which the social environment becomes translated into physiological and psychological processes that influence health remains unclear. The aim of this longitudinal study is to compare changes over time and the relationship between socioeconomic position (SEP) indicators and different biomarkers in a nationally representative sample of older adults in England.

*Methods:* The study population consisted of participants aged 50 and older who took part in the 2004 and 2008 waves of the English Longitudinal Study of Ageing (ELSA), a prospective national cohort study of people aged 50 years and over. The analysis focuses on biomarkers associated with adverse outcomes as well as those associated with improved health and well-being. Risk factors considered here include indicators of cardiovascular disease (lipid profile, fibrinogen, C-reactive protein) and anthropometric measures such as body mass index and waist circumference. Protective factors included include high density lipoprotein (HDL) cholesterol, insulin-like growth factor (IGF-1) and dihydroepiandrosterone sulfate (DHEAS). The changes in these markers over time were modelled using three measures of socioeconomic status: total (non-pension) wealth, subjective social status and childhood SEP. Analyses were adjusted for confounding variables (age, sex and marital status).

*Results:* The increase in levels of both inflammatory markers (CRP and Fibrinogen) was larger among the wealthier groups. High total cholesterol levels have decreased from Wave 2 to Wave 4 in both men and women and this decrease is larger among the poorest. Prevalence of both overweight and obese categories and raised waist circumference decreases with increases in wealth. A socioeconomic gradient is evident for both IGF-1 and DHEAS markers, with increases in levels with increased wealth.

*Conclusion:* The present findings suggest an association between biomarkers and socioeconomic position. However, the direction of the social gradient observed varied for the different biomarkers highlighting the need for further investigation.

## S2.4.3

### **Childhood and adult socioeconomic position and incidence of type 2 diabetes in a national sample of middle-aged and older adults. The English Longitudinal Study of Ageing**

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#### **Abstract**

*Objective:* Currently, there is limited evidence for the association between socioeconomic position (SEP) and incident type 2 diabetes at older ages. We examined whether childhood SEP assessed by paternal occupational class and adult SEP assessed by total net non-pension household wealth (categorized by tertiles), educational attainment, occupational class (NS-SEC) and subjective social status were related to incident type 2 diabetes over 45.3 months of follow-up.

*Methods:* The sample consisted of 7,363 men and women aged 50 and over from the English Longitudinal Study of Ageing. The associations between childhood and adult SEP and incident type 2 diabetes were assessed by Cox proportional hazard regression models.

*Results:* The inverse graded association between wealth and incident diabetes remained significant after adjustment for sociodemographic, clinical, anthropometric and behavioural characteristics and all SEP markers but subjective social status. The inclusion of subjective social status in the fully adjusted model made the association marginally non-significant. Educational attainment was related to diabetes risk in women but not in men, but this association was explained by elevated depressive symptoms, unhealthy behaviours and BMI. Small employers, self-employed workers and people in intermediate occupations such as intermediate level administrative, clerical or technical professions had a lower risk of developing diabetes compared to higher level managers and professionals in the fully adjusted model. The difference in diabetes risk between higher level managers and professionals and people in lower supervisory and routine professions was not significant. The inverse graded association between subjective social status and risk of developing diabetes became marginally non-significant only when wealth was included in the fully adjusted model. Middle-aged and older people with lower childhood SEP had higher risk of developing diabetes but this association was explained by elevated depressive symptoms, health behaviours and BMI in adulthood.

*Conclusions:* Markers of contemporary SEP such as wealth and subjective social status were inversely associated with the risk of developing type 2 diabetes in the fully adjusted model. Childhood SEP was associated with the risk of developing diabetes through depression, health behaviours and BMI.

## S2.4.4

### Social mobility after retirement – how can it be measured?

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#### **Abstract**

*Objective:* Most studies about social mobility have referred to changes from inter-generational changes in social class or status or to changes during working ages. However, we may now live up to 40 years after stopping paid work. Life expectancy for those aged 65 in 2006 is projected to be 20.6 years for males and 23.1 years for females. Currently we lack an accepted measure of social mobility after retirement so lack the means to assess whether social mobility can continue to influence health and wellbeing in later life. The aim of this study is to explore potential measures of social mobility in older age.

*Methods:* to use the English Longitudinal Study of Ageing (ELSA) to explore the degree of change over time in various socioeconomic factors among people aged 50 and over.

*Results:* Some preliminary analysis was undertaken using the first and third waves of ELSA, which took place 4 years apart. Of the usual measures of socioeconomic position some vary little over time among older people (education, occupational classification, housing tenure), while income varies considerably making it somewhat unstable (over half had changed income quintile after a four year period). For wealth one-third of those not in paid work had changed quintile after four years but 40% of women in paid work and 29% of men in paid work.

*Conclusions:* the standard measures all have problems. Wealth is most promising but difficult to measure so an indicator involving the type of resources available to people is to be tried using four waves of ELSA spanning a six year period between first and last interview.

## **S3.1.0**

### **Symposium: Long-lasting influences on adult health**

**David Blane<sup>1,2\*</sup>, Meena Kumari<sup>1,3</sup>, Elizabeth Webb<sup>1,2</sup> and Morten Wahrendorf<sup>1,4</sup>**

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#### **Abstract**

The symposium examines long-term influences on different domains of adult health including physiology (cortisol), anthropometry (height) and quality of life (CASP). The three presentations are based on longitudinal data from, respectively: Whitehall II Study; English Longitudinal Study of Ageing (ELSA); Survey of Health, Ageing and Retirement in Europe (SHARE) and National Child Development Study (NCDS). The symposium demonstrates consistent results across these different studies and dimensions of health.

### S3.1.1

## Maternal separation in childhood and cortisol secretion in mid-life: findings from the Whitehall II study

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#### Abstract

*Objectives:* Animal studies suggest that maternal separation is associated with lifelong alterations in the hypothalamic-pituitary-adrenal (HPA) axis through effects that occur in a critical period following birth. Evidence of an association of cortisol secretion, a product of the HPA axis, with maternal separation in man is equivocal. Here we examine whether maternal separation in childhood is associated with diurnal cortisol secretion, measured in mid-life..

*Methods:* Cortisol was assessed from six saliva samples over the course of a normal weekday collected at waking, waking+30mins, +2.5hours, +8hours, +12hours and bedtime (n=3519) . Two aspects of cortisol secretion were calculated; the cortisol awakening response (CAR) and the diurnal slope in cortisol secretion. Participants were asked about separation from mother for one year or more in childhood and age and reason for the separation. Co-variables, collected in adulthood included social position, emotional and material deprivation in childhood, depressive symptoms and three dimensions of perceived parenting: warmth; strictness; expectations.

*Results:* In this cohort of participants in early old age (mean age 61), 12% reported separation from mother in childhood. Compared to those that did not report separation in childhood, maternal separation was associated with flatter slopes (a shallower decline across the day) in cortisol secretion (decline of 0.1292 nmol/l/h in those not reporting separation vs. 0.1262 nmol/l/h in those reporting separation, p=0.01) and a larger CAR (7.19 nmol/l vs 8.36 nmol/l, p=0.047). The age at which separation occurred was not significantly associated with cortisol secretion. Cortisol secretion was not associated with perceived parenting style but slope in cortisol secretion was flatter in those reporting emotional deprivation in childhood (p=0.048). The association of slope in cortisol secretion with maternal separation remained statistically independent of all co-variables examined (a decline of 0.1295 nmol/l/h in those not reporting separation vs. 0.1263 nmol/l/h in those reporting separation, p=0.02 following adjustment for all covariates). Association between the CAR and childhood maternal separation was partially mediated by childhood psychosocial and material factors and adult smoking status (7.18 nmol/l vs. 8.26 nmol/l, p=0.117).

*Conclusions:* Our findings suggest that maternal separation in childhood is associated with alterations in cortisol secretion in early old age.



## **S3.1.2**

### **Adult height as an indicator of childhood socio-economic circumstances**

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#### **Abstract**

*Objectives:* When cohorts are established to study middle and older aged people, contemporary data on early life socioeconomic circumstances (SEC) is usually unavailable, and retrospectively collected data is subject to recall bias. One solution is to use adult height as a proxy indicator for early life SEC, as a more advantaged childhood is associated with greater adult height. This has been shown to be a reliable method, with strong relationships between height and its components and measures of early life SEC, however concerns remain. The variation in adult height explained by differences in childhood SEC may be too small to justify the use of height as a proxy measure. In addition, with ageing comes height loss, beginning around the age of 40, after which age measures of adult height do not represent maximum achieved height. Methods for estimating height lost, taking into account age and sex as predictors of height loss, have been developed. However, loss of height may be influenced by other factors, such as life course SEC. If more disadvantaged children go on to experience greater loss of height in older age, the use of an adult height measure taken in middle or older age as a proxy for childhood SEC will magnify the apparent influence of a disadvantaged childhood on adult health outcomes. This paper aims to establish whether there is an influence of life course socioeconomic circumstances on height loss at older ages.

*Methods:* The paper will use height measurements from waves 0, 2 and 4 of the English Longitudinal Study of Ageing (ELSA), and life course socioeconomic data from the ELSA Life History data. ELSA is a cohort of non-institutionalised adults aged 50 years or older and living in England in 2002. Latent growth curves will be used to investigate how height changes over time. Changes in height will be predicted using age, gender and measures of life course SEC.

*Results and conclusions:* Results and conclusions are not available at this stage. Full analyses will be performed upon release of the ELSA wave 4 Nurse Data.

### **S3.1.3**

## **Childhood influences on quality of life at age 50 years: evidence from National Child Development Study (1958 British Birth Cohort Study)**

**David Blane<sup>1,2\*</sup>, Elizabeth Webb<sup>1,2</sup>, Morten Wahrendorf<sup>1,3</sup> and Gopalakrishnan Netuveli<sup>1,2</sup>**

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### **Abstract**

*Objectives:* The increase in life expectancy at middle age prompts the question whether greater quantity is accompanied by quality. Health at middle age is influenced by childhood factors independently of adult circumstances; is the same true of quality of life? Previous investigations of this question suggest that quality of life at older ages is influenced primarily by current circumstances, with any effect of early life acting indirectly.

*Methods:* These results came from retrospective data on a relatively small sample of the Boyd Orr Study, using a measure of positive quality of life at older ages (CASP; acronym Control, Autonomy, Self-realisation, Pleasure). The recent age 50 year sweep of the National Child Development Study included the CASP measure, allowing a test of replication in prospective data from a large sample.

*Results:* CASP scores at age 50 years in NCDS were found to be graded by accumulated deprivation during childhood & adolescence; and by childhood psycho-social disruption. Path analysis showed these associations were indirect via, respectively, adult material and psycho-social circumstances, with no direct effects.

*Conclusions:* Quality of life differs from health. The policy implications are encouraging. Access to good quality of life at older ages does not depend upon events from early life.

## **S3.2.0**

### **Symposium: The epidemiology of neurogenetic diseases in the Cypriot population**

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#### **Abstract**

*Objective:* To present initial clinical, genetic and epidemiological studies on neurogenetic diseases in the Cypriot population and to initiate regular follow up and reporting on these diseases over the next decades.

*Methods:* The Cyprus Institute of Neurology and Genetics (CING) has been offering clinical and genetic services to the Cypriot population for the past 20 years. It is the main neurology and genetics centre on the island and the majority of patients with neurogenetic diseases are referred to CING both for clinical evaluation and follow up as well as for molecular genetic diagnosis. Respective neurogenetic disease patients were identified from the clinical and neurogenetic data bases of CING. Genetic studies were performed after written informed consent of the subjects. Demographic, clinical and genetic data were reviewed for the purposes of the epidemiological studies.

*Results:* The prevalences of familial amyloidotic polyneuropathy, Huntington disease, Charcot-Marie-Tooth disease and hereditary ataxias in the Cypriot population have been estimated. Genetic characteristics of the Cypriot patients with the above neurogenetic diseases have been documented. Clusters of families have been identified that originate from specific geographic parts of the island, such as Friedreich ataxia in the Paphos district, familial amyloidotic polyneuropathy in the Kyrenia and Limassol districts and Huntington disease in the Famagusta district.

*Conclusion:* Epidemiological data on neurogenetic diseases in the Cypriot population have recently emerged through studies of the CING. The Cypriot population being relatively small and isolated provides a good manageable population for such studies. We would like to initiate reporting of long term observations on this field in the Cypriot population for the next decades.

## **S3.2.1**

### **Epidemiology of Huntington disease in Cyprus**

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#### **Abstract**

*Objective:* Huntington disease (HD) is an autosomal dominant neurodegenerative disease of midlife onset. It is caused by a CAG repeat expansion in exon 1 of the HTT gene on chromosome 4p16.3. It is characterized by motor impairment with either excessive movements such as chorea and rarely rigidity, cognitive deterioration and behavioral disturbances. The number of CAG repeats affects age of onset and probably disease severity. Most European populations show relatively high prevalence of 4-8 per 100,000. Our aim is to provide extended epidemiological findings about HD in Cyprus.

*Methods:* The clinical and neurogenetic databases of the Cyprus Institute of Neurology and Genetics were used to identify individuals with CAG repeat number >36, symptomatic and presymptomatic. In all cases demographic, clinical and family data were reviewed.

*Results:* A total number of 32 living symptomatic and asymptomatic HD patients were identified giving a prevalence of HD in Cyprus in 2010 of proximally 4 per 100,000. The total number of individuals with HD diagnosed in Cyprus by genetic testing since 1994 is 48 (21 females). Forty-seven patients were Greek Cypriot and one was Danish. Pathological alleles ranged from 40 to 60 CAG repeats with one juvenile case of 120. Normal alleles ranged from 15 to 25. Two patients had no family history (4%). All patients with family history belong to 14 families originating from the southern Famagusta area. Mean age of onset (AO) was 40 years old. In 6 cases (12,5%) the AO was >55 years old and there was one juvenile case with AO 2 years old. Initial symptomatology was involuntary movements in 45,8% and psychiatric abnormalities in about 27%. In 3 cases the main movement disorder was rigidity (rigid variant of HD). Duration of the disease from initial symptomatology to death averaged at 11,6 years.

*Conclusion:* The prevalence of HD in Cyprus and the clinical and genetic findings are comparable with previous reported data in other European countries. The genetic cluster of HD in the southern Famagusta district indicates a possible founder effect. We will report epidemiological findings of HD in the Cypriot population every five years.

### S3.2.2

## Epidemiological, clinical and genetic study of familial amyloidotic polyneuropathy in Cyprus and the long term effects of liver transplantation

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### Abstract

**Objective:** Familial amyloidotic polyneuropathy (FAP) is a lethal autosomal dominant sensorimotor and autonomic neuropathy due to deposition of amyloid fibrils, made up of aberrant transthyretin (TTR) molecules. In FAP TTRVal30Met the mutated TTR has methionine substituted for valine at position 30 which causes polymerization into  $\beta$ -pleated sheets. A previous report suggested that there may be a high frequency of FAP TTRVal30Met in Cyprus. The aims of the current study were to formally study the epidemiological, clinical and genetic aspects of FAP TTRVal30Met on the island and create a database to assess the effects of liver transplantation on disease survival.

**Methods:** The clinical and neurogenetic databases were used to identify probands with FAP TTRVal30Met and detailed family trees were constructed. Transthyretin was completely sequenced in patients and potential carriers. The phenomena of penetrance and anticipation were estimated.

**Results:** Thirty-six patients carrying the TTRVal30Met mutation (one homozygote) from 22 families were identified. On 1 December 2003 the prevalence of FAP was 3.72/100,000 while the incidence is estimated to be 0.69/100,000 per year. The phenotype observed was characteristic for a length dependent sensorimotor and autonomic neuropathy with neuropathic pain. Mean age of onset was 46 years. Penetrance is estimated to be 28% and positive anticipation in the age of onset is found. Out of the original cohort of 36 patients 25 had liver transplantation and will be followed up to establish the natural history of transplanted TTRVal30Met patients.

**Conclusion:** FAP TTRVal30Met is relatively prevalent in Cyprus which may be considered as another endemic focus of the disease in Europe. The mean age of onset and penetrance is different from the Portuguese and Swedish populations. Understanding the biological factors that determine these differences could potentially lead to therapeutic advances. Further data on post transplanted patients will be provided with the passage of time.

### S3.2.3

## Epidemiology of Charcot-Marie-Tooth disease in Cyprus

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### Abstract

*Objective:* Charcot-Marie-Tooth disease (CMT) is the most common inherited neuropathy and is classified into two main subgroups: demyelinating and axonal type. Further subdivisions within these two main categories exist and intermediate forms have also been described. Inheritance can be autosomal dominant, recessive or X-linked. CMT has thus far been associated with 25 causative genes and there remain many more genes to be identified. The aim of this study is to characterise and long term follow-up CMT in Cyprus at the clinical, genetic and epidemiology levels.

*Methods:* Patients were identified from the clinical and neurogenetic data bases of the Cyprus Institute of Neurology and Genetics, the main neurology and genetics referral centre on the island. Thirty-three Cypriot families and eight sporadic patients were ascertained. Eighteen families and one sporadic patient had demyelinating, eleven families and seven sporadic patients had axonal and four families had intermediate CMT forms. Patients with demyelinating CMT were initially investigated for the PMP22 duplication. Patients and families negative for the PMP22 duplication were further investigated according to an existing protocol and prioritised based on the specific clinical and neurophysiological characteristics. PCR amplification and automated sequence analysis of exons of candidate genes were performed. The prevalence of CMT was estimated based on the most recent population census of 1st October 2001.

*Results:* The prevalence of CMT in Cyprus on 15th January 2009 is estimated to be 16/100,000. Thirty-three families and eight sporadic patients were ascertained. CMT was demyelinating in 52%, axonal in 33% and intermediate in 15% of patients. Thirteen families had the PMP22 duplication, three families had the PMP22 S22F mutation, four families had GJB1/Cx32 mutations, two families had different MPZ mutations, one of them novel, and two families had different MFN2 mutations. Nine families and eight sporadic patients were excluded from the common CMT genes.

*Conclusion:* The most frequent CMT mutation worldwide, the PMP22 duplication, is also the most frequent CMT mutation in the Cypriot population. Five out of the eight other mutations are novel, not reported in other populations. We will report CMT characteristics in the Cypriot population every five years.

### S3.2.4

## Genetic epidemiology of hereditary ataxias in the Cypriot population

**Christina Votsi, Pantelitsa Koutsou, Paschalis Nicolaou, Anthi Georghiou, Marios Pantzaris, Kleopas A. Kleopa, Savvas Papacostas, Theodoros Kyriakides, Kyproula Christodoulou and Eleni Zamba-Papanicolaou\***

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#### **Abstract**

*Objective:* To perform a genetic epidemiology study of hereditary ataxias in the Cypriot population.

*Methods:* Patients with hereditary ataxias are referred to the Cyprus Institute of Neurology and Genetics for more than 20 years now. Patients are clinically evaluated and possible acquired ataxia cases are excluded following the paraclinical investigation. Investigation of the possible hereditary ataxic patients/families continues with more specific biochemical examinations with vitamin E levels, a-fetoprotein levels, hexosaminidase a&b, in order to better classify them according to the phenotype but also biochemical findings. Family pedigrees are drawn and blood is collected from all consenting affected and non-affected family members. Molecular genetic analysis is carried out according to the clinical classification. Genetic investigation includes FRDA frataxin GAA triplet repeat test, SCA1, SCA2, SCA3, SCA6, SCA7, SCA12 CAG triplet repeat test, SCA8 CTA/CTG repeat test, SCA10 ATTCT repeat test, SCA17 CAG/CAA, DRPLA CAG triplet repeat test and APTX gene sequencing test. Further studies include linkage investigation at the known genes and loci of recessive ataxias (SETX, POLG, TDP1, SACS, SYNE1, C10orf2, SCAR7).

*Results:* The most frequent mutation identified in our population thus far is the GAA repeat expansion in intron 1 of the frataxin gene. Twenty-seven Cypriot Friedreich ataxia (FRDA) patients have been ascertained until today. A SETX novel mutation has been identified in a single Cypriot family with 5 affected individuals. The genetic diagnosis is still pending for twelve Cypriot autosomal recessive (AR) families, one autosomal dominant family and 53 sporadic hereditary ataxia patients.

*Conclusion:* The most frequent hereditary ataxia in the Cypriot population is Friedreich ataxia with increased frequency of carriers in the Paphos district. The vast majority of familial ataxias in our population still remain unknown. None of the sporadic ataxia patients is carrying a mutation in the most frequent so far identified genes. In other populations only 50% of the sporadic patients remains without a genetic diagnosis. A novel mutation in the SETX gene has been identified in a single AR family. We will report genetic epidemiology findings of hereditary ataxias in the Cypriot population every five years.

### **S3.3.0**

## **Symposium: Methodological approaches to analysing life course trajectories of inequalities and health**

**Jenny Head<sup>1,2\*</sup>, Paola Zaninotto<sup>2</sup>, Noriko Cable<sup>1,2</sup> and Tarani Chandola<sup>1,3</sup>**

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### **Abstract**

This symposium brings together four papers illustrating different methodological approaches to the analysis of life course data.

Using data from the English Longitudinal Study of Ageing, the first paper uses latent growth curve models to study age-related trajectories of physical functioning. The paper shows how the use of ageing-vector graphs can reveal both changes in physical functioning as people age and trends in the sum of changes up to a given age.

The second paper based on data from two British birth cohort studies uses path analysis to show how changing social contexts lead to differences in the paths through which socioeconomic position influences educational attainment.

Using data from the Whitehall II study, the third paper describes trajectories of health and well-being before and after retirement. This paper demonstrates how piecewise growth curve models can be used to disentangle the influence of critical periods such as retirement from general ageing effects on health trajectories.

The final paper focuses on the important problem of attrition in longitudinal studies. Using selection models to perform sensitivity analyses, this paper explores whether or not selective attrition may lead to underestimation of social inequalities in health decline.



### **S3.3.1**

## **Age-trajectories of physical functioning among older adults: findings from ELSA**

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### **Abstract**

*Objective:* to explore age-trajectories of physical functioning and influences on them in a 6-year period among older adults living in England.

*Methods:* Data come from the English Longitudinal Study of Ageing (ELSA), a large panel study where non-institutionalised individuals aged 50 and over are followed every two years. Physical functioning was assessed in participants aged 60 and over using a gait speed test, which involved timing how long it took to walk a distance of 8 feet.

Latent Growth Curve (LGC) model was used to describe both the average change in populations and individual differences in trajectories of change. Latent factors representing intercept (initial status) and slope (rate of change) components are extracted from three observations across time (Wave 1 (2002-03), Wave 2 (2004-05), Wave 3 (2006-07) and Wave 4 (2008-2009), for physical functioning. Predictors of individual change of physical functioning were examined by regressing the intercept and conditional slope on several predictors such as health, socioeconomic circumstances; demographic characteristics and social network. The physical functioning trajectories for each age group over the follow-up period are expressed in graphical form by a series of vectors, namely ageing-vector graphs. Ageing-vector graphs reveal both the changes as people age and trends in the sum of changes up to a given age.

*Results:* There are several factors influencing the trajectories of physical functioning at older ages. People with intermediate and minimal conditions have low levels of physical functioning.

*Conclusion:* People with optimal and intermediate conditions reach critical level of physical functioning after the age of 90. A centenarian starting with optimal conditions can have higher physical function than someone aged 70 with intermediate conditions.

### **S3.3.2**

## **Exploring pathways leading to social inequality in educational qualification attainment: a comparison of two British Birth Cohort Studies**

**Noriko Cable<sup>1,2\*</sup>, Anne McMunn<sup>1,2</sup>, Mel Bartley<sup>1,2</sup> and Yvonne Kelly<sup>1,2</sup>**

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### **Abstract**

*Objectives:* To examine if educational qualification was determined by school absences and overcrowding, if school absences are influenced by childhood common illness due to overcrowding, if childhood common illness and overcrowding are socially determined and to assess consistency in the model between two cohort studies which are conducted 12 years apart.

*Methods:* We used two British Cohort studies, the National Child Development Study (NCDS, born in 1958) and the 1970 British Cohort Study (BCS70, born in 1970).

The outcome variable is educational qualification based on exam scores obtained at age 16. Father's social position at birth is treated as an exogenous variable in this study. We also included school absences obtained at age 16, incidence of medically treated throat infection (BCS70) or throat and or ear infection (NCDS) and overcrowding collected at middle childhood and at age 16 in the model.

Using path analysis, pathways originating from father's social position at birth to educational qualification through overcrowding, medically treated throat or ear infection, and school absences were examined. All effects are adjusted for the effects from gender, maternal smoking at birth, and early childhood factors such as intelligence, maternal reading, and psychosocial adjustment. All coefficients were calculated using the full-information maximum likelihood approach, based on 12696 cases for the NCDS and 10589 cases for the BCS70.

*Results:* In both cohort studies, educational qualification attainment was determined by school absences and overcrowding at age 16. The pathway from overcrowding to throat or ear infection to school absences was only supported at age 16 in the NCDS. The pathway from father's social position at birth to educational qualification at age 16 is only supported through overcrowding at two time points.

*Conclusion:* In summary, social context of a pathway leading to educational attainment has changed in its shape over time. The negative effect of socially determined overcrowding on educational attainment starts from middle childhood; however, the effect became weaker in the later born cohort.

### S3.3.3

## Piecewise growth curve models to describe trajectories of health and well-being before and after retirement

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### Abstract

*Objectives:* The period around early old age and retirement is associated with two contrasting health trajectories- improvement in mental well-being and declines in physical health. Recent research has shown that retirement changes the trajectory of self-reported health (a measure that combines mental and physical well-being), so that the general decline in self-reported health before retirement is reversed around retirement age. However, these trajectories before, during, and after retirement may differ for mental and physical health. Piecewise growth curve models are a useful method to disentangle these health trajectories around a critical period such as retirement. This paper fits different growth curve models to repeated measures of physical and mental well-being and discusses the substantive interpretation of these different models.

*Methods:* Data from the Whitehall II civil servants study (1985-2009) with repeated measures of the GHQ-30 and the physical and mental component scores of the SF-36 were analysed. Single-piece and piecewise repeated measures regression models with separate intercepts and slopes, before and after retirement age were estimated.

*Results:* Single-piece and the piecewise model that assumes that the initial status post-retirement is a function of the initial status and growth trajectory pre-retirement, suggest mental well-being increases with age, before and after retirement. However, the piecewise model that allows for different growth rates and initial states at pre- and post-retirement stages suggest a different picture of decreasing well-being with age pre- and post-retirement, but a big increase in well-being upon retirement. No such differences between the models were observed for physical health measures. Interactions between these trajectories and occupational class suggest widening health inequalities at retirement for both physical and mental health measures.

*Conclusion:* The generalised piecewise model that estimates separate intercepts and slopes in the pre- and post-retirement stage is the best fitting model for trajectories of mental well-being in early old age. Previous results that suggest improving mental well-being trajectories with age may be incorrect as they do not take into account changes in well-being upon retirement. Retirement is a critical period of the life course that widens inequalities in health.

### S3.3.4

## Estimating social inequalities in trajectories of health decline in studies with informative drop-out

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### Abstract

*Objective:* A major aim of longitudinal studies in ageing research is to identify risk factors for health decline. Such studies face problems of drop-out and missing data. The potential bias arising from selective attrition is particularly acute at older ages where attrition may be related to age-related change in health status and functioning. An additional source of health selection in longitudinal studies of ageing is mortality. Methods for missing data are now readily available in standard software packages for situations where the missing data mechanism can be assumed to be missing at random (MAR) but methods for dealing with missing data which are not missing at random (NMAR) are less easily implemented. Using selection models, we apply methods for dealing with informative (NMAR) drop-out to analysis of social inequalities in trajectories of health decline.

*Methods:* Using repeated measures of physical functioning from the Whitehall II longitudinal study of 10, 308 civil servants, latent growth curve modeling was used to investigate social inequalities in trajectories of health decline. Results were obtained under three different assumptions for the dropout mechanism a) dropout is completely at random b) dropout is random and depends on observed measurements preceding dropout c) dropout is informative and depends on unobserved current health status.

*Results:* There were social inequalities in rates of decline in physical functioning with people in lower socio-economic positions having steeper declines than those in higher socio-economic positions. Estimates of differences in rates of decline were more marked if dropout was allowed to depend on previous levels of physical functioning. Social inequalities in health decline were most marked in the third model that allowed dropout to depend on current health status (NMAR).

*Conclusion:* Results suggest that differences in rates of decline in physical health functioning among socioeconomic groups may be underestimated if drop-out is assumed to be independent of current health status.

## **S3.4.0**

### **Approaches to health services research and health policy evaluation using longitudinal, whole-population medical record linkage**

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#### **Abstract**

*Background:* Research using linked data is both time- and cost-effective compared with performing de-novo longitudinal studies, as it maximises the use of available data and makes it feasible to follow-up entire populations over extended periods. In addition, it enables retrospective studies to be conducted many years after exposure to an agent or policy, and minimises loss to follow-up and reliance on self-reported data.

The Western Australian Data Linkage System (WADLS) is unique in Australia and constitutes a powerful source for conducting longitudinal health outcomes research on a population of >2.3 million people. It combines seven core health administrative datasets, variously dating back over 30 years, linked to >30 external research and other government databases.

*Objective:* This session will overview the work performed using the WADLS and explore emerging opportunities for using linked routine databases for longitudinal health services and health policy research, as a means to encourage researchers and policy makers to exploit these burgeoning resources for research.

*Symposium overview:* This session will initially provide a summary of the current and historical research using WADLS linked data and the impacts on health care policy and practice. This will be followed by a series of presentations describing recent studies using novel approaches to analyze linked medical/health data to address areas of public health significance, including: i) Evaluating the impact of variations in primary health care contact on disease progression, hospital admission and mortality from 1990-2006 in Western Australian patients with chronic disease including diabetes mellitus, asthma, COPD and epilepsy, ii) Evaluating the impact of national policy changes to government-subsidized medicines from 2000-2009 on the utilisation of prescription drugs in Australia and subsequent impact on health outcomes, iii) Whether increasing physician fee-for-service payments can improve regularity of health service contact in elderly patients with chronic disease, iv) Quantifying long-term risk and type of sequelae attributable to exposure to enteric infections occurring in childhood and adolescence from 1985-2000.

*Outcomes:* A greater understanding of the most recent developments in medical record linkage, the potential for using linked routine medical/health data to generate world class health services research, and the possibilities for forming new research collaborations.

### S3.4.1

## Long-term health risks after infective gastroenteritis: a population-based cohort study

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### Abstract

*Objective:* Gastroenteritis presents a considerable burden on communities and health systems. In addition to the immediate health consequences long-term adverse sequelae have been associated with gastroenteritis; however, the risk and type of sequelae attributable to previous exposure to enteric infections have not been quantified. The objective of this study was to quantify the risk and type of sequelae attributable to previous exposure to enteric infections occurring in childhood and adolescence.

*Methods:* This was a population-based retrospective cohort study comprising all individuals born in Western Australia between 1 January 1985 and 31 December 2000 using linked administrative records from the Western Australian notifiable infectious diseases database, the Western Australian hospital morbidity data system and Western Australian death notifications. The risk of first-time hospitalisation for sequelae for those exposed to an enteric infection was modelled using Cox proportional regression analysis controlling for other health and socio-demographic factors.

*Results:* After adjusting for confounding there was a significant increase in the rate of first-time hospitalisation for sequelae in those exposed to enteric infections by 64% for any sequelae; 52% for intra-gastrointestinal sequelae and 63% for extra-gastrointestinal sequelae compared with non-exposed individuals. This equated to an increased attributable risk of 39% for all sequelae, 34% for intra-gastrointestinal and 39% for extra-gastrointestinal sequelae. Extra-gastrointestinal sequelae occurred predominantly in the first five years after exposure; in contrast, most intra-gastrointestinal sequelae had onset 10 years or more after exposure.

*Conclusions:* Infective gastroenteritis in childhood or adolescence increases the risk of first-time hospitalisation for intra-gastrointestinal and extra-gastrointestinal disease over the following two decades. This highlights the importance of developing appropriate risk management strategies for those exposed to enteric infections.

## S3.4.2

### Regular primary care decreases the likelihood of mortality and morbidity in older people with chronic disease

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#### Abstract

**Objectives:** To investigate the effect of regular general practitioner (GPs) visits on the likelihood of all-cause death and hospitalisation in older ( $\geq 65$  years) Western Australian (WA) epilepsy and chronic respiratory disease (CRD) patients.

**Methods:** We used routinely-collected, whole-population linked, administrative medical data to ascertain the study population, the exposure and outcomes. We identified 3537 older patients with epilepsy and 108,455 older patients with CRD during 1992-2006 in WA. Pattern of GP visits was determined in the first three years of observation, followed by up to 11.5 years of follow-up for outcome ascertainment. A GP visit regularity index was calculated and quartiles of GP visit regularity derived. Cox proportional hazard models, adjusted for multiple confounders, including GP visit frequency, were used to achieve the study aim.

**Results:** Epilepsy: Patients in the least regular GP visit quartile had the worst all-cause survival with the difference in survival curves between GP visit regularity quartiles being significant ( $p=0.0005$ ). Compared with patients in the least regular quartile, patients in the 2nd least regular (HR= 0.62, 95%CI=0.41-0.93), 2nd most regular (HR=0.37, 95%CI=0.22-0.62) and most regular (HR=0.42, 95%CI=0.23-0.78) quartiles had a significantly decreased likelihood of all-cause death. GP visit regularity did not appear to affect the likelihood of a repeat hospitalisation for epilepsy. CRD: Differences in survival curves and hospital avoidance pattern between the GP visit regularity quintiles were statistically significant ( $p=0.0279$  and  $p<0.0001$ , respectively). Higher GP visit regularity protected against first CRD hospitalisation compared with the least regular quintile (medium regular: HR=0.84, 95%CI=0.77-0.92; 2nd most regular: HR=0.74, 95%CI=0.67-0.82; most regular HR=0.77, 95%CI=0.68-0.86).

**Conclusions:** Higher regularity between GP visits, as distinct from higher GP visit frequency, reduces the likelihood of subsequent mortality and morbidity in patients with epilepsy and CRD.

### **S3.4.3**

## **Can increasing physician fee-for-service payments improve service regularity in elderly patients with chronic disease?**

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### **Abstract**

*Objective:* To assess the influence of increased fee-for-service values on regularity and frequency of primary care visits, and examine the independent effects of demographic factors (age and gender) and chronic disease history.

*Methods:* We performed a retrospective, population-based, longitudinal cohort study, linking routinely collected primary care claims (Medicare Benefits Schedule) and hospital separation data (Hospital Morbidity Data System) in people aged 65 or more years from Western Australia from 2001 to 2006. We used polytomous/multinomial logistic regression to evaluate changes in the likelihood of increased primary care service regularity and frequency in exposed and unexposed individuals, adjusting for age, gender and recent chronic disease history.

*Results:* The higher value services significantly and substantially increased likelihood (up to 14 times) of higher regularity of visits with no corresponding higher frequency of GP contact. The increased likelihood of higher primary care regularity was consistent across regularity quintiles and year of service. Increased regularity was more likely to occur with increasing age, except in the oldest age group (90+ years). Some chronic disease histories (e.g. diabetes) conferred a higher likelihood of improved regularity than others (e.g. hypertension).

*Conclusions:* The study suggests a potential for modification of physician and patient behaviour using incentives within the current fee-for-service system in Australia. This type of incentive could be adopted in systems, which are not based on fee-for-service, as an additional incentive or bonus payment.



### S3.4.4

## The impact of pharmaceutical policy changes on utilisation of medicines in Australia: An analysis of administrative health data

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### Abstract

*Objective:* Patient co-payments for medicines subsidised under the Australian Pharmaceutical Benefits Scheme (PBS) increased by 24% in January 2005. We investigated whether this increase and two related co-payment changes were associated with changes in dispensings of selected subsidised medicines in Australia.

*Methods:* We analysed national aggregate monthly prescription dispensings for 17 medicine categories, selected to represent a range of treatments (e.g. for diabetes, cardiovascular diseases, gout). Trends in medication dispensings from January 2000 – December 2004 were compared with those from January 2005 – September 2007 using segmented regression analysis.

*Results:* Following the January 2005 increase in PBS co-payments, significant decreases in dispensing volumes were observed in 12 of the 17 medicine categories (range: 3.2%-10.7%), namely anti-epileptics, anti-Parkinson's treatments, combination asthma medicines, eye-drops, glaucoma treatments, HmgCoA reductase inhibitors, insulin, muscle relaxants, non-aspirin antiplatelets, osteoporosis treatments, proton-pump inhibitors and thyroxine. The largest decreases were observed for medicines used in treating asymptomatic conditions or those with over-the-counter substitutes. Decreases in dispensings to social security beneficiaries were consistently greater than for general beneficiaries following the co-payment changes (range: 1.8%-9.4% greater,  $P=0.028$ ).

*Conclusions:* The study findings suggest that recent increases in Australian PBS co-payments have had a significant effect on dispensings of prescription medicines. The results suggest large increases in co-payments impact on patients' ability to afford essential medicines. Of major concern is that, despite special subsidies for social security beneficiaries in the Australian system, the recent co-payment increase has particularly impacted on utilisation for this group. Additional work by our team has shown that these decreases in dispensings have not been offset by increases in the number of doses supplied per prescription. Patients now fund more than one quarter (28%) of all prescription medicine costs in Australia, placing it in the mid-upper range compared with other OECD countries with universal pharmaceutical subsidies. Data on the impact of rising out-of-pocket costs and decreasing utilisation of medicines on patient health outcomes is now warranted. We plan to analyse linked pharmaceutical, hospital and other health services data available through the Western Australian Data Linkage System, to determine the health impact of the recent PBS cost increases.

## F1

### **The impact of the length of the follow-up period on the predictive power of major cardio-vascular risk factors**

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#### **Abstract**

*Objective:* The aim of the present study was to investigate how the length of the follow-up period influences the predictive power of the major cardiovascular (CV) risk factors regarding the three different outcomes myocardial infarction (MI), stroke and heart failure during a prolonged follow-up period.

*Methods:* 2322 men aged 50 were investigated regarding CV risk factors in 1970-74. The follow-up time was 33 years. The hazard ratio (HR) was calculated yearly for each risk factor regarding the three separate outcomes.

*Results:* During the follow-up 571 cases of MI, 381 cases of stroke and 384 cases of heart failure occurred. Regarding the influence of the follow-up time on risk prediction, three patterns were found. First, a gradual decline in the HR over time. This pattern was seen for blood pressure regarding all three outcomes, with the most rapid decline for heart failure and stroke. This pattern was also seen for BMI regarding MI and heart failure and for smoking regarding MI and stroke. Second, a gradual increase in HR to a maximum at 20-25 years follow-up and thereafter a decline. This pattern was seen for the apoB/A1 ratio, diabetes and triglycerides regarding MI and heart failure. Third, a fairly consistent HR over time was seen for HDL regarding MI and heart failure.

*Conclusion:* The length of the follow-up period influenced the predictive power of traditional CV risk factors in different ways during a long follow-up period. The 10-15 year risk is however for most risk factors well preserved after 33 years follow-up.

## F2

### **What do we know about light drinking in pregnancy and child development?**

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#### **Abstract**

The link between heavy alcohol consumption during pregnancy and consequent poor developmental outcomes in children and young people is well established. Until recently little work had been done on whether or not light drinking in pregnancy is also linked to adverse developmental outcomes in children.

In the UK and elsewhere there are lively public and policy debates around the safety of light and moderate alcohol consumption during pregnancy. In many countries policy recommends that expectant mothers should abstain from the consumption of any alcohol. Associated with this are ethical discussions – the right of the unborn child *versus* the right of the mother. But what does the research tell us?

Over the last couple of years there has been a re-ignition in interest in this field of study reflected in a large number of published articles from across Europe and elsewhere. This paper reviews what is known to date, gives an overview of emerging approaches to investigation in this area, and presents new results from analysis of the UK Millennium Cohort Study.

## F3

### Does physical activity contribute to sustained BMI improvement in overweight and obese 5-10 year old children? Community based longitudinal study

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#### Abstract

**Objectives:** Childhood overweight and obesity remain difficult to reverse. Though a cornerstone of treatment, surprisingly little is known about the contribution of physical activity to children's weight loss. We aimed to determine, in a community sample of overweight and mildly-obese 5-9 year olds, whether physical activity predicts over 3-4 years: (1) reduced BMI z-score; (2) odds of a lower BMI category; and (3) clinically-significant weight loss ( $\geq 0.5$  SD BMI z-score).

**Methods:** Design – Longitudinal study. Setting – 66 general practitioners (GPs) in Melbourne, Australia. Participants – 258 overweight/obese (IOTF criteria) 5-9 year old children recruited into the LEAP2 trial from a survey of 3,958 children visiting their GP May 2005-July 2006. Very obese children (UK BMI z score  $\geq 3.0$ ) were excluded. Outcomes – Change in BMI ( $\text{kg/m}^2$ ) between 6 months and 3 years. Predictor – Physical activity (PA, counts/minute (cpm)) by 7-day multi-axial accelerometry at 6 and 12 months and 3 years. Analysis – Multivariable linear regression (Aim 1), multinomial logistic regression (Aim 2), and multivariable logistic regression (Aim 3), adjusted for intervention status and potential confounders.

**Results:** 182 children (71% retention) took part at 3-4 years, with a mean (SD) outcome BMI z-score of 1.81 (0.68). Mean (SD) PA fell from 334 (111) and 339 (134) cpm at 6 and 12 months to 284 (104) at 3-4 years. PA at 6 months did not predict change in any BMI outcome. However, every 100cpm PA increase between 6 months and 3-4 years resulted in: (1) adjusted BMI z-score 0.11 ( $p < 0.01$ ) lower; (2) greater odds of not being in a higher BMI category ( $p = 0.05$ ) and (3) OR 1.96 ( $p = 0.09$ ) of a clinically-significant weight loss. Findings were similar for the 6-12 month and 12 month-3-4 year epochs. In post-hoc analyses, increased % time in moderate-vigorous ( $p = 0.008$ ), but not sedentary ( $p = 0.16$ ) or light ( $p = 0.96$ ), PA predicted better BMI outcomes.

**Conclusion:** Higher physical activity can improve long-term BMI in overweight/obese children, but only if increases are made and then sustained. The short-term nature of most intervention programs may explain the lack of efficacy reported in the 2009 Cochrane systematic review of childhood obesity treatment.

## F4

### **Emotional and behavioural problems among children with chronic illness: The role of parent-child relationship**

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#### **Abstract**

*Objective:* Children with a chronic illness are known to have a higher likelihood of experiencing emotional and behavioural problems. A number of hypotheses have been put forward to explain this relationship. One suggests that the relationship maybe due to conflict between parents and children due to the stress of caring for chronically ill children and possible over-protectiveness but no studies to date have presented evidence on this hypothesis.

*Methods:* Data on 8570 nine year old children was collected as part of the Growing Up in Ireland Cohort Study. Parent reported information on chronic illness was coded using ICD-10 codes. The Strengths and Difficulties questionnaire (SDQ) was used to collect information on the extent of emotional and behavioural problems. The Pianta scale was used to measure level of conflict between children and parents. Bivariate statistics of mean differences between chronically ill children are compared to healthy peers. Path analytic models are estimated to identify the direct and indirect effects of chronic illness, the latter acting through via parent-child conflict.

*Results:* A chronic illness was reported for 871 (11%) of children in the study. Asthma constituted 46% of reported chronic conditions. Children reported as having asthma were 2.2 times more likely to have a score at or above the 90<sup>th</sup> percentile on the SDQ total score. Children with other chronic illnesses were 2.3 times as likely as healthy peers. Children with chronic illness had significantly higher levels of conflict with parents even controlling for mother and household characteristics. Controlling for confounders, chronically ill children were more likely to have high SDQ total scores but analysis showed that the effect of chronic illness on SDQ was completely mediated by the level conflict between parent and child.

*Conclusions:* Children with chronic illness are more likely to experience emotional and behavioural problems but the likely cause is highly modifiable if the interaction of parents and children can be altered.

## F5

### **Inequality during the early years: Child outcomes and readiness to learn in Australia, Canada, the United Kingdom and the United States**

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#### **Abstract**

*Objective:* A comparative analysis of the relationship between parental socio-economic status (SES) and early child cognitive and socio-emotional outcomes in the US, UK, Canada and Australia.

*Methods:* The study uses data from four 21st century nationally representative longitudinal birth cohort studies: the US Early Childhood Longitudinal Study Birth Cohort; the UK Millennium Cohort Study; the National Longitudinal Study of Children and Youth Canada from Canada; and the Longitudinal Study of Australian Children. We compare the gradients in mean child outcomes by parental SES across countries (contrasting SES measurement by education and income). Child outcomes at age 4 to 5 cover cognitive measures (such as the Peabody Picture Vocabulary Test) and non-cognitive measures (such as the Strengths and Difficulties Questionnaire).

*Results:* We find evidence of a stronger relationship between cognitive test scores and parental SES in the US than in the other three countries, a difference driven by greater disparities between the most advantaged and middle-SES families. Disparities in socio-emotional outcomes are smaller in general and show less systematic differences across countries, although inequalities in these outcomes are generally the lowest in Canada.

*Conclusion:* Research has shown that intergenerational persistence in SES is strong in the US and the UK by international standards, but much weaker in Canada and Australia. The results of this study suggest that the greater transmission of parental advantage in the US begins very early in life, before children enter school or the labour market. We discuss differences in the cultural, economic and social welfare systems of the four countries, highlighting the fact that the US relies more heavily than the other countries on the private market for early childhood care, education and health care.

## F6

### Greek migrants to Australia: Obese but metabolically healthy?

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#### Abstract

**Objective:** Central obesity is a key feature of the metabolic syndrome and increases diabetes and cardiovascular disease (CVD) risk. Greek migrants to Australia present a paradox: they are obese, and have an increased prevalence of diabetes, however continue to have low CVD mortality compared with the Australian-born population despite more than 50 years since migration. We aim to determine whether a Mediterranean style diet is associated with a more metabolically healthy obesity phenotype which could contribute to the lower CVD risk of Greek migrants in Australia.

**Methods:** In a cross-sectional study we recruited 432 Greek and Australian-born men and women aged 44-83yrs with and without type 2 diabetes, and measured dietary intake, body composition, medical history, smoking and other lifestyle factors, as well as novel CVD risk factors.

**Results:** Three CVD risk factor patterns were identified using principal components analysis (PCA). Pattern 1, labeled 'diabetes', included positive factor loadings for HbA1c, fasting insulin, triglycerides, low HDL, obesity (high % body fat and intra-abdominal adipose tissue (IAAT)), and C-reactive protein (CRP). Pattern 2, labeled 'pre-diabetes', included positive factor loadings for HbA1c (but not fasting insulin), systolic and diastolic blood pressure, triglycerides, IAAT, and urinary ACR. Pattern 3, labeled 'healthy obesity', included positive factor loadings for obesity (% body fat), and HDL, and negative factor loadings for smoking, HbA1c, fasting insulin, urinary ACR, and homocysteine. The healthy obesity factor was positively associated with Greek ethnicity ( $p < 0.001$ ), and negatively associated with prevalent CHD ( $p < 0.002$ ). Furthermore, healthy obesity was positively associated with consumption of a traditional Greek Mediterranean diet ( $R^2$  0.164;  $p < 0.01$ )

**Conclusion:** The traditional Greek Mediterranean diet may reduce the risk of CVD by attenuating the detrimental effects of obesity.

The authors are currently analyzing follow-up mortality data from this cohort to examine whether the metabolically healthy obesity phenotype is associated with lower mortality rates (all-cause and CVD) and they will be in a position to present this data at the conference in October.

## T1.1.1

### Is Mediterranean Diet during pregnancy protective for foetal growth retardation? Results from two mother-child cohorts in Spain and Greece

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#### Abstract

**Objective:** Dietary intake of specific nutrients or food groups during pregnancy could play a role in fetal growth, but scant evidence is available on effects of dietary patterns.

We evaluated the impact of Mediterranean Diet (MD) adherence during pregnancy on foetal growth in two population based mother-child cohorts in Spain and Greece.

**Methods:** We studied 2481 mother-newborn pairs from the Spanish multicenter "INMA" study, and 889 pairs from the Greek "RHEA" study. Maternal dietary intake during pregnancy was assessed by food frequency questionnaires and MD adherence was evaluated through a priori scores. Fetal growth restriction was based on a customized model, and multivariate log-binomial and linear regression models were used adjusting for several confounders.

**Results:** MD scores differ significantly between the Spanish cohorts in the Atlantic area (INMA-Atlantic), the Mediterranean area (INMA-Mediterranean), and the Cretan cohort (Rhea). Women in INMA-Atlantic reported higher intakes of fish and dairy products, while women in RHEA had higher intakes of fruits, nuts, and olive oil. Women with high MD adherence had a significantly lower risk of delivering a foetal growth-restricted infant for weight (RR: 0.5; 95% CI: 0.3, 0.9) in INMA-Mediterranean, but this was not the case for INMA-Atlantic and Rhea. In INMA-Mediterranean, high MD adherence was associated with a birth weight gain of 88gr (SE: 33.4) and length gain of 0.30cm (SE: 0.1). Stratified analysis by smoking revealed that higher MD adherence increased birth weight and length in smoking mothers, whereas this effect was not apparent in non-smoking mothers.

**Conclusion:** Several types of Mediterranean diet exist across European Mediterranean countries. High MD adherence may modify the detrimental effect of smoking on birth size, but overall effects of diet were not universal for the studies in this analysis.



## T1.1.2

### Maternal diet and fatty acids levels in pregnancy in relation to child IQ

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#### **Abstract**

*Objective:* To investigate the relationship between maternal diet in pregnancy and fatty acid levels in maternal blood and how these relate to cognitive development of the child at age 8 years.

*Methods:* Blood samples and food frequency questionnaires (FFQ) were collected from pregnant women in the Avon Longitudinal Study of Parents and Children (ALSPAC). Their children were followed up at 8 years and IQ assessed using WISC, in both verbal and performance domains. Markers of social status were collected by questionnaire. Maternal blood samples were assayed for 13 saturated, 11 monounsaturated, 8 omega-6 and 7 omega-3 fatty acids. The FFQ provided information on dietary intake of 50 food groups. The relationship between maternal fatty acid levels and child IQ was investigated using appropriate statistical packages. Fatty acid levels in pregnancy in relation to food groups eaten will be investigated.

*Results:* Fatty acid levels in maternal blood were available from 4400 mothers, 9500 provided FFQ data and child IQ was available for 6000 children. Data on fatty acids and IQ were available for 2790 mother/child pairs. Verbal IQ showed stronger associations than performance IQ. Strong positive associations (unadjusted) were seen with 15:0, 19:0, 18:2 and 22:6 with 18:1 n-9 showing a strong unadjusted negative association. Adjusted associations will be explored and the relationship between diet and blood levels of the fatty acids investigated.

*Conclusions:* Univariable associations were found between fatty acid levels in pregnancy and child verbal IQ at age 8 years. These will be explored further and related to diet in pregnancy and presented at the conference.

### T1.1.3

## Maternal intake of fish oil during pregnancy and blood lipid status in adulthood: follow up study over two decades from a randomized controlled trial

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### Abstract

**Objective:** Nutritional influences on cardiovascular disease (CVD) operate throughout life. Studies in both experimental animals and humans have suggested that changes in the peri- and early post-natal nutrition can affect the development of the various components of the metabolic syndrome in adult life. This has led to the hypothesis that n-3 fatty acid supplementation in pregnancy may have a beneficial effect on lipid status in the offspring. The aim of the present study was to investigate the effect of supplementation with 2.7 grams of long chain n-3 fatty acids (fish oil) during third trimester of uncomplicated pregnancies on serum triglyceride and cholesterol concentrations in the 19 year old offspring compared to controls.

**Methods:** The study was based on long term follow-up of the offspring of 533 pregnant women enrolled in a randomised controlled trial from 1990. The women were randomised to fish-oil (2.7g n-3 fatty acids/day; n=266), olive-oil (4g/day; n=136) or no oil (n=131). In 2009, the offspring were invited to a physical examination including blood sampling.

S-triglyceride and s-cholesterol data were logtransformed due to skewness and a t-test was used to compare lipid concentrations between the fish-oil and olive-oil groups.

**Results:** A total of 243 of the offspring participated (fish-oil n=108, olive-oil n=72 and no oil n=63). Lipid values did not differ between the fish-oil and olive-oil groups. The unadjusted ratio between lipid concentrations with 95%-confidence intervals were 0.98 (0.90; 1.07) for LDL cholesterol, 1.05 (0.98;1.13) for HDL cholesterol and 0.97 (0.84;1.11) for triglyceride concentrations.

**Conclusion:** We could not detect any effect of fish-oil supplementation during third trimester of pregnancy on offspring blood lipid values in adolescence.

## T1.1.4

### Long-term health effects on the next generation of Ramadan fasting during pregnancy

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#### **Abstract**

*Objectives:* Each year, many pregnant Muslims fast from dawn to sunset during the Islamic holy month of Ramadan. Maternal nutrition during pregnancy is known to have long-term effects on the health of the offspring. These effects often increase in size as the offspring ages. Yet, although signs of accelerated starvation and insufficient 24-hour time span energy intakes have been demonstrated among Ramadan fasting pregnant women, virtually no research exists on long-term effects of this. The present study aims to establish how the health of people of various ages is affected by prenatal exposure to maternal Ramadan fasting.

*Methods:* Using a large Indonesian cross-sectional database ( $N > 22,000$ ), potential prenatal Ramadan exposure is established using dates of birth, average length of human gestation, and start and end dates of all Ramadans in the last century (Ramadan each year falls about 11 days earlier in the commonly used Gregorian calendar). The health of potentially exposed Muslims (i.e. there was overlap between gestation and a Ramadan) is compared to that of certainly not exposed Muslims (i.e. no overlap), controlling for age, season of birth and sex. Comparing potentially to certainly not exposed Muslims leads to lower bound estimates of the health effect. Health measures include general health – (a rating given by nurses after taking measurements of a diverse set of physical and health variables) – and reports of own health and sickness.

*Results:* Muslims under the age of 45 whose mother had fasted during pregnancy receive general health ratings that are about 5% of a standard deviation lower than ratings received by otherwise similar not exposed Muslims. For Muslims of 45 years and older, the negative health effect increases to 18% of a standard deviation. Self-reports of own health and sickness confirm the negative health effect of prenatal Ramadan exposure, which is larger for older people.

*Conclusions:* Muslims whose mother observed the Ramadan fast during pregnancy have a worse general health and are sick more often than otherwise similar others. These effects get larger as the prenatally exposed person gets older.

## T1.2.1

### The interaction between BDNF, 5-HTTLPR and childhood adversities on depression scores could not be replicated in the TRAILS study

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#### Abstract

*Objectives:* The three-way interaction between the functional polymorphism in the serotonin transporter gene linked promotor region (5-HTTLPR), the val66met polymorphism in the brain-derived neurotrophic factor (BDNF) gene, and childhood adversity in the prediction of depression in children, has only been confirmed in adult samples. This study examines the gene-by-gene-by-environment interaction in an adolescent sample.

*Methods:* 1096 complete data sets were obtained from the TRAILS (TRacking Adolescents' Individual Lives Survey) cohort. Depression scores were assessed with the Youth Self Report at ages 11, 13.5 and 16. Pregnancy and Delivery adversities and Childhood Events were assessed in a parent interview at age 11. Long Term Difficulties until age 11 were assessed with a parent questionnaire at age 13.5. Blood or buccal cells were collected for genotyping at age 16. A hierarchical linear regression model with three-way interaction effects was fitted on the data to predict mean depression score over the three measurement waves.

*Results:* Correlations between the three types of childhood adversities were low ( $.1 < r < .2$ ). Biserial correlations between genotypes and childhood adversities were all below  $r = .1$ . Depression score over the three measurements was not significantly predicted by any interaction between genotypes and childhood adversities. This non-replication was confirmed when regression equations were performed separately for each childhood adversity.

*Conclusions:* We were not able to confirm the three-way interaction in a representative, population based sample of adolescents. The large sample resulted in adequate power, in combination with the reliability of our measures; this gives confidence in our findings. Exposure to childhood adversities was not different between the genotypes, given the low biserial correlations. The only explanation for our non-replication seems to be the bias of researchers to submit positive findings, of editors to send positive findings to reviewers, and of reviewers to evaluate studies with positive findings more positively.

## T1.2.2

### Genetic variants in the FADS cluster and ELOVL5, colostrums PUFA levels, breastfeeding and child cognition

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#### Abstract

**Objective:** Polyunsaturated fatty acids (PUFA) uniquely available in breast milk are proposed to mediate breastfeeding effects on cognition, but controversy persists. We aimed to identify maternal genetic variants in the FADS cluster and ELOVL5 genes influencing PUFA levels in colostrum; and to assess whether child's genetic variants in these PUFA metabolizing enzymes modify the effects of breastfeeding on cognition in two population-based birth cohorts: the AMICS-Study and the Sabadell-INMA cohort.

**Methods:** PUFAs were measured in colostrum samples by gas chromatography. Colostrums FADS1, FADS2 and ELOVL5 activities were estimated from (C20:4n-6):(C20:3n-6), (C20:3n-6):(C18:2n-6), and (C22:5n-3):(C20:5n-3) ratios, respectively. Eighteen tag SNPs were successfully genotyped with SNPlex technology (11 in the FADS cluster, and 7 in ELOVL5). Detailed information on breastfeeding was completed by interviewer-administered questionnaires. Child cognition scores were assessed by Bayleys and McCarthy tests at 14 months and 4 years of age. The statistical analysis was performed using a likelihood ratio test from a linear model adjusting for main confounders.

**Results:** According to PUFA in colostrum and maternal genetic variants, the minor alleles of rs174537 and rs968567 located in the FADS cluster were associated with higher FADS2 activity ( $p < 9e-06$ ). The minor alleles of seven SNPs in FADS cluster (rs174537, rs968567, rs2072114, rs526126, rs174626, rs174627, and rs174464) were associated with lower FADS1 activity ( $0.0031 \leq p \leq 2.40e-29$ ), and the minor allele (A) of rs174468 with higher activity ( $p = 0.0078$ ). In addition, the minor allele (G) of rs2397142 was associated with higher ELOVL5 activity ( $p = 0.0362$ ). Regarding child genetic variants, we replicated two statistically significant interactions in both cohorts. We found that not being breastfed conferred a disadvantage on cognition (8-9 points) among children GG homozygotes for rs174468 (lower FADS1 activity) but not among those carrying allele A (higher FADS1 activity). In addition, not being breastfed resulted in a disadvantage in cognition (5-8 points) among children CC homozygotes for rs2397142 (lower ELOVL5 activity), but not among those carrying allele G (higher ELOVL5 activity). In contrast, breastfed children did not differ in cognition score irrespectively of their genetic variants both in rs174468 and rs2397142.

**Conclusion:** Polymorphisms in FADS cluster and ELOVL5 genes determined PUFA metabolism in colostrum. Child genetic variants in FADS cluster and ELOVL5 modified the effect of breastfeeding (an environmental background universal before formula feeding) on intelligence development.

## T1.2.3

### Interaction between prenatal nutrition and common genetic variants on the risk of type 2 diabetes mellitus: evidence from the Dutch Hunger Winter Families Study

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#### Abstract

*Objective:* Genome wide association studies have identified single nucleotide polymorphisms (SNPs) that are associated with type 2 diabetes mellitus (DM). Associations have also been reported between fetal malnutrition and DM. We use the circumstances of the Dutch Hunger Winter of 1944-45 to assess possible interactions between maternal food availability during pregnancy and high-risk genotypes as predictors of DM risk in the offspring.

*Methods:* We studied (1) adults born in one of three hospitals in affected cities in the western Netherlands to mothers exposed to famine immediately before pregnancy (0-10 weeks before the last menstrual period) or during pregnancy (n=423), (2) adults born in the same hospitals to mothers not exposed to famine during pregnancy (n=223) as time-controls, and (3) non-exposed same-sex sibling controls of individuals (n=305) in the above two groups. Famine exposure was defined in relation to distributed nutrition rations. Diabetes mellitus was defined by either a previous diagnosis of diabetes, a fasting glucose of 7.0 mmol/L or more, or a 2-h post-challenge glucose of 11.1 mmol/L or more by oral glucose tolerance test. We evaluated common variants in the *NOTCH2*, *HHEX*, *CDC123*, *SLC30A8*, *IGFBP2*, *ADAMTS9*, *KCNJ11*, *CDKALI1*, *THADA*, *TSPAN8*, *JAZF1*, and *TCFL2* genes related to diabetes. For each individual we obtained a genetic risk score by summing the number of risk alleles in the genes. The score was categorized as high vs low, relative to the median. Institutional ethics committees gave the appropriate approvals for the study.

*Results:* At mean age 58 y, the prevalence of DM in the adults with prenatal famine exposure was 17.5%, in unexposed time-controls 9.7%, and in sibling controls 11.4%. The genetic risk score ranged from 3-17. DM was independently associated with prenatal famine exposure (OR 1.81; 95% CI: 1.24 to 2.63) and with a high genetic risk score (OR 1.45; 95% CI: 1.00-2.12) but there was no statistical interaction with regard to DM risk.

*Conclusions:* In this study, we found no interaction between prenatal exposure to famine and a high genetic risk score for common genetic variants for the risk of type 2 diabetes mellitus. Further analyses are in progress.

## T1.2.4

### Nicotinic acetylcholine receptors (nAChRs) variants, nicotine dependence and lung function decline in the general population

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#### Abstract

**Objective:** Single nucleotide polymorphisms (SNPs) rs1051730 and rs8034191 in nicotinic acetylcholine receptors (*nAChRs*) cluster have been identified in genome-wide association studies as a risk for nicotine dependence, lung cancer and COPD. The aim is to investigate whether SNPs in *nAChR* cluster are associated with smoking habits and lung function decline, and if these potential associations are independent of each other.

**Methods:** The SNPs rs1051730, rs569207 in *nAChR* and rs8034191 nearby *nAChR* were analyzed in the population-based cohort Vlagtwedde-Vlaardingen (n=1390) which was followed for 25 years with lung function measurements every 3 years (last survey: 51.4% males, median age 52 yrs, 35.2% current smokers, mean FEV<sub>1</sub>%pred. 92.6). GEE models were used to assess the associations of *nAChR* SNPs with smoking habits such as quitting or restarting smoking within smokers respectively ex-smokers. LME models were used to assess the associations of the SNPs with quitting smoking and the course of FEV<sub>1</sub>.

**Results:** Smokers homozygote for rs569207 were more likely to quit smoking (OR (95%CI) = 1.58 (1.05-2.38)) compared to wild type smokers. Smokers homozygote for rs1051730 were less likely to quit smoking (0.64 (0.42-0.97)) compared to wild type smokers. None of the SNPs was significantly associated with the annual FEV<sub>1</sub> decline for smokers or ex-smokers, with or without correction for quitting or restarting smoking respectively. Smokers who quit smoking improved the annual FEV<sub>1</sub> decline with 18.12ml/yr (4.5-31.8) as compared with those who continued smoking.

**Conclusion:** Our study shows that rs569207 and rs1051730 in *nAChR* are associated with an increased respectively decreased ability to quit smoking, but have no effect on the annual FEV<sub>1</sub> decline for smokers or ex-smokers, suggesting a potential role of these SNPs in COPD via smoking habits rather than lung function among smokers and ex-smokers.

### T1.3.1

## Grip strength relationships between parents and children: Findings from the Southampton Women's Survey

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### Abstract

*Objective:* Relationships between birth weight and grip strength throughout the lifecourse suggest that early influences on the growth and development of muscle are important for long-term muscle function. However little is known about parental influences on children's grip strength. We aimed to assess the relationship between grip strength in children aged four years and that of their parents, taking account of birth weight, body size and lean mass.

*Methods:* The Southampton Women's Survey is a prospective general population cohort study from before conception through childhood. Grip strength was measured using a Jamar handgrip dynamometer in the mother at 19 weeks' gestation and her partner and in the child at age four years. Pre-pregnancy heights and weights were measured in the mothers, reported weights and measured heights were available for the fathers. In the children, we measured height and weight and assessed body composition (lean mass) using dual energy x-ray absorptiometry. Multiple regression was used to relate grip strength of the children to that of their parents allowing for adjustment for confounding factors.

*Results:* Complete data on parents and children were available for 444 trios. In univariate analyses, both parents' grip strengths were significantly associated with that of the child ( $r=0.17$ ,  $p<0.001$  for mothers,  $r=0.15$ ,  $p=0.002$  for fathers). Confounding influences of height and weight of the parents and the child, and the child's birth weight and lean mass at age 4 years were explored. In the final model, the mother's but not the father's grip strength was significantly associated with the child's grip strength; for each 1kg increase in maternal grip strength the child's grip strength increased by 0.035kg (95%CI: 0.006 – 0.064kg).

*Conclusion:* Children's grip strength at age 4 years is associated with that of their parents, but after adjustment for current height and lean mass of the child, the relationship with the father's grip strength is attenuated. The stronger association between children and their mothers than their fathers after adjustment for current size supports a role for trans-generational influences transmitted through the maternal line and suggests that the effects of the materno-foetal environment on muscle development persist into childhood.



## T1.3.2

### **Childhood trauma and offspring birth characteristics – an intergenerational study of siblings**

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#### **Abstract**

*Objectives:* Early influences on children's development may extend into the next generation, for instance into offspring birth characteristics. The evidence for girls' early environment having such an effect is stronger than that for boys, but even for boys this could be possible. Our main objective was to find out 1) if the death of a parent during childhood might have intergenerational effects. We hypothesized that both boys and girls having such an experience may see their own children being on average smaller at birth; and asked 2) if there was a specific age of vulnerability, when a parent's death may matter more.

*Methods:* We identified all same-sex sibling pairs in the Swedish population, where both siblings experienced the death of a parent during childhood. Childhood was grouped into ages 1-4, 5-9, 10-14 and 15-19. When the two siblings fell into different age groups at the event of parental death we could analyse age-dependent vulnerability. Thus we compared, within sibling pairs, each sibling's firstborn offspring's size at birth by age at exposure to parental death. In separate analyses, not based on siblings, we compared size at birth of offspring to children with and without parental death during childhood.

*Results:* For boys, the experience of the death of a parent at ages 5-9, rather than at ages 1-4, was associated with their future offspring being smaller at birth. Offspring to boys who experienced parental death at ages 5-9 were on average 270 grams lighter, 1 cm shorter and had a somewhat smaller head circumference (0.7 cm) than offspring to their brothers who experienced the same event at ages 1-4, but not significantly different from brothers who were older at parental death. For girls, who lost their mother or father, the age at which this happened did matter less, or not at all.

*Conclusion:* The death of a parent may influence the social and biological development of that child in such a way that the foetal growth of its offspring is affected. For boys, the experience of such trauma after age 5, rather than earlier may be associated with a larger intergenerational effect.

### T1.3.3

## Maternal birth characteristics and perinatal mortality in twin offspring. An intergenerational population-based study in Norway 1967-2008

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#### Abstract

*Objective:* To investigate if maternal preterm birth and birth weight in one generation affect perinatal mortality in their twin offspring in the next generation.

*Methods:* Population-based cohort study from the Medical Birth Registry of Norway 1967-2008 comprising linked generational data with 9,426 mother-twin pair units. Twin offspring were linked to their mothers by means of the unique national identification numbers.

The main outcome measure was perinatal mortality in twin offspring

*Results:* The twin incidence was not dependent on the mother's gestational age at her birth, but did increase by birth weight in term mothers. The mother's gestational age at her own birth was strongly and inversely associated with risk of perinatal death in one or both of her twin offspring, and the risk was more than doubled for twin offspring compared to singleton offspring. Compared to term mothers, preterm mothers born in gestational weeks 27-31 and 32-34 had a relative risk (RR) of 3.83 (95% confidence interval: 1.56-9.36) and RR 2.41 (95% CI: 1.29-4.50), respectively. There was an interaction between preterm born mothers, the use of assisted reproductive technologies (ART) and perinatal mortality in twin offspring ( $P=0.03$ ). Further, term mothers with birth weight-by-gestational age Z-scores  $\leq -2$  had more than twice the risk of a perinatal loss in their twin offspring compared to mothers compared with the most favourable birth weight-by-gestational age (Z-scores = 1-1.99). [RR 2.42 (95% CI: 1.37-4.29)]

*Conclusions:* Women born preterm had increased risk of perinatal mortality in their twin offspring and particularly after ART treatment. Very low birth weight-by-gestational age in term mothers was also associated with this adverse outcome. A twin pregnancy is a high risk pregnancy in general, but even more so if the mother herself was preterm born or growth restricted at birth.

## T1.3.4

### Factors influencing susceptibility to CMV infection: evidence from the Leiden Longevity Study and the Longitudinal Study of Aging Twins

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#### Abstract

*Objective:* The herpesvirus cytomegalovirus (CMV) is a common latent and persistent infection, which may play an important role in the aging of the immune system. Little is known of the underlying causes affecting susceptibility to CMV infection. The purpose of this study was to disentangle the role of genetic, early and adult life environmental influences on susceptibility to CMV infection.

*Methods:* We measured CMV seroprevalence in two genetically informative cohorts. From the Leiden Longevity Study we selected sib pairs age 90+, their offspring and the spouses of the offspring (n = 2296). From the Longitudinal Study of Aging Danish Twins a sample of 604 (302 pairs) same-sex monozygotic (MZ) and dizygotic (DZ) Danish twins aged 73-94 participated.

*Results:* LLS offspring had significantly lower seroprevalence of CMV compared with their partners (offspring: 42% vs. partners: 51%, p = 0.003). Of the 744 offspring living with a CMV-positive partner, only 58% were infected themselves. The corresponding number for the partners was 71% (p < 0.001). This pattern suggests that subjects enriched for longevity infect their partners, whereas the partners are less likely to infect the subjects enriched for longevity. In the Longitudinal Study of Aging Danish Twins, the MZ and DZ twins had high and similar CMV-positive concordance rates (MZ: 90% vs. DZ: 88 %, p = 0.51) suggesting that shared family environment accounts for the similarity within twin pairs. This is further supported by the finding that the 90+ year-old siblings in LLS had CMV-positive concordance rates significantly lower (75%) than DZ twins (88%, p < 0.001) who have the same genetic similarity as sibs, but more similar early environment.

*Conclusion:* Susceptibility to CMV infection – even under continuous within-partnership exposure – appears to be more strongly influenced by early life environment than by adult environment and genetic factors.

## T1.4.1

### Parents' education, social attainment, and major depressive episode

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#### **Abstract**

*Objectives:* Few longitudinal studies have investigated the relationship between parents' education and major depression in adults. Education plays a critical role in the inter-generational transmission of parental socioeconomic position (SEP) to adult SEP; and adults of lower SEP are more likely to suffer from major depression. Using a life course perspective, the aim of this study was to estimate the relationship between parents' education and major depressive episode (MDE) in adults. We also examined the mediating effects of several adverse childhood experiences (ACE), adult SEP (education, income adequacy, employment status, and student status), psychosocial factors (chronic stress and sense of mastery) and physical health (number of chronic conditions).

*Methods:* Data came from seven waves (1994/95 to 2006/07) of the Canadian longitudinal National Population Health Survey (NPHS), and included 1,267 participants that were between the ages of 12 and 24 at the first wave. Parents' education was measured in wave 1, while ACEs were collected retrospectively during waves 1, 4, and/or 7. Measures of adult SEP, psychosocial factors, and physical health were collected in waves 4 (2000/01) and/or 5 (2002/03). Individuals who met the criteria for past-year MDE in waves 6 (2004/05) and/or 7 (2006/07), according to the Composite International Diagnostic Interview-Short Form for Major Depression (CIDI-SFMD), were classified as having experienced an MDE at follow-up. Logistic regression analysis was used to estimate the effect of parent's education and other early-life and adult risk factors on adult depression.

*Results:* No effect was observed for father's education. However, respondents of mothers with less than a secondary school diploma were at increased risk for MDE (OR = 2.04, 95% CI: 1.25, 3.32) compared to respondents of more educated mothers. Adjusting for the respondent's ACEs, adult SEP, psychosocial factors, and physical health did not reduce the impact of maternal education.

*Conclusion:* These results suggest that early-life may be a sensitive period for the development of major depression in adulthood, and that maternal education may play a significant role in the aetiology of depression.

## T1.4.2

### **Do the stability and co-morbidity of anxiety and depression symptoms over time differ by social class?**

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#### **Abstract**

*Objective:* Socioeconomic inequalities in anxiety and depression constitute an unknown mix of higher incidence and greater stability of symptoms over time in disadvantaged groups. Also anxiety and depression symptoms are often grouped together without addressing which arise first. This paper investigates social class differences in the stability and longitudinal co-morbidity of anxiety and depression in order to better understand how socioeconomic inequalities develop.

*Methods:* Data are from the West of Scotland Twenty-07 Study, with 4,510 respondents in three cohorts aged 15, 35 and 55 at baseline in 1987/88. The Hospital Anxiety and Depression Scale (HADS) was included at each of four subsequent visits spanning 20 years up to 2007/08. Anxiety and depression are defined as scores of 8+ out of 21 on the appropriate HADS subscale. A multiple-group analysis of a multilevel cross-lagged panel model was used to examine social class differences in the stability and co-morbidity of anxiety and depression symptoms in each cohort, adjusting for age and sex.

*Results:* Anxiety symptoms were more common than depression at all ages, and depression symptoms rarely preceded anxiety, though both appeared concurrently as often as anxiety appeared first. In those aging from 15-35 there were no significant social class differences in the stability or co-morbidity of symptoms, but for those aging from 35-55, those in manual classes with anxiety were more likely at the next measurement to have anxiety again (OR 1.74, 95% CI 1.13-2.70) than someone with anxiety from a non-manual class. For those aging from 55-75 those from manual classes were more likely to have symptoms initially than those from non-manual classes, and the stability of symptoms was very high in this cohort. Those in manual classes with anxiety were also more likely to have depression at the next measurement (OR 2.33, 95% CI 1.23-4.42) than someone with anxiety from a non-manual class. Preliminary investigations of gender differences in these effects suggest complex interactions.

*Conclusion:* Socioeconomic inequalities in anxiety and depression arise in later life as people who are disadvantaged are less likely to recover from anxiety in middle age and more likely to experience symptoms worsening from anxiety to depression in old age. High stability of symptoms in old age perpetuates these inequalities. Understanding when and how these inequalities develop may help research into their causes and efforts to intervene.

### T1.4.3

## Social differentials in psychiatric admission among the depressed. A register-based study of 228 877 community-dwelling Finns

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#### Abstract

*Objectives:* Depression is a major public health burden due to its high prevalence. Depression also contributes to the social gradient in health as it is found more prevalent among those with low socioeconomic position and the unpartnered. However, the burden of depression is not fully determined by its prevalence but also by its consequences. Some manage better with their illness, whereas among some, the symptoms tend to escalate, causing repeated hospitalisation. Using longitudinal register data, this study seeks to identify social factors that predict psychiatric hospitalisation among depressed outpatients and inpatients.

*Methods:* A register-based random sample of community dwelling Finns aged 40–64 at the end of 1997 was assessed for depression, using data on antidepressant use and psychiatric hospital care in 1996–1997. Depressed outpatients (antidepressant users without psychiatric hospital care, n=12,806) and discharged inpatients (those with hospital care for depression, n=837) as well as those with no records of psychiatric care (n=215,234) were followed up for psychiatric admission in 1998–2003. Cox proportional hazards models were used to assess differentials in admission according to education, occupational class, household income, home ownership, union status, and co residence with children.

*Results:* Among depressed outpatients, only socioeconomic factors which measured material hardship, namely being in the lowest income quartile (HR 2.03, 95% CI 1.66–2.48) and not owning a home (1.16, 1.01–1.33), predicted psychiatric admission when other social factors were adjusted for. Also, not having a co resident partner (1.27, 1.09–1.47) or children (1.58, 1.36–1.84) were independent predictors of psychiatric admission among depressed outpatients. Similarly, among depressed inpatients, low income, not owning a home, and being unpartnered predicted psychiatric admission. However, only being unpartnered remained a significant predictor (1.33, 1.03–1.72) after mutual adjustment for all social factors.

*Conclusions:* Those with higher socioeconomic position and those living with a partner seem to manage better with depression, avoiding psychiatric admission. Particularly material hardship seems to be detrimental among the depressed. This potentially causes a double burden to those with fewer material and family resources, as they have both a higher prevalence of depression and a higher risk for adverse outcomes.

## T1.4.4

### Trajectories of depression and anxiety in adolescents from 10 to 17 years: the TRAILS study

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#### Abstract

*Objectives:* The aim is to identify distinctive patterns of depression and anxiety symptoms over adolescence. We hypothesize a large stable group with low depression/anxiety, and smaller groups that increase/decrease in different patterns. Two main hypotheses in literature are that of anxiety preceding depression (developmentally) and that of depression and anxiety symptoms increasing together due to shared etiological factors.

*Methods:* A community sample of 2230 boys and girls was assessed biennially across a 5/6-year interval. The age range was 10-12 at baseline and 14-17 at the third follow-up. Symptom scores of depression and anxiety were analyzed with Growth Mixture Models. All analyses were stratified by gender.

*Results:* For both girls and boys, a three-class depression and a three-class anxiety trajectory model best fit the data. We found a large stable low-depression trajectory (girls: 80.6%, boys: 85.0%) and a large stable low-anxiety trajectory (girls: 91.6%, boys: 81.0%), confirming our hypothesis. Secondly, we found increasing and decreasing patterns for depression and anxiety. For depression, a trajectory with strong increase (girls: 9.3%) or stable moderate levels (boys: 7.1%) was identified, as well as a trajectory with a high-level start and decrease over adolescence (girls: 10.1%, boys: 6.2%). For girls only, a trajectory with steep increase in anxiety from middle adolescence on was found (2.6%), and for boys only, a trajectory with a steep decrease in early adolescence (8.3%). For both genders the third anxiety trajectory was a "transient anxiety trajectory", with an initial increase of anxiety symptoms between the ages of 10 and 13 and a gradual decrease of anxiety between the ages of 13 and 17 (girls: 4.1%, boys: 10.7%). The majority (52%) of the girls in the increasing anxiety trajectory concurrently increased in depression, whereas only 19% of girls in the increasing depression trajectory concurrently increased in anxiety. 22% of the girls in the "transient anxiety trajectory" followed the increasing trajectory of depression, and 51% the decreasing depression trajectory. In boys no increase in depression was found, therefore anxiety preceding depression could not be tested. A concurrent decrease in anxiety and depression was present in 34% of those on a decreasing trajectory.

*Conclusions:* In the general population, distinct gender-specific longitudinal patterns of symptom levels of anxiety and depression over adolescence exist and are interrelated. There was less support for anxiety preceding depression than for concurrent changes in anxiety and depression.

## T1.5.1

### **Long-term impact of weight change on blood pressure, lipids and metabolic control among patients with type 2 diabetes**

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#### **Abstract**

*Objectives:* Although weight loss in patients with type 2 diabetes is very important, the data on the effect of long-term weight change on blood pressure (BP), lipids and metabolic control among these patients are limited. The aim of this study was to assess the long-term impact of weight change on BP, plasma lipids and metabolic control among patients with type 2 diabetes.

*Methods:* During the mean (SD) follow-up period of 9.3 (3.4) (range 2-15) years, 9,205 patients with type 2 diabetes have been examined to determine changes in weight, BP, plasma lipids and glycaemic control. Their weight, BP, plasma lipids and HbA<sub>1c</sub> at the last clinic visit was compared with the initial visit data. The mean (SD) age of participants was 51.5 (10.6) years with a mean (SD) duration of diabetes of 6.4 (6.4) years at initial registration.

*Results:* The change in systolic and diastolic BP, fasting plasma glucose, HbA<sub>1c</sub> and cholesterol from baseline to last follow-up examination was significantly more favourable in those who lost weight during follow-up than those with stable weight. But loss of weight related to increase risk for hypertension, plasma lipids and worsen glycaemic control after adjustment for possible confounding factors such as age, gender, and BMI.

*Conclusions:* Although this population of Iranian type 2 diabetes had negligible weight change over mean 9.3 years. Weight loss in patients with type 2 diabetes was associated with significant reduction in BP, plasma lipids and HbA<sub>1c</sub>.



## T1.5.2

### **Life-course BMI trajectories and cardiovascular disease risk factors in mid-adulthood**

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#### **Abstract**

*Objective:* High BMI is associated with increased cardiovascular disease (CVD) risks. Trajectories of BMI have changed over time as younger generations experience the obesity epidemic at earlier life stages than older generations. Less is known about the extent to which life-course BMI trajectories are associated with adult outcomes. We aim to investigate associations between child-to-adult BMI trajectories and adult CVD risk factors.

*Methods:* We used the 1958 British birth cohort, all born in one week, March 1958, followed-up to adulthood. Measures considered included BMI, derived at multiple ages from childhood to adulthood, and CVD risk factors, including systolic and diastolic blood pressure, LDL- and HDL-cholesterol, triglyceride level at 45 years. We applied a joint model to repeated BMI measures and CVD risk factors, adopting a piecewise linear model to allow for distinct BMI slopes in childhood and adulthood. Correlations between unobserved characteristics for BMI trajectories and CVD risk factors were estimated.

*Results:* Given the BMI trajectories, BMI at 45 years was positively associated with blood pressure, LDL-cholesterol and triglycerides, and negatively associated with HDL-cholesterol. There was little association between BMI at 7 years and adult CVD risk factors, but the associations strengthened with increasing age. BMI slopes in childhood and adulthood were independently associated with risk factors for CVD, with stronger association for adult slope (i.e. rate of BMI gain).

*Conclusion:* These findings suggest that control of excessive weight gains throughout the life-course, child-to-adulthood, are likely to have a beneficial effect on adult CVD risks.

### T1.5.3

## Ten-year change of cardiovascular risk markers and life style habits among 30-70 year old Swedish men and women

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#### Abstract

*Objective:* To evaluate 10-year changes of cardiovascular risk markers, life style and self-reported health among adults.

*Methods:* Västerbotten Intervention Programme is ongoing in the county of Västerbotten, Northern Sweden, since 1985. All citizens are invited to a health screening at ages 30, 40, 50 and 60 years. During 2008 a pilot was added, targeting all 70 year olds living in three small municipalities. An oral glucose tolerance test, measurements of blood pressure, weight and height are done and participants answer a comprehensive questionnaire. In this report panels including yearly cohorts of VIP-participants in 1990-1999 who returned to a follow-up 10 years later are analyzed.

*Results:* Between 1990 and 2009 a total number of 126 296 health examinations were performed and 33 138 subjects participated twice 10 years apart. The prevalence of overweight and obesity was high already among 30-year olds (36.7% and 7% among men and 20.9% and 6.8% among women), and each 10-year period obesity increased with 5-10% until age 70, and most pronounced in the younger age-groups. Diabetes prevalence was around 1% at age 30 and then more than doubled during each decade and reached 15% and 19% among 70 years old men and women. Blood pressure levels increased rapidly from age 40, and 50% of 60-year olds and 70-80% of those who were 70 years old were hypertensive. Sedentary lifestyle decreased slightly and similarly between examinations in all panels, except among men aged 30 years and women aged 60 years at baseline, who became more sedentary. Smoking decreased in all groups. Self rated health decreased between examinations up to 60 years of age, but thereafter increased until age 70.

*Conclusion:* These longitudinal data reveal a high prevalence of obesity and a peak in the increase of obesity among young adults, and, in spite of decreasing sedentary lifestyle and smoking, this precedes the deterioration of other cardiovascular risk markers, such as diabetes and hypertension. Between ages 60 and 70 years, the cardiovascular risk profile seems to aggravate considerably, while self-reported health improves. Effective strategies for the prevention of weight gain among the young and prevention of cardiovascular risk factors from ages 40+ should be implemented.

## T1.5.4

### Incidence of type 2 diabetes in relation with adiposity

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#### Abstract

*Objective:* To investigate incidence of type 2 diabetes and its relationship with body mass index and adipokines in the MONICA-Catalonia cohort of men.

*Methods:* A general population random sample cardiovascular survey was carried out during 1986-88 in men aged 35 to 69 years (n=1011, response rate 76%). The cohort was re-examined in 1996-97 (n=904) with the same methods and team. Methods followed the WHO-MONICA protocol, plus the diabetes questionnaire of the Hispanic NHANES. Height and weight was measured with a roman balance. BMI calculated by Quetelet index. Blood pressure was measured with random zero mercury sphygmomanometers. 12-hour fasting venous blood sample analyzed for lipids and glucose with conventional enzymatic methods. HDL-cholesterol by manual precipitation. Adiponectin and insulin were measured in serum, kept frozen at -80°C, by X-Map luminex technology. Type-2 diabetes was defined as 12-hour fasting glucose  $\geq 7.0$  mmol/l or self-report of diabetes diagnosed or treated by a doctor. Incident diabetes defined as absence of these criteria at baseline but presence at re-examination. Prevalent diabetes excluded from the analysis. X2 test, ANOVA and Cox regression were calculated with SPSS-13©.

*Results:* Incidence of diabetes was 10.3 per %/year (95% CI, 8.4-12.7). Obese men had lower levels of adiponectin than overweight ( $25 < \text{BMI} < 30 \text{ kg/m}^2$ ) or lean ( $\text{BMI} < 25 \text{ kg/m}^2$ ) men ( $17.6 \pm 8.8$ ;  $20.1 \pm 9.4$ ;  $23.7 \pm 12.2 \mu\text{g/ml}$ ,  $p < 0.001$ ) respectively. Incidence of diabetes increased with BMI (age-adjusted HR=1.18, 95%CI, 1.12-1.25). The risk decreased but remained significant after adjusting for adipokines or for adipokines and metabolic syndrome variables.

*Conclusion:* Incidence of diabetes is high in Catalonia and BMI was a significant risk factor for diabetes independently of other factors.

## T1.6.1

### **Does type of milk feeding in infancy influence food choice in adult life? Results from the Hertfordshire Cohort Study**

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#### **Abstract**

*Objective:* To determine whether type of milk feeding in infancy is related to adult diet.

*Methods:* From 1911 to 1948, health visitors kept detailed records on all infants born in Hertfordshire, UK, including the type of milk they were fed. This was summarised at the end of the first year as breastfed only, breast & bottle-fed, or bottle-fed only. In 1998, 7106 men and women who were born between 1931 and 1939 were traced. 3217 of these men and women had their diets assessed by food frequency questionnaire. Their most important dietary pattern, identified using principal component analysis, was a 'prudent' pattern. This described compliance with healthy eating recommendations, such that high 'prudent' diet scores indicated diets characterised by frequent consumption of fruit, vegetables and wholemeal cereals.

*Results:* 60% (1937) of the men and women were breastfed in the first year, 31% (984) were breast & bottle-fed, and 9% (296) were bottle-fed. Type of milk feeding was not related to social class at birth, but was related to weight at birth and to growth in the first year; higher birthweight babies were more likely to be breastfed, but conditional weight gain in infancy was lower amongst breastfed infants (both  $P < 0.001$ ). Type of milk feeding in infancy was related to 'prudent' diet scores in adult life. Independent of birthweight, conditional weight gain in infancy, gender and age at leaving school, there was a graded association with diet scores across the 3 milk feeding groups ( $P = 0.008$ ); men and women who had been breastfed only had the highest mean 'prudent' diet score.

*Conclusion:* For the men and women in this cohort the type of milk they had been fed in infancy was related to their dietary choices as adults. Greater exposure to breastmilk was associated with 'healthier' diets in adult life.

## T1.6.2

### **Children's cognitive development: does breastfeeding really make a difference?**

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#### **Abstract**

*Objective:* As well as being associated with significant health benefits for children, breastfeeding is also associated with better cognitive outcomes. However, research in this area is beset by the difficulty of establishing the causality behind this relationship. Does breastfeeding /cause/ the more favourable outcomes observed in breastfed children? Or does the association arise because breastfeeding is more likely to be practised by mothers whose characteristics (higher social class, higher IQ, higher education) are themselves associated with better outcomes for children? There are practical and ethical problems in researching this question via randomised controlled trials; statistical attempts to study the relationship include twin studies and instrumental variables. Here, we use propensity score matching – a technique which social scientists have applied in many contexts, but which has not yet been applied to infant feeding.

*Methods:* Propensity score matching is an analytical technique which simulates an experimental situation by synthesising matched 'treatment' and 'control' samples and comparing outcomes between them. PSM is applied using data from the Avon Longitudinal Survey of Parents and Children (ALSPAC), a longitudinal study of around 12,000 children born in the Avon area during the early 1990s. ALSPAC contains measures of children's cognitive and academic outcomes from a few months to 16 years; detailed data on infant feeding practices from birth to over two years; and background variables including (crucially) information on parents' attitudes and intentions to breastfeeding prior to birth.

*Results:* Our findings suggest that a substantial part of the relationship between breastfeeding and cognitive development is explained by differences between women who do and do not breastfeed; however, even after controlling for these differences, a smaller but significant relationship between breastfeeding and cognitive outcomes remains; this relationship is evident through from infancy to age 16. Crucially, we find that this estimated relationship is stronger and more significant for children who are not breastfed, than for those who are.

*Conclusion:* Propensity score matching is a valuable analytical technique in the study of infant feeding and associated outcomes; our results indicate that breastfeeding has a causal effect on cognitive outcomes smaller than the raw association between the two, but significant. The potential gains for the types of children who currently would not typically be breastfed are likely to be larger than the gains for children who are currently likely to be breastfed; this finding has important implications for policy.

### T1.6.3

## Breastfeeding and the risks of asthma related symptoms in preschool children. The Generation R study

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### Abstract

*Objective:* Breastfeeding reduces the risk of childhood asthma. It is not clear whether this association is due to the duration or exclusivity of breastfeeding, and whether similar associations are present in early childhood. Our aim was to examine the associations of the duration of exclusivity of breastfeeding with the risks of asthma related symptoms during the first four years of life.

*Methods:* This study was embedded within the Generation R Study, a population-based prospective cohort study from early fetal life onwards in Rotterdam, The Netherlands. Information about breastfeeding (never, ever); and exclusivity (never, partial < 4 months, exclusive > 4 months) and asthma-related symptoms (wheezing and shortness of breath) were assessed using annual questionnaires until the age of 4 years. Adjusted logistic regression analyses were performed in 5,864 subjects.

*Results:* As compared to children who were not breastfed, those who were breastfed tended to have lower risks of wheezing and shortness of breath at all ages, and the strongest effect estimates were observed at the age of 4 years (OR 0.67 (95% CI: 0.42, 0.93) and OR 0.56 (95% CI: 0.38, 0.84), respectively). Stronger effect estimates were observed for frequent (> 4) episodes of wheezing and shortness of breath. Also, the duration of exclusive breastfeeding was associated with lower risks of wheezing and shortness of breath at the ages of 1 and 2 years (p-trends < 0.05). Similar but non-significant tendencies were observed at the ages of 3 and 4 years. Partial breastfeeding during the first 4 months had weaker protective effects.

*Conclusions:* Prolonged exclusive breastfeeding was associated with lower risk of frequent episodes of wheezing and shortness of breath in preschool children. Our findings support health policies strategies to promote prolonged duration of exclusive breastfeeding in industrialised countries.

## T2.1.1

### Characteristics of participants and non-participants and analyses of attrition in a youth cohort

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#### **Abstract**

*Objective:* The need for knowledge on non-participants has become of special importance in recent years. Over the years decreasing rates of participation have been reported in population based studies. Consequently, differences between participants and non-participants in distribution of the exposure to an outcome may be present. This questions the generalisability of the results. The objective in this study is therefore to present differences in participants and non-participants in a longitudinal youth cohort.

*Methods:* The Danish Youth Cohort (DYC) is a recently established longitudinal cohort focusing on development of health behaviours and health from adolescence into adulthood. A total of 12,498 students participated in first wave (mean age: 13.4 years). The participation rate for the Danish Youth Cohort 2005 was 63%. The sample of 12,498 adolescents represents 18.2% of the total population in the 7th grade in schools in Denmark. Participants born in 1991 (N=10,666) were compared with adolescents born in 1991 who did not participate in The Danish Youth Cohort (N=56,619) through registries in Statistics Denmark. Further, participants at baseline with follow-up in 2007 (N=3777) were compared with participants at baseline with no follow-up (N=8721).

*Results:* We found that non-participants were more likely to belong to lower socio-economic groups. Regarding attrition, we found that adolescents who at baseline had tried drinking one unit of alcohol (OR=0.87, CI: 0.81-0.94), had experienced being drunk (OR=0.85, CI: 0.77-0.94), and who smoked (OR=0.65, CI: 0.49-0.88) were less likely to have follow-up two years after baseline.

*Conclusion:* Our study confirms what already is known from many other previous study cohorts; that lower socio-economic groups are underrepresented in epidemiological studies. Methods to account for low participation rates in cohort studies have been introduced. Future analysis in the Danish Youth Cohort may overcome the rather low participation rate, and hereby the skewed sample by for example using multiple imputation. Regarding attrition, only 25% was followed up from baseline in 2005 to second follow-up in 2007. Loss to follow-up was only associated with drinking and smoking and all other factors were not associated with attrition. Therefore, when using data from the Danish Youth Cohort to investigate research question that require longitudinal data, these variable should be cautiously used and interpreted with care.

## T2.1.2

### Comparisons of methods for dealing with missing data in longitudinal studies

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#### **Abstract**

*Objective:* To compare three methods for dealing with missing data in a longitudinal study.

*Methods:* The data are from the first 3 waves (2002-2008) of the English Longitudinal Study of Ageing (ELSA), a panel study where individuals aged 50 and over are re-interviewed every two years. Using a random intercept model we want to explore the impact of Coronary Heart Disease (CHD) on Quality of Life (QoL) and seek for possible gender differences. The data consist of one incomplete dependent variables (QoL), three complete covariates (Age, Sex, CHD) and six incomplete covariates (marital status, wealth, depression, physical activity, smoking status and alcohol consumption). The sample size is 4,496 in wave1; 3,465 in wave2 and 3,031 in wave3. 1,998 participants had complete data on all variables at the 3 waves (44.4% of the sample in wave1). In order to find the best method to deal with missing data, we compare the performance of the Full Information Maximum Likelihood (FIML), Multiple Imputation under the normal model and the two-fold Fully Conditional Specification (FCS). For this purpose we set up a simulation study, which was based on the real data for 1,998 individuals, the reference population for a complete data analysis. Simulations were done using 1000 replications, in each of which 55.6% missing data was generated using random uniform numbers. Then each of the 1000 replications were analyzed as follows: 1) In Mplus to perform the FIML estimation, 2) In SAS, using the MI procedure to generate 5 imputed datasets under the normality assumption, 3) In Stata, to perform the two-fold FCS, generating 5 imputed datasets.

*Results:* All methods show small bias effects and that the standard error of the parameter estimates are very close to target values. However, the two-fold FCS estimates recover the population coefficients to an impressive extent.

*Conclusion:* The two-fold FCS is the best method to recover parameter estimates; nevertheless, given that the two-fold FCS is computationally intense and given the small gain over the estimates obtained using the FIML, researchers may prefer the FIML method.



## T2.1.3

### Exploring the protocol used to quantify biological analytes at UK Biobank and the influence of that protocol on the power of genetic association studies

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#### Abstract

*Objectives:* UK Biobank processes biological samples within 36 hours from collection. A certain proportion of the variation between subjects may be due to difference in processing time. If the contribution of delayed processing to the overall variation between subjects is not adjusted for, it can bias the results of association studies using biological analytes as measures of environmental determinants of disease.

*Methods:* The data are longitudinal and hierarchical. Two variance component analyses were carried out in MLwiN to determine the contribution of delayed processing to the overall variation between subjects and the rate of change in concentration. The impact of delayed processing on the power of a case-control study was investigated through simulations by comparing the sample size required to reach a power of 80% when analytes are measured at different times to that required when analytes are measured at the same time. When the samples are drawn manually to quantify analytes, a misclassification can occur so that an assay is carried out for the right analyte but for the wrong sample. The impact of such sample misclassification on the power was investigated through simulations.

*Results:* 16 of the 47 analytes have a contribution of processing delay  $\approx$  10% of the overall variation between subjects. For these 16 analytes a sample size increase between 10% and 160% is required to compensate for the reduction of power due to delayed processing. If the sample misclassification rates are respectively 10% , 5% and 1%, the sample size required has to be multiplied by 1.24, 1.11 and 1.05 to compensate for the power drop.

*Conclusion:* If cases and controls for a particular analysis are derived from different studies, it is critical that care is taken to ensure that protocols for processing delay were similar or to adjust for the difference between protocols. It is important to specify a limited delay in processing for analytes that are very sensitive to delayed assay. The error arising from manual misclassification of samples may have a high impact on power in the presence of well measured data as it will then be the main source of error. The findings are very important as they help toward providing well measured data and increasing the power of association studies which are two of the main goals of large scale biobanks.

## T2.1.4

### **Biobanking primary teeth collected from children within the Norwegian Mother and Child Cohort Study**

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#### **Abstract**

*Objective:* Primary teeth can be used as biomarkers of environmental exposures, nutrition and disease. The Norwegian Mother and Child Cohort Study (MoBa) is a national study comprising 100 000 pregnancies. Mother, father and child are included and data is collected using questionnaires and biological samples. Specific aetiological hypotheses may be tested by estimating the association between exposure and disease. MoBaTooth, a biobank of primary teeth, is established within MoBa to strengthen the biological material of the cohort study. The main objective of the study is to present and evaluate the registration of the biobank tooth collection.

*Methods:* An invitation to donate one or more primary teeth is sent to all MoBa-participants the year the child is seven years, during 2008-15. Received teeth are registered and stored in dry conditions at room temperature in polypropylene tubes marked with an identification code that can be linked to the MoBa-database. Information on tooth type, caries status, root length, crown attrition and internal discoloration is registered. The method of registering tooth variables was evaluated for inter- and intra individual variation (Kappa). The project is approved by all relevant authorities in Norway.

*Results:* A total of 1,803 teeth, representing 1,424 children, have been registered into the MoBaTooth database. Response rate was about 22%. Boys and girls were equally represented. The response time varied from a few days to more than one year, possibly because some children may not have shed teeth at seven years or may have discarded them before receiving the invitation letter. Inter- and intra-individual variation for registrations of variables showed that the intra-observer agreement (A1/A2) was good (Kappa values; 1 thru 0.68). The inter-observer agreement (A/B) varied between 1 thru 0.57, with moderate correlation for the variables tooth type and attrition. Altogether 46% were upper and 51% lower front teeth, 97% of the teeth had no carious lesion, 82% had more than 2/3 of the root resorbed and 62% of the teeth were markedly worn at the incisal edge. Five teeth had internal discoloration.

*Conclusion:* Method for registration in the biobank and intra- and inter-observer agreement were acceptable.

## T2.2.1

### Sex-specific effects of famine on the placental programming of hypertension

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#### Abstract

*Objective:* People who were small at birth are at increased risk of hypertension. This may reflect foetal programming by undernutrition. Foetal nutrition depends on the mother's diet and the placenta's ability to transport nutrients. Undernourished foetuses generally have small placentas, but in some circumstances they expand the placental surface. We hypothesized that maternal undernutrition, as a result of the Dutch wartime famine, would alter the way in which placental size and shape predicted later hypertension.

*Methods:* We studied 860 subjects born in one hospital in Amsterdam during 1943-47. Two diameters of the placental surface and placental thickness were recorded. At age around 58 years, 216 were taking anti-hypertensive medication. We examined the associations between placental size and later hypertension.

*Results:* Famine changed the association between placental size and shape and later hypertension among men. In those who were not exposed to famine in utero hypertension was associated with a small, oval-shaped placental surface. The odds ratio for hypertension was 0.83 (95% CI 0.70 to 1.00) for a 40 cm<sup>2</sup> increase in surface area. Among men who were exposed to famine in utero hypertension was associated with a large placental surface. The odds ratio for hypertension was 1.34 (95% CI 0.99 to 1.80) for a 40 cm<sup>2</sup> increase ( $p$  for interaction = 0.008). Among women, hypertension was not associated with placental size or shape.

*Conclusion:* Hypertension in men may be programmed by disruption of two normal processes of placental development. Famine exposure changes the placental programming in men, possibly because boys invest less in placental growth and depend more on the mother's current diet than on her metabolism.

## T2.2.2

### Birth weight, childhood body mass index and risk of coronary heart disease in adults

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<sup>9</sup>The NordNet project is a Nordic collaborative research project focusing on the role of prenatal and childhood growth in relation to the risk of cardiovascular disease using existing Nordic cohorts

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#### Abstract

**Objective:** To determine the individual and combined associations of birth weight and childhood body mass index (BMI) with the risk of coronary heart disease (CHD) in adulthood.

**Methods:** Birth weight and BMI at age seven years were available in 216,771 Danish and Finnish individuals born 1924-1976. Linkage to national registers for hospitalization and causes of death identified 8,805 CHD events during up to 33 years of follow-up (mean=19.63±7.84) after age 25 years. Analyses were conducted with Cox regression based on restricted cubic splines.

**Results:** Using the median birth weight of 3.4 kg as reference, a non-linear relation between birth weight and CHD was found. It was not significantly different between cohorts, or men and women, nor was the association altered by childhood BMI. For birth weights below 3.4 kg, the risk of CHD increased linearly and reached 1.28 (95% confidence interval [CI]: 1.13 to 1.44) at 2 kg. Above 3.4 kg the association weakened, and from about 4 kg there was virtually no association. BMI at age seven years was strongly associated with the risk of CHD and the relation was not altered by birth weight. Thus, birth weight and BMI at age seven contributed independently to the risk of CHD, with a 44% (95% CI: 30% to 59%) excess risk in individuals with a birth weight of 2.5 kg and a BMI of 17.7 kg/m<sup>2</sup> at age seven years.

**Conclusion:** Birth weights below 4 kg were inversely related to CHD risk in adulthood, but above this the association with CHD levelled off. The association was not altered by childhood BMI, nor was the association between BMI and CHD altered by birth weight. These findings suggest that little will be gained with regard to reducing the risk of CHD by increasing birth weights above 3.4 kg. On the other hand, treatment and prevention of childhood obesity should indeed be given high priority, especially in individuals with excess relative weight in childhood and a further increased disease risk because of a birth weight below the average.

## T2.2.3

### Childhood behaviour problems and health at midlife: 35 year follow-up of a Scottish birth cohort

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#### Abstract

*Objectives:* To describe long-term health outcomes associated with externalizing and internalizing childhood behaviour problems, reported by school teachers in a Scottish birth cohort.

*Methods:* The Aberdeen Children of the 1950s (ACONF) is a longitudinal study, sampling 12,500 children born 1951 to 1956 in the Aberdeen area, Scotland. Data were recorded at birth (i.e. socio-economic status of origin) and at age 6 to 12 (i.e. intelligence and behaviour problems). 7,183 cohort members completed a follow-up questionnaire aged 46 to 51 and reported on their health status, including details on physician-diagnosed conditions (long-term disease, diabetes, and high blood pressure), general health, well-being, weight, smoking, and alcohol intake.

*Results:* Two dimensions of externalizing (aggression and restlessness) and one of internalizing (anxiety) behaviour problems, assessed at age 6 to 12 by teacher ratings on the Rutter scale, were associated with health at age 46-51. Childhood aggression was related to an increased risk of long-term disease (males: odds ratio (OR) 1.15; 95% confidence interval (CI) 1.02 to 1.29; females: OR 1.26; CI 1.08 to 1.47), obesity (males: adjusted OR 1.16; CI 1.01 to 1.33; females: adjusted OR 1.38, CI 1.14 to 1.68), cigarette smoking (males: OR 1.20; CI 1.07 to 1.34; females: OR 1.17; CI 1.01 to 1.35), and lower well-being. Childhood restlessness was associated with the earlier initiation of smoking in men and women; smoking more cigarettes in women; and binge-drinking and a higher frequency of hangovers in men. Internalizing behaviour was related to a reduced the risk of ever smoking (males: OR 0.87; CI 0.80 to 0.95; females: OR 0.92; CI 0.85 to 0.99) and to healthier drinking patterns. In women but not men, internalizing problems also predicted a later age of smoking onset. Adjusting for socio-economic status of origin, childhood intelligence, education and age had negligible effects on these results.

*Conclusions:* Childhood behaviour problems are associated with a series of lifestyle choices and health related habits that at least partially explain links between problem behaviours in childhood and future mortality.

## T2.2.4

### Survival effects of prenatal famine exposure

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#### Abstract

*Objective:* Adverse intrauterine conditions are known to be associated with an increased risk of chronic diseases in adult life. Previously, we demonstrated that prenatal famine exposure increased the incidence of cardiovascular and metabolic diseases in adulthood. Here we examine the association between prenatal famine exposure and overall and cause specific adult mortality.

*Methods:* We studied adult survival among 1,991 term singletons born in Amsterdam around the time of the Dutch Famine by Cox proportional hazard models. We compared overall and cause specific adult mortality (between 18 and 63 years of age) among persons exposed to famine in late, mid, and early gestation to those unexposed to famine in utero. Since the associations may differ in the two sexes, we performed sex-specific analyses.

*Results:* 206 people (10%) had died by the end of follow-up in 2007. Forty-eight deaths were due to cardiovascular disease (23%) and ninety-three deaths were due to cancer (45%). Compared to unexposed women, women exposed to famine in early gestation had a significantly increased risk of overall adult mortality (HR 1.8, 95% CI 1.0 to 3.3) and cancer mortality (HR 2.3, 95% CI 1.1 to 4.8), and a higher risk of cardiovascular mortality (HR 3.2, 95% CI 1.0 to 10.8). Among these women there was also an increase in breast cancer mortality (HR 4.2, 95% CI 0.9 to 19.0). In men exposed to famine in early gestation these associations were HR 0.4 (95% CI 0.2 to 1.1) for overall adult mortality, HR 0.9 (95% CI 0.3 to 3.1) for cardiovascular mortality, and HR 0.3 (95% CI 0.0 to 1.8) for cancer mortality compared to unexposed men.

*Conclusion:* Women exposed to famine in early gestation are at an increased risk of overall adult and cancer mortality. These women have also higher risks of cardiovascular and breast cancer mortality compared to unexposed women. Men exposed to famine in early gestation have lower risks of overall adult and cancer mortality compared to unexposed men.

## T2.3.1

### Patterns of weight gain in pregnancy and their determinants: findings from the Avon Longitudinal Study of Parents and Children

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#### Abstract

*Objective:* To describe changes in weight gain during pregnancy and the associations of these with maternal characteristics.

*Methods:* We developed multilevel linear spline models for repeated antenatal weight measurements of 10,366 women in the Avon Longitudinal Study of Parents and Children (ALSPAC) who had singleton, term live births. The maternal characteristics considered as exposures were: age (<20, 20-25, 25-30, 30-35 and >35 years); height (cm); parity (0, 1, 2, >2); smoking (never, smoker but stopped during pregnancy, smoked throughout pregnancy); and education (CSE/vocational, 'O' Level, 'A' level, degree).

*Results:* We identified three distinct periods of weight change: 0-14 weeks, 14-36 weeks and >36 weeks. Average pre-pregnancy weight for a woman in the reference category of all exposures (aged 25-30, height 150cm, parity 0, never smoker, with 'O' levels) was 53.7kg, with average weight gain of 0.13kg/week (0-14 weeks), 0.48 kg/week (14-36 weeks) and 0.47 kg/week (>36 weeks). Pre-pregnancy weight was positively associated with parity and height, and inversely associated with maternal education and smoking. Parous women put on more weight during weeks 0-14 but less weight thereafter than nulliparous women (0.07 and 0.21kg/week less during weeks 14-36 and >36 respectively for those with parity 3 than those with parity 0). Older women put on more weight initially but less from 14 weeks onwards (0.14kg/week more during weeks 0-14 and 0.04 and 0.11 kg/week less during weeks 14-36 and >36 for those aged >35 than those aged 25-30), as did women with higher education (0.05kg/week more during weeks 0-14 and 0.02 kg/week less during weeks 14-36 and >36 for those with a degree than those with 'O' levels). Smokers put on 0.06kg/week more weight during week 0-14 but less weight thereafter (0.04kg/week and 0.08kg/week less during weeks 14-36 and after week 36) than never smokers.

*Conclusions:* These novel methods allowed associations between maternal characteristics and both pre-pregnancy weight and weight gain during pregnancy to be investigated. Being in the worst combination of categories (parity 3, age >35, degree, and smoker) was associated with weight gain of 0.17kg/week and 0.42kg/week less than the average (0.48kg/week and 0.47kg/week) during weeks 14-36 and >36.

## T2.3.2

### The contribution of overweight and obesity to the occurrence of adverse pregnancy outcomes: Population attributive risks for Amsterdam

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#### Abstract

*Objective:* Obesity contributes to morbidity and mortality, also during pregnancy. However, it is uncertain which proportion of adverse birth outcomes in a population is attributable to obesity, also in comparison to the often studied risk factor smoking during pregnancy. Therefore, the objective of this study was to assess, in a large prospective cohort, the population attributive fraction of overweight/obesity for small-for-gestational-age (SGA), large-for-gestational-age (LGA) infants and preterm birth (PTB) in Amsterdam, and make comparisons to smoking.

*Methods:* Data were used from a prospective multiethnic community-based cohort study of 8266 pregnancies from the Amsterdam Born Children and their Development (ABCD) study. Pre-pregnancy body mass index was self-reported by questionnaire (12th week of pregnancy). Exclusion criteria were multiple births and gestational age at delivery  $\leq 24$  weeks. The analysis included 7871 pregnancies. Binomial log-linear regression analyses were performed to estimate Rate Ratios (RRs) expressing the association between overweight/obesity and SGA, LGA, PTB ( $< 37$  weeks) and extremely PTB ( $< 32$  weeks), controlling for parity, maternal age, education level and smoking. Next, the RRs were used to estimate the population attributive fraction (PAF) for Amsterdam and for several ethnic groups separately.

*Results:* PAFs for overweight/obesity were: SGA -4,9%, LGA 15,3%, PTB 6,6% and extremely PTB 22,0%. In absolute terms, this corresponds to -47 SGA infants, 126 LGA infants, 35 PTB and 20 extremely PTB per year in Amsterdam. Except for SGA, these PAFs were higher than those for smoking (6,2%, -3,9%, 5,5% and 10,6%). The contribution of overweight/obesity to LGA and PTB was higher in Non-Western immigrant groups. For example, for LGA and extremely PTB the contributions were 23,8% and 32,9% for Moroccan and 26,4% and 35,7% for African-descent women.

*Conclusion:* Overweight/obesity is an important contributor to the occurrence of adverse pregnancy outcomes in Amsterdam, especially among non-Western immigrant groups. For most outcomes, these contributions are larger than those for smoking. Obesity prevention programs are required for young women, especially in immigrant groups, to prevent adverse pregnancy outcomes.



## T2.3.3

### Maternal age and blood pressure in different trimesters of pregnancy. The Generation R study

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#### Abstract

*Objectives:* Age is related to the risks of hypertension and cardiovascular disease. Maternal age might be a risk factor for the development of hypertensive disorders during pregnancy. We examined the associations of maternal age with systolic and diastolic blood pressure in different trimesters of pregnancy and the risks of pregnancy-induced hypertension and preeclampsia in a population-based prospective cohort study from early pregnancy onwards of 8623 mothers in the Netherlands.

*Methods:* Maternal age was assessed at enrolment. Systolic and diastolic blood pressures were measured in each trimester of pregnancy. Information about preeclampsia and pregnancy-induced hypertension was obtained from medical records. Information about potential socio-demographic variables and lifestyle related determinants was obtained from questionnaires. Multivariate linear and logistic regression analyses were used.

*Results:* Maternal age was not associated with first trimester systolic and diastolic blood pressure. In second and third trimester, we observed an inverse association between maternal age and systolic blood pressure (-0.86 mmHg (95% CI: -1.41,-0.30) and -0.57 mmHg (95% CI: -1.12,-0.02), per additional 10 maternal years, respectively). Older maternal age was associated with a higher third trimester diastolic blood pressure (0.47 mmHg (95%CI: 0.04, 0.90 per additional 10 maternal years). As compared to mothers aged 30 to 34.9 years, those aged 20 to 24.9 years had a lower risk of preeclampsia (odds ratio of 0.53 (95% CI: 0.32, 0.90)). Maternal age was not associated with the risk of pregnancy-induced hypertension.

*Conclusions:* Our results suggest that older maternal age is associated with lower second and third trimester systolic blood pressure, but higher third trimester diastolic blood pressure. Younger maternal age tends to be associated with lower risk of preeclampsia. The hemodynamic mechanisms underlying these associations should be further studied.

## T2.3.4

### Patterns of blood pressure change in pregnancy and their determinants: findings from the Avon Longitudinal Study of Parents and Children

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#### Abstract

*Objective:* To investigate the pattern of blood pressure (BP) change in normal pregnancy and the associations of risk factors for pre-eclampsia with variation in gestational BP change.

*Methods:* We examined repeat antenatal BP measurements (median 14 per woman) of 11,789 women in the Avon Longitudinal Study of Parents and Children (ALSPAC) who had a live birth between 37-44 weeks gestation with no evidence of pre-eclampsia or a previous diagnosis of hypertension. Linear spline random effects models for systolic BP (SBP) and diastolic BP (DBP) were developed, with gestational age as the exposure. The models had three knots (change in gradient and/or direction); at 18, 30 and 36 weeks gestation. Baseline was set at 8 weeks gestation. The maternal characteristics of age, parity, pre-pregnancy body mass index (BMI), smoking, education and number of foetuses were subsequently included together in the models as main effects and interactions with the splines.

*Results:* On average, both SBP and DBP decreased slowly from 8 until 18 weeks gestation, and then rose from 18 weeks onwards, with the rate increasing at 30 and then again 36 weeks. Pre-pregnancy BMI category was positively associated with SBP and DBP at 8 weeks gestation. The BP of obese women showed a smaller change between 18-30 weeks compared with women of a normal BMI, but rose more rapidly between 30-36 weeks and more slowly after 36 weeks. Twin pregnancies were associated with faster gains in BP from 30 weeks onwards compared with singleton pregnancies. Multiparas had lower BP at 8 weeks and a slower increase in DBP from 30 weeks and SBP from 36 weeks onwards than nulliparas. Women who smoked throughout pregnancy had lower BP at 8 weeks and throughout pregnancy than women who never smoked, while women who only smoked in the first trimester soon attained the same pattern of change as never smokers. Women aged over 35 years had higher BP at 8 weeks than 25-29 year olds and a more rapid rise in SBP from 36 weeks onwards.

*Conclusions:* The gestational BP nadir is 18 weeks, slightly earlier than the previously reported 20 weeks which defines pre-eclampsia. In general risk factors for pre-eclampsia were associated either with BP at the start of pregnancy (8 weeks) or patterns of BP change in later gestation.

## T2.4.1

### Maternal smoking as a risk factor of atherosclerosis in young adult male offspring

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#### Abstract

*Objectives:* Low birthweight contributes not only to metabolic syndrome in adult life but also to atherosclerosis. However, the mechanism underlying this association remains unknown. The main aim of the present study is an exploration of maternal risk factors which may be responsible for the relationship between birthweight and atherosclerosis risk in adulthood.

*Methods:* This retrospective cohort study was performed in 119 males aged 27-32 years whose mothers had been prospectively examined during pregnancy from the first trimester till delivery in one district in Warsaw in 1974-1977. The subjects' right CIMT was measured using ultrasound scan and components of metabolic syndrome (serum high density cholesterol, triglycerides, and fasting glucose levels, systolic and diastolic blood pressure, waist circumference) were measured in the out-patient clinic in 2000-2004. CIMT >0.6 mm was arbitrarily assumed as an indicator of atherosclerosis risk. Data concerning risk factors of low birth weight were taken from the clinical records that had been created during the prospective study.

*Results:* Among the considered risk factors of low birth weight (smoking during pregnancy, primiparity, hypertension in 2<sup>nd</sup> or 3<sup>rd</sup> trimester of pregnancy and prematurity), only maternal smoking during pregnancy and prematurity were statistically related to CIMT >0.6 mm. These effects remained significant after controlling for the presence of current metabolic syndrome in the offspring (OR for smoking during pregnancy – 3.71, 95% CI: 1.49-9.26, OR per one week of GA increase –0.80, 95% CI: 0.64-0.99). Although hypertension during pregnancy failed to show statistical significance, OR=9.81 indicated potential harmful effect as well.

*Conclusions:* Smoking during pregnancy and prematurity may contribute to atherosclerosis risk in young adult males.

## T2.4.2

### Maternal smoking during pregnancy, foetal growth and the risks of asthma-related symptoms in early childhood. The Generation R Study.

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#### Abstract

*Objective:* The independent effects of risk factors to which a foetus is exposed during pregnancy with asthma-related symptoms in childhood are not well established. Maternal smoking during pregnancy and foetal growth retardation might adversely affect early lung development and increase the risks of asthma-related symptoms. Our aim was to study the associations of maternal smoking during pregnancy and foetal growth measured in different periods of pregnancy with asthma-related symptoms in early childhood.

*Methods:* This study was conducted within the Generation R Study, a population based prospective cohort study from foetal life onwards in Rotterdam, The Netherlands. Foetal growth retardation was defined as a decrease of 1 gestational age adjusted standard deviation score in weight from 3<sup>rd</sup> trimester to birth. Maternal smoking during pregnancy (no, first trimester only, continued) and asthma-related symptoms (wheezing, lower respiratory tract infections (LRTI), doctor-diagnosed asthma) at the age of 1 to 3 years were assessed by questionnaires. Adjusted logistic regression analyses were performed in 2,805 subjects.

*Results:* Maternal first trimester only smoking was not associated with asthma-related symptoms in the children. Continued maternal smoking was associated with wheezing at the age of 1, 2 and 3 years (adjusted OR 1.49 (aOR (95% confidence interval: 1.14 to 19.4), aOR 1.51 (1.13, 2.10) and aOR 1.60 (1.09, 2.37) respectively) and with LRTI at the age of 2 years (aOR 1.69 (1.19, 2.41)) but not with doctor-diagnosed asthma. Foetal growth retardation was not associated with any asthma-related symptoms. Children of continued smoking mothers with foetal growth retardation had no higher risks of wheezing than children of smoking mothers without foetal growth retardation.

*Conclusions:* Continued maternal smoking during pregnancy is associated with increased risks of wheezing in early childhood. These associations are equal in children with and without foetal growth retardation.

## T2.4.3

### Moderate alcohol intake during pregnancy and risk of foetal death

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#### **Abstract**

*Objective:* The aim of this study was to assess the risk of foetal death and its compartments, spontaneous abortion and stillbirth, according to maternal alcohol consumption within the limits of normal social drinking.

*Methods:* Participants for this study were 92,719 pregnant women enrolled into the Danish National Birth Cohort between 1996 and 2002. These women participated in a computer-assisted telephone interview about e.g. lifestyle and reproductive history while pregnant or, in case of an early pregnancy loss subsequent to the termination of pregnancy. Outcome of pregnancy (spontaneous abortion, stillbirth, live birth, and other pregnancy outcomes) and gestational age at end of pregnancy were obtained through register linkage with the Civil Registration System and the National Discharge Registry. Data were analysed using Cox-regression models, taking the varying gestational age at recruitment into account.

*Results:* Fifty-five percent of the participants abstained from alcohol drinking during pregnancy and only 2.2 % reported to drink 4 or more drinks per week. Women who consumed even small amounts of alcohol during pregnancy had increased risk of foetal death within the first 16 weeks of pregnancy. The risk was especially increased for first trimester miscarriages, the adjusted hazard ratios were 1.05 (95% CI 0.94-1.18), 1.66 (95% CI 1.43-1.92), and 2.82 (95% CI 2.27-3.49) for consumption of ½-1½ drink per week, 2-3½ drinks per week, and 4 or more drinks per week, respectively. Maternal alcohol consumption within the limits of normal social drinking was not associated with spontaneous abortions later than the first 16 weeks of pregnancy or with stillbirth.

*Conclusion:* Even light drinking on a weekly basis during pregnancy increases the risk of spontaneous abortion substantially. The results indicate that the foetus is especially susceptible to alcohol early in pregnancy.

## T2.5.1

### **Poverty and income dynamics and their impact on mental health: Evidence from three cohorts followed over 20 years in the West of Scotland**

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#### **Abstract**

*Objective:* Income dynamics over time are likely to have a greater impact on mental health than income measured at one time point. However, key determinants of income – employment, marriage/cohabitation and parenting – may also affect mental health. This paper investigates the effect of income change on mental health after adjustment for other key life changes.

*Methods:* Data are employed from the West of Scotland Twenty-07 Study; 4,510 respondents, in three cohorts aged 15, 35 and 55 at baseline in 1987/88, have been followed up four times, most recently in 2007/08. For working-age respondents, household income, measured at each wave, was adjusted for family composition and inflation and used to investigate income change (greater than 30%), controlling for income level, and movements in and out of poverty (defined as 60% median income). Hierarchical repeated-measures models were produced separately for anxiety and depression cases (score of 8+ on subscales of the Hospital Anxiety and Depression Scale) against between-wave income change, or movements in and out of poverty, controlling for gender, period and cohort. Changes in employment, marriage/cohabiting and parenting were then added to the models to assess whether income had an independent effect.

*Results:* Preliminary findings suggest that for anxiety, those staying poor between waves, leaving poverty or moving into it, all had raised odds for being a case, but only entering poverty was statistically significant (OR 1.55, 95%CI:1.07-2.24) after controlling for other key life changes. For depression, after full adjustment, those staying poor had an odds ratio of 1.50 (CI:1.03-2.20), those leaving poverty 1.54 (CI:1.09-2.19) and those moving into poverty 1.67 (CI:1.18-2.35) in comparison to those not experiencing poverty between waves. The income change variable was not significantly related to depression or anxiety in the fully adjusted models. Gender differences were evident, with women more likely to experience anxiety when moving into poverty and depression when staying poor between waves. Depression was more likely for men than women when leaving poverty.

*Conclusion:* Poverty, rather than income, dynamics was associated with adverse mental health outcomes. This was true of both leaving as well as entering poverty; a finding that requires further investigation.

## T2.5.2

### **Inequalities in later life depression: An empirical investigation of the materialist, psychosocial and behavioural hypotheses**

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#### **Abstract**

*Objectives:* To empirically compare the materialist, psychosocial and behavioural theoretical mechanisms of socio-economic variation and estimate the relative influence of early life and current socioeconomic position (SEP) on depression.

*Methods:* We use data from the four waves (2002 – 2009, n = 11,391) of the English Longitudinal Study of Ageing (ELSA), a nationally representative multi-purpose sample of the population aged 50 and over living in England. We developed latent indices of SEP, material resources, perceived control, perceived social capital and health related behaviour from observed variables available in ELSA. The depression outcome was modelled with a latent growth curve model, with latent random effects for the initial level (intercept) and change over time (slope). A path analytic model that enabled us to estimate the indirect effects of SEP on depression was combined with the latent curve model within the generalised latent variable modelling framework. We included participants with non ignorable missing data in the analysis, and modelled this with the Diggle – Kenward selection model. All models were estimated with the robust maximum likelihood estimator, with adaptive quadrature in Mplus 6.

*Results:* After adjustment for covariates such as gender, age, cognitive ability, retirement status, marital status and presence of chronic illness, social capital and perceived control had the most prominent mediating role on the association between SEP and depression, although their mediating effects were partially explained by the availability of material resources. Material resources and health related lifestyle were also – albeit less – influential. We did not observe a direct effect of early life SEP on depression, but the indirect effect via current SEP was substantial.

*Conclusion:* The psychosocial pathway had the most prominent mediating role on the association between SEP and later life depression, a finding that provides further evidence for the social stress hypothesis. However, large part of its effect was explained by the availability of material resources. It appears therefore that from a policy perspective, population interventions to reduce later life depression differentials and thus improve the overall mental health of the older population should be primarily targeted on material resources.

## T2.5.3

### **Influence of racism and context on ethnic differences in adolescent mental health trajectories: the Determinants of Adolescent Social well-being and Health (DASH) study**

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#### **Abstract**

*Objective:* There is some evidence that ethnic density in neighbourhoods may buffer the adverse effect of racism on mental health in adulthood. We previously reported generally better mental health for ethnic minority groups in early adolescence, despite socio-economic disadvantage. Here we investigate whether this resilience persists in late adolescence, and the interplay between racism and the context of schools and neighbourhoods.

*Methods:* Repeated measures of psychological well-being (Total Difficulties Score (TDS) from Goodman's Strength and Difficulties Questionnaire), racism and characteristics of individuals (socio-economic position and family type), schools (n=49) and neighbourhoods (n=3495) were obtained for 4744 adolescents aged 11-17, surveyed at two waves (2003, 2005/06). Ethnic groups included: White-UK (n=870); Mixed-Black Caribbean/White (n=260); Indian (n=417); Pakistani (n=295); Bangladeshi (n=149); Black Caribbean (n=770); Nigerian/Ghanaian (n=501); Other-African (n=380); Other ethnicities (n=1102). Context measures included neighbourhood White-ethnic density and deprivation, school White-ethnic density, academic performance, and free school-meals.

*Results:* The prevalence of racism increased between wave 1 (girls: 18%; boys: 19%) and wave 2 (girls: 29%; boys: 27%). Ethnic minority adolescents reported better mental health (lower TDS) throughout adolescence relative to White-UK peers, particularly among Nigerian/Ghanaian boys (coefficient (95% CI): -2.27 (-2.97, -1.58) and Indian girls: -1.74 (-2.54, -0.94), adjusted for age, socio-economic position, racism and context. TDS improved throughout adolescence for boys. Effects of racism were not ethnic specific, but associated with higher TDS for boys: 1.50 (1.21, 1.79) and girls: 1.88 (1.54, 2.22) through adolescence. Compared to White-UK peers, ethnic minority adolescents were disproportionately situated in less well-performing schools with higher rates of free-meals and lower White-ethnic densities, and more deprived neighbourhoods with lower White-ethnic densities. No variation in TDS was observed between schools or neighbourhoods. Context had little effect on TDS directly, or through modification of the association between racism and TDS.

*Conclusions:* Poorer ethnic-specific mental health patterns among adults do not appear to emerge during adolescence. Boys from all ethnic minority groups and Indian girls reported better mental health. Racism was associated with poorer mental health for all ethnic groups. Targeting intervention in adolescence may be a critical opportunity for preventing ethnic differences in mental health in later life.



## **T2.5.4**

### **Adult emotional and behavioural outcomes of children with a public care experience from the BCS70 cohort**

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#### **Abstract**

*Objective:* Longitudinal data from the 1970 British Cohort Study were used to examine the long-term, adult outcomes of those who as children were placed in public care.

*Methods:* Two estimation models were employed to determine whether public care and placement patterns were associated with adult psychosocial outcomes. Seven emotional and behavioural outcomes measured at age 30 were considered, including depression, life dissatisfaction, self-efficacy, alcohol problems, smoking, drug abuse, and criminal convictions.

*Results:* The analyses examining public care status in childhood and subsequent adult outcomes at age 30 revealed a significant association between public care status and adult maladjustment on five of the seven outcomes. Adult outcomes tended to vary with cohort member's placement patterns, including age at placement, number of placements, and type of care.

*Conclusion:* Overall, the study findings suggest an association between admission to public care and adult well being, which remained significant after adjusting for childhood confounding factors.

## T2.6.1

### Predictors of childhood physical activity: The Gateshead Millennium Study

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#### Abstract

*Objective:* With a number of studies suggesting associations between early life influences and later chronic disease risk, it has been suggested that associations between early growth and later physical activity (PA) may be a mediator. However, conflicting evidence exists for association between birth weight and childhood PA levels. In addition, it is important to know what other, potentially modifiable, factors may influence PA in children given its' association with childhood and later adiposity. The objective of this analysis was to use the Gateshead Millennium Study (GMS) to identify predictors of childhood PA levels.

*Methods:* The GMS is a population based cohort of 1029 infants born in 1999-2000 in Gateshead in Northern England. Throughout infancy and early childhood, detailed information was collected. Assessments at age 9 years included body composition, objective measures of habitual PA (using Actigraph GT1M accelerometers during waking hours) and the child's food and PA environment. Mean total volumes of PA (accelerometer count per minute, cpm) and moderate-vigorous intensity PA (MVPA), and the percentage of time spent in sedentary behaviour (%SB) were quantified and related to potential predictors using linear regression.

*Results:* Data were collected on 508 children, aged 9 years. Highly significant differences were seen in all three outcome variables between males and females ( $p < 0.001$ ). No significant associations were seen with birth weight, gestational age, being born preterm or with Townsend socioeconomic status. Having ever been breast fed was significantly associated with a decreased %SB, which remained after adjustment for sex and socioeconomic status ( $p = 0.03$ ). Increased paternal age was associated with significant increases in %SB and decreases in cpm and MVPA ( $p < 0.033$ ). Significant associations with BMI at 9 years were in the expected directions. Increased time spent in sports clubs was significantly associated with decreased %SB ( $p = 0.02$ ) and increased MVPA ( $p = 0.01$ ), but not cpm ( $p = 0.13$ ).

*Conclusion:* Although we found no evidence for an effect of birth weight on PA, there were associations with having ever been breast fed which go beyond confounding by socioeconomic status. Having an older father appeared to have a negative impact on the child's PA levels, while participation in sports clubs increases time spent in MVPA, but not cpm.

## T2.6.2

### Physical (in)activity throughout the life-course: impact on adult blood pressure in the 1958 British cohort

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#### Abstract

*Objective:* High blood pressure manifests mainly in adulthood but is thought to be influenced by factors, such as physical (in)-activity, acting throughout life. However, long-term effects of physical (in)-activity (PA) on adult blood pressure (BP) remain unclear. Objectives of this study are to examine: (1) relationships of PA and TV viewing at different life-stages with adult BP, (2) whether the effect of PA on BP is accumulative from early to mid adulthood, and (3) if these associations are independent of BMI.

*Methods:* Data were from the 1958 British birth cohort (n=9,927), including all born in England, Wales and Scotland in 1958 with follow-up through to adulthood. We analysed PA and TV viewing from early to mid-adulthood (23, 33, 42 and 45y) and BP at 45y. Linear regression was undertaken for systolic, diastolic and pulse pressure and logistic regression for hypertension.

*Results:* There was a trend of increasing BP with increasing frequency of TV viewing. For example, for TV viewing at 45y, one level increase on a 5 category scale (e.g., from 1-2 to 2-3h/day) was associated with a 1.1mmHg increase in systolic BP. Similar trends were observed for diastolic, pulse pressure and hypertension. Relationships were modest between PA and BP demonstrating no evidence of a trend across frequency categories. The main distinction was seen between active and non-active groups: e.g. adjusted for gender only, systolic BP was 1.5mmHg higher for individuals who were non-active at 23y vs. those who were active. In addition, there was evidence that the association between PA/TV-viewing and BP was accumulative from earlier adulthood (i.e. 23y). While findings attenuated slightly when adjusted for covariates, such as diet and socio-economic position, the strength of associations diminished when adjusted for concurrent BMI.

*Conclusion:* PA and TV viewing in adulthood were associated with BP, with evidence of additional contributions of earlier life-stages. BMI and other covariates appeared to mediate associations of PA and TV viewing with BP. The work is supported by the Public Health Research Consortium, funded by the Department of Health Policy Research Programme. Views expressed are not necessarily those of the funder.

## T2.6.3

### Physical activity and TV viewing over 20y in adulthood: associations with adult lipids levels in the 1958 British birth cohort

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#### **Abstract**

*Objectives:* Effects of physical activity (PA) and TV viewing on blood lipids are well-documented. Less is known about the long-term association of physical (in)activity with lipid levels. This study aims to investigate associations of PA and TV viewing between 23y and 45y with lipid levels in mid-adulthood.

*Methods:* Data from early to mid-adulthood in the 1958 British birth cohort (n=7824) were examined. Using linear regression, we analysed prospectively reported frequency of PA (23, 33, 42 and 45y) and TV viewing (23 and 45y) in relation to total cholesterol, triglycerides, LDL (LDL-C) and HDL cholesterol (HDL-C) at 45y.

*Results:* In general, greater frequency of PA and lower duration of TV viewing were associated with a better lipids profile in simple analyses: e.g., adjusted for gender only, PA >4 days/week vs no exercise at 42y was associated with higher HDL-C (0.05 mmol/L,  $p<0.001$ ) and one level increase in PA (e.g., from 1 to 2-3 days/week) with 2% lower triglycerides among men ( $p<0.001$ ). For TV viewing at 45y, one level increase (e.g., from 1-2 to 2-3h/day) was associated with a 0.02 mmol/L lower HDL-C and 6% higher triglycerides ( $p<0.001$ ). Less consistent trends were seen for total cholesterol and LDL-C. When 33 and 42y PA were examined simultaneously, there was some additional contribution of both ages to lipid levels at 45y; similarly, there was a contribution of TV viewing at both 23 and 45y. When adjusted for covariates, the strength of associations with lipids for both PA and TV were substantially reduced, mainly due to lifestyle factors.

*Conclusion:* PA and TV viewing were associated with lipid levels in mid-adulthood, particularly HDL-C and triglycerides. Importantly however, associations of PA and TV viewing with lipids were largely due to other lifestyle factors. The work is supported by the Public Health Research Consortium, funded by the Department of Health Policy Research Programme. Views expressed are not necessarily those of the funder.

## T2.6.4

### Longitudinal changes in children's body composition and physical activity: The Gateshead Millennium Study

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#### Abstract

*Objective:* Despite a global increase in childhood obesity, few studies of longitudinal changes in physical activity (PA) and body composition in children exist. The objective of this analysis was to use the Gateshead Millennium Study (GMS) to identify how change in body composition and change in physical activity in children might be related.

*Methods:* The GMS is a population based cohort of 1029 children born in 1999-2000 in Gateshead in northern England. Throughout infancy and early childhood, detailed information was collected. Assessments at age 7 and 9 years included objective measures of habitual PA (using Actigraph GT1M accelerometers during waking hours) and body composition – height, weight, waist circumference and bioimpedance. Four physical activity variables were calculated from accelerometry: changes in mean total volume of PA (mean accelerometer count per minute, cpm), minutes of moderate-vigorous intensity PA (MVPA), and the percentage of time spent in MVPA and sedentary behaviour (% MVPA, % SB). Fat and lean masses were calculated from impedance values and published age and sex-specific hydration constants. Change in waist circumference, BMI, fat mass and lean mass were calculated, and related to physical activity variables using linear regression, corrected for baseline variables.

*Results:* Repeat data were available for 403 children. There were significant increases in all body composition variables and % SB, and decreases in mean cpm, MVPA minutes and % MVPA. Change in BMI was significantly and negatively associated with change in MVPA minutes. Change in waist circumference was significantly and negatively associated with change in % MVPA. Change in lean mass was significantly and negatively associated with both MVPA minutes and % MVPA. Change in fat mass was significantly associated with sex, with girls showing an increased change in fat mass, negatively associated with MVPA minutes and % MVPA, and positively associated with % SB.

*Conclusion:* The data present evidence for the protective effect of MVPA on increasing fat mass in children, and the detrimental effects of SB. The results should strengthen public health efforts to increase MVPA in primary-age children. Further longitudinal work is needed to see if these changes continue into adolescence.

### **T3.1.1**

## **Cognitive ability in childhood and cognitive decline in mid-life: evidence from two British longitudinal birth cohort studies**

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### **Abstract**

*Objective:* To examine factors influencing cognitive change from childhood to midlife.

*Methods:* Multivariable regression models were used to analyse data from two British longitudinal, population-based birth cohort studies of 1,907 men and women born in 1946 (NSHD) and 8,369 men and women born in 1958 (NCDS). Childhood cognition was measured by the NFER General Ability Test at 11 years. Cognition in midlife was tested by Word Recall, Animal Naming and Letter Cancellation at age 53 in NSHD and at age 50 in NCDS. These analyses focus on memory. Residuals obtained from regressions of memory score in childhood cognitive ability were used as the outcome.

*Results:* In both cohorts better memory than predicted by childhood cognitive ability were associated with female sex, greater educational attainment (although there were no additional effects of social class), and physical exercise. In the 1958 cohort worse memory than predicted by childhood cognitive ability was associated with alcohol dependency, but in both cohorts there were no independent effects of BMI.

In separate analyses there was no effect of being predominantly a smoker on cognitive change in the 1946 cohort, but ex-smokers in the 1958 cohort were more likely to have better memory than predicted than non-smokers. Although there were no effects of self-rated general health in the 1958 cohort, there was a negative effect of depressive symptoms.

*Conclusion:* The most important independent positive factors predicting cognitive change from childhood to midlife are educational attainment and physical exercise. Women show better memory than predicted by their childhood cognitive ability than men. On the other hand, while several studies suggest that moderate alcohol consumption is protective of cognitive ageing, alcohol dependency appears to have detrimental effects.

## **T3.1.2**

### **Fluctuating asymmetry associated with cognition across 76 years: The Lothian Birth Cohort 1921 study**

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#### **Abstract**

*Objectives:* To examine whether developmental imprecision is an early biological marker of lifecourse cognitive ageing.

*Methods:* We assessed bodily fluctuating asymmetry (FA) based on digital images and measurements taken in 173 members of the Lothian Birth Cohort 1921, assessed at age 87. In a series of linear regression models (controlling for MMSE and parental status), this marker of early developmental precision related to Moray House IQ scores across the 76 year period from age 11, 79, 83, and 87, and to old-age scores on the Raven intelligence, Letter-number sequencing and Logical Memory.

*Results:* Lower FA was significantly associated with better verbal, spatial, and abstract reasoning at age 87, and to intelligence tested 76 years earlier. The effect size was constant at around .17 across this time span. No main effects of sex, parental social status or measures of growth such as height were found for FA, and the significant influence of FA on ability did not interact with these independent effects.

*Conclusions:* Developmental precision measured by FA appears to be a persistent archaeological marker of early development, and an indicator of brain and cognitive reserve. Early developmental precision may be a basis of the “common cause” of cognitive and bodily aging, indicating that a determinant of cognitive aging can be studied and perhaps modified in youth.

### T3.1.3

## Associations between white matter lesion intensity and cognitive abilities in youth and old age in The Disconnected Mind Study

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### Abstract

*Objective:* We investigate how the distribution, extent and severity of white matter lesions (WML) relates to measures of cognitive ability obtained in youth and old age in the Lothian Birth Cohort 1936 (LBC1936).

*Methods:* The study population was the first 140 participants of the LBC1936, none of whom showed signs of dementia or MCI (MMSE > 23). All underwent structural MRI, specifically T<sub>2</sub>-, T<sub>2</sub>\*-, T1- and FLAIR-weighted sequences on a GE Signa LX 1.5T scanner. Their IQ was tested at age 11 in June 1947 using the Moray House Test (MHT) No. 12 of verbal reasoning. Sixty years later (2004-07) they took a battery of mental tests, including the same version of the MHT, six subtests of the Wechsler Adult Intelligence Scale III, three subtests of the Wechsler Memory Scale III, and measures of information processing speed (simple and 4-choice reaction time, and inspection time). The MR images were pre-processed using FSL tools and the WMLs were segmented using a novel multispectral method developed in-house – MCMxxxVI – and subdivided into intense (iWMLs) and less intense (liWMLs) lesions.

*Results:* The distribution of iWMLs was predominant in frontal regions while liWMLs were mainly located posteriorly. The maximum frequency of iWMLs was located in the periventricular regions adjacent to the frontal horns of the lateral ventricles, while the maximum frequency of liWMLs spreads between the midbody of the corpus callosum and the superior and posterior corona radiata. Both were highly correlated ( $r = 0.70$ ), indicating that subjects with high iWML load also had high liWML load. WMLs were significantly associated with various cognitive abilities, but relationships were stronger for iWMLs than liWMLs in young and old age, e.g. age11 IQ  $r = 0.26$  vs.  $r = 0.21$  ( $p < 0.01$ ) and age70 IQ  $r = 0.38$  vs.  $0.30$  ( $p < 0.001$ ). iWMLs relate to cognition independent of liWMLs, but the reverse was not true.

*Conclusions:* Our findings support the central role of white matter for higher cognitive abilities and the “frontal ageing” hypothesis, which predicts that age-related brain change would selectively impact frontal regions. They also show that there are relationships between early life cognitive ability and disease burden in old age.



### T3.1.4

## The relationship between late-life cognitive decline and brain reserve: a multi-state modelling approach.

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#### Abstract

*Objective:* There is great interest on the impact of modifiable factors such as education and lifestyle upon the progression of cognitive decline and the development of dementia. This is commonly referred to as the brain reserve hypothesis. The main premise of the model is that individual differences result in different cognitive performances in persons with similar underlying neuropathology. Factors commonly associated with reserve include late-life social engagement, educational attainment, and adult occupation. The aim of this analysis was to study the association between brain reserve and cognitive change in a population-based cohort of older persons from five sites across England and Wales.

*Methods:* Data came from 13,004 participants of the Medical Research Council Cognitive Function and Ageing Study who were aged 65 years and over at the start of the study in 1991. Cognition was assessed at multiple waves over a 16 year follow-up period using the Mini-Mental State Examination. Subjects were grouped into four cognitive states (no impairment, mild impairment, moderate impairment, and severe impairment). Brain reserve was assessed as a composite measure of education, occupation, and current social engagement. A multi-state model was used to test the effect of brain reserve on cognitive transitions.

*Results:* Hazard ratios for brain reserve showed significant differences between those in the upper compared to the lower tertile with brain reserve protecting against transitions from no impairment-mild impairment (HR 0.6 (0.5, 0.7)) and from no impairment-death (0.8 (0.7, 0.9)), increasing the chance of a back transition from mild impairment-no impairment (2.9 (1.3, 6.3)), but increasing the risk of transitioning from severe impairment-death (1.3 (1.1, 1.4)).

*Conclusion:* These results support a brain reserve hypothesis with greater education, socioeconomic status, and social engagement in old-age protecting against cognitive decline. Whilst it takes longer for those with greater reserve to reach a severely impaired cognitive state, once this happens they are more likely to have a faster transition to death.

### T3.2.1

## Parametric and nonparametric approaches to model growth in infancy using comparative data from two birth cohorts

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### Abstract

*Objectives:* Growth models aim at summarising individual growth data into a reduced number of parameters. These are then used to compare growth patterns between individuals or populations. Analyses of this type of data often involve parametric linear mixed models, despite their rigid algebraic form often leading to poor fits of individual growth curves data. Recently semi-parametric generalizations of these models have been proposed. These allow a common non-parametric specification of the shape of the growth trajectory (e.g. via regression splines) while individual departures from that shape are modelled via normally distributed random effects. The implementation of these models is however not as straightforward as that of linear mixed models.

Our objective is to compare the performance of parametric and semi-parametric mixed models in analyses of early weight growth using data from two comparative birth cohorts.

*Methods:* Data from two Southern European birth cohorts will be used: the Geração XXI (GXXI), based in Portugal, and the web-based Italian NINFEA study. Performance of parametric and semi-parametric model are compared. The effect of time-fixed exposures (i.e. gender, maternal smoking status during pregnancy) are also considered.

*Results:* The two studies vary in terms of ages and numbers of growth measurements, and of data completeness and quality. Preliminary analyses show some difficulties in fitting the semi-parametric model when the growth measurements are sparse. However the semi-parametric model suggested by Beath and Cole leads to parameters which are more easily interpretable. The extension of the parametric and semi-parametric models to include a time-varying exposure is undergoing as well as the examination of the contribution of confounding factors and data completeness on these results.

*Conclusions:* In comparison with standard parametric approaches, more flexible semi-parametric models appear to be more appropriate to describe the complex process that characterises infant growth, in particular to study its determinants. User friendly routines were used for their implementation.

## T3.2.2

### Age and body mass index at adiposity peak and adiposity rebound and adult metabolic outcomes in the Northern Finland Birth Cohort 1966

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#### Abstract

**Objectives:** To evaluate associations between age and body mass index (BMI) at infant adiposity peak (AP) and childhood adiposity rebound (AR) in relation to adult metabolic outcomes.

**Methods:** Age and BMI at AP and AR were derived from random effects models fitted at >0-1.5 years and >1.5-13 years (N=3,265 infants and N=4,121 children with minimum 3 measurements per age window). Metabolic outcomes at age 31 years included BMI, waist circumference (WC), HDL, LDL and total cholesterol, triglycerides, glucose, insulin, systolic and diastolic blood pressure (SBP, DBP) and metabolic syndrome (MetS). Associations were analysed by fitting regression models with adjustments for confounding factors, after replacing missing values using the multiple imputation method.

**Results:** Average age and BMI at AP and AR were 9 months, 18.1 kg/m<sup>2</sup> and 5.7 years, 15.4 kg/m<sup>2</sup>, respectively. Age and BMI at AP were positively associated with adult BMI and WC, independently of birth weight and infant height growth. 2SD (2.19 kg/m<sup>2</sup>) higher BMI at AP associated with 4.7% (95%CI: 3.5-5.8%), i.e. 1.2 kg/m<sup>2</sup>, higher BMI at 31 years. Later age at AR associated strongly with a better metabolic profile at age 31 years (p<0.0001 for all outcomes). BMI and insulin were about 14% lower, WC and triglycerides about 10% lower, and the odds of MetS 74% (95% CI: 72-75%) lower per 2SD (1.86 years) higher age at AR. BMI at AR had generally weaker but still highly significant positive association with metabolic outcomes (negative with HDL). These associations strengthened after adjustment for infant height growth and BMI at AP. 2SD (2.20 kg/m<sup>2</sup>) higher BMI at AR associated with 20.3% (95%CI: 18.8-21.8%), i.e. 5.0 kg/m<sup>2</sup>, higher BMI at 31 years. When age and BMI at AR were both included in the same model, the associations between BMI at AR and metabolic outcomes weakened, but only a slight attenuation was observed for age at AR.

**Conclusions:** Age and BMI at infant AP were associated with adult adiposity but not with other metabolic outcomes. Earlier timing of AR was a risk factor of an adverse metabolic profile, independently of early growth or BMI at AR.

### T3.2.3

## Periods of infant growth associate with flow mediated dilatation in adulthood. The Helsinki Study of Very Low Birth Weight Adults

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#### Abstract

**Objectives:** As adults those with a very low birth weight (VLBW, < 1500 g) have been found to express a higher blood pressure and higher fasting insulin. Infant growth may associate with later cardiovascular disease. Within the Helsinki Study of VLBW Adults, we investigated weight gain in infancy and its associations with a sign of vascular health in adulthood.

**Methods:** We measured brachial artery flow mediated dilatation (FMD) in 92 adults with VLBW and in 66 age- and sex-matched term-borns. Birth weight means (and SDs) were 1140 (210) and 3662 (470) grams, gestational ages 29.7 (2.4) and 40.2 (1.1) weeks. Age at assessment was 18 to 27 years. A low FMD is associated with early atherosclerosis. We analyzed the effects of growth separately in the groups with age and sex adjusted multiple regression models predicting FMD.

**Results:** Among the VLBW young adults, baseline diameter of the brachial artery was 3.28 mm (SD, 0.56) in contrast to 3.49 mm (0.64) among the term born (P=0.003). FMD was 6.9 % (3.9) in VLBW and 5.8 % (3.3) in term subjects (P=0.06). Within the VLBW group a higher FMD was associated with faster weight gain during the 2 first weeks of life (1.1, percent units per each 100 g weight gain, 95 % CI: 0.2 to 2.0). Association was positive also at 5 weeks of life and at 72 postmenstrual weeks but negative at 60 postmenstrual weeks.

**Conclusions:** Although VLBW birth is associated with cardiovascular disease risk factors, it was not associated with a lower FMD that would be a sign of impaired vascular health. In our cohort faster gain in weight was either a benefit or a disbenefit for adult vascular health, depending on the period of interest.

## T3.2.4

### Growth pattern in childhood and attributes of metabolic disorders in adult life in a high birth weight population

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#### Abstract

*Background:* Low birth weight and rapid childhood growth has been associated with metabolic disorders in adult life. Tracking this association in populations of relatively high birth weight has been minimally addressed.

*Methods:* 2566 Icelanders born in Reykjavik (1917-1935) were medically examined during recruitment (1967-1991) into the Icelandic Heart Association longitudinal Reykjavik study. Based on examination at recruitment, individual attributes of metabolic disorders were assessed according to WHO guidelines. Size at birth and at age 8-13 years were extracted from National Registries. Growth patterns of individuals with attributes of metabolic disorders were compared to normal weight, non-hypertensive individuals with normal blood lipids and glucose values (reference-group). Using piece wise linear assumptions, changes in childhood weight were calculated between 8-10 and 10-13 years ( $\Delta\text{weight}/\text{year}=\text{weight-velocity}$ ) and the birth weight adjusted associations with attributes of metabolic disorders were explored.

*Results:* The mean birth weight was 3730g. Compared to the reference-group (42%), individuals with either elevated ( $>1.7\text{mmol/L}$ ) blood triglycerides (18%) or hypertension (49%) in adulthood, weighed significantly more between the age of 8 to 13 years, while modest non-significant differences were observed for birth weight. Individuals with either impaired glucose tolerance (11%) or type-II diabetes (3.6%) had significantly lower birth weight, but modest non-significant differences in childhood weight were observed.

Accelerated weight changes between 8-10 and 10-13 years were associated ( $P<0.05$ ) with higher adult blood triglycerides and blood pressure. Using the lowest quintile in the weight-velocity distribution for 10-13 years as a referent, individuals in the highest quintile had 4.4mmHg (95%CI: 1.8-7.1) higher systolic and 2.6mmHg (95%CI: 1.0-4.1) diastolic blood pressure; and 0.2mmol (95%CI: 0.1-0.3) higher blood triglycerides. When dichotomizing these outcome measures, a positive association with adult hypertension and elevated blood triglycerides ( $>1.7\text{mmol/L}$ ) were observed. Non-significant trends were, however, observed for type-II diabetes and impaired glucose tolerance.

*Conclusions:* In this high birth weight population, individuals with hypertension or elevated blood triglycerides appear to follow a different growth pattern compared to individuals with impaired-glucose intolerance or type-II diabetes. Accelerated changes in childhood weight between 8-13 years also appear to be more strongly associated with adult blood pressure and blood triglycerides than blood glucose.

### T3.3.1

## Harmonisation potential of 50 large bioclinical studies using the DataSHaPER

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### Abstract

*Objective:* Most individual cohort studies provide insufficient number of cases to help us properly understand the interactions of genetic, lifestyle, environmental and social factors in modulating the risk and progression of chronic diseases. Understanding the etiological structure of chronic diseases increasingly has to rely on effective data sharing and implementation of large-scale pooled meta-analyses. The DataSHaPER (Data Schema and Harmonization Platform for Epidemiological Research) tool was developed with this in mind; providing a flexible, but structured approach to the harmonization and synthesis of information between studies. In this presentation, DataSHaPER will be used to determine the potential of synthesizing 150 reference variables using baseline questionnaires and physical measures from 50 large population-based studies (over 5.5M participants).

*Methods:* The DataSHaPER approach to harmonization is threefold. Firstly, rules reflecting the formal criteria that determine if a particular reference variable can be recreated from the assessment items of each study are defined. These rules also determine the quality of the match between reference variables and assessment items. Secondly, rules are applied for each reference variable and for each study participating in the harmonization process. Finally, results from this exercise are tabulated to illustrate the data sharing potential between participating studies.

*Results:* A number of important reference variables can potentially be shared by a majority of participating studies (e.g. Occurrence of diabetes, 44 studies; Use of alcohol, 41 studies). To illustrate the potential for co-analysis, 15 studies (over 1.5 million participants) can simultaneously generate Blood pressure, Body mass index, Level of physical activity, Use of alcohol, Quantity of cigarettes smoked and some post-secondary education completed. Finally, results show that certain study design and variable characteristics impact markedly on the potential for harmonization.

*Conclusion:* The potential for synthesis of study data demonstrated by the DataSHaPER tool is an important step towards more collaborative epidemiology. We encourage people to join the growing international network of bioscientists that is now collaborating to develop and use the DataSHaPER. An expanding network of partners will improve this emerging methodological tool; for it is the rigour with which the DataSHaPER is developed and used that determines its scientific value.

## **T3.3.2**

### **Combining longitudinal survey data and register data – opportunities and difficulties**

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#### **Abstract**

*Objective:* The objective of our presentation is to study the opportunities and difficulties that social scientists are facing when they combine longitudinal survey data with data from registers. In Denmark social science researchers have unique opportunities to combine survey data with a rich variety of register data. When combining these data, however, the researchers face difficulties in organising, analysing and interpreting the data.

*Methods:* Using a Danish longitudinal study of children placed in out-of-home care as a case we will study the experiences gathered during the first two waves of data productions and analysing, and the strategies being developed for the third data wave. The study includes all children from the 1995 cohort who are or have been placed in out-of-home care. The study includes survey data on parents, child protection social workers, the care environment and the children themselves as well as data drawn from several public registers at Statistics Denmark.

*Results:* When combining survey and register data some of the challenges are: Discrepancy between survey and register data, identifying and combining the units of data, identifying the characteristics of the variable being measured, identifying the time sequence of the data collection, deciding what to draw from registers and what to produce by survey, and registration practises (of e.g. health care professionals, social workers).

*Conclusion:* We identify several areas where the discrepancy of survey and register data is distinct. For instance, there is little – if any – accordance between out-of-home care history from survey data and register data. The explanations of the discrepancies include a variety of the presented problems. Based on our analysis we present recommendations to closely examine the production of both register and survey data. Further the researcher should keep these challenges in mind when analysing and interpreting the data.

### T3.3.3

## Using calibration samples to enable cohort comparisons: Methods and design

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#### Abstract

*Objectives:* How do we estimate trends in mental health when the measures used keep changing? Maughan et al (2004) presented findings on adolescent behaviour and emotional problems as reported in 1974 and 1986 from the UK 1958 and 1970 birth cohort studies and the 1999 ONS cross-sectional study (CAMHS-1999). They used a comparatively small additional sample of adolescents rated on two measures, the Rutter A-scale (1958 & 1970 cohorts) and SDQ (1999) to estimate a calibration equation from the newer questionnaire to the older, and multiple imputation methods from the missing-data literature were used to impute and analyze the scores. They found progressive increases in antisocial behaviour, more recent increases in emotional distress, but no time trend in changes for attention/hyperactive problem behaviours. We consider alternative analytical methods, study designs and findings from these cohorts.

*Methods:* Using this study and simulation we compare estimates obtained using manual calculation from regression theory, multiple imputation and structural equation modelling with respect to bias and efficiency. We examine how the correlation across the measures influences the calibration study in terms of size and sampling design. We extend the methods to use both the within and the between cohorts information that repeated/longitudinal measurement allows in order to assess where within childhood the increasing rates derive from and whether these trends will persist.

*Results:* We show that the alternative analytical methods are convergent in the simple case but that multiple imputation lends itself to greater efficiency through the ease in which it is possible to use item-level, subscale or auxiliary information. With weaker correlation between measures, increased attention to the comparability of main study and calibration samples is necessary in order to avoid bias due to estimates/imputation being shrunk away from main study means towards those of the calibration sample.

*Conclusion:* Calibration samples provide an effective tool for extending the scope for cohort comparisons and analysis using structural equation and particularly multiple imputation methods is straightforward. The appeal of opportunistic samples needs to be tempered by the need for adjustment to remove potential bias.



### T3.3.4

## Considering ethical aspects of merging longitudinal datasets for epidemiologic research: An example of Linnaeus database

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### Abstract

*Objective:* To discuss ethical aspects of creating and working with large longitudinal datasets by merging micro-data from multiple sources.

*Method:* The discussion is based on the experience of newly created Linnaeus database at Ageing and Living Conditions Programme (ALC), Umeå University, Sweden. The database merged demographic, geographic, socioeconomic and health data on the whole Swedish population aged 30+ in 1960-2006 and detailed data on lifestyle and cognition of sub-samples from northern Sweden.

*Results:* All research must comply with several laws guaranteeing secrecy of the individual data in Sweden. The creation and the research on Linnaeus database was approved by the University ethical committee and by the national institutions providing the data. The data were anonymous and could not be traced back to individuals. Public was informed about the Linnaeus database by publications and announcements. To ensure the research quality and further guarantee the data safety, ALC established a set of routines on working with the Linnaeus database. The database is stored on a separate server and only approved researchers can enter ALC. No researcher has access to a full database. Applications for extraction of data for individual research projects are reviewed by the ALC board. Data extraction is conducted and documented by special personnel.

Consideration of multiple ethical aspects when designing the Linnaeus database imposed several limitations. They were however balanced by the strengths of the Linnaeus database: being a complex database combining merged micro-data from several sources, it provides excellent ground for extensive epidemiologic research while not compromising individual integrity.

*Conclusion:* Merging micro-data for epidemiologic studies is aimed at restoring and protecting the health of the population. However, while it is the general population that benefit from such studies, the risks are threatening individuals whose data are merged. The protection of individual integrity should be integrated in all stages of creating and working with complex datasets comprising micro-data from multiple sources. While this might impose some limitations (e.g., longer ethical reviews, limited extent of the database, long-winded update procedures), it is an effective approach to maximizing the benefit to the society while minimizing the risk to individuals.

### T3.4.1

## Social origin, schooling, individual changes in intelligence during childhood and mortality until age 78

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### Abstract

*Objective:* In this paper we test the hypothesis that individual changes in the performance on IQ tests between age 10 and 20 are associated with mortality later in life. We base this on the controversial idea that such changes are true and valid changes of the underlying intelligence, rather than artefactual and/or transient changes.

*Methods:* The analyses are based on a data material defined as all boys who attended third grade in Malmö, Sweden, in 1938. They took an IQ test (age 10) and another at conscription (age 20). Structural equation models were used to estimate the associations between the two latent intelligence scores at age 10 and 20 with paternal and own education and of all these variables with mortality rates. Of 834 individuals, 610 (73 percent) had full data on all variables and were used in the analyses.

*Results:* The results suggest (1) that individual change in intelligence between age 10 and 20 is related to mortality in adulthood independent of the initial intelligence level, (2) that this change in intelligence is driven by the amount of schooling received between the two measurements, (3) that the change in intelligence in fact mediates the influence of own education on mortality and (4) that adult differences in intelligence (and consequently in mortality) over social origin are partly explained by the tendency for sons of highly educated fathers to receive longer schooling, irrespective of the sons' initial intelligence levels.

*Conclusion:* The findings are promising when it comes to reducing inequalities, promoting intelligence and prolonging life.

## T3.4.2

### Prenatal undernutrition and cognitive function in late adulthood

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#### Abstract

**Objective:** At the end of World War II, a severe famine struck the western Netherlands. The famine lasted five months and at its peak the rations dropped to as low as 400 calories a day. In 1972, it was reported that cognitive performance in 19-year old male Dutch conscripts was not affected by exposure to the famine before birth. We investigated whether prenatal exposure to famine is related to a number of diverse aspects of cognitive functioning in late adulthood.

**Methods:** The Dutch Famine Birth Cohort study is a population-based study in men and women born as term singletons around the time of the Dutch famine. A total of 1423 cohort members were eligible of which 740 were enrolled at a mean age of 58 years. Cognitive function was measured in four different domains: general intelligence with the AH4 test, memory with immediate and delayed paragraph recall, perceptual motor learning with a mirror tracing task and selective attention with a Stroop color-word incongruence task.

**Results:** At age 58, head circumferences were smaller in those prenatally exposed to famine ( $B = -0.5$  cm [95% CI: -0.7 to -0.3],  $P < 0.001$ ) compared to those unexposed to famine. Men and women who had been exposed to famine during early gestation performed worse on the Stroop task ( $B = -85$  [-139 to -32],  $P = 0.002$ ). Adjusting for potential confounders (including sex, head circumference at birth and in adulthood, placental area, education, socio-economic status, alcohol consumption and score on the Hospital Anxiety and Depression Scale) minimally changed the association ( $B = -75$  [-131 to -19],  $P = 0.009$ ). Prenatal famine exposure was not associated with other cognitive outcomes.

**Conclusion:** Prenatal undernutrition during early gestation seems to affect selective attention, a cognitive ability usually declining with increasing age.

### **T3.4.3**

## **Type 2 diabetes mellitus and cognitive decline in middle-aged men and women. The Doetinchem Cohort Study**

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### **Abstract**

*Objective:* To test the hypothesis that type 2 diabetes mellitus is associated with greater decline in cognitive function in middle-aged individuals.

*Methods:* As part of the Dutch prospective, population based Doetinchem Cohort Study, cognitive functioning was measured twice within a five year time interval in 2613 men and women. Participants were aged 43-70 years at baseline (1995-2002), and no one had a history of stroke. Change in scores on global cognitive function as well as on specific cognitive function domains (memory, speed of cognitive processes, and cognitive flexibility) were compared for respondents with and without type 2 diabetes (self reported diabetes verified by the GP, or random plasma glucose levels  $\geq 11.1$  mmol/l).

*Results:* At 5-year follow-up, the decline in global cognitive function in diabetes patients was 2.6 times greater than in persons without diabetes. For persons aged 60 years or older, incident and prevalent diabetes patients showed a 2.5 respectively 3.6 times greater decline in cognitive flexibility than persons without diabetes. For most cognitive domains, the magnitude of cognitive decline in incident diabetes patients was intermediate between that of persons without diabetes and that of patients with diabetes at baseline.

*Conclusion:* Middle-aged persons with type 2 diabetes showed a greater decline in cognitive function than middle-aged persons without diabetes.

### T3.4.4

## Relationships between children's cognitive performance and maternal and childhood obesity status

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### Abstract

**Objective:** Obesity is a recognised risk factor for cognitive decline in older age. Inconsistent reports have linked obesity with impaired cognition in childhood. Proposed mechanisms include direct effects of endocrine mediators, e.g. leptin and triglycerides, on the central nervous system (CNS). It is conceivable that hormonal changes in pregnancy could influence foetal CNS development. A recent study reported differences in anxiety, spatial learning, and CNS inflammation in offspring of obese rats vs. controls. Using a contemporary longitudinal cohort of 18,818 UK children (Millennium Cohort Study), our objective was to investigate any relationships between childhood & maternal body mass index (BMI) and children's cognitive performance.

**Methods:** Children were assessed using subscales of the British Abilities Scales assessment battery at 5 (Picture Similarities, Naming Vocabulary, Pattern Construction) and 7 (Word Reading, Pattern Construction) years of age, and NFER Progress in Maths test at 7 years. Principal component factor analysis was used to generate underlying general cognitive ability factors (*g*) from the individual tests at age 5 and 7 (mean 100, s.d. 15). Children's height and weight was measured at 5 years, and resulting BMI was categorised into 'normal', 'overweight', and 'obese' using International Obesity Taskforce age-specific cut-offs. Maternal pre-pregnancy BMI was calculated from self-reported height and weight, and categorised according to WHO criteria. Multi-level linear models were used for analysis, controlling for; child's sex, ethnicity, birth weight, maternal socioeconomic class, maternal education, maternal age, family poverty status, and geographical clustering.

**Results:** Maternal obesity (BMI $\geq$ 30) was associated with significantly lower cognitive performance (*g*) in children aged 5 ( $b = -0.99, t = -2.24, p = 0.025$ ) and 7 years ( $b = -2.65, t = -5.44, p = <0.001$ ). Maternal overweight (BMI 25-30) was associated with significantly lower '*g*' at 7 years ( $b = -1.00, t = -2.86, p = 0.004$ ), but the relationship was non-significant at 5 years. There was no significant relationship between childhood BMI status and cognitive performance.

**Conclusions:** We identified a small, but statistically significant, reduction in cognitive performance in children of overweight and obese mothers. The effect size increased with child's age. Further research is required to investigate whether these findings are related to differences in parenting / upbringing, or are the result of biological effects on the foetus in utero.

### T3.5.1

## Women and men born with low birthweight are more often smokers as adults. A generational study

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### Abstract

*Objective:* The association between birth size and later coronary heart disease has been demonstrated in many studies. However, not all of these studies have controlled for socioeconomic condition and smoking habits. Smoking is an example of a socially-related factor that increases the risk for cardiovascular disease and reduces birthweight. To the degree that smoking and social status persist across generations, infants with low birthweight may be particularly likely to smoke as adults. Thus, smoking may contribute to an observed association between birthweight and adult disease. We used data from the Medical Birth Registry of Norway for 1967-2008 to examine the birth characteristics of men and women registered as mothers and fathers in the registry, and to assess woman's likelihood of smoking in adulthood. We used maternal education as a measure of socioeconomic position.

*Methods:* Women born in Norway in 1967 or later (and therefore registered at birth in the Medical Birth Registry), have given birth to 344,000 infants in the period 1999-2008. Similarly, men born in 1967 and later have fathered 312,000 infants. Smoking habits during pregnancy is known for mothers in the last generation. We used these data to study whether women's own birthweight influence the chance of smoking during pregnancy. We do not have smoking patterns of fathers, but can indirectly assess his smoking habits through his partner. Thus, similarly we assessed whether men's birthweight influence the chance of his partner being a daily smoker during her pregnancies.

*Results:* Mothers were more likely to smoke if they themselves were small at birth. The prevalence of women's smoking ranged from 18% to 10% depending on her birthweight, with a clear dose-response relationship. Smoking habits are strongly linked to socioeconomic factors. Among mothers with low education, close to 40% smoked, while among mothers with high education, less than 5% smoked. The associations between birth weight of the parents and their adult smoking were strongest in the lower SES group. Previous reports indicate a near-zero correlation between birth weights of mothers and fathers. In our material we estimate this correlation to be 0.023. Still, a low birth weight mother is slightly more likely to find a partner who also had low birth weight (OR=1.30 (95% C.I. 1.10-1.55)).

*Conclusion:* We find a strong relation between a mother's birthweight and her smoking in adulthood. This presumably contributes to the observed relation between birthweight and risk of adult disease. Unexpectedly, the association between the father's birthweight and the partner's smoking habit was nearly as strong. This is presumably due to the couple's shared social factors, including similar smoking habits.

## T3.5.2

### Smoking and risk of coronary heart disease in younger, middle-aged, and older adults

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#### Abstract

**Objective:** Results from some studies suggest that the risk of coronary heart disease associated with smoking attenuates by age, implying that having survived to a certain age, smoking is less of a risk factor for CHD. In the other end of the age scale, relatively more cases of CHD among younger adults may be attributable to genetic causes. This study examined how the risk of CHD according to smoking depends on age.

**Methods:** Data from a pooled analysis of 8 prospective studies from North America and Europe including 192,067 women and 74,919 men was used.

**Results:** As compared with never smokers, the relative risk of CHD in current smokers was highest in the youngest and lowest in the oldest women and men. For example, the relative risk among men who smoked compared with never smoking men was 4.72 (95% CI: 2.93, 7.58) among the 40-49 year-old and 2.02 (95% CI: 1.54, 2.66) among the  $\geq 70$  year-old. In contrast, higher incidence rate differences were observed in the oldest men than in the youngest men. For example, the incidence rate difference (per 100,000 years) among men who smoked compared with never smokers was 202 (95% CI: 108, 295) among the 40-49 year-old and 611 (95% CI: 516, 706) among the  $\geq 70$  year-old. The CHD-attributable fraction among smokers was highest among the youngest and lowest among the oldest women and men. However, in all age groups, a substantial proportion of cases among smokers could be attributed to smoking. For example, attributable fractions among smokers were 88% (95% CI: 82%, 94%), 81% (95% CI: 77%, 85%), 71% (95% CI: 65%, 76%) and 68% (95% CI: 53%, 82%) among women aged 40-49, 50-59, 60-69 and  $\geq 70$  years.

**Conclusion:** Smoking is causing a large fraction of CHD cases in all age groups. Hence, smoking prevention and efforts to encourage individuals to stop smoking is important regardless of age.

### T3.5.3

## Longitudinal associations between childhood and adolescent emotional problems, behavioural problems and substance use

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### Abstract

**Objectives:** Emotional and behavioural problems are commonly associated with substance use in adolescence, but it is unclear whether substance use causes or is a consequence of mental health problems. The aim was to study longitudinal associations between early emotional and behavioural problems and the initiation of substance use among adolescents.

**Methods:** The sample was a longitudinal Population based Northern Finland 1986 Birth Cohort (n= 6,349; 3,103 male). Subjects' emotional (internalizing) and behavioral (externalizing) problems were assessed with Rutter scales (teachers' and parents' ratings at age 8) and Youth Self- Report (adolescents' ratings at age 15 to 16). Information related to regular smoking, alcohol, cannabis and other substance use was collected by self-reports at the age of 15 to 16 years. Adolescents' hospital diagnoses for emotional disorders and their violent and property offences, reflecting later behavioral problems, were collected from nationwide registers until age of 20 years.

**Results:** Both among males and females, behavioural problems at age 8 were associated (P<0.05) with later smoking and other substance use than alcohol or cannabis (Adjusted Odds Ratios, OR, between 1.5 and 2.3). Early emotional problems were not a risk for later substance use. Cannabis (OR = 6.7; 95% Confidence Interval: 2.3 to 19.6) among females predicted emotional disorders in the follow-up. Substance use predicted later criminality in both genders; associations were stronger among males.

**Conclusions:** Mental health problems and substance use are strongly associated in adolescence and early adulthood. Behavioural problems often both precede and follow adolescent substance use, whereas emotional problems may follow adolescent substance abuse, especially among females. Males with substance use are at high risk for criminal offences. These associations were robust even when taking into account childhood and adolescence mental health problems.



## T3.5.4

### Mortality among drug users: following up a sample of drugged drivers

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#### Abstract

*Objective:* Mortality among drug users has been studied among cohorts using iv-drugs and those admitted for detoxification or treatment programs. This concerns, however, only a very small proportion of drug users. Our aim is to analyze mortality among a very different kind of sample of drug users: people suspected of driving under the influence of drugs (DUID). This study analyzed mortality rates and causes of death among drugged drivers in Finland and compared them with the general Finnish population during 1993–2006.

*Methods:* The material consisted of register data on 5,832 DUID suspects apprehended by the police. A reference group of 74,809 of individuals was drawn from the general Finnish population. Deaths were traced from National Death Register. The survival and the differences in mortality hazard were estimated by using Kaplan-Meier plots and Cox regression models.

*Results:* Almost two-thirds of DUID suspects were under the influence of drugs or alcohol at the time of death, whereas less than one-fifth of the general population was intoxicated at the time of death. Both male and female DUID suspects had around ten times the hazard of death in comparison with the general population. Male DUID suspects had twice as high hazard of death as females. Among male DUID suspects cause-specific hazards were highest for poisoning/overdose, violence and suicide. Cases with a finding for one drug only were likely to survive longer than cases with poly-drug findings. DUID suspects who had a finding for medicinal drugs (especially benzodiazepines) had a higher hazard of death than DUID suspects with a finding for illicit drugs (especially amphetamines).

*Conclusion:* Our sample of drug users, the DUID suspects apprehended by the police, had a greatly increased risk for premature death, in all observed causes of death. Findings for medicinal sedatives/tranquillizers indicated excess mortality over findings for illegal drugs, especially stimulants.

### T3.6.1

## Comparison of wheezing phenotypes in the first 8 years of life in two large birth cohort studies: PIAMA and ALSPAC

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### Abstract

**Objective:** Asthma has its origins in early childhood. Systematic classification of early life wheezing patterns to allow cross-cohort comparisons will facilitate large scale investigations of early life risk factors for asthma development. Recently, wheezing phenotypes were identified by longitudinal latent class analysis (LLCA) in the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort (Thorax 2008). The aim of this study was to compare wheezing phenotypes in children from the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study with those in the ALSPAC study.

**Methods:** Repeated measures from birth to 8 years of parent-reported wheezing of 2810 children from PIAMA and 5760 children from ALSPAC were modeled using LLCA. Wheezing phenotypes from the best fitting models were compared between cohorts. Associations between wheezing phenotypes and outcomes of asthma and atopy at 8 years were analyzed using weighted multinomial logistic regression.

**Results:** A model with five wheezing phenotypes (NI, Never/Infrequent wheeze; TE, Transient Early wheeze; IO, Intermediate Onset wheeze; LO, Late Onset wheeze and P, Persistent wheeze) provided the best fit in the PIAMA study. Two more phenotypes (PE, Prolonged Early; TI, Transient Intermediate wheeze) were identified in an extended version of the previous published model in the ALSPAC study. Measures of model fit differed slightly between the PIAMA study ALSPAC study. The strongest associations with doctor diagnosed asthma at age 8 were for P and LO, with OR (95% CI) = 71.5 (36.5-140.2), 50.5 (21.9-116.5), respectively, when compared with NI. Sensitization against allergens was strongly associated with IO and LO, with OR (95%CI) = 5.1 (2.7-9.8) and 4.2 (1.8-9.9), respectively. P and TE were strongly associated with a lower FEV<sub>1</sub> %predicted at age 8 (mean difference (95%CI) = -4.4 (-8.0,-0.8) and -2.1 (-4.1,-0.1) respectively).

*Conclusion:* Wheezing phenotypes during childhood identified by LLCA were highly comparable in two large birth-cohorts. We confirmed the newly identified phenotype Intermediate Onset wheeze, which starts after age 2 and is strongly associated with atopy development. This study supports the hypothesis that wheezing in the first years of life is associated with lower lung function, and wheezing after 2 years of age with atopy development.

## T3.6.2

### Risk factors for wheezing illness in Ukrainian children: Ukraine ELSPAC study

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#### Abstract

**Objective:** The prevalence of wheezing illness in children varies markedly across countries. Since 1991 Ukraine has undergone rapid social and economic transition which may affect the risk factors for wheezing illness in children. The objective of this study is to determine the prevalence and risk factors for wheezing illness in 7 year old Ukrainian children.

**Methods:** We conducted a case cohort study of wheezing illness among 2127 6-8 year old children who participated in the *Family and Children of Ukraine* longitudinal cohort study in three cities in Ukraine (Ukraine ELSPAC study).

**Results:** The prevalence of wheezing illness was highest (14.4%) in Kyiv, the capital and most westernized city. In addition to city of residence, factors significantly ( $p < 0.05$ ) associated with increased risk of wheezing illness at age 7 in adjusted analyses included mother's asthma (OR=3.4), mother's allergy problems (OR=1.5), water entering the home during pregnancy (OR=1.7), and inadequate heating of the home during pregnancy (OR=1.7). Factors protective of wheezing illness at age 7 included delivery by Caesarean section (OR=0.4), attending kindergarten (OR=0.7), weekly contact with other furry animals (OR=0.4), and amount of ingestion of certain root vegetables (turnips, cabbage turnips, and parsley) at age 18 months to 3 years (OR=0.84). Lower respiratory infections at any age over 6 months and upper respiratory infections at any age over 18 months were significantly associated with wheezing illness at age 6-8 years.

**Conclusions:** Most risk factors for wheezing among Ukrainian children are similar to those reported from other developed countries.

### T3.6.3

## Temporal changes in the prevalence of childhood asthma and allergies in urban and rural areas in Cyprus

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#### Abstract

**Objectives:** The rise in the frequency of asthma and allergies in childhood has reached a plateau in many European countries in the last decade. In Cyprus, first time investigation into the prevalence of asthma and allergies in 1999 using the ISAAC questionnaire showed an overall low prevalence of asthma and allergies, but a significantly higher prevalence in urban compared to rural areas. The present study aimed at investigating changes in the prevalence of asthma and allergies in Cyprus after a period of 8 years and more specifically whether these have been differential between urban and rural areas.

**Methods:** Consistently with the original design, 2216 children aged 7-8 years residing in the same urban and rural areas participated in a cross sectional study in 2008. The parents completed the ISAAC questionnaire enriched with questions on possible risk factors. The findings were compared to those of the earlier study using logistic regression analysis.

**Results:** At 8.6% in 2008, the prevalence of current wheeze was significantly higher than 6.9% observed in 2000 (OR=1.41, 95% CI 1.11-1.79). Significant increases were also seen in the prevalence of ever wheeze (OR=1.46, CI 1.24-1.72) and diagnosis of asthma (OR=1.66, CI 1.38-2.00), eczema (OR=1.84, CI 1.48-2.28) and hayfever (OR=1.78, CI 1.27-2.49). The odds of current wheeze increased significantly in rural areas (OR 2.00, 1.36-2.95) while no difference was observed in urban areas (OR 1.23, 0.93-1.63); p value for effect modification = 0.02. Rises in asthma and rhinitis prevalence, but not eczema were generally more pronounced in rural compared to urban areas.

**Conclusions:** In Cyprus the prevalence of allergic diseases is still increasing; however, recent rises appear more pronounced among children living in rural areas, possibly implicating the role of environmental and lifestyle changes in these communities.

### T3.6.4

## Patterns of antibiotic use in early life as a marker of susceptibility to asthma

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### Abstract

**Objective:** The assessment of patterns of antibiotic use in early life may have major implications for our understanding of asthma. The hygiene hypothesis suggests that antibiotic use in infancy is causally related to the development of childhood asthma (via the effect on gut microbiota). However, in this study, we hypothesise that early-life antibiotic use, rather than being causally related to asthma, is a marker of susceptibility to asthma with a heightened response to exposure.

**Methods:** The Manchester Asthma and Allergy Study is a population-based birth cohort study designed to determine early life factors for the development of asthma and allergic disease. Subjects were recruited prenatally and followed prospectively. A trained physician extracted information on antibiotic prescription receipt and symptoms of asthma/wheezing from primary care medical records (n=800). Within the generalized linear latent and mixed models framework, we use longitudinal latent class analysis to characterize these children according to susceptibility based on patterns of early-life antibiotic use. We then investigate whether these phenotypes of susceptibility are predictive of contemporaneous and future asthma and wheeze symptoms.

**Results:** We identified a model with three distinct latent classes of susceptibility based on patterns of antibiotic use within the first 2 years of life. Based on our interpretation of the model, Class 1 were children resilient to infection (31.1%), Class 2 showed a normal immune response (55.7%) and Class 3 were susceptible to infection (13.2%). Compared to Class 1 and Class 2, children in Class 3 had a significantly higher hazard of experiencing asthma or wheeze symptoms within the first 3 years of life (HR=3.72 [95% CI 2.72 – 5.10, p<0.01] and 1.61 [95% CI 1.25 – 2.09, p<0.01] respectively). Class 2 had a greater hazard of experiencing exacerbations of asthma and wheeze symptoms than Class 1 (HR=1.90 [95% CI 1.21 – 2.98, p<0.01]) however, after the third year of life, this hazard ratio ceased to be statistically significant (HR=1.39 [95% CI 0.79 – 2.45, p=0.25]).

**Conclusion:** By analysing trajectories of antibiotic use in early life, we are able to establish that antibiotic use in early life, rather than being causally related to asthma, is a phenotypic marker of susceptibility to asthma.

## T4.1.1

### Relative contributions of early and later life influences on blood pressure at age 50 years

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#### Abstract

*Objective:* While a large number of previous studies have suggested an association between birth weight and blood pressure in later life, others have not. Where associations do exist there have also been suggestions that they may be mediated through factors operating later in the life course. A further issue surrounds the relative importance of these associations. The objective of this study was to investigate the relative contributions of a range of factors from across the life course to variations in systolic and diastolic blood pressure at age 50 years in the Newcastle Thousand Families Study birth cohort.

*Methods:* All 1142 babies born in the city of Newcastle upon Tyne in May and June 1947 were recruited into a cohort study and detailed information collected prospectively throughout childhood. At age 50, 412 study members attended for clinical examination and a self-completion questionnaire, returned by 574, was used to ascertain socio-economic and lifestyle factors. Systolic and diastolic blood pressure were measured. Multiple linear regression was used to identify significant predictors of both blood pressure variables. Path analyses were used to identify significant direct and indirect associations and also to ascertain the relative importance of the significant predictors.

*Results:* After adjustment for all other significant variables, birth weight, standardized for sex and gestational age, ( $p=0.014$ ), body mass index (BMI) at age 50 ( $p<0.001$ ) and alcohol consumption at age 50 ( $p=0.002$ ) were all independently associated with both systolic and diastolic blood pressures. BMI was found to be the most important predictor. An inverse relationship of standardized birth weight with blood pressures was the only directly associated early life factor however it was of small relative contribution. A 1kg increase in unstandardised birth weight was associated with a 2mmHg decrease in systolic blood pressure. Full path diagrams will be presented.

*Conclusion:* Adult blood pressure is influenced by numerous factors, acting both directly and indirectly during an individual's lifetime. Inverse associations of standardised birth weight, although statistically significant, were found to be of relatively small importance, with the majority of variation in data being explained by factors in adulthood, in particular adult BMI and alcohol consumption.

## T4.1.2

### Is accelerated postnatal growth associated with blood pressure in childhood?

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#### Abstract

*Objective:* To investigate whether variations in growth patterns in early-life are associated with blood pressure at age 11.5 years by modelling detailed, individual growth trajectories between birth and 8.5 years of age.

*Methods:* We analysed multiple measures of weight from birth to age 8.5 years in 8,448 children from Belarus who were born in one of 31 hospitals that participated in a cluster randomised trial of a breastfeeding promotion intervention. We analysed all 13 possible childhood growth measurements to develop a best-fitting linear spline random-effects model with 3 knots (thus dividing follow-up into 4 time periods, each with its own trajectory). The spline models were used to generate 5 random effects coefficients: birthweight; 'early infant weight velocity' (birth – 3 mo); 'late infant weight velocity' (3 mo – 1 yr), 'early childhood weight velocity' (1 yr – 4 yr) and 'mid childhood weight velocity' (4 - 8.5 yrs). Each coefficient denotes an individual's deviance from average birthweight or velocity at each time period; together, the coefficients are a within-subject summary of each child's growth curve from birth to 8.5 years. The coefficients were converted into age-standardised z-scores to render them directly comparable. Our outcomes were systolic and diastolic blood pressure (mmHg) measured at age 11.5 years. Sex-specific linear regression was used to investigate associations of each coefficient with blood pressure, controlled for baseline confounders.

*Results:* Birthweight was not associated with blood pressure. Weight velocity in each time-period was positively associated with blood pressure in boys. The change in systolic blood pressure per z-score increase in growth was 1.1 (95% CI 0.7 to 1.5) for 'early infant weight velocity'; 1.1 (0.7 to 1.5) for 'late infant weight velocity', 1.9 (1.5 to 2.2) for 'early childhood weight velocity' and 1.3 (1.0 to 1.6) for 'mid childhood weight velocity'. Associations were similar for girls, but with a larger coefficient for 'mid childhood weight velocity' (1.7, 95% CI 1.3 to 2.2).

*Conclusion:* Children's growth trajectory between birth and 8.5 years was positively associated with blood pressure at age 11.5 years. Associations increased in magnitude with age, with a more marked pattern for girls than boys.



### T4.1.3

## Path analysis of the association between birth length and adult systolic blood pressure in the Northern Finland Birth Cohort 1966

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### Abstract

**Objectives:** Low birth length has been shown to be associated with adult hypertension. The mechanisms are still unclear. We investigated whether this association could be entirely mediated via accelerated height growth in infancy which is often observed in children born small and is a known risk factor for adverse metabolic profile in adulthood.

**Methods:** The study population consisted of 5851 singletons belonging to the Northern Finland Birth Cohort 1966. We used path analysis to estimate the associations between birth length (BL), peak height velocity (PHV) in infancy, and height and systolic blood pressure (SBP) at age 31 years. The analysis also accounted for gender, gestational age, maternal height, age, smoking, parity, socio-economic status (SES) and subject's own smoking, drinking, SES and BMI at 31 years. Frequent height measurements at 0-2 years were used to estimate individual height curves, and PHV was derived as the maximum value of the growth velocity curve, typically occurring immediately after birth.

**Results:** An inverse association between BL and SBP was observed ( $\beta = -0.40$  mmHg/cm,  $SE = 0.09$ ) after controlling for all the assumed relationships in our path model. Low BL was also associated with increased PHV in infancy, which in turn was associated with increased adult height but not with SBP adjusted for adult height. Mediation of the BL association on SBP was observed via PHV and height at 31 years (total indirect effects  $\beta = 0.20$  mmHg/cm,  $SE = 0.03$ ). In the assumed model, the sum of the direct and indirect effects, that is the total effect of BL on SBP, remained negative ( $\beta = -0.21$  mmHg/cm,  $SE = 0.08$ ).

**Conclusions:** About one third of the low BL effect on high adult SBP was mediated via increased PHV in infancy and current height, but a direct effect remained. Recently, genetic variants associated both with lower birth weight and type 2 diabetes have been identified. Expanding the model to include genetic variants could further improve our understanding of the causal paths between small birth size and high adult SBP.

## T4.1.4

### Weight change is associated with rising blood pressure, in particular in elderly people: the Doetinchem Cohort Study

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#### Abstract

*Objective:* To study the longitudinal association between weight change on the one hand and change in blood pressure levels on the other hand in the general Dutch population.

*Methods:* The Doetinchem Cohort Study is a longitudinal population-based cohort study that started in 1987 to investigate the impact of (changes in) lifestyle factors and biological risk factors on the incidence of CVD and other chronic diseases. A total of 7769 men and women aged 20-59 at baseline have been re-invited every five years. Data from the first four examinations are used. Weight, height, systolic and diastolic blood pressure (SBP and DBP) were measured at every examination. Hypertension was defined as SBP  $\geq$ 140 mmHg and/or DBP  $\geq$ 90 mmHg and/or use of antihypertensive medication. We used generalized estimating equations (GEE) to perform longitudinal linear regression analyses (proc GENMOD in SAS). People with complete data on weight and blood pressure for all four examination were included (n=3598).

*Results:* The population consisted of 1773 men and 1825 women with a mean age at baseline of 39.7 ( $\pm$  10) yrs and a prevalence of hypertension of 15.5%. A total of 1605 normotensive individuals developed hypertension during follow-up. The mean change in weight between examination 1-2, examination 2-3 and examination 3-4 was +2.7 ( $\pm$  4.5), +2.2 ( $\pm$  4.4) and +1.02 ( $\pm$  4.6) kg, respectively. The corresponding mean changes in SBP were +3.5 ( $\pm$  13.6), +3.9 ( $\pm$  14.0) and +7.5 ( $\pm$  15.3) mmHg and in DBP +2.6 ( $\pm$  10.0), +1.6 ( $\pm$  10.3) and +5.4 ( $\pm$  10.2) mmHg, respectively. After adjustment for age and sex, weight gain of 1 kg was associated with a rise in SBP of 0.50 (0.43-0.57) mmHg and in DBP of 0.38 (0.33-0.43) mmHg (longitudinal linear regression coefficient (95% confidence interval)). The association between weight change and SBP change was stronger in older vs younger baseline age-groups: SBP 0.32 (0.18-0.46) mmHg in the 20-29 years age-group vs 0.63 (0.43-0.84) mmHg in the 50-59 years age-group. Adjustment for hypertension, physical activity, alcohol intake or total daily energy intake only slightly affected these associations.

*Conclusions:* Weight change was associated with rising blood pressure in this population-based study, in particular in people over 50 years of age. Therefore, interventions aimed at weight loss or weight maintenance may also affect the development of elevated blood pressure and should not be restricted to young people.

## T4.2.1

### Physical exercise during pregnancy and foetal growth measures: a study within the Danish national birth cohort

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#### Abstract

*Objectives:* The objective of the study was to examine the association between physical exercise during pregnancy and foetal growth measures.

*Methods:* We used data on 79,692 liveborn singletons from the Danish National Birth Cohort collected between 1996 and 2002. We calculated mean differences in birthweight, length, ponderal index, head and abdominal circumference and placental weight as well as hazard ratios of small- and large-for-gestational-age according to amount and type of maternal physical exercise. In addition, 5521 pairs of siblings were studied to examine whether changes in exercise between two pregnancies correlated with birthweight measures.

*Results:* Our data indicated smaller babies in exercising women compared with non-exercisers, but the differences were small, and only a few were statistically significant. Exercising women had a slightly decreased risk of having a child small for gestational age (hazard ratio, 0.87; 95% confidence interval, 0.83-0.92) and large for gestational age (hazard ratio, 0.93; 95% confidence interval, 0.89-0.98). In a sibling analysis we found that women who changed exercise level between pregnancies had on average larger babies than women who exercised at the same level in the two subsequent pregnancies. Yet, conclusions are not clear, since this association was seen both for increasing and decreasing exercise levels between pregnancies. The type of exercise (a proxy measure of intensity) was only of minor importance; the largest decrease in birthweight was seen among women engaged in high-impact activities and horseback riding in late pregnancy, but no statistically significant estimates were found.

*Conclusions:* These findings do not indicate sizable effects on foetal growth measures related to exercise apart from a modest decreased risk of small- and large-for-gestational-age infants. Hence, our results do not speak against advising pregnant women to be physically active during pregnancy.

## T4.2.2

### **Association of maternal psychosocial stress and personality traits with adverse pregnancy outcomes in the mother-child cohort (Rhea study) in Crete, Greece**

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#### **Abstract**

*Objective:* There is conflicting evidence regarding the effect of psychosocial stress on reproductive outcomes. The purpose of the present study was to investigate the contribution of antenatal anxiety, depression and personality traits to adverse pregnancy outcomes, such as preterm birth and foetal growth restriction in the population-based mother-child cohort study ("Rhea" Study), in Crete, Greece 2007-2009.

*Methods:* We evaluated 580 women with singleton pregnancies, recruited in the "Rhea" Study (Crete, Greece), with complete data for psychosocial stress and birth outcomes. Participants were asked to self-complete questionnaires on trait anxiety, depression and personality traits at 28-32 weeks of gestation. Antenatal trait anxiety was assessed by the trait subscale of the State-Trait Anxiety Inventory (STAI-Trait), and depressive symptoms were measured by the Edinburgh Postpartum Depression Scale (EPDS) both translated and validated into Greek. The Eysenck Personality Questionnaire-Revised (EPQ-R) was used to assess personality traits, such as neuroticism, psychoticism, and extraversion. Information on newborns' anthropometric measures at birth was obtained from the hospital delivery logs and medical records. Foetal growth restriction was based on a customized model, and multivariate linear regression models were used adjusting for several confounders.

*Results:* The results indicated that a 5 unit increase in the STAI-Trait score increased the risk for foetal weight growth restriction by 23% (RR=1.23, 95 percent CI: 1.02, 1.47) after adjusting for maternal age, maternal education, parity and smoking during pregnancy. A per unit increase in the EPQNeuroticism scale increased the risk for foetal weight growth restriction by 9% (RR=1.09, 95 percent CI: 1.02, 1.17), and for foetal head circumference growth restriction by 7% (RR=1.07, 95 percent CI: 1.00, 1.15) after adjusting for several confounders.

*Conclusion:* These findings suggest that the risk for foetal growth restriction may be increased among women with high levels of trait anxiety and neuroticism. Further research is needed to better understand the biological mechanisms underlying these relationships.

## T4.2.3

### Is regular exercise during pregnancy associated with a reduced risk of caesarean delivery in nulliparous women?

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#### Abstract

*Objective:* Caesarean section (CS) rates have increased during the last decades in developed countries. A corresponding increase in non-medical indications for caesarean delivery is also reported, implying that some of the CS performed may be medically unnecessary exposing both woman and fetus to risks without proven benefits. Participation in regular exercise during pregnancy is recommended for all pregnant women without complications. However, knowledge on the possible association with mode of delivery, particularly caesarean delivery, is sparse. Previous studies have suggested that an association may exist between exercise during pregnancy and a decreased risk of CS, although other studies showed increased risk or reported mixed results. The aim of this study is to assess the association between regular exercise during pregnancy and caesarean delivery, both emergency and elective CS, in nulliparous women.

*Methods:* Using data from the Norwegian Mother and Child Cohort study (MoBa), conducted by the Norwegian Institute of Public Health, 27,229 nulliparous singleton pregnancies enrolled between 2001 and 2006 were included. Recreational exercise was assessed by self-report in weeks 17 and 30, and defined in terms of frequency per week. Outcome variable was caesarean delivery (all types) and emergency caesarean delivery as registered in the Medical Birth Registry of Norway. We used logistic regression analysis to estimate the associations, and the results are presented as crude and adjusted odds ratios (aOR) with 95% confidence intervals (95% CI). The following covariates were included: maternal age, pre-pregnancy BMI, education, assisted reproduction, hypertension, preeclampsia, and fear of childbirth.

*Results:* The prevalence of caesarean delivery was 15.8% (n=4306), whereas 10.7% were emergency CS. Regular exercise performed 1-2 times a week in gestational weeks 17 was negatively associated with having all types of caesarean delivery aOR= 0.78 (95% CI 0.70-0.88). The greatest protective effect on emergency CS was observed in women exercising at least 3 times a week in week 30 aOR=0.58 (95% CI 0.53-0.64). However, including fear of childbirth in the model, diluted the effect of exercise aOR=0.76 (95% CI 0.67-0.86).

*Conclusion:* Women exercising during pregnancy are less likely to have a caesarean section.

## T4.2.4

### Sleeping habits during pregnancy and adverse birth outcomes in the mother-child cohort (Rhea study) in Crete, Greece

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#### Abstract

*Objective:* The association of sleeping habits in pregnancy with adverse birth outcomes still remains elusive and the exact mechanisms involved are not well established. The objective of this study, was to examine the association between sleeping habits in the third trimester of pregnancy and adverse pregnancy outcomes including low birth weight (LBW), Foetal weight Growth Restriction (FwGR), and preterm births, in the population-based mother-child cohort study ("Rhea" Study), in Crete, Greece 2007-2009.

*Methods:* We evaluated 1087 women with singleton pregnancies, recruited in the "Rhea" Study (Crete, Greece), with complete data for sleeping habits and birth outcomes. Participants were asked to complete detailed questionnaires that covered demographic and medical features and sleeping habits. Information on anthropometric measures at birth was obtained from the hospital delivery logs and medical records. Fetal growth restriction was defined based on a customized model, and multivariable logistic regression models were used to estimate the association between sleeping habits during pregnancy and the outcomes of interest, adjusting for maternal age, smoking during pregnancy, pre-pregnancy BMI, gestational diabetes, and gestational hypertension.

*Results:* Women with severe snoring habits were at high risk for low birth weight OR 3.17 (95%CI 1.32-7.65), and for foetal weight growth restriction OR 2.44 (95%CI 1.07-5.59), after adjusting for potential confounders. Women with sleep deprivation (<5 hours sleep) were at high risk for preterm births OR 1.89 (95%CI 1.04-3.46), with the highest risk observed for medically indicated preterm births OR 2.33 (95%CI 0.82-6.66) after adjusting for potential confounders.

*Conclusion:* These findings suggest that snoring, and sleep deprivation during pregnancy could be associated with increased risk for intrauterine growth restriction, and preterm births respectively. Further epidemiological and mechanistic evidence is needed.

### T4.3.1

## Magnetic resonance imaging (MRI) determined childhood abdominal adiposity and its association with subsequent cardiovascular risk factors in adolescence: Prospective cohort study

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### Abstract

*Objective:* To compare the degree of association between MRI determined intra-abdominal adiposity, BMI or waist circumference and cardiovascular risk factors in adolescents.

*Methods:* Data were used from a random sub-sample of ALSPAC in whom abdominal MRI scans were completed at age 12 years (N=85; 40% girls). Blood pressure and fasting blood samples for assessment of glucose, insulin and lipids were assessed at age 15 years.

*Results:* In the full eligible cohort (N=5235) there were similar associations of BMI, WC and DXA determined total fat mass measured in childhood (mean age 12) with adverse cardiovascular risk factors measured in adolescence (mean age 15). For example, for a 1SD greater level of adiposity mean differences in systolic blood pressure (SBP) were 1.54 (95%CI: 1.21, 1.87), 1.54 (1.18, 1.89) and 1.59 (1.24, 1.93) mmHg for BMI, WC and DXA fat mass, respectively. For a 1SD greater level of adiposity the ratio of geometric means of fasting insulin was 1.13 (95%CI: 1.12, 1.14), 1.14 (1.13, 1.16) and 1.14 (1.13, 1.16) for BMI, WC and DXA fat mass, respectively. In the sub-sample with MRI scans (N=85) greater intra-abdominal adiposity in childhood was positively associated with SBP (mean difference 0.03 (-3.42, 3.49) mmHg), DBP (1.19 (-1.28, 3.67)), fasting glucose (0.02 (-0.07, 0.11) mmol/l) and insulin (ratio of geometric means 1.03 (0.89, 1.19)) in adolescence, but all associations were imprecise with wide confidence intervals that included the null value. Paradoxically there were inverse associations with LDLc and triglycerides and positive associations with HDLc, but again these were imprecisely estimated and consistent with the null. Within this subgroup of 85 participants associations of BMI, WC and fat mass were also imprecisely estimated and consistent with the null.

*Conclusions:* Greater intra-abdominal adiposity in childhood was positively associated with cardiovascular risk factors of systolic and diastolic blood pressure, fasting glucose and insulin in adolescence. MRI scans of intra-abdominal adiposity are feasible within a subgroup of large prospective cohort studies, but our results suggest that considerably greater numbers needed to be included in these subgroups to obtain precise estimates of the associations of intra-abdominal adiposity with later cardiovascular risk factor outcomes.

## T4.3.2

### Adiposity trajectories across childhood and their association with DXA-assessed fat mass and cardiovascular risk factors at age 15

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#### Abstract

**Objective:** Overweight in childhood is known to be associated both with overweight and increased cardiovascular risk factors in later life, but few large studies have been able to explore these associations prospectively. In particular, few studies have modelled trajectories of adiposity across childhood and examined the associations of adiposity changes in different periods of childhood with later adiposity and cardiovascular risk factors.

**Methods:** Using data from the Avon Longitudinal Study of Parents and Children, we modelled individual trajectories of adiposity (N=4,601) across childhood using random effects linear spline models for ponderal index between birth and two years and body mass index between two and ten years. We explored how adiposity trajectories were associated with DXA determined today body fat mass and a range of cardiovascular risk factors (systolic and diastolic blood pressure, fasting LDL and HDL cholesterol, triglycerides, C-reactive protein, glucose, insulin) measured at 15 years. Associations between the adiposity trajectories and fat mass and cardiovascular risk factors at age 15 were explored using linear regressions adjusted for a wide range of potential confounding factors.

**Results:** The period of adiposity change from birth to ten years most strongly associated with DXA-assessed fat mass at age 15 was two to five years. In boys, a one standard deviation increase in the rate of adiposity change between two and five years of age was associated with a 0.55 standard deviation increase (95% CI 0.51, 0.60) in DXA-assessed fat mass at age 15 (equivalent result for girls 0.31, 95% CI 0.27, 0.35). However, subsequent periods of adiposity change also demonstrated strong associations with DXA-assessed fat mass. Adiposity changes in childhood were associated with a wide range of cardiovascular risk factors in adolescence; associations tended to be strongest for adiposity changes in later childhood (ages 8.5-10).

**Conclusion:** Although adiposity increases from 2-5 years are strongly associated with DXA-assessed fat mass at age 15, adiposity change in later years is also associated with later DXA-assessed fat mass and a range of cardiovascular risk factors, meaning that obesity prevention initiatives should be targeted across childhood.



### T4.3.3

## **Childhood and adolescent obesity: long-term effects of lifestyle, socioeconomic, child and parental factors. Results from a Greek longitudinal study**

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### **Abstract**

*Objective:* To examine the long-term effects of lifestyle, socioeconomic, and parental parameters on childhood and adolescent BMI, and on change in BMI from childhood to adolescence in a representative Greek birth cohort.

*Methods:* A longitudinal study of 1845 adolescents born nationwide in April 1983 and followed up at 7 and 18 years. BMI z-scores at 7 and 18 years, and change in BMI z-score between 7 and 18 years were the outcomes in linear regression analyses. The independent variables assessed included child (gender, birthweight, mental health status), lifestyle (physical activity, television viewing, eating behaviour, perceptions), socioeconomic (parental education, material consumerism, housing conditions), and parental characteristics (parental BMI, stress, maternal smoking during pregnancy, breastfeeding and physical punishment).

*Results:* At 7 years, socioeconomic parameters, such as parental education and better housing conditions (with less persons per room), child birthweight, fussiness with food and higher conduct problems scale scores were positively associated with zBMI. In addition, early parental practices, such as maternal smoking during pregnancy and duration of breastfeeding, could predict higher zBMI in childhood. At 18 years, zBMI was positively associated with BMI in childhood, birthweight, maternal BMI, and overconsumption of material goods in childhood. Boys were more prone to higher BMI levels, while incorrect perception of self-image, dissatisfaction with self-appearance, breakfast skipping, use of weight control methods, and emotional eating also showed a significant positive association with zBMI at 18 years. Change in zBMI from childhood to adolescence was associated with male gender, fussiness with food in childhood, incorrect perceptions of self-image, lower parental education and paternal stress.

*Conclusions:* Our research suggests any interventions for childhood obesity should begin before the age of 7 years. Attaining healthy eating habits and minimizing material goods in youth could be powerful tools for reducing obesity. Finally, attempts should be made by parents to support adolescents in order to build up a positive and correct opinion of them and adopt stress coping strategies.

## T4.4.1

### **Socioeconomic inequalities in physical and developmental health outcomes for Australian children, birth to 6 years**

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#### **Abstract**

*Objectives:* The impact of family socioeconomic position (SEP) on physical and developmental health in the early years of life is widely recognised. However, it remains unclear at what age health inequalities emerge, and whether SEP relationships vary across ages and health outcomes. We address these issues using cross-sectional data on the physical and developmental health of children at ages 0-1, 2-3, 4-5 and 6-7 years.

*Methods:* Two cohorts of 5000 Australian children each from the Longitudinal Study of Australian Children were assessed in 2004 and 2006. SEP was measured using a composite variable derived from indicators of parental education, occupation and household income. Physical health outcomes assessed at all ages were general health, special health care needs, illness with wheeze, sleep problems and injury. Developmental health outcomes were socio-emotional problems and emotional competence, communication skills, vocabulary and emergent literacy skills, assessed at developmentally appropriate ages.

*Results:* At all ages, lower SEP was associated with increased odds for poor general health, illness with wheeze, sleep problems and poorer outcomes on all developmental health indicators. SEP associations were not found for injury, and were only evident in the oldest age group for special health care needs.

*Conclusions:* There was no evidence of age-limited or cumulative effects on any outcomes, and inequalities were apparent on most measures from the first assessment point. Linear gradients were observed for most physical health outcomes. For the developmental outcomes, linear gradients, thresholds and accelerating (J-relationships) effects were each found across outcomes. The latter associations indicated a marked worsening of outcomes for the most disadvantaged members of the cohorts. Findings confirm pervasive socioeconomic inequalities from early life and highlight the need for comprehensive, early life interventions.

## T4.4.2

### Using Longitudinal Study of Australian Children (LSAC) to identify attributable causal effects of the gaps in health outcome between Indigenous and non-Indigenous Australian infants

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#### Abstract

*Objectives:* The disturbing health gaps between adult Indigenous and non-Indigenous populations sparked many policy attention and national soul-searching. However, little was known about the infant health gaps at a national level between two populations. No study examined the intervening pathways and their attributable effects on the gaps in a longitudinal setting. We aimed to explore two research questions: 1) is there a health gap between Indigenous and non-Indigenous Australia infants; 2) what is the magnitude of individual attributable effect to the gap for a group of risk factors?

*Methods:* We used the baseline and follow-up data from infant cohort of the LSAC study. We identified 34 potential risk factors at individual, socioeconomic and environmental/ecological level and 10 measures of access to health care at baseline. We applied a structural equation modelling approach in deriving the total effect and indirect effect of each interested causal pathways on the follow-up health outcomes. We honoured the complex design of the data in our analysis.

*Results:* Indigenous infants had significant poor global health rating and physical health outcomes at follow-up. The most significant intervening pathways in improving Indigenous overall health outcome were marital status (attributable effect: 0.147), smoking during pregnancy (0.14), social economic position score (0.129), private health insurance (0.122), family income (0.084), receive any of government benefits(0.075), education (0.07), hardship (0.061), mother's age groups (0.06), depression (0.046), stressful life events (0.046), couple relationship (0.041) and drinking during pregnancy(0.038). The attributable effect of neighbourhood belonging and liveability, postcode SEIFA score to the health gap were 0.042, 0.039 and 0.033 respectively. Other less strong significant attributable effects included attachment to friends (0.018) and argumentative relationship (0.014). Similar results were identified for the physical health outcome.

*Conclusions:* Using the national representative longitudinal data from LSAC, we identified the most important attributable effects to the health gaps between Indigenous and non-Indigenous infants. The unique modelling approach that we applied can be used in other settings in understanding the determinants of inequality and inequity in health outcomes. These results provided evidence-base to design the target intervention initiatives in closing the gaps in health outcomes between Indigenous and non-Indigenous infants.

### T4.4.3

## Does the home environment influence inequalities in unintentional injury in early childhood? Findings from the UK Millennium Cohort Study

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### Abstract

*Objectives:* To explore the home environment as a potential mediator between socio-economic circumstances (SECs) and preschool injuries in the home.

*Methods:* We used data on 14,378 children from the Millennium Cohort Study, a large cohort of children born in the UK in 2000-2002. Home environment was represented by proxy measures of housing quality (build type, storey, garden access, rooms per capita, heating type, presence of damp) and safety equipment use (fire guards, safety gates, electric socket covers, smoke alarms) at age 9 months. Risk ratios (RR) for being injured in the home between 9 months and 3 years were estimated using Poisson regression, according to 5 measures of SECs (social class, maternal education, lone parenthood status, area deprivation, and tenure) (captured at 9 months). The home environment measures were then entered into the models, as potential mediators between SECs and injury.

*Results:* Children from less advantaged SECs were more likely to be injured than those from the highest SECs, for all measures of SECs ( $p < 0.05$ ). For example, the RR was 1.42 (95% CI 1.24-1.63) for children whose mothers had no educational qualifications compared to those whose mothers had a degree; and 1.35 (1.24-1.46) for those who lived in socially rented accommodation compared to those living in owned/mortgaged homes. All aspects of the home environment were socially distributed ( $p < 0.05$ ). For example: the RR for living in homes where the main living accommodation was not on the ground floor was 8.46 (6.53-10.97) for children living in socially rented accommodation compared to owned/mortgaged homes; the RR for living in a home without a garden was 3.36 (2.54-4.43) for those whose mothers had no educational qualifications (compared to those with a degree); and homes in the most deprived areas were more likely to not own safety gates (1.63 [1.49-1.77]) than those in the least deprived areas. However, controlling for aspects of the home environment did not alter the association between SECs and injuries.

*Conclusions:* Findings from this observational study imply that steps to improve home environments are, in isolation, unlikely to reduce inequalities in childhood injuries, though they may bring about other benefits.

## T4.4.4

### Impact of socioeconomic position on children's risks for multiple problems in physical, socio-emotional and cognitive functioning

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#### Abstract

*Objective:* A substantial body of literature demonstrates that childhood socioeconomic disadvantage is related to adverse outcomes in physical and developmental health. Most studies have examined single outcomes. Little research has examined the impact of socioeconomic position on the accumulation of multiple adverse outcomes in childhood. This paper examines the association between socioeconomic disadvantage and risks for multiple concurrent adverse outcomes in childhood, in physical health (global health, special health care needs, illness with wheeze, caries, sleep problems, physical quality of life) socio-emotional adjustment and school functioning from infancy to age 9 years.

*Method:* Data were examined for two nationally-representative cohorts from the Longitudinal Study of Australian Children (LSAC). The cohorts, each of approximately 5000 children, were aged 0-1, 2-3, and 4-5 years (birth cohort) and 4-5, 6-7 and 8-9 years (child cohort). Thirteen outcomes were assessed by parent report, teacher report or direct assessment: global health, special health care needs, illness with wheeze, caries, sleep problems, physical quality of life (physical health); conduct, attention and emotional problems (socio-emotional adjustment); and receptive vocabulary, school readiness, school functioning and academic ratings (cognitive domain). Logistic regression analyses examined risks for multiple poor outcomes within each of the three outcome domains and across the domains.

*Results:* Socioeconomic inequalities were apparent in children's physical, socio-emotional and cognitive outcomes at all ages. Inequalities were stronger when considering risks for multiple problems within domains, compared to single outcomes, and stronger again when considering multiple outcomes across all three domains.

*Conclusion:* Socioeconomic disadvantage has substantial and broad-ranging effects on children's physical and developmental health, which are likely to persist into adulthood. The impact was most evident when risks for multiple poor outcomes were considered, illustrating a pervasive effect that is likely to significantly impact on a range of areas of functioning in later life. Conversely, these findings suggest that early interventions to reduce inequalities may have benefits beyond the domain of functioning that may be the central focus. They provide further strong impetus for policy makers to direct resources towards addressing childhood inequalities as a way of improving population health and wellbeing.

## T4.5.1

### **Type of employment relationship and mortality: Prospective study among Finnish employees in 1984–2000**

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#### **Abstract**

*Objectives:* The study investigated the relationship between the type of employment (permanent / temporary) contract and mortality. Factors through which temporary employment was expected to be associated with increased mortality were the degree of satisfaction with the uncertainty related to temporary work situation (Study 1), and the voluntary/involuntary basis for temporary work (Study 2).

*Methods:* In Study 1 the data consisted of representative survey on Finnish employees in 1984 (n = 4502), which was merged with register-based follow-up data in Statistics Finland covering years 1985–2000. In Study 2 the data consisted of representative survey on Finnish employees in 1990 (n = 3502) with register-based follow-up data covering years 1991–2000. The relative risk of death was examined by conducting Cox proportional hazards analyses for the permanent, and the two temporary employment groups, respectively.

*Results:* In Study 1 temporary employees feeling the insecure situation unsatisfactory had a 1.95-fold higher risk of mortality than permanent employees (95% CI 1.13–3.35) after adjusted for background, health- and work-related factors. In Study 2 employees in the position of having a temporary job on the involuntarily basis had a 2.59-fold higher risk of mortality than permanent employees (95% CI 1.16–5.80).

*Conclusions:* The present study confirmed that temporary employees are not a homogeneous group, which holds true even for mortality. Those temporary employees, who either felt the insecure situation unsatisfactory or who worked in temporary work involuntarily, had higher risk of mortality than permanent employees.

## T4.5.2

### **Labour force status, unemployment spells and the effect on psychological well-being set points**

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#### **Abstract**

*Objectives:* This study explores the effect that returning to employment or inactivity after unemployment has on psychological well-being set points. Specifically, we are interested to know whether people return to pre-unemployment levels of psychological well-being.

*Methods:* Data came from the British Household Panel Survey. Psychological well-being was measured using the GHQ-12 and a question on life satisfaction; participation in the labour force was self-reported. Multilevel regression models were used to explore associations among males and females.

*Results:* Findings showed differences by gender and post-unemployment labour force status. Previously employed males who returned to employment following unemployment experienced a return to their GHQ set point; a similar pattern was seen for previously inactive males who gained employed following a period of unemployment. Previously employed males who left the labour force following unemployment experienced a return to their life satisfaction set point, but not their GHQ set point. Previously employed females also experienced a return to their GHQ-12 and life satisfaction set points after employment. No other significant associations were observed for females.

*Conclusions:* Findings suggest that males and females return to their GHQ-12 set point only if they become re-employed after experiencing unemployment. If they become economically inactive, their psychological well-being does not return to the level it was prior to unemployment.

### T4.5.3

## Investigating the effects of labour market position on minor psychiatric morbidity across the business cycle: longitudinal analysis of the British Household Panel Survey, 1991-2007

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### Abstract

*Objective:* Existing longitudinal evidence suggests that the link between joblessness and minor psychiatric morbidity (MPM) is likely to be causal, but that many complex processes are at play. This study seeks to contribute to the field by assessing the relationship between labour market position and MPM across the business cycle, looking at the effects of permanent sickness and other economic inactivity as well as registered unemployment.

*Methods:* This study is based on working-age (16-65 years), original sample members of the British Household Panel Survey. All seventeen currently available waves of the study are used (1991-2007). MPM is measured in the BHPS using the 12-item version of the General Health Questionnaire (GHQ-12). The analysis presented uses a binary outcome (MPM caseness). A series of nested random effects logit models are presented, showing the association between labour market position and MPM before and after adjustment for confounding and mediating factors. Covariates included macroeconomic conditions, educational attainment, physical health problems, spousal GHQ12 and unemployment, perceived job security level of the employed, housing tenure, substance abuse, equivalised household income and subjective assessment of financial situation. The models also adjust for lagged GHQ12 score, to control for any propensity towards MPM and are stratified by sex.

*Results:* Prevalence of MPM is significantly greater among the jobless than the employed. In the fully adjusted model, compared to the employed: the unemployed were more likely to be MPM cases (OR=1.66,  $p<0.001$ ), as were the permanently sick (OR=2.30,  $p<0.001$ ) and the 'other inactive' category (OR=1.21,  $p<0.026$ ). Stratification by sex shows that it is important to treat male and females separately with regards to labour market exposure. Males who were permanently sick were more likely to be MPM cases than their female counterparts (OR= 2.58,  $p<0.001$  and OR=1.99,  $p<0.001$  respectively). Unemployed women were at higher risk of MPM than their male counterparts (OR=1.77,  $p<0.001$  and OR=1.44,  $p=0.005$  respectively). Adjustment for macroeconomic conditions across the business cycle produced no difference in the odds ratios reported.

*Conclusion:* This study shows that joblessness is significantly associated with minor psychiatric morbidity even after full adjustment for a wide range of confounders.



## T4.5.4

### Sickness absence in men and women

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#### **Abstract**

*Objective:* Women are generally considered to have higher sickness absence rates than men, a difference that is especially salient in the Scandinavian countries. Deriving from previous studies, indicating that men exhibit a less help-seeking health behavior than women and experience not working as more stigmatic, we propose that psychological factors play an important role in explaining this gender gap. We use the theory of planned behavior (TPB) to capture psychological determinants of sickness absence behavior. According to the TPB human behavior is determined by the intention to perform the behavior which in turn is a function of attitudes, subjective norms, and perceived behavioral control with regard to the behavior. TPB also states that these manifest approaches reflect underlying beliefs (i. e., behavioral, normative and control beliefs). We apply a prospective, longitudinal cohort study using both survey data and objective measures to predict sickness absence from TPB-determinants.

*Methods:* A random sample of 5000 individuals drawn from all Swedish citizens aged 20-59 years received a survey in December 2008 (response rate 48 %) on health, work situation and TPB-determinants concerning the intention to work in a year. The questionnaire was designed by the Swedish Social Insurance Agency in collaboration with researchers at Uppsala University. The survey data was supplemented with some socio-demographics from Statistics Sweden and register data on sickness benefit payment during 1st January 1995 until 20 January 2010 from The Swedish Social Insurance Agency.

*Results:* We tested the model using Structural equation modeling (SEM) and the behavior was measured as net days with sickness benefit payment during 2009. The analysis revealed that the intention to work significantly predicts sickness absence in a negative direction, however, the relationship is stronger for men than women. Social norm is the most important predictor of the intention to work in both sexes, though, for men there is a stronger indirect effect of social norm on the intention to work, mediated by perceived behavioral control and attitude. Men also have higher scores on average in the social norm variable.

*Conclusion:* The results support the hypothesis that men and women differ with regard to psychological determinants of sick leave behavior. Social norm seems to be a more central underlying attitude component in men's intention to work, thus indirectly the sick leave behavior. The fact that men on average also score higher on social norm could be an important explanation of the gender gap in sick leave.

## T4.6.1

### **The SOFIA study: A multi-disciplinary large scale longitudinal study of social, behavioral, and physical development**

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#### **Abstract**

*Objectives:* SOFIA (SOcial and PHysical development, Interventions and Adjustment) is a Swedish longitudinal study of children's social, behavioural and physical development, started in March 2010. The overall objective of the study is to better understand the development of children's social, physical and mental health, including antisocial behaviour. The study also aims to study when, why, and how children with special needs get professional support. Design, implementation and baseline prevalence data of the study will be presented.

*Methods:* All 2487 children in municipal and private preschools in the municipality of Karlstad in Sweden, born in 2005, 2006 or 2007 constituted the target population. The children are followed once a year for three years to begin with. The long term plan is to follow them into adulthood. Data is gathered primarily via web-based questionnaires answered by pre-school staff, principals and the child's parents. The study is led by a multidisciplinary research group including researchers in psychology, medicine, social work, pedagogic, and public health science. It is conducted in collaboration between the research group and the municipality of Karlstad in Sweden. Before the start of the study, a "SOFIA group" was formed, consisting of researchers, the municipality's development manager and principals from preschools involved in the study. A "SOFIA folder" including all required information enabled the preschool staff to be a vital link between the research group and the parents, throughout the data collection period.

*Results:* The first data collection has been finalized and as many as 86% of the children's parents accepted to participate in the study, in total 2112 children. Preschool staff and principals have filled in questionnaires for 100 percent of these children and the response rate among parents is 94 %. Baseline prevalence data on i.e. antisocial behaviour, chronic health conditions and early interventions will be presented.

*Conclusions:* A successful collaboration between researchers, managers and practitioners can secure the interests in a large scale longitudinal study for all the involved partners and result in a high participation rate.

## **T4.6.2**

### **Family and children of Ukraine: a long-term epidemiological study of children's state of health in Ukraine's cities**

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#### **Abstract**

The Family and Children of Ukraine (FCOU) study is the Ukrainian component of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC). The FCOU study is a birth cohort study of 7,500 Ukrainian families that was initiated in 1993 and follows the cohort to the present time. The purpose of the study is to investigate the influence of multilateral factors on the course of pregnancy, labor, health and development of children from their birth up to their graduation from school.

The FCOU study recruited pregnant women living in Ukraine's urban regions: in the cities of Kyiv, Dneprodzerzhinsk, Mariupol and Krasny Luch. Data collection has been carried out through questionnaires and medical record abstraction. The study protocol and data collection instruments were developed by the ELSPAC study group and the coordinating center at the University of Bristol and adapted for Ukraine's conditions by the Institute of Pediatrics, Obstetrics and Gynaecology of the Academy of Medical Sciences of Ukraine (POG AMS). The questionnaires are completed by the mother or caregiver. Children complete their own questionnaires beginning at age 11. Medical record abstraction is performed by medical personnel. In addition to the ELSPAC questionnaires and medical record abstraction, we have also carried out several focused studies, including studies on environmental exposures, obesity, and wheezing illness.

The FCOU studies are carried out under the general supervision of the Institute of POG AMS of Ukraine (Department of Medical-Social Family Problems) with the participation of the Great Lakes Center for Occupational and Environmental Safety and Health at the University of Illinois in Chicago, National Medical University, and the Departments of Public Health of the stated regions. Local health care providers participate in the data collection. Research training support for the FCOU study has been provided by the Fogarty International Center at the U.S. National Institutes of Health. The FCOU research program is focused on the determination of biological, social, medical, ecological, psychological and cultural factors that influence on the health and survival possibilities of fetuses, babies, on children's harmonic development, and consequently on the survival, health and development of Ukraine's young generation.

We are currently studying somatic, intellectual, and reproductive health problems of children who are between 15 and 18 years of age.

The data collected in the FCOU research program continues to be systematically analyzed with the goal of designing and implementing effective measures for prevention.

## T4.6.3

### The SELMA study – research for a healthier future

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#### Abstract

*Objective:* SELMA (Swedish Environmental Longitudinal, Mother and child, Asthma and allergy) is a study on the importance of early life exposure for environmental factors and life styles for development of asthma and allergy and other chronic diseases in Swedish children. The study aims to investigate the importance of early life exposure (during pregnancy and infancy) for modern exposures such as endocrine disrupting chemicals (EDCs) for the development of asthma and allergies, reproductive effects neuro-psychiatric disorders, overweight, diabetes, etc. in human offspring later on in life.

*Method:* The SELMA study started in September 2007 and is designed to follow a birth cohort of 2,500 pairs of mothers and children from 10<sup>th</sup> week of pregnancy, over birth and until school age of the child and further. Medical examinations and bio-sampling (blood and urine) will be conducted for both the pregnant women and the child. Questionnaires and interviews will be used to collect information about background factors as well as life style factors of the family. Environmental exposures will be estimated by analyzing air and dust samples from the homes during pregnancy and infancy period. This multidisciplinary study includes scientists within the area of medicine, epidemiology, statistics, engineering, public health sciences, chemistry and biomedical science and is a collaboration between 12 international institutions from Sweden, Denmark, Norway, Taiwan, China and USA.

*Results:* The recruitment of pregnant women started in September 2007 and ended in March 2010. Of 6,649 invited pregnant women, 2,577 accepted to participate, corresponding to a participation rate of 40% and 1,855 children has so far been born. 2,311 blood samples (90%), 2,319 urine samples (90%) and 2,021 answers of the first questionnaire (78%) have been received. A non-respondent questionnaire was distributed to women that did not want to participate in the study. Results of this showed that participating woman have more allergy (58 vs 38%), live in a single family house to a higher degree (68 vs 60%) and have a higher education level (51 vs 36%), but smoke to a lower extent (13 vs 19%).

*Conclusion:* This study is a result of a multi disciplinary collaboration between institutions and countries. One main strength with the SELMA study is that we will be able to evaluate the health relevance of exposing foetuses and infants for modern chemicals since such data is lacking.

## T4.6.4

### **The 11-year follow-up of the CCC 2000 birth cohort study: Psychosis-like experiences (PLE) in children**

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#### **Abstract**

*Objectives:* The CCC2000 study investigates risk mechanisms of psychopathology from the first year of life. The 11 year follow-up will describe the prevalences, risk factors and correlates of mental illnesses – and of the early signs and symptoms along the continuum from mental health problems to mental disorders. The perspective is to define longitudinal phenotypes closer to genetic endophenotypes, and to propose early 'at risk' states that may be useful targets for indicated prevention.

The present study of psychosis-like experiences (PLE) aims to define an 'at risk of psychosis' mental state characterized by the presence of PLE combined with developmental lags and problems regarding social, language and/or motor abilities and/or emotional/behavioural functioning. A nested case-control study aims to identify disorder-specific sub-components of cognitive deficits.

*Methods:* The study population consists of 6090 children born in Copenhagen County, Denmark, in the year 2000. The cohort is representative of the Danish population. The follow-up studies have demonstrated that risk mechanisms and signs of psychopathology can be identified from early infancy. The 5-7 year follow-up of CCC 2000 has described the prevalence and pattern of comorbidity of the mental health problems and disorders in that age. Due to attrition of 188 children a total of 5902 children will be investigated at age 11. The key measures of the 11-year follow-up are self-report questionnaires answered electronically by child, parent and teacher. Child mental health problems and disorders will be assessed by Strength and Difficulties Questionnaire (SDQ) and Development and Well Being Assessment (DAWBA), also used in the 5-7 year follow-up. PLE will be screened by the section T in DAWBA. All Children who screen positive for PLE (and screen negative controls) will be assessed for psychotic-like symptoms by trained professionals using a semi-structured psychopathological interview (SCAN, PSE, part 2). The Case-control study of cognition will include a representative sample of the children with verified psychotic-like symptoms, ADHD, or autism spectrum-disorder. Controls are matched by gender, parent education and household income.

*Results and conclusion:* aim to inform future early identification and intervention of mental health disorders.

## T5.1.1

### Developing a Child Cohort Research Strategy for Europe: the CHICOS project

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#### **Abstract**

*Objectives:* Over the last two decades, a number of pregnancy and birth cohorts have been established in Europe with the shared purpose to follow participants from the intrauterine period, throughout childhood and adolescence into early adulthood. Some are large general cohorts with multiple aims, whilst others are smaller and more focused on specific risk factors or specific diseases. Some have been following children for many years, whereas others have just started. In total, such cohorts comprise more than 350,000 children and their parents across Europe and they form an important resource for child health and life-course research. However, data are, by nature, non-uniform across cohorts and improved coordination at European level is needed to take full advantage of this important infrastructure of existing cohorts.

*Methods:* The European Commission's 7<sup>th</sup> Framework Programme has recently funded the coordination project CHICOS ("Developing a Child Cohort Research Strategy for Europe") to develop an integrated strategy for birth cohort research in Europe. This will be achieved by the development of a comprehensive inventory of birth cohorts, by an evaluation of existing data on child health outcomes and risk factors, by identification of gaps in knowledge and coverage of the cohorts, and by an assessment of how contribution of cohorts to policy may be improved. Working groups will focus on main topics of policy relevance in the areas of pregnancy outcomes, asthma and allergies, obesity, cognitive and behavioural development, infectious diseases, injuries, childhood cancer, social and cultural factors, nutrition, physical activity, environmental pollutants, and genetic factors.

*Results:* The CHICOS project brings together partners from some of the oldest and largest cohorts in Europe with important newer cohorts, and cohorts from relatively underrepresented regions of Europe. All other relevant cohorts in Europe will be asked to join the project workshops, the inventory, and the working groups.

*Conclusions:* In this presentation we will present the CHICOS aims, work plans, and vision for close collaboration between European birth cohorts.

## T5.1.2

### **ENRIECO: European Inventory of Birth Cohorts with Environmental Exposures**

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#### **Abstract**

*Background:* It is well recognised that the foetus and infant are especially vulnerable to the effects of environmental contaminants, and that these effects may manifest themselves throughout the lifetime and even over generations. Pregnancy and birth cohort studies have played a prominent role in studying these effects. There are many such cohorts in Europe, but data are often of fragmented nature. Therefore, the EC has funded the ENRIECO project to coordinate European birth cohort research in the area of environmental exposures. An inventory of cohorts is a prerequisite for improved coordination.

*Objective:* To create an inventory of all existing pregnancy and birth cohorts in Europe with data on environmental exposures and make this publically available as a web-based searchable database.

*Methods:* Criteria for inclusion of cohorts in the inventory were: collection of data on at least one environmental exposure topic; start enrolment during pregnancy or at birth; at least one follow-up point after birth; and inclusion of at least 200 mother-child pairs. An inventory questionnaire collected information on basic protocol details, and exposure and outcome assessments, including contaminants, methods and samples, timing, and number of subjects.

*Results:* Questionnaires were completed by 31 cohorts with information for more than 300,000 children. In most of cohorts (N=17) children are now aged between 5-10 years, in 11 cohorts children are 10-20 years old and in only 2 cohorts children are over 20 years. All of the 31 cohorts are assessing exposures to environmental tobacco smoke, 27 collect information on parental occupation, whilst 22 are assessing air pollution. Fewer cohorts collect biomarker data on specific exposures such as metals (N=12 mercury and lead, N=9 cadmium) or persistent organic pollutant (N=16). All cohorts have information on birth outcomes, 27 on asthma/allergy, and 25 on child neurodevelopment. Working groups within the ENRIECO project are carrying out further evaluations of European birth cohort data on all these topics.

*Conclusion:* This web-based inventory will be the first place that provides detailed information on exposures and outcomes measured in all European birth cohorts with environmental exposure data. It will facilitate future collaboration and effective use of existing data.

## T5.1.3

### Family-based longitudinal database of Norwegian citizens

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#### **Abstract**

*Objective:* Investigating early life exposures and later health outcomes in study designs that increase strength of causal inference generally need large sample sizes. This is because methods will require formal statistical testing, such as difference between paternal and maternal effects, grandparental effects, within and between sibship comparisons and associations between genetic variants and later disease. We will here present a comprehensive longitudinal and multigenerational database of the Norwegian population.

*Methods:* Data of all participants in the Censuses from 1960 through 2001 which includes all Norwegian citizens (n=6,7 million records) was linked to the Norwegian Birth Registry (1967-2009), the Cancer registry (1960-2009), the Cause of death registry (1960-2008), the Disability Registry (1992-2008) and the Cohort of Norway (CONOR). CONOR is a pool of Norwegian health surveys from 1994-2002 (n=173,000) including blood samples. The multigenerational database was constructed by using the personal identity number which includes family information for most individuals born after 1952 and the Census in 1960 which extended household based family information, including parents and siblings, for those born between 1940-1952.

*Results:* 1,3 million siblings were identified in the total population participating in the Censuses 1960-2001. Of all those Norwegians born after 1940 90% of their parents could be identified. There were 240,000x4 grandparents with offspring births recorded in the Medical Birth Registry. Other outcomes from the Disability registry and Cancer registry will be presented. In CONOR there were 30,000 siblings and 19,000 father, mother offspring trios.

*Conclusions:* This multigenerational data base provides potential to conduct large scale family based studies. In order to take full advantage of this and other similar data bases in future collaborative research, the complexity of the data needs to be better communicated.



## T5.1.4

### Prospects for contextual analyses in longitudinal ageing research: the case of the Linnaeus database

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#### **Abstract**

*Objective:* The objective of the paper is to present the so-called Linnaeus database, recently developed at Umeå University. One objective of the research is to improve the possibilities to analyse the influence of individual versus contextual effects on the prospects for successful ageing.

*Methods:* The Linnaeus Database is designed for longitudinal analyses of the interrelations between health and socio-economic conditions over the life course. The database includes anonymised individual data for the whole population with rich socio-economic information as well as information about death, death causes, hospitalisation, and diagnosis. For the people included in the two local regional investigations even more detailed information is available for instance about, life style, social support, self-reported health and data from cognitive tests etc. Since the data contains information about place of residence, working place and family links for all individual in the country, it has allowed the researchers to design contextual variables including all residents in any geographical context, the composition of employed in any work place as well as the characteristics of family networks.

*Results:* By combining socio-economic and health data from Swedish registers with information from two local investigations on health and cognition (VIP and Betula) a unique research database has been created. As a major part of the data is longitudinal and annual for the period 1990 – 2006 it allows for thorough analyses of relations between health and socio-economic conditions related to the individual and to various social environments, such as neighbourhoods, work places and family networks. Due to the rich information, the data also allows for matching methods and for considering selection effects.

*Conclusion:* The design of the Linnaeus Database has demonstrated the potential of micro-data based on entire populations, since it is possible for researchers to be flexible when making contextual variables. Hence this kind of data allows for new research questions on the interrelations between health and socio-economic conditions over the life-course.

## T5.2.1

### Common variants near LEPR and PCSK1 are associated with infant BMI

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#### Abstract

**Objectives:** To identify associations between common genetic variation and changes in infant body mass index (BMI) through a meta-analysis of genome-wide association studies (GWAS) using longitudinal growth data.

**Methods:** Four population-based birth cohorts of European ancestry born in 1934-2006 were included in the analysis (Helsinki Birth Cohort Study, Northern Finland Birth Cohort 1966, Generation R Study from Rotterdam, and LISA Study from Munich; N=6,222). Age and BMI at infant adiposity peak (AP) were estimated from mixed effects models fitted on repeated BMI measurements from 2 weeks to 1.5 years. These phenotypes were regressed on imputed genotypes from ~2,500,000 single nucleotide polymorphisms (SNPs), assuming an additive genetic model. The cohort-specific results were meta-analysed using an inverse variance fixed effects model.

**Results:** Common polymorphisms near two genes that contain rare mutations causing severe obesity, leptin receptor (LEPR;  $p=6 \times 10^{-8}$ ) and proprotein convertase subtilisin/kexin type I (PCSK1;  $p=1 \times 10^{-6}$ ), were associated with BMI at AP, occurring at ~9 months of age. Both loci contained a cluster of associated SNPs, and the most strongly associated SNP from each locus was selected for replication in other cohorts that have DNA and infant growth data available (replication results pending). Leptin hormone, which regulates adipose-tissue mass, acts through the LEPR gene. The protein encoded by the PCSK1 gene converts pro-hormones into functional hormones that regulate energy metabolism. Therefore both of them are plausible candidate genes for obesity-related traits. The locus with the strongest association with adult BMI to date, FTO, was not associated with BMI at AP (SNP rs9939609  $p=0.71$ ), which supports earlier findings suggesting an age-dependent BMI effect.

**Conclusions:** This is the first GWAS meta-analysis to identify common variants associated with infant BMI near candidate genes for obesity (LEPR and PCSK1). The methodological novelty is the use of estimates from longitudinal models as phenotypes. Larger samples are needed to identify more variants involved in infant/child BMI regulation. If these studies turn out to be successful, a genetic component could be added to future risk prediction algorithms for infant/child obesity.

## T5.2.2

### Association between common variation at *FTO* locus and changes in body mass index from birth to adolescence: Longitudinal analysis of over 19,000 children of European ancestry

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#### Abstract

**Objectives:** To meta-analyze the association between variation at the *FTO* locus (rs9939609) and BMI in longitudinal collections with samples aged 2 weeks to 13 years from eight cohorts of European ancestry (N > 19,000).

**Methods:** ge-stratified cross-sectional analyses and longitudinal analysis using mixed effects modelling and extensions to this (skew-t) to fit growth curves in infancy (2 wks–1.5 yrs) and childhood (1.5–13 yrs). The association between *FTO* rs9939609 and change points in BMI – infant adiposity peak (AP) and childhood adiposity rebound (AR) – was explored.

**Results:** In cross-sectional analysis we identified a positive association between additional minor (A) alleles and BMI from 5.5 years onwards. In contrast, an inverse association was observed between additional minor alleles and BMI below age 2.5 years. In longitudinal analysis, the same variation was associated with lower BMI in infancy (AA vs. TT -0.11 kg/m<sup>2</sup> (95% CI: -0.20, -0.03),  $p=0.007$ ), higher BMI in childhood (AA vs. TT 0.13 kg/m<sup>2</sup> (95% CI: 0.06, 0.20),  $p=9E^{-05}$ ), and a faster BMI growth rate in childhood (AA vs. TT 0.039 kg/m<sup>2</sup>/year (95% CI 0.028, 0.051),  $p=7E^{-12}$ ). The A-allele at rs9939609 was also associated with a higher average BMI at the age of AR (AA vs. TT 0.848 % (95%CI: 0.515, 1.181),  $p=6E^{-07}$ ). Carriers of 2 minor alleles had on average 0.28 years (95%CI: 0.21, 0.34) earlier AR than non-carriers ( $p=1E^{-17}$ ).

**Conclusions:** This study found evidence for a strong and expected association between variation at *FTO* and BMI in childhood, but only after an inverse association between the same variant and BMI in infancy. Whilst we are unaware as to the exact cause of these effects, this pattern is similar to that predicted by a simple hastening of normal developmental trajectory. The positive association between rs9939609 and BMI in childhood was manifest in both differential rates of BMI change and points of inflection in modelled BMI curves. The age-dependent nature of the association between *FTO*rs9939609 and BMI provides an important contribution to our knowledge of longitudinal gene effects and further evidence of our limited understanding of the role of *FTO* in adiposity.

## T5.2.3

### Association studies of the common variant in the *FTO* gene – The Finnish Diabetes Prevention Study

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#### Abstract

**Objectives:** The common single nucleotide polymorphism (SNP) in the *FTO* (fat mass and obesity associated) gene has been consistently associated with an increased risk of obesity and related metabolic traits. We examined whether this variant (rs9939609, T/A) in the first intron of the *FTO* was associated with body mass index (BMI), inflammatory markers, serum lipids, long-term weight changes and cardiovascular disease (CVD) risk in the Finnish Diabetes Prevention Study (DPS).

**Methods:** Altogether 522 (BMI  $\geq$  25 kg/m<sup>2</sup>) subjects with impaired glucose tolerance were randomized to a lifestyle intervention or a control group. SNP rs9939609 was genotyped by Illumina protocol from 502 subjects. Cardiovascular morbidity and mortality data were collected during the median follow-up of 10.2 years.

**Results:** At baseline those with the AA genotype had higher BMI than subjects with other genotypes ( $p=0.006$ ), but the association was observed only in women ( $p=0.016$ ). During the follow-up, the subjects with the AA genotype had consistently the highest BMI ( $p=0.009$ ) in the entire study population. The magnitude of weight reduction was greater in the intervention group. The risk allele did not modify weight change in either of the groups. In men, the AA genotype was associated, independently of BMI, with increased RANTES (Regulated on Activation, Normal T Cell Expressed and Secreted) ( $p=0.002$ ) and decreased HDL cholesterol concentrations ( $p=0.007$ ). During the follow-up, the AA genotype was associated with an adjusted 2.09-fold risk (95% CI 1.17-3.73,  $p=0.013$ ) of CVD, but only in men.

**Conclusions:** Our results confirm the association between the common *FTO* variant and BMI cross-sectionally and during the long-term lifestyle intervention. We did not observe association between the *FTO* variant and the magnitude of weight reduction. Thus, it is unlikely that the common variant of the *FTO* gene affects the success of lifestyle modification on weight loss. Our data provide also preliminary evidence that the *FTO* rs9939609 polymorphism contributes to variation in RANTES concentration in men. Furthermore, we suggest that the variation in the *FTO* gene might increase the risk of cardiovascular diseases in men.

## T5.2.4

### Associations between the pubertal timing-related variant in LIN28B and BMI vary across the life-course

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#### Abstract

*Objective:* To explore the association between genetic variation in LIN28B (rs314276), a robust marker for earlier age at menarche and other pubertal traits, with body mass index (BMI) across the life-course. Since this variant was previously shown to be unrelated to prepubertal BMI or body weight, we hypothesised that such associations may be indicative of the effects of the timing of puberty on obesity risk.

*Methods:* rs314276 in LIN28B was genotyped in 1242 men and 1209 women born in 1946 and participating in the MRC National Survey of Health and Development. Birth weight was extracted from medical records and height and weight were measured or self-reported repeatedly at 11 time-points between ages 2 and 53 years. Polynomial mixed models were used to test whether additive genetic associations with standard deviation scores (SDS) for BMI and height changed with age between 0 to 53 years.

*Results:* Longitudinal analyses revealed age-dependent associations between rs314276 genotype and BMI ( $p < 0.001$  for genotype-by-age<sup>2</sup> interaction) and body weight ( $p < 0.001$  for genotype-by-age<sup>2</sup> interaction) in women, but not in men. In women only, the common 'C' allele at rs314276 (which confers earlier age at menarche) was associated with higher BMI SDS from ages 15 through to 43 years. In contrast, 'C' allele associations with shorter height SDS were apparent in both men and women and did not vary with age.

*Conclusion:* A common genetic variant in LIN28B that confers earlier puberty was associated with a prolonged increase in BMI during adolescence and early to mid-adulthood in women only. Examination of such genetic associations in a longitudinal setting may provide new insights into the direct effects of pubertal timing on subsequent weight gain.

## **T5.3.1**

### **Families with parental depression – are preventive interventions effective in reducing children’s psychosocial symptoms**

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#### **Abstract**

*Objectives:* The aim is to document the effectiveness of a preventive family intervention (Family Talk Intervention) and a brief psychoeducational discussion with parents on children’s symptoms and prosocial behaviour in families with parental mood disorder, when the interventions are practiced as part of the treatment protocol for adult psychiatric patients. We also studied whether changes in parental depression modified the findings.

*Methods:* Patients with mood disorder were invited to participate with their families in the trial. Consenting families were randomized to the two intervention groups. The initial sample comprises 119 families and their children aged 8-16, and of these 109 completed the interventions and the baseline evaluation. Mothers, fathers and children filled out questionnaires including standardized rating scales for children’s symptoms and prosocial behaviour at baseline and at four, ten and eighteen months post intervention. The final sample to be used in mixed effects models consisted of parental reports on 148 children.

*Results:* Parental reports showed significant positive changes in children’s emotional symptoms and prosocial behaviour particularly in the Family Talk Intervention group. Parental depression pressure in the families tended to moderate the change.

*Conclusions:* The study supports the effectiveness and applicability of the Family Talk Intervention in health services for families with depressed parents. The study documents further how even a brief discussion with depressed parents about children, coupled with a guide book, is associated with favourable changes in child well-being according to parental reports. Our findings provide support for including preventive measures as part of psychiatric services for mentally ill parents.

## T5.3.2

### Early onset puberty and psychosocial adjustment in earlier childhood: National Australian longitudinal study

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#### Abstract

**Objective:** Mental health problems, particularly major depression and anxiety disorders, increase in prevalence between childhood and adolescence. Recent studies have implicated the pubertal process itself in this rise, but none has had the capacity to examine these pubertal changes in the context of earlier childhood mental health and behaviour. We aimed to determine whether early-onset puberty is related to poorer concurrent and earlier childhood mental health in a national Australian population-based sample.

**Methods: Participants:** Members of the Longitudinal Study of Australian Children, which recruited 4,983 4-5 year olds in 2004 (59% response) and followed them at ages 6-7 and 8-9 years. **Main measures:** (1) Pubertal onset (yes/no) at age 8-9 years from parent-reported breast development, skin changes, body hair, and adult body odor. (2) Parent-reported mental health and psychosocial functioning at each wave (SDQ Total Difficulties Score, PedsQL Psychosocial Health Summary Score). **Analysis:** Linear regression analysis to determine (1) cross-sectional and (2) longitudinal associations of early-onset puberty with SDQ and PedsQL scores.

**Results:** Of 4,331 children at 8-9 years (87% retention), 3,687 took part in all three waves including data on early puberty. 16% of girls and 6% of boys had definite puberty onset. Early puberty was associated with poorer psychosocial health concurrently (eg 8-9yr PedsQL mean for early vs not early puberty, 72.9 vs 76.2,  $p \leq .001$ ; SDQ 8.0 vs 7.8,  $p = .04$ ). Poorer scores were already evident by ages 4-5 and 6-7 years in the early puberty group (eg 6-7yr PedsQL: 76.7 vs 77.9,  $p = .04$ ), and these discrepancies widened with puberty onset. Effects were seen across emotional, social and school functioning subscales (eg. 8-9yr PedsQL: emotional 69.9 vs 73.2,  $p = .001$ ; social 75.2 vs 79.2,  $p \leq .001$ ; school 74.0 vs 76.1,  $p = .001$ ). There was a suggestion that some effects were stronger for boys than girls.

**Conclusion:** Children who had commenced puberty by age 8-9 years had poorer mental health and psychosocial health scores, at least partly antedating the pubertal process. We therefore speculate that early psychosocial stressors may affect the timing of puberty. Alternatively, both early-onset puberty and mental health problems could reflect a shared life-course vulnerability from very early in development.



### T5.3.3

## Maternal hypertensive disorders during pregnancy and mild cognitive limitations in the offspring

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### Abstract

*Objective:* The proportion of children having mild cognitive limitations (intelligence quotient 50-85) has been estimated about six percent. The most robust effects of this condition are educational and occupational attainment problems. Environmental factors contributing to differences in intelligence can be modified, e.g. by perinatal and educational factors. There is a paucity of studies of the relative roles of biological environmental factors on childhood intelligence. The aim of our study was to explore the association between maternal hypertensive disorders during pregnancy and mild cognitive limitations in the offspring.

*Methods:* Our 11.5 year follow-up study is population-based and belongs to longitudinal Northern Finland Birth Cohort 1986 study (NFBC 1986). The total number of mothers and deliveries was 9 432. The present study includes 8 649 singleton children, who did not refuse the use of their data. Of these children 198 had mild intellectual limitations. Maternal hypertension was defined as de novo hypertension arising after mid-pregnancy to normotensive mother (systolic blood pressure of  $\geq 140$  mm Hg or diastolic blood pressure of  $\geq 90$ ). The data on maternal blood pressure were collected from recordings of maternal health care centers and antenatal clinics. Data on intellectual level was based on psychometric test results collected from hospitals, institutions, family counseling centers and school psychologists in the study area.

*Results:* Maternal gestational hypertension emerged as having an independent risk for mild intellectual limitations in the offspring (OR, 2.70, CI 1.48-4.91, p-value 0.001). In addition, male-gender, SGA-status of the newborn, family SES lower than professional, high maternal prepregnancy BMI and high parity had an independent effect on intellectual limitation in the multiple regression analyses.

*Conclusion:* Adverse intrauterine environment appearing as maternal gestational hypertension has an association with mild cognitive limitations in the offspring. The mechanisms responsible for this association need further study.

## T5.3.4

### **Applying Latent Class Growth Analysis to the investigation of developmental trajectories of pure or combined psychopathological problems**

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#### **Abstract**

*Objective:* The current work aims to provide evidence that Latent Class Growth Analysis (LCGA) can be used for the identification of different groups of individuals exhibiting normative, pure or combined developmental trajectories of distinct psychopathological problems. For the purposes of the current paper, LCGA is used to investigate the development of pure and co-occurring internalizing and externalizing problems from age 2 to age 12. LCGA can also aid in the identification of (1) possible factors that might place individuals at higher risk for exhibiting pure or combined psychopathology, and (2) developmental outcomes that might be related to higher risk groups of individuals. Thus, in addition to the development of externalizing problems, we also examine how antecedents (temperament, cognitive functioning, maternal depression, and home environment) during the first two years of life and early adolescent outcomes (delinquency and peer relationship variables) are related to differential trajectories of pure and co-occurring internalizing and externalizing problems.

*Methods:* The sample (NICHD study of Early Child Care) consisted of 1232 children (52% male). Mother self-reports on the Child Behavior Check List (CBCL) were used to construct the trajectories of externalizing and internalizing problems. Antecedents were based on interviews, assessments, self-reports, and observations. Early adolescent outcomes were based on questionnaires completed by teachers, mothers, the study's children, and friends of the study's children.

*Results:* The findings suggested the existence of different groups of children, exhibiting pure and co-occurring internalizing and externalizing problems. Children exhibiting continuous externalizing or co-occurring internalizing and externalizing problems were more likely to (1) engage in risky behaviors, (2) be associated with deviant peers, (3) be rejected by peers, and (4) be asocial with peers. However, children exhibiting pure internalizing problems were only at higher risk for being asocial with peers. Moreover, the additive effects of both individual and environmental risk factors influenced the development of chronic externalizing problems, although pure internalizing problems were uniquely influenced by maternal depression.

*Conclusions:* Studies using the LCGA method can offer a more comprehensive view of co-occurrence when compared to studies investigating point by point change or average trajectories of change over time. The current investigation provides important information for the co-occurrence between different behavioral problems, which is considered to be a major research challenge for developmental psychopathology research. The findings also suggest that taking into account the concept of co-occurrence is essential for explaining the development and understanding the etiology of externalizing and internalizing problems

## T5.4.1

### Dietary patterns and cardiovascular disease mortality in older Australians

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#### Abstract

**Objectives:** Despite having the second longest life-expectancy in the world, cardiovascular disease remains a major cause of mortality in Australians. Due to the effects of diet on cardiovascular disease, dietary pattern analysis is of increasing interest in cardiovascular research. To identify major patterns of dietary intake using Principal Components Analysis [PCA] and assess their impact on the 5-year incidence of cardiovascular mortality

**Methods:** Older community-dwelling Australians (n = 343) were recruited from the prospective Melbourne Collaborative Cohort Study. At baseline, conventional cardiovascular risk factors were determined [fasting glucose and lipids were measured in plasma while albumin and creatinine were measured in 24 h urine], and dietary intake was assessed by food frequency and portion-size questionnaires. A personal lifestyle questionnaire provided medical, family, and activity information. CVD mortality was determined from data held at national registries.

**Results:** Using the components above the (first) break in the Scree plot [Scree criterion], we identified a set of two major dietary patterns. The first was a Mediterranean-style dietary pattern, characterized by plant foods, while the second was a dietary pattern in which highly processed [fried/sweet/salty] foods featured more prominently than plant foods. In a fully adjusted Cox regression model, the dietary pattern featuring processed foods was associated with a significantly higher 5-yr incidence of CVD mortality [hazard rate ratio (95% CI) 1.83 (1.03, 3.25)], while a protective trend was apparent for the Mediterranean-style dietary pattern [hazard rate ratio (95% CI) 0.59 (0.32, 1.10)].

**Conclusions:** A Western-style dietary pattern characterized by highly processed foods featuring fat, salt and sugar was associated with higher CVD mortality in older Australians, supporting the promotion of a less-processed diet based on fresh foods, such as the Mediterranean diet.

## T5.4.2

### Associations of vitamin D, parathyroid hormone and calcium with cardiovascular risk factors in US adolescents

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#### Abstract

*Objective:* Evidence from adult studies suggest that lower circulating vitamin D (25(OH)D), higher parathyroid hormone (PTH) and higher calcium levels are associated with cardiovascular disease and risk factors. Current evidence for these associations in adolescents is limited. We aimed to examine independent associations of 25(OH)D, PTH and calcium with a range of cardiovascular risk factors in adolescents.

*Methods:* We conducted a cross-sectional analysis of data for adolescent participants of three NHANES cycles (2001-02, 2003-04, 2005-06). Associations were examined using multivariable linear regression.

*Results:* 25(OH)D was inversely associated with systolic blood pressure (-0.068 (-0.118, -0.018) standard deviations (SD)), and positively associated with HDL-c (0.101 (0.040, 0.162)SD) and HbA1c (0.073 (0.021, 0.125)SD) after adjustment for gender, age, ethnicity, socioeconomic status and waist circumference. In adjusted models, PTH was inversely associated with triglycerides (-0.115 (-0.188, -0.042)SD) and LDL-c (-0.133 (-0.207, -0.060)SD). In adjusted models, calcium was positively associated with fasting insulin (0.110 (0.060, 0.160)SD), postload glucose (0.116 (0.000, 0.232)SD), HbA1c (0.130 (0.005, 0.255)SD), triglycerides (0.182 (0.122, 0.242)SD), HDL-c (0.049 (0.010, 0.088)SD) and LDL-c (0.137 (0.080, 0.195)SD). The associations of each exposure with risk factors remained after mutual adjustment for each other.

*Conclusion:* Higher calcium levels might be a more important predictor of increased cardiovascular risk in adolescents than lower 25(OH)D levels, but our findings require replication in additional studies and examination in prospective studies.

### T5.4.3

## Fish and long-chain n-3 polyunsaturated fatty acid intakes in relation to risk of hypertensive and cardiovascular disease in women

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### Abstract

*Objective:* Previous observational studies and randomized controlled trials have indicated a protective effect of long-chain n-3 polyunsaturated fatty acids (LCn3FAs) against hypertensive and cardiovascular disease; however, the overall evidence remains uncertain and controversial. Research into modifiable cardiovascular risk factors in women is needed and large pregnancy cohorts provide an opportunity for such studies. Therefore, the aim of this study was to explore the association between intake of fish and LCn3FAs and the risk of hypertensive and cardiovascular disease in a large prospective cohort of women.

*Methods:* Exposure information from the Danish National Birth Cohort, which contains information on 91,827 women recruited throughout the country between 1996-2002, was linked to the Danish National Patients Registry for data on hospital contacts based on diagnosis of hypertensive, cerebrovascular and ischaemic heart disease used to define the outcome measure. Intake of fish and LCn3FAs was assessed in midpregnancy by a food-frequency questionnaire and in gestation weeks 12 and 30 by telephone interviews. A total of 48,627 women were included in the study sample.

*Results:* During the 6-12 years (median, 8 years) of follow-up, 577 women with an outcome event were identified. Of these 328 were cases of hypertensive, 146 cases of cerebrovascular and 103 were cases of ischaemic heart disease. A low intake of fish and LCn3FAs was associated with an increased risk of hypertensive and cardiovascular disease: adjusted hazard ratio (HR) for women in the lowest vs highest fish intake group was 1.51 (95%CI:1.11-2.05) (p for trend 0.03); and 1.91 (95%CI:1.26-2.90) for women in lowest vs highest LCn3FA-intake group (p for trend 0.02). For the other intake groups, risk estimates were close to one and confidence limits included unity. When applying a strict measure of consistently reported frequency of fish intake in both telephone interviews and the FFQ, the effect estimate for the lowest intake group was even higher, adjusted HR 2.91 (95%CI:1.45-5.85).

*Conclusion:* Our findings based on a large prospective cohort of relatively young and initially healthy women indicate that no, or a very low intake of fish and LCn3FAs is associated with an increased risk of cardiovascular and hypertensive disease.

## T5.4.4

### No association between repeated measures of an energy-dense, high saturated fat, low fibre dietary pattern, and incidence of cardiovascular events

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#### Abstract

*Objective:* Little is known about the associations between diet and cardiovascular risk independent of weight within severely obese populations. We investigated associations between repeated measures of a dietary pattern (DP) derived using Reduced Rank Regression (RRR) and the incidence of cardiovascular events (myocardial infarction and stroke) in the non-surgical group of the prospective intervention study Swedish Obese Subjects (SOS).

*Method:* The analysis included 2011 severely obese individuals (BMI  $41 \pm 4$  kg/m<sup>2</sup>) followed for 8-22 years without specific intervention. Dietary intake was assessed using a dietary questionnaire and outcomes measured using the Swedish Hospital Discharge Register (HDR). At registration into the study, a DP was derived using RRR based on intakes of 39 food groups with dietary energy density (DED), saturated fat (SF) and fibre density (FD) as response variables. To account for changes in the DP, the DP at registration was projected onto 9 subsequent follow-up measurements (over 10-years). This provided a DP z-score at each follow-up relative to the DP identified at registration. Repeated measures Cox-proportional hazards models were used to assess the association between repeated DP scores and CVD incidence. Models were adjusted for sex and time-dependent variables such as age, smoking, BMI, physical activity and relevant medication use.

*Results:* A total of 29,904 person years of follow up and 211 (91 MI and 112 stroke) cases were included. The DP explained 71.2%, 31% and 60.4% of the variation in DED, SF and FD respectively. The DP score was positively weighted towards SF ( $w=0.44$ ) and DED ( $w=0.66$ ) and inversely weighted to FD ( $w=-0.61$ ). The DP was high in chocolate, full-fat-spreads, low-fibre bread and low in fruits and vegetables. Repeated measures of the DP were not associated with CVD incidence.

*Conclusion:* An energy-dense, high saturated fat, low fibre DP was not associated with CVD incidence in this severely obese population. This suggests that diet composition alone is not sufficient to modulate CVD risk in the severely obese.

## T5.5.1

### Differences in time to virological failure, treatment changes and cessation, between persons treated soon after HIV seroconversion and in chronic infection

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#### Abstract

*Objectives:* Since treatment failure experienced early in human immunodeficiency virus infection may limit the number of therapeutic options in chronic disease, we compared the risk of treatment failure in patients starting treatment close to seroconversion vs those starting therapy during chronic infection.

*Methods:* We used data from CASCADE of HIV infected persons with well-estimated dates of seroconversion. Follow-up data include CD4 and HIV RNA measurements, antiretroviral drugs prescribed, vital status and date of last clinical assessment. We examined the effect of beginning treatment within 12 months of seroconversion ('early') vs beginning later on three competing events: the risk of virological failure, of changing, or of interrupting therapy. Timing of treatment failure was defined as the date of first HIV RNA of >1000 copies/ml after previous viral suppression to <500 copies/ml, or >500 copies/ml after six months following therapy initiation. The association between therapy initiation and each of these events was studied using the Fine and Gray approach, controlling for class of therapy, sex, age, HIV risk group, and CD4 cell count, HIV RNA and calendar period at the time treatment was initiated. CD4 and HIV RNA measurements were first jointly modelled to obtain predicted values at the relevant times.

*Results:* All analyses were based on 1454 patients, respectively 392 treated early and 1062 treated later. Of these 71 and 223 experienced treatment failure, 119 and 287 changed therapy, 132 and 167 interrupted treatment. The adjusted subdistribution hazard for treatment failure was similar for early and late treated patients (sub-hazard ratio (sub-HR) = 0.91, 95%CI: 0.67-1.23) as was the adjusted subdistribution hazard for treatment change (sub-HR=1.11, 95%CI: 0.87-1.41). The adjusted subdistribution hazard of treatment interruption was higher for early compared to late treated patients (sub-HR=1.83, 95%CI: 1.39-2.40).

*Conclusions:* Rates of treatment failure do not appear to differ between HIV patients treated in primary and chronic infection.

## T5.5.2

### Changes in antidepressant prescribing and switching in women: a United Kingdom population-based study

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#### Abstract

*Objective:* In the UK antidepressants are mainly prescribed in primary care. Guidelines have been introduced to regulate antidepressant prescribing, however, no large-scale longitudinal studies describe practical changes in patterns of antidepressant prescribing regarding the first-line drug treatment and switching of drug classes at a population level over time in the UK.

*Methods:* As part of a larger study on maternal depression, we identified women age 15-45 years with first antidepressant prescriptions between 1990 and 2004 in The Health Improvement Network nationally-representative electronic primary care database. The first three consultations with antidepressant prescriptions were extracted for each woman. Potential changes in primary care prescribing were examined yearly throughout the study period. Different antidepressants were grouped into three classes (tricyclic and related antidepressants [TCAs], selective serotonin re-uptake inhibitors [SSRIs] and other antidepressants that were neither TCAs nor SSRIs). We calculated the percentage of different classes of antidepressants prescribed as a proportion of all antidepressants for the first prescription and the percentage of people prescribed the same drug class for the first three prescriptions.

*Results:* We identified 75,853 women with first antidepressant prescriptions between 1990 and 2004. The median length for each prescription was 28 days (interquartile range 28-30). The percentage of TCAs as first prescriptions decreased steadily from 88.2% in 1990 to 11.8% in 2004 in contrast with a substantial increase in SSRIs (5.1% and 76.5% in 1990 and 2004 respectively). There were no remarkable changes for other antidepressants (6.7% and 11.8% respectively). The number of women prescribed the same drug class for their first three prescriptions increased for those initially prescribed an SSRI (57.7% in 1990 and 93.6% in 2004) or other antidepressant (28.9% and 91.7% respectively), but very slightly for those initially with a TCA (70.5% and 75.0% respectively).

*Conclusions:* Antidepressant prescribing and switching of drug classes have changed substantially since 1990. Women are increasingly prescribed SSRIs as the first choice antidepressant instead of a considerable decrease of TCAs. Subsequent drug switching within the same drug class rather than to a different class progressively happens in women initially prescribed an SSRI or other antidepressant but not in those with a TCA.



### T5.5.3

## **The influence of frequency and periodicity of primary health care contact on disease progression, unplanned hospitalisation and mortality in patients with type II diabetes**

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#### **Abstract**

*Objectives:* Evidence is growing that timely provision of primary medical care maintains population health for chronic diseases. However, the evidence in support of its importance in reducing utilisation of secondary health care services or preventing premature mortality is mixed and there is a lack of robust longitudinal investigation in this area. Furthermore, while previous research has focussed on frequency of contact, little attention has been paid to the regularity/periodicity of such service provision. Consequently, previous studies have been unable to differentiate between routine and reactive primary care contact.

The primary objective of this study was to evaluate the impact of frequency and periodicity/regularity of primary health care contact on the likelihood of disease progression, hospital admission and death in Western Australian (WA) diabetic patients from 1992-2006.

*Methods:* This study comprised a 15-year retrospective cohort study of 57,473 WA patients with diabetes using whole-population linked primary care, hospital inpatient, pharmaceutical and death data. Patients were stratified depending on type of diabetes-related pharmacotherapy. Exposure of interest was the level of primary care contact determined by frequency and regularity of visitation. Cox regression was used to determine the association between primary health care contact and disease progression, diabetes-related complication, hospitalisation and death, controlling for multiple sociodemographic and clinical factors.

*Results:* Increased regularity of contact with primary health care significantly decreased the likelihood of diabetes-related complications and hospitalisation in all patient groups, with strongest associations in patients treated with insulin (HR=0.53, 95%CI: 0.41-0.69). Increased regularity was also associated with a reduced likelihood of diabetes-related death in patients treated with oral hypoglycaemics (HR=0.91, 95%CI: 0.84-0.98) or insulin (HR=0.83, 95%CI: 0.69-1.95). Higher contact regularity was associated with a 23.8% increased likelihood of progression of diabetes pharmacotherapy in all patients. In contrast, frequency of care was only associated with development of diabetes-related complications in patients receiving insulin.

*Conclusions:* Regular, as opposed to frequent, contact with primary health care decreases the likelihood of adverse diabetes-related outcomes. This protective effect was more pronounced, although not limited to, patients treated with more robust pharmacotherapy regimes. These findings highlight the importance of regular management-focussed, as distinct from 'reactive', primary medical care for diabetic patients.

## T5.5.4

### Regular primary care plays a significant role in secondary prevention of ischemic heart disease

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#### Abstract

*Objective:* To assess the association between regular general practitioner (GP) visits and death or second IHD hospitalisation in older ischemic heart disease (IHD) patients in Western Australia (WA).

*Methods:* Patients aged  $\geq 65$  years ( $n=65,641$ ) who had been hospitalised at least once for IHD during 1992-2006 were retrospectively ascertained from administrative, health data routinely collected on the whole WA population. Frequency of GP visits was determined during a three-year exposure period at the beginning of follow-up and a regularity score was calculated that measured the regularity of intervals between the GP visits. The regularity score ranged from 0 to 1 and was divided into quartiles. Patients were then followed for maximum 11.5 years for determination of outcomes. Hazard ratios and confidence intervals were calculated using Cox proportional hazards models.

*Results:* Patients in the least regular GP visit quartile had the worst all-cause death and IHD death survivals as well as emergency hospitalisation survival, with the differences in survival patterns between the regularity quartiles being statistically significant ( $p < 0.0001$ ,  $p < 0.0001$  and  $p = 0.0059$ , respectively). Compared to the least regular quartile, patients in the most regular quartile had significantly decreased risks of all-cause death (HR=0.70, 95%CI=0.61-0.79) and IHD death (HR=0.64, 95%CI=0.50-0.81).

*Conclusions:* Visiting GPs at regular intervals protects against mortality and hospital admissions in older people with IHD. The findings demonstrate the importance of scheduled, regular GP visits for the secondary prevention of IHD.

## T5.6.1

### **Effect of retirement on major chronic conditions and fatigue: The French GAZEL occupational cohort study**

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#### **Abstract**

*Objectives:* To determine, using longitudinal analyses, if retirement is followed by a change in the risk of incident chronic diseases, depressive symptoms, and fatigue.

*Methods:* We used repeat measures surveys from 7 years before through 7 years after retirement in a large prospective French occupational cohort of 11,246 men and 2,858 women (the GAZEL study). Data were collected by questionnaire each year from 1989 through 2007 inclusive. The main outcome measures used were respiratory disease, diabetes, coronary heart disease and stroke, mental fatigue, and physical fatigue, measured annually over the 15-year observation period, and depressive symptoms measured at four time points.

*Results:* Repeated-measures logistic regression with generalised estimating equations (GEE) showed that the cumulative prevalence of respiratory diseases, diabetes, coronary heart disease and stroke increased with age, with no break in the trend around retirement. In contrast, we found retirement to be associated with a substantial decrease in the prevalence of both mental fatigue (odds ratio for fatigue one year after versus one year before the retirement 0.19; 95% confidence interval 0.18 to 0.21) and physical fatigue (0.27; 0.26 to 0.30). A slightly smaller decrease was observed in depressive symptoms (0.60; 0.53 to 0.67). The decrease in fatigue around retirement was more pronounced among those with chronic disease before retirement.

*Conclusions:* Longitudinal modelling of repeat data shows that retirement does not change the risk of major chronic diseases, but is associated with a substantial reduction in mental and physical fatigue and depressive symptoms, particularly among those with chronic disease.

## T5.6.2

### Self-rated health as a predictor of disability pension: a register based follow up study

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#### Abstract

*Objective:* Self-rated health is a generic measure of health predicting mortality, many diseases, sickness absence and need for care. Whether self-rated health also predicts early retirement due to disability is poorly understood. We examined associations of self-rated health with subsequent disability retirement, and factors related to work, health behaviours, prior diseases and occupational class as potential explanations.

*Methods:* Self-rated health and the explanatory factors were obtained from the Helsinki Health Study baseline mail surveys in 2000-2002 among municipal employees aged 40-60 (n=8960, 80% women, response rate 67%). Data for disability retirement (n=525) along with the diagnosis were linked from the Finnish Centre for Pensions, with a follow-up by the end of 2008 (n=6525). Hazard ratios (HR) and their 95% confidence intervals were calculated using Cox regression analysis.

*Results:* Poor self-rated health predicted women's disability retirement due to all diagnoses (HR=5.55, 95% CI=4.51-6.84) as well as musculoskeletal (HR=7.44, 5.01-11.03) and mental (HR=6.88, 5.03-9.39) diagnoses. Men's corresponding hazard ratios were 6.42, 3.26-12.62; 3.55, 2.43-5.18 and 3.49, 1.84-6.65. Physical work exposures, job control, occupational class and prior diseases somewhat explained the found associations, which nevertheless remained for both diagnosis groups as well as women and men. The only interaction showed that among obese women self-rated health was a weaker predictor.

*Conclusions:* Self-rated health is a strong predictor of disability retirement. This cannot be explained by factors related to work, behaviours and health. Self-rated health provides a tool for detecting employees with a high risk of disability retirement.

### **T5.6.3**

## **Health of the elderly in left-behind households: Some evidence from the Indonesia Family Life Surveys**

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### **Abstract**

*Objective:* The Indonesia Family Life Survey is a longitudinal household survey that collects a vast array of information from individuals, households, communities, and health and education facilities. The paper uses data from four waves of the Indonesia Family Life Survey, IFLS1(1993), IFLS2(1997), IFLS3(2000), and the new IFLS4(2007) to explore the relationship between migration and health of the elderly.

*Method:* The analysis is based on 3252 households where elderly aged 56 years and above are living in 2007. Distinction is also made for migrant and non-migrant households. Migrant households are households in which in 2007, one or more members age 15 and above are no longer in the household.

The longitudinal nature of the data will help us see whether a household has lost members to migration between survey waves and how living arrangements in the household have shifted after the migration. It may be possible, for example, to see from the data, households in which elderly members suddenly find themselves without someone to care for them. We will then look at health outcomes in 2007 among the elderly, during which some proportion of households had some members migrating and the rest did not.

Using logistic regression we use two models in this paper for three age groups of the elderly: age 56-61, age 62-68 and age 69 and above.

*Result and Conclusion:* The data give us insight about the importance of the presence of other prime age household members in the household on the health of the elderly left behind. The loss of members due to migratio does not have much adverse effect on health of the elderly as long as there is other adult member presence in the household who could take care of them. Remittance does not seem to have any significant effect to cushion the adverse effect on health of the elderly due to migrating members. The negative relationship of remittance and the health of the elderly left behind could also signify the practice that family members made more transfers at the time of need such as sickness of the elderly.

## T5.6.4

### The prognostic value of the patients' self-assessment of subjective health conditions and of various short-term rehabilitation success markers for early retirement: results of a prospective cohort-study

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#### Abstract

*Objectives:* The objective of this study was to evaluate the prognostic value of various short-term rehabilitation success markers and of the patients' self-assessment of their health status on early retirement by means of a prospective cohort study.

*Methods:* We included 1416 patients aged 45-57 years with musculoskeletal diseases who underwent an in-patient rehab programme between January and December 2001 in 10 LVA Baden-Württemberg (Germany) rehab clinics. Follow-up information with regard to disability was collected until 2006. During follow-up (mean duration: 3.9 years) 146 (10.3%) patients retired because of health-related disability. The prognostic value of the patients' self-assessment questionnaire and of the standardized documented items of short-term rehabilitation success markers was estimated by proportional hazards regression.

*Results:* After adjustment for sex, age and social index, a better self-assessment of functional status and pain status, respectively, was statistically significant associated with reduced risk for early retirement. Compared to patients within the lowest tertile of distribution of functional status scale, hazard rate for patients within the upper tertile of distribution was 0.3 (95%CI 0.2 – 0.6); compared to patients within the lowest tertile of distribution of pain scale, hazard rate for patients within the upper tertile of distribution was 0.3 (95% CI 0.1 – 0.5). Pain reduction reported as short-term rehabilitation success marker by physician was also of prognostic relevance. Patients with unsuccessful pain reduction had an increased risk for early retirement compared to patients, for whom physicians had not reported pain reduction as short-term rehabilitation success marker (HR 2.4, 95% CI 1.4-4.3).

*Conclusions:* Self-assessment of pain as well as reduction of pain reported as short-term rehabilitation success marker by the physician clearly demonstrated a prognostic value in terms of risk for subsequent early retirement among patients with musculoskeletal diseases.

## **T6.1.1**

### **Understanding Society: design features and analysis potential**

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#### **Abstract**

*Objective:* This paper provides an overview of the key design features of Understanding Society including the sample design and data collection plan, an Innovation Panel for methodological research, an ethnic minority oversample, the collection of bio-markers, data linkage to administrative records and the potential for linked qualitative studies.

Understanding Society, the UK Household Longitudinal Study, is a new annual household panel survey of 40,000 households and the successor study to the British Household Panel Study (BHPS).

*Methods:* Fieldwork for wave 1 of Understanding Society began in January 2009 and wave 2 commenced in January 2010. The BHPS sample is incorporated within Understanding Society from wave 2 of the study.

*Results:* The paper describes central features of the study, including the ethnicity strand. In addition to a large sample size with an ethnic minority boost sample and dedicated question time, the questionnaire content has been developed after a wide consultation with users of ethnicity related research to meet such research needs. The paper also outlines the long-term content plans for the study and discusses the analysis potential for users of longitudinal data. These include the possibilities offered by the large sample size, the household panel design, the multi-topic content for interdisciplinary use, and the new forms of data being collected or added to the study. The rationales for decisions made in incorporating the BHPS into the new study to provide longitudinal consistency while reconciling the competing demands for continuity and innovation are also discussed.

*Conclusions:* Understanding Society is a fruitful data source for epidemiologists focusing on social and ethnic inequalities.

## T6.1.2

### The Southampton Women's Survey: from observation to intervention

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#### **Abstract**

*Objective:* Epidemiological longitudinal studies are designed to inform our understanding of influences on health. However, to establish causality and to lead to improvements in health, the findings need translation into interventions. We established the Southampton Women's Survey to understand the maternal and early life influences on the health, growth and development of children, and to use the findings to develop interventions to improve these outcomes in children.

*Methods:* The Southampton Women's Survey is a longitudinal birth cohort with data collected on the mothers before conception. 12,583 Southampton women aged 20-34 years were recruited and assessed when not pregnant. Over 3,000 of them were followed through a subsequent pregnancy and the children are being followed-up.

*Results:* Strong relationships were found between a woman's educational attainment and the quality of her diet before conception, which in turn predicted the quality of the diet of her infant and child. Maternal vitamin D levels in pregnancy were positively associated with markers of bone development in the newborn infants and at four years of age. Variations in infant diet were related to body composition at the age of four years.

These findings, in conjunction with results from other studies, have led to: (1) a randomised controlled trial of vitamin D in pregnancy (MAVIDOS) to improve bone health of the offspring, (2) an intervention to develop the skills of staff working in disadvantaged areas to engage in 'healthy conversations' with young women. These conversations focus on enabling the women to identify their own ways of improving their diets and physical activity (Southampton Initiative for Health), and (3) a laboratory project with school children in Southampton to teach them the long-term impact of their lifestyle on their own health and that of future children, and to motivate behaviour change (LifeLab).

*Conclusions:* The Southampton Women's Survey, a longitudinal birth cohort study, has led to the development of targeted interventions to improve health of women and their children. Cohort studies contribute to our understanding of influences on health, and we have shown that the findings can be translated into intervention studies.



### T6.1.3

## Utilising routine healthcare data for the longitudinal study of chronic disease: Four approaches; one chronic disease

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### Abstract

*Objective:* With changing population demographics, diagnostics and disease definitions, understanding chronic disease epidemiology remains a cornerstone of health research, and planning. Following large cohorts of people can be challenging and expensive. With increasing computerisation of healthcare records there is an opportunity to study diseases using routinely collected, electronic data. Chronic kidney disease (CKD) is an ideal model. A new definition, rising risk factors and increasing recognition have resulted in the identification of large numbers of people for whom we know little about the natural history of their disease. ARRC aims to develop a programme utilising routine healthcare data to better understand the epidemiology of CKD.

*Methods:* A range of routine healthcare data sources have been utilised to provide a resource for the study of chronic kidney disease and draw on data from population surveys, primary care, laboratory and hospital contacts.

*Results:* Strengths – Each approach adopts a different aspect of patient identification. Changes over time in clinical practice are reflected in the data. GLOMMS II and P-CKD allow setting of different definitions and thus can be used to test the predictive value of future changes. The use of routine data affords efficient and optimal resource use. Limitations – No single source captures all aspects. Each requires different ethics procedures and has own complex data issues. Illustration of key findings and outputs – P-CKD: In 2006/7, 4.3% of population had evidence of kidney impairment but few had a recorded CKD diagnosis (<0.2% of the population). Changes to improve early diagnosis and management have resulted in an increase in recording of diagnosis (~3% of population in 2009). – P-CKD: used as baseline population data for development of Markov model for CKD. BRHS: Unique 20 years follow up of population screening: at least 35% of patients with mild/moderate CKD at baseline showed no deterioration in kidney function at follow up. SHHS: eGFR<50ml/min/1.73m<sup>2</sup> independently associated with increased risk of cardiovascular death. GLOMMS I: at 6years, 36% have not died/required RRT.

*Conclusions:* The use of routine healthcare data provides a valuable resource for chronic disease epidemiology. In Scotland, the ability to link different healthcare data sources through a unique identifier enables existing data to be enriched.

## T6.1.4

### Recruitment strategies for Irish Traveller women into the Traveller birth cohort study on island of Ireland: challenges and solutions

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#### Abstract

*Objectives:* Irish Travellers are a minority group primarily based on island of Ireland (IOI) and characterised by a nomadic lifestyle, specific culture, and significant socio-economic and health disadvantage. When last documented in 1986, their child health indicators were one of the worse in Europe. The purpose of this study was to investigate prospectively the health status and health care needs of Traveller infants.

*Methods:* A two-stage recruitment process was undertaken through (1) the All Ireland Traveller Health Study census, using an innovative audio-visual computer package delivered by peer researchers to overcome literacy issues, and subsequently (2) consents for the study were obtained by the Public Health Nurses (PHN). High level of illiteracy and the tradition of oral communication posed methodological challenges. For study promotion, simplified culturally-appropriate leaflets, and oral promotion by Traveller health workers ensured trust and acceptance. Identification of study participants in ROI was through birth notification forms, the national metabolic screening registers, PHNs' local knowledge and Traveller health projects, and in NI, by Health Visitor notifications and informal local Traveller networks. All Traveller babies were eligible, born over a one year period (13<sup>th</sup> October 2008 to 14<sup>th</sup> October 2009), born on the island of Ireland, whose parents self-identify as Irish Travellers. Eligible mothers and infants were followed up for a year. The participating mothers carry a specifically designed 'Parent-held Child Record'. Birth estimates calculation used updated census and this assisted in recruitment of participants. Linkage-data to maternity hospital records was also planned.

*Results:* Estimated births were 1000-1100 per annum. 982 births were identified (89-98% ascertainment, on going); 915 in ROI and 67 in NI; of these 968 were singleton births. 468 (51.6%) mothers consented in ROI, while 34 (48.5%) have consented in NI (in progress). Median maternal age was 25 years old (25% centile= 21, 75% centile= 30). Births occurred in 24 maternity hospitals in IOI, 30% in the 3 major maternity hospitals in Dublin.

*Conclusions:* Ascertainment challenges exist, especially in a predominantly mobile minority group. Specific challenges include gaining trust and employing culturally-friendly methodology. This novel linkage cohort study will provide important policy relevant data for ethnic minority research generally.

## T6.2.1

### Child mental health problems and youth educational attainment in the UK

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#### **Abstract**

*Objective:* To explore the relationship between the timing, persistence and type of symptoms of childhood mental health problems between the ages of 3 and 13 and educational achievement at age 16.

*Method:* We use data on 6000 children from the Avon Longitudinal Study of Parents and Children born in the early 1990s in the UK. Mental health symptoms are measured by the parent-report Strengths and Difficulties Questionnaire (SDQ), a screener designed measure children's behaviour along five dimensions: Hyperactivity/Inattention; Conduct Problems; Peer Problems; Emotional Symptoms and Prosocial Behaviours. We relate longitudinal data from the SDQ at six ages – 47, 81, 97, 115, 140 and 157 months – to children's achievement in compulsory national academic assessments at age 16. We use regression-based techniques to explore how the effects of childhood behaviour problems differ with a) age at onset, b) degree of persistence over time, c) severity of symptoms, and d) type of problem.

*Results:* Children in the highest quartile of the overall behaviour problems index at 47 months are significantly less likely to reach the national benchmark in educational qualifications at 16 than other children. The role of persistence in symptoms is crucial and children whose early symptoms abate by adolescence suffer little if no penalty. Hyperactivity symptoms stand out as the strongest predictor of all the sub-scales, while the association of Emotional Symptoms with educational outcomes is weak.

*Conclusion:* Previous studies in the economics literature have shown a link between childhood mental health and educational and economic success, and speculated that the economic pay-off to effective mental health interventions in childhood could be large. Our results suggest children with persistently high levels of hyperactivity symptoms are much more vulnerable to educational failure than those with more transitory problems, or those with aggressive or internalizing behaviours, and so may benefit disproportionately from targeted treatment.

## T6.2.2

### The role of infant development in human capital formation: evidence from a longitudinal birth cohort study

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#### Abstract

*Objective:* A number of theories from various domains have suggested that the positive effects of superior development in early life will increase and accumulate with age, producing more advantageous outcomes in older ages. Conversely, the negative effects of inferior development will also accumulate with age. These theories, which have utilised data from childhood but not from infancy to support their findings, suggest that it is mainly educational and health advantages / disadvantages that accumulate from these early life advantageous / disadvantageous positions. The same theories support that this accumulation of advantage and disadvantage is what leads to an increasing heterogeneity in a number of outcomes over the life course, and hence greater inequality. Exploiting the availability of rich longitudinal birth cohort data from the 1966 Northern Finland Birth Cohort Study, this study aims to evaluate the association of developmental outcomes during the first year of life with indicators of socio-economic position during adulthood, such as occupational social class, income, educational attainment, and unemployment. Identifying a link between these outcomes over the life course will provide further evidence that the first few months of development comprise a critical period, which may set individuals on pathways which go on to influence their entire life course.

*Methods:* The study is conducted using data from the 1966 Northern Finland birth cohort (NFBC1966), a prospective mother-child birth cohort which included all pregnant women with an expected date of delivery in 1966 as well as their children. Their development and health have been followed up at various intervals, from gestation to 31 years of age, through questionnaires and clinical examinations. This study will focus on measures of infant motor and language development.

*Results:* Measures of development in infancy were associated with indicators of socioeconomic position in adulthood, with more advanced developers being in a higher occupational social class, reporting a higher household income, higher educational attainment, and being unemployed for shorter periods than their less developed peers.

*Conclusion:* Infant developmental outcomes are associated with indicators of socioeconomic position in adulthood, highlighting the importance of early life development in human capital formation in adulthood. Part of the socioeconomic inequality observed throughout the life course can be traced back to the period of infancy, where precocious or delayed infant development can set individuals on advantageous or disadvantageous socioeconomic trajectories.

## T6.2.3

### The dynamics of skill formation: evidence from a Flemish cohort study

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#### Abstract

*Objectives:* In this paper, we focus on the evolution of both cognitive and non-cognitive skills during adolescence, using Heckman's framework in which skill formation is modelled as a dynamic process. We first discuss the formalization of these dynamics by self-productivities, cross-productivities and complementarities. Next, we estimate such models for a cohort of Flemish students during adolescence, supplementing the out-of-school, family-based drivers of skill differences by a vector of school investments. This allows us to focus on the impact of differential treatment within the educational system on the generation of skill differences. In the process of dynamic skill formation, tracking reinforces the cumulative effect of earlier investments by differentiating inputs in the skill formation process (curricula, teachers, peers) and causes skill gaps to widen. To identify tracking effects, both pre-track and post-track investments are modelled dynamically, since tracking itself is based on past performance and background. In order to examine the effects of tracking we use various measures of differentiated investment indicating specialisation (number of hours on mathematics and languages).

*Methods:* In order to identify causal relationships, the problem of endogeneity of inputs, resulting from omitted variables or reverse causality, has to be addressed. Following Cunha and Heckman (2008), we estimate a dynamic factor model to solve the problems of endogeneity of inputs and multiplicity of inputs relative to instruments. Modelling cognitive and non-cognitive skills, as well as parental and school investments as low dimensional latent variables, allows us to identify the dynamics generating the evolution of skills using a multiple indicator-multiple cause (MIMIC) model.

*Results:* First, the estimates provide evidence of strong self-productivities both in the formation of cognitive and non-cognitive skills (1). Second, skill formation entails cross productivity effects from non-cognitive skills to next period cognitive skills (but not vice versa) (2). Thirdly, both parental and school investment drive cognitive and non-cognitive skill differences (3). Finally, the estimates suggest complementarity in cognitive skill development among adolescents is stronger than in non cognitive skill development (4).

*Conclusions:* Findings 1, 2 and 4 corroborate the existence of dynamics effects in processes of skill formation among adolescents. While previous empirical estimates on the dynamics of skill formation found only weak and statistically insignificant effects of school inputs on outputs, findings 3 suggests this weak relation is due to poorly measured schooling inputs and not to the fact that skill formation during adolescence is governed by dynamic effects. While correcting for endogenous inputs and vector error autocorrelation, estimates confirm that tracking causes skills gaps to increase. Efficiency and equity implications of our findings are pointed out.

## T6.2.4

### Child height, health and human capital: Evidence using genetic markers

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#### Abstract

*Objective:* We examine the causal effect of child height at different ages on a wide range of outcomes in late childhood and early adolescence: academic performance, IQ, self-esteem, depression and behavioural problems (including hyperactivity, emotional, conduct, and peer problems).

*Methods:* Height is influenced by a wide range of environmental factors experienced in childhood, some of which may also be determinants of our outcomes of interest. To deal with this potential endogeneity, we use instrumental variables, specifying carefully chosen genetic markers as instruments for children's height; an approach also known as 'Mendelian randomization'. Genes are randomly distributed at conception. Whilst this random allocation is at a family trio level, at a population level it has been shown that genetic variants are largely unrelated to the many socioeconomic and behavioural characteristics that are closely linked with each other and that confound conventional observational studies.

*Results:* OLS findings show that taller children perform better in school tests, have higher IQ, and are less likely to have emotional problems, but more likely to have peer problems. We find no evidence of differences in self-esteem, depression scores, hyperactivity and conduct problems for children of different heights. The IV results suggest that height indeed increases IQ, but this is not reflected in children's test scores. In addition, height increases peer problems, emotional problems and hyperactivity. We find some small differences when examining height at different ages during childhood, though our main findings are robust.

*Conclusions:* Our findings suggest that child height is an important factor in children's human capital accumulation both in childhood and during adolescence.

## T6.3.1

### Rate and predictors of induction of labour in the mother-child cohort study (Rhea study) in Crete, Greece

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#### Abstract

*Objective:* The rate of induction of labour (IoL), one of the most common interventions in obstetrics, is rising in many countries. The objective of this study was to assess the rate of induction of labour and its predictors in the population-based mother-child cohort study ("Rhea" Study), in Crete, Greece.

*Methods:* The "Rhea" Study examines a population sample of women who became pregnant during one year starting February 2007 at the prefecture of Heraklion; 1610 women agreed to participate and 1317 were followed up until delivery. There were 888 women with singleton pregnancies, complete follow-up until delivery and known status of IoL; 471 were excluded due to having a caesarean delivery (CD); 6 additional women were excluded due to previous CD and 2 due to unknown type of delivery or status of previous CD, finally resulting in a sample of 409 women who had vaginal delivery and were included in the analysis. Timing of drug administration in relation to the initiation of labour was not available, so we were not able to differentiate between induction and augmentation of labour, thus IoL in the present study includes both. Multivariable Poisson regression models with robust error were fit to estimate the associations [Relative Risk (RR), 95% CI] of sociodemographic, health or pregnancy-related variables with IoL. Probable predictors of IoL with a p value  $\leq 0.2$  in the bivariate models were included in the final multivariable model: maternal age, maternal education (low, medium, high), smoking status (smoker, ex-smoker, non-smoker), parity (primiparous / multiparous), type of delivery hospital [university hospital (public), general hospital (public), private clinics].

*Results:* 274 of the 409 women (67%) had an IoL. Women with medium education had a higher risk for IoL than women with lower education (medium vs. low education: RR 1.19, 95%CI 1.00, 1.42; and high vs. low education: RR 1.06, 95%CI 0.83, 1.34). Women giving birth in the university hospital had a lower risk for IoL compared with women giving birth in private clinics (university hospital vs. private clinics: RR 0.71, 95%CI 0.6, 0.84; and general hospital vs. private clinics: RR 1.02, 95%CI 0.88, 1.19).

*Conclusion:* IoL was quite frequent in this study population. Findings suggest that the association between the type of delivery hospital and IoL differs depending on the type of the hospital. Future population-based studies in Greece need to investigate these questions further.

## T6.3.2

### Predicting live birth, preterm and low birth weight infant after in-vitro fertilisation: A prospective study of 144,018 treatment cycles

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#### Abstract

*Objectives:* (i) To compare a new prediction model for successful live birth in couples treated with in-vitro fertilisation (IVF) to the Templeton model that was established in the 1990s prior to widespread use of intra-cytoplasmic sperm injection (ICSI); (ii) To identify predictors of low birthweight, macrosomia and preterm birth in women with a singleton live birth following IVF.

*Methods:* We utilised the Human Fertilisation and Embryology Authority database to examine the predictors of live birth in all IVF cycles undertaken in the UK between 2003 and 2007 (n=144,018). In the novel prediction model we used the same characteristics as those used in the Templeton model but included all causes of infertility, the source of the oocyte (donor or patient's own), type of hormonal preparation (antioestrogen, gonadotrophin or hormone replacement), whether or not ICSI was used and the number of treatment cycles (1, 2 or ?3). For those cycles that resulted in a live singleton (n=25,490), we determined the associates with preterm birth, low birthweight and macrosomia.

*Results:* The overall rate of at least one live birth was 23.4 per 100 cycles (95%CI: 23.2, 23.7). The odds of a live birth decreased with increasing maternal age, increasing duration of infertility, a greater number of previously unsuccessful IVF treatments, use of own oocytes, necessity for a second or third treatment cycle, or if it was not unexplained infertility. A previous IVF live birth increased the odds of future success (OR 1.58, 95% CI 1.46, 1.71) more than previous spontaneous live birth (OR 1.19, 95% CI 0.99, 1.24), p< 0.001 for difference in coefficients. Use of ICSI increased the odds of live birth and in couples who did not receive ICSI male infertility was related to reduced risk of live birth; in those receiving ICSI there was no association of male causes of infertility with successful live birth. The existing Templeton model had poor calibration; our new model had excellent calibration. Preterm birth and low birthweight were increased in younger women, if oocyte donation was required or if there was a history of pregnancy loss. Cervical causes of infertility were associated with marked reduced odds of live birth and where live birth occurred with increased risk of preterm, low birth weight and macrosomia.

*Conclusions:* Couple and treatment specific factors accurately predict live birth.



### T6.3.3

## Recurrence of stillbirth in sibships: population based cohort study

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### Abstract

*Objective:* We aimed at studying 'gestational age' and 'weight-by-gestation specific' stillbirth recurrence, and to evaluate time trends in a population based cohort study from the Medical Birth Registry of Norway, 1967 to 2004.

*Methods:* Singleton births, including stillbirths from 20 weeks' gestation, were linked to their mothers by national identification numbers. Stillbirth rates in second pregnancies among mothers with (N=5,091) and without (N=562,057; reference) a stillbirth in first pregnancies were compared across four gestational age and three weight-by-gestation groups. Time trends in stillbirth recurrence were also studied.

*Results:* A remarkable symmetric pattern of 'gestational age specific' recurrence of stillbirth was found, with highest odds of stillbirth in the same age group. The adjusted odds ratios (OR<sub>adj</sub>) associated with preterm stillbirth recurrence were high, e.g. 25.7(95%CI: 19.8,33.3) for stillbirth at 20-27 weeks' gestation (73/1,511 versus 1,021/562,057), while lower for term stillbirth: OR<sub>adj</sub> 2.3(1.2,4.7) (9/1,844 versus 1,021/538,499). Women experiencing a first stillbirth at any of the endpoints of the gestational age range (lowest or highest groups) did not have significantly increased odds of a stillbirth at the other endpoint in their next pregnancy relative women with a first live birth. The proportion of second early stillbirth in the population attributable to previous early stillbirth was 6.4%, compared to 0.5% for second term stillbirth. Over time, recurrence of early stillbirth decreased, whereas that of mid/late stillbirth did not change significantly. A symmetric pattern of recurring stillbirth in similar weight-by-gestation groups was not found.

*Conclusion:* It is known that women with a previous stillbirth are at increased risk of a recurrent stillbirth. The present study suggests that this recurrence risk is mostly due to a tendency to repeat a stillbirth with similar gestational age as the first stillbirth. These results may be useful for clinicians in risk assessment and counseling.

## T6.3.4

### Recurrence of prolonged and post-term pregnancy across generations: maternal and paternal contribution

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#### Abstract

*Objective:* The objective of the current study was to estimate intergenerational recurrence risk of prolonged pregnancy and to assess the maternal and paternal contribution to this risk.

*Methods:* We used data from the Medical Birth Registry of Norway, covering the years 1967 to 2006, including more than 2.3 million births. Intergenerational data sets of post-term singleton mothers and fathers giving birth to singleton children were formed. The main outcome measures were prolonged pregnancy  $\geq 287$  days of gestation (41 completed weeks), post-term pregnancy of  $\geq 294$  days (42 completed weeks) and prolonged pregnancy of  $\geq 301$  days (43 completed weeks) in the second generation.

*Results:* We identified 497 526 mother-child units and 367 344 father-child units. A post-term mother had a 49% increased risk of giving birth to a post-term child (relative risk 1.49, 95% confidence interval 1.46 to 1.51) and a post-term father had a 25% increased risk of fathering a post-term child (relative risk 1.25, 95% confidence interval 1.22 to 1.28). The relative risks for prolonged pregnancy  $\geq 287$  days was 1.29 and 1.16 for mother and father, respectively. The similar relative risks for prolonged pregnancy  $\geq 301$  days were 1.54 and 1.21, and also highly statistically significant. The relative risk of post-term pregnancy in the second generation was 1.58 (95% confidence interval 1.52-1.65) if both mother and father were post-term.

*Conclusions:* There is a familial factor related to recurrence of prolonged pregnancy across generations and both mother and father contribute to this risk. Genetic effects on gestational age seem to be more important in the post-term period than in the preterm period.

## T6.4.1

### **Relations between characteristics of social network, health-related quality of life and mortality patterns in older age. Cracow study**

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#### **Abstract**

*Objectives:* Theoretical concepts presented in social epidemiology showed that size, density and boundedness of social network as well as social support significantly influenced not only health-related quality of life in older people but also directly and indirectly the patterns of all-caused mortality. The aim of the study was to assess the role of different dimensions and characteristics of social network in older stage of life in relation to health-related quality of life and its effects on mortality patterns.

*Methods:* Relation between characteristics of social network and social support has been based on cross-sectional study performed as a part of Central European Network on Healthy Ageing. Base-line study was performed in simple random sample of 552 older Kraków citizens (65-85yrs old), using face-to face interviews, based on Polish validated version of Dutch questionnaire, focused on assessment of health status in older part of population. Such scales as SF-20 test, GARS, SSL12-I, de Jong-Gierveld Loneliness Scale and Cantril's ladder were used. Data on mortality was ascertained/gathered by monitoring city vital records and general mortality was analyzed. Statistical analysis was performed with Cox proportional hazard model, using SPSS 15 for Windows software.

*Results:* During 8 years of monitoring mortality patterns among elderly citizens of Kraków 32.1% of the study population died. Cox proportional hazard model revealed that the highest risk of death was observed in men with low social support who additionally met their neighbours less than once per two weeks (HR=2,29, 95%CI=(1,21;4,36)). In women, low frequency of contacts with neighbours remained a significant factor influencing risk of death, irrespective perceived social support, though those with low social support had higher risk of death (HR=3,61, 95%CI=(1,99;6,56)) than those with high social support (HR=2,25, 95%CI=(1,21;4,16)). In men, primary education connected with high level of emotional loneliness was an independent predictor of mortality (HR=2,51, 95%CI=(1,17;5,38)). Higher numbers of contacts with children was an independent predictor of mortality, reducing risk of death both in men (HR=0,77, 95%CI=(0,61;0,97)) and women (HR=0,79, 95%CI=(0,63;0,99)).

*Conclusion:* Presented results showed that factors concerning both health-related quality of life and properties of social networks remain significant predictors of mortality in elderly men and women.

## T6.4.2

### A personal accounting of time, health and quality of life

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#### **Abstract**

*Objectives:* Time has been described as the currency of life. The way people spend their time and experience life influence their wellbeing. Time spent in unpleasant activity had been shown to correlate well with how people feel. These studies were characterised by small sample sizes, cross-sectional nature of the data, and a small set of variables. In the present study, we explore how the 'consumption patterns' of time influence quality of life and health in older ages.

*Methods:* We used data from the British Household Panel Survey (BHPS), which has calibrated time use data for waves 4 to 14. Health outcomes were self-rated health and limiting long-standing illness. The quality of life was measured using CASP-19 in waves 11 and 16. The sample was restricted to those who were 50 years or more and had time use and CASP-19 data in wave 11 (N= 3473). Cross-sectional and longitudinal analyses were done.

*Results:* The pattern of time use varied with age groups, gender and socio-economic position. Men, younger age groups and those in better socio-economic position would be spending more time in paid employment compared to women, older age groups and those in disadvantaged socio-economic position. While total work at home was similar for men and women, women did more routine chores. The extra time available as people exited from paid employment was consumed in leisure and domestic activities. Good self-rated health was positively associated with time spend on activities, while limiting illness was negatively associated. Duration of time spend on sleep was negatively associated. For health outcomes, the effect of time use pattern was low albeit statistical significance. CASP-19 scores also showed similar effect but stronger; strongest impact was for time spend on leisure activities. There were no gender differences in any of these results. Longitudinal analyses are in progress.

*Conclusions:* The preliminary results from cross-sectional analyses presented here suggest that health and quality of life are influenced by the time spent on activities. The longitudinal analyses will address limitations of these results especially the potential for reverse causation.

## T6.4.3

### Quality of life concordance among older couples in Europe

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#### **Abstract**

*Objectives:* This study aims to investigate the concordance between partners' quality of life (CASP-12) in older community based couples in Europe. It will also consider the influence of gender and welfare regimes, controlling for individual level covariates (education, health, age and depression) and couple level covariates (self-rated economic difficulty, outside help provided to the household). The strength of this concordance will also be compared across welfare regimes.

*Methods:* Secondary analysis of Wave 2 of the Survey of Health, Ageing and Retirement in Europe (SHARE) was undertaken on the final sample (n= 8521) using multiple level modelling to account for the dyadic structure of the sample (individuals within couples). Cross-national comparisons using welfare regime typologies are also undertaken between the thirteen European countries featured in SHARE.

*Results:* A strong concordance was evident between partners' quality of life, this remained so even when individual level and household level covariates were included. Welfare regime and gender (although not their interactions) also predicted quality of life. Although concordance between quality of life scores was present in each welfare regime, the strength of this association did vary between them.

*Conclusion:* The observations of quality of life scores between individuals who are married cannot be assumed to be independent. The importance of dyadic data analysis and multilevel models for understanding quality of life in older couples has been highlighted. Cross-national comparisons also suggest that institutional arrangements may be associated with the strength of quality of life concordance for couples.

## T6.5.1

### Polymorphisms in *ADAM33* are associated with total mortality and with COPD and cardiovascular mortality in the general population

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#### Abstract

**Objective:** Single nucleotide polymorphisms (SNPs) in *ADAM33* are associated with accelerated lung function decline in the general population. It is known that low lung function is associated with increased mortality risk, in particular due to Chronic Obstructive Pulmonary Disease (COPD) and cardiovascular diseases (CVD). The objective of this study was to assess the association between SNPs in *ADAM33* and total mortality, COPD mortality, and CVD mortality, independently of lung function level.

**Methods:** The vital status of all participants in the Vlaardingen/Vlagentwedde study at 31-12-2008 was assessed. This longitudinal cohort study of the general population started in 1965 and the last survey was in 1989/1990. In total 8465 subjects were included and the maximum number of visits per subject was 8. DNA-samples from 1390 subjects who participated in the last survey in 1989/1990 were genotyped for 8 SNPs in *ADAM33*. We analyzed five SNPs in *ADAM33* that were previously described to be associated with asthma, airway hyperresponsiveness, COPD, or excessive decline in FEV<sub>1</sub>: rs17548907 Q-1 (C/T), rs3918396 S\_1 (Val-Iso), rs528557 S\_2 (G/C), rs2280091 T\_1 (Met-Thr) and rs2280090 T\_2 (Pro-Ser). Cox regression adjusted for gender, age, FEV<sub>1</sub>, height, place of residence and packyears of smoking was used to assess the association of SNPs with total (excluding external causes of death), COPD, and CVD mortality.

**Results:** At 31-12-2008 284 (20.4%) of the 1390 included subjects had died (20 due to COPD and 107 due to CVD). Individuals homozygous for the minor allele of T\_1 and T\_2 had an increased total mortality risk compared to wild types [HR (95% CI): 3.11 (1.58-6.12) and 3.63 (2.00-6.74) respectively]. Individuals homozygous for minor allele of S\_1, S\_2, T\_2 or Q\_1 had a significantly increased risk to die of COPD. Individuals homozygous for minor allele of T\_2 had increased risk to die of CVD compared to wild types, HR=3.42 (1.23-9.52).

**Conclusions:** This study for the first time showed associations between polymorphisms in the *ADAM33* gene and total, COPD, and CVD mortality. These associations were independent of the level of lung function and other potential confounders. Previously, *ADAM33* has been identified as an asthma and COPD susceptibility gene. The current study suggests *ADAM33* might play a role in general morbidity and mortality as well.

## T6.5.2

### Epigenetic variation in T2D susceptibility genes is associated with phenotype

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#### Abstract

*Objectives:* Genotype clearly plays a role in type 2 diabetes (T2D) susceptibility. However, the role of DNA methylation and its interaction with genotype is poorly understood. This study aims to identify whether variation in DNA methylation pattern is associated with risk of T2D or associated traits. A targeted approach was adopted; genes which harboured SNPs identified by genome wide association studies (GWAS) were analysed for variation in methylation patterns.

*Methods:* Methylation analysis was conducted in two genes, FTO and ADCY5, using the Sequenom® EpiTYPER® platform. DNA samples were derived from the Relationship between Insulin Sensitivity and Cardiovascular Disease (RISC) cohort; a group of healthy individuals aged between 30-60 years of age. DNA samples were collected at baseline and 3 year follow-up alongside detailed biological, physiological and lifestyle measures.

*Results:* DNA methylation was analysed at 11 CpG sites in ADCY5 (average n=304) and 10 CpG sites in FTO (average n=287). Spearman's tests for correlation between methylation and T2D related traits revealed a number of statistically significant observations including an inverse relationship between ADCY5 methylation and fat free mass ( $\rho = -0.179$ ;  $p = 0.001$ ) and an association with age ( $\rho = 0.148$ ;  $p = 0.007$ ). In FTO, methylation correlated with BMI ( $\rho = 0.139$ ;  $p = 0.011$ ) and basal glucose ( $\rho = 0.125$ ;  $p = 0.022$ ).

*Conclusion:* Both FTO and ADCY5 genes showed inter-individual variation in methylation and in turn were associated with T2D-related traits within the RISC cohort. These data suggest that, in addition to effects of genetic polymorphisms on T2D risk, epigenetic variants in the same genes may also contribute to disease risk.

## T6.5.3

### Common genetic determinants of vitamin D insufficiency

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#### Abstract

**Objective:** Vitamin D is crucial for maintaining musculoskeletal health. Recently, vitamin D insufficiency has been linked to a number of extraskeletal disorders, including diabetes, cancer, and cardiovascular disease. Determinants of circulating 25-hydroxyvitamin D (25-OH D) include sun exposure and dietary intake, but its high heritability suggests that genetic determinants may also play a role.

**Methods:** We performed a genome-wide association study of 25-OH D among ~30,000 individuals of European descent from 15 cohorts. Five cohorts were designated as discovery cohorts (n=16,125), five as in silico replication cohorts (n=9,366), and five as de novo replication cohorts (n=8,378). Association results were combined using z-score-weighted meta-analysis. Vitamin D insufficiency was defined as 25-OH D <75 nmol/L.

**Results:** Variants at three loci reached genome-wide significance in the discovery cohorts, and were confirmed in the replication cohorts: 4p12 (overall  $P=1.9 \times 10^{-109}$ ); 11q12 ( $P=2.1 \times 10^{-27}$ ); 11p15 ( $P=3.3 \times 10^{-20}$ ). Variants at an additional locus (20q13) were genome-wide significant in the pooled sample ( $P=6.0 \times 10^{-10}$ ). All confirmed variants were biologically relevant, showing direct associations with 25(OH)D synthesis, clearance, or binding. Participants in the top quartile of genotype scores had 2.5-fold elevated odds of vitamin D insufficiency ( $P=2.3 \times 10^{-48}$ ).

**Conclusion:** Variants near genes involved in synthesis, hydroxylation, and vitamin D transport influence vitamin D status. Genetic variation at these loci identifies individuals of European descent who have substantially elevated risk of vitamin D insufficiency.



## T6.5.4

### Genome wide profiling of blood pressure in children six years of age

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#### Abstract

**Objective:** A large number of genes, each with a small contribution, seem to explain the heritability of blood pressure. So far, genome wide association studies (GWAS) aiming to identify genes regulating blood pressure, focused on middle and old age. Not much is known about genetic variants related to blood pressure in childhood. The aim of this study was to assess to what extent multiple genetic variants contribute to blood pressure levels in childhood using genome-wide profiling.

**Methods:** Genetic risk profiles for systolic (SBP) and diastolic blood pressure (DBP) were defined based on a meta-analysis of GWAS on blood pressure conducted in the CHARGE-blood pressure consortium (n=29,136; age range 38-72 years). Different profiles were created, using ranges of p-values of the CHARGE meta-analysis results (p-value ranges: 0-1x10<sup>-7</sup>, 0-1x10<sup>-6</sup> etc. until 0-0.1, 0-0.2 etc. until 0-1.0) for selecting single nucleotide polymorphisms (SNPs). Subsequently, genetic risk scores for all profiles were calculated in a population based cohort sample of 1,034 children aged 6 years. To evaluate the role of the genes in early life, these risk scores were added to the baseline model for SBP and DBP, including gender, age and body mass index (BMI) and the change in explained variance was evaluated.

**Results:** The baseline model explained 5.2% of the variance in SBP and 1.4 % of the variance in DBP in children aged 6 years. The genetic risk scores significantly increased the explained variance when added to the baseline model for SBP and DBP. The risk score including all SNPs with a p-value of 0-0.1 in the CHARGE meta-analysis (151,178 SNPs) additionally explained 0.5% of the variance in SBP in children. For DBP, a genetic risk score including all SNPs with a p-value of 0-0.3 (427,346 SNPs) additionally explained 1.5% of the variance.

**Conclusion:** These findings suggest the presence of many genetic loci with small effects on SBP and DBP in early life. The variance explained in DBP by these genes is similar to that explained by age, sex and BMI. To assess the joint genes determining blood pressure at early and late age will require large and long-term follow-up studies.

## T6.6.1

### How stable are physical activity habits among adults? The Doetinchem Cohort Study

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#### **Abstract**

*Objective:* Leisure-time physical activity in compliance with recommended levels is associated with improved health and lower mortality, but little is known on whether these physical activity habits are stable among adults and what characteristics predict physical activity changes. Our objective was to determine change in the levels of leisure-time physical activity among adults over a period of ten years.

*Methods:* Detailed information on time spent on cycling, gardening, doing odd-jobs and sports from three measurements (1993-1997, 1998-2002, 2003-2007) of the population-based Doetinchem Cohort Study was used to define being active: spending at least 3.5 hours a week on moderate to vigorous physical activities, an approximation of the Dutch recommended level.

*Results:* Almost one third (31.4%) of the population was active at all three points in time, 3.6% was inactive and 45.0% of the participants changed their level of physical activity, almost equally distributed over decreasers, increasers and varying. Not smoking (OR=1.47 95%CL 1.14 1.89) and high socioeconomic status (OR=1.43 95%CL 1.07 1.92) were associated with staying active. Inactive men (OR=0.73 95%CL 0.57 0.94) had the highest risk of staying inactive, while a good perceived health was associated with becoming active (OR=1.49 95% CL 1.09 2.03).

*Conclusion:* The finding that in a decade almost half of the population changed from active to inactive or vice versa affects the interpretation of the long-term health effects of physical activity measured only once, and it stresses the importance of interventions not only on increasing physical activity levels, but also on maintaining a physically active lifestyle.

## T6.6.2

### Daily profiles of energy and nutrient intakes- are eating patterns changing over time?

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#### Abstract

*Objective:* It is commonly believed that eating patterns in the UK have changed in recent decades, with omission of breakfast more often, greater amounts eaten late in the day, and an increased frequency of eating, with implications for obesity and chronic disease risk. However, little longitudinal data are available to examine this. The National Survey of Health and Development (NSHD) (1946 British birth cohort) has collected detailed dietary information repeatedly in adulthood, allowing changes in patterns of eating over time to be explored.

*Methods:* Dietary intakes were assessed at 36 years (1982), 43 years (1989) and 53 years (1999), using a 5d estimated food diary. Intakes were coded into eight timeslots (seven for 36 years), from early morning until late evening. Each timeslot was analysed for total and % contribution to daily energy and nutrient intakes. Only survey members for whom data was available for all 3 timepoints were included in analyses (1263 for dietary data; 917 for diet and social class).

*Results:* Mean distribution of energy across the day changed little over the period studied. For the three assessments in 1982, 1989 and 1999, breakfast accounted for 14-15% energy, lunch 27 – 28% and dinner + late evening 41-44%. Fat, protein and carbohydrate also showed little change; lunchtime alcohol consumption decreased steadily from 14% in 1982 to 8% in 1999, but increased at dinner from 26% in 1989 to 35% in 1999. Energy distribution was similar by sex and social class, although individuals from a non-manual occupational social class ate more at dinner and less in the late evening than those from a manual class in 1999. Alcohol consumption showed distinct patterns by social class with non-manual groups consuming more at lunch and dinner and less in the late evening, a pattern which was consistent over time.

*Conclusion:* Assumptions about recent changes in eating patterns are not borne out by longitudinal data from the 1946 birth cohort. Average patterns of energy intake over a day have remained steady over time, while the pattern of alcohol intake has changed; differences by social class seen in recent years require further examination.

## T6.6.3

### Tracking of an energy-dense, high saturated fat, low fibre dietary pattern over 10 years in the severely obese: The Swedish Obesity Study

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#### Abstract

**Objective:** The consideration of dietary changes over time is important in studies of diet and disease risk. However, there has been no work on dietary tracking in obese adults, who may be particularly likely to exhibit changes in their diet. We investigate the tracking of a dietary pattern (DP) in a severely obese population using repeated dietary measurements taken over a 10-year period.

**Methods:** Dietary intake was assessed in 2037 severely obese individuals (BMI  $41 \pm 4$  kg/m<sup>2</sup>) from the non-surgical group within the Swedish Obese Subjects (SOS) study using a dietary questionnaire. At registration into the study a DP was derived using RRR based on intakes of 39 food groups, with dietary energy density, saturated fat and fibre density as response variables. A similar DP was identified at each follow-up. Accordingly, the DP at registration was able to be projected onto the 9 follow-up measurements (over 10-years) and scores for the DP estimated at each follow-up.

Tracking of the DP was examined using generalised estimating equations (GEE) (Twisk et al 1996). We regressed repeated measurements of the DP score against the DP score at registration, adjusting for time between each measurement. The standardised regression coefficient was interpreted as the tracking coefficient for the DP. This coefficient falls between 0 (no tracking) and 1 (perfect tracking). We investigated adjustments for age and smoking on the tracking coefficient.

**Results:** The energy-dense, high saturated fat, low fibre DP was high in chocolate, full-fat-spreads, low-fibre bread and low in fruits and vegetables. The tracking coefficient for men was 0.40 and 0.41 for women (both  $p < 0.0001$ ). Adjustments for smoking and age made little difference to tracking coefficients.

**Conclusion:** During 10 years of follow-up, there is only low to moderate tracking of this DP in this population of severely obese adults. This suggests that diet measured at only one time point maybe a poor reflection of long-term dietary intake in obese individuals. This may in part explain the poor association seen between diet and long term health outcomes in many studies.

## T6.6.4

### Changes over time in social class differences in food habits: a follow up study

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#### **Abstract**

*Objectives:* Social class differences in food habits have been found, but how these differences might change over time is poorly understood. Our aim was to prospectively examine whether social class differences in food habits among middle-aged women and men narrow or widen over a five to seven years follow up.

*Methods:* At baseline all participants, aged 40-60, were employed by the City of Helsinki, Finland. The data were derived from the Helsinki Health Study cohort baseline mail surveys in 2000-02 (n=8960, response 67%) and follow-up survey in 2007 (n=7332, response 83%). The measures included seven food habits recommended in the national dietary guidelines, four hierarchical occupational social classes and socio-demographic variables. Age adjusted prevalence and slope index of inequality (SII) were calculated with 95% confidence intervals.

*Results:* Following the dietary guidelines varied by food habit. Apart from consuming fish twice a week and choosing vegetable-based margarine on bread, the proportion of those following each recommended food habit was higher among women than men. Following the recommendations either improved or remained stable over time depending on the food habit. The social class differences in the recommended food habits largely remained. However, among women the differences slightly widened for fresh vegetables, as upper class women increased their vegetable consumption (SII at baseline 2.38, 1.93-2.95 and at follow up 2.47, 2.01-3.03). Among men widening class differences were observed for the consumption of fresh vegetables, fruit and berries, and fish. For the use of dark bread and vegetable-based margarine on bread the social class differences were reverse, with larger proportions among the lower classes following these food habits. For milk and cooking fat social class differences were negligible.

*Conclusions:* Following recommended food habits improved among employees over a period of five to seven years in the early 2000s. This increase was mostly similar throughout the social classes, with upper classes following better the dietary guidelines. There were signs of widening social class differences, but overall the class differences in recommended food habits remained stable. Measures are needed to promote healthy food habits and reduce their differences across social classes.

## T7.1.1

### **Size at birth and early life social characteristics predict educational outcomes: consistency across Swedish cohorts born 1915-1929 and 1973-1980**

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#### **Abstract**

*Objective:* Adverse birth characteristics and early-life social disadvantage impact negatively upon cognitive development and educational attainment. We investigate: Which early-life characteristics independently predict (a) school achievement and (b) education continuation? How far are early-life effects on education continuation mediated by school achievement? Do any of these effects differ by gender or social class?

*Methods:* The Uppsala Birth Cohort Multigenerational Study includes manually collected archive data on a representative and well-defined cohort born in Uppsala University Hospital 1915-1929 and information on descendants of the cohort obtained through linkage to routine registers. 12,674 males and females born 1915-1929 (generation 1, G1) and 9,706 of their grandchildren born 1973-1980 (G3) were included in this analysis. School achievement was the mean of school marks received in the spring term of the third grade (G1) and grade average in the ninth grade of elementary school (G3).

*Results:* Predictors of educational outcomes were very similar in the two cohorts, and the effect sizes were usually at least as large in the younger cohort. In both cohorts, the independent predictors of better school marks were: female gender, higher birthweight, lower birth order, older mother, married mother and higher family social class. There was no evidence of any independent effect of preterm or twin status, but weak evidence of a disadvantage to postterm infants. The same characteristics predicted education continuation (secondary school attendance and entrance to tertiary education), with the exception that in the older cohort (the G1s) there was a marked male advantage but no effect of birthweight. In the G3s, the lower probability of education continuation among males and lighter birthweight individuals seemed to be mediated by poorer school achievement. By contrast, even after adjusting for school achievement, continuation to tertiary education was still predicted in both cohorts by lower birth order, older mother, married mother and higher family social class. In cross-generational analyses, better educational outcomes in the grandchildren were predicted by heavier birthweight, lower birth order and higher social class in the grandparents. These associations became non-significant and/or were substantially attenuated after adjusting for grandchild socio-economic position at birth.

*Conclusion:* This paper demonstrates Sweden's success in increasing the proportion of young people entering tertiary education and equalising participation by gender. Nevertheless, for most early-life characteristics the pattern of relative advantage and disadvantage changed little over the twentieth century.

## T7.1.2

### School performance at age 7 of children born late preterm (34-36+6)

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#### **Abstract**

*Objective:* Late preterm infants represent the less studied premature population. The question that our study aims to address is whether the outcome of these children more closely parallels that of term neonates or more worryingly that of more premature infants.

*Methods:* As part of a nationwide, cross-sectional study all births in April 1983 in Greece were recorded. At age 7, from the original cohort, 76% was traced and followed-up by questionnaires. After excluding twins, a target population of 8150 was derived of which 94.4% were full term (FT), 4% late preterm (LP) and 1.6% preterm (PT). Teacher evaluation was used to determine the children's progress in school, using a scale of above average/average/below average. Data were analyzed with SPSS.

*Results:* Scores for below average skills were studied; Overall school performance showed statistical significance ( $p < 0,005$ ), with 36.5% of the PT group, 17.5% of the LP and 15.6% of the FT being below average. The results were similarly statistically significant ( $p < 0,005$ ) for reading, mathematics, expression, initiative and hearing problems, with the PT infants mainly carrying the burden of disability. Although PT infants had more visual problems and poorer environmental awareness, those differences were not found to be significant in our study. We then analyzed the data specifically for the FT and LP infants. There was no statistic difference for overall below average performance and for specific competences with the exception of more visual problems in the LP group 10.9% vs 6.1% ( $p < 0.005$ ).

*Conclusion:* Prematurity does have a negative effect on school performance, however results for LP infants appear reassuringly similar to FT ones. Further studies are needed to validate this preliminary result.

### T7.1.3

## The influence of social background and gestational age on school performance

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#### Abstract

*Objectives:* Our main aim was to explore the combined influence of social background and gestational age on school performance.

*Methods:* We use all Swedish children born 1973-81 that were rewarded a complete grade in primary school (9th grade). Grades were awarded on a relative basis, using a 1-5 scale where 5 was highest. Total mean grade in our population was 3.24 and regressions were performed on 597023 children. Linear regressions were applied to estimate differences in mean grade over parental household class (employees only) and gestational age (25-41 weeks).

*Results:* There were clear gradients in mean grades over both household class and gestational age. The grade distance between the non-manual classes were about 0.2, and between the manual classes 0.1. Across gestational categories the differences were smaller, very preterm births (24-32 weeks) corresponded to a decrease in mean grades of approximately 0.1 in comparison with our reference full term category (39-41 weeks). Early term births (37-38 weeks) and moderately preterm births (33-36 weeks) were in between. Making comparisons within classes, we found an interaction between class and gestational age. In both minimally and fully adjusted models we found that the detrimental effect of both early term birth and moderately term birth was smaller for more advantageous classes. In the higher non-manual class, early term birth did not influence school performance in our fully adjusted model, and moderately preterm birth changed the mean with a score of -0.02 (95% CI -0.40, -0.00). In the unskilled manual class, the figures were -0.02 (95% CI -0.40, -0.003) and -0.06 (95% CI -0.77, -0.04) respectively.

*Conclusions:* In line with previous research we found that social background and gestational age had independent influences on school performance. We also conclude that that the detrimental influence of a shorter gestational age was smaller for children born into more advantaged classes with the exception of very preterm births. Finding out more about how children with a shorter gestational age born into more socially advantaged families reduces the consequences of this challenge, could provide information on how to support less socially fortunate children to do the same.



## T7.1.4

### **Language and learning difficulties at 8 years and school performance at 16 years in small-for-gestational-age children – a longitudinal study of the Northern Finland Birth Cohort 1986**

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#### **Abstract**

*Objectives:* Children with small for gestational age (SGA) often experience language and learning difficulties (LLDs) and problems in academic achievement later on. The aim of the present study was to assess if LLDs at the age of 8 years affect later school achievement in 16-year-old adolescents born SGA with low birth weight (LBW) or normal birth weight (NBW).

*Methods:* The Northern Finland Birth Cohort (NFBC) 1986 included 9432 live-born children and there were 9357 eligible children at the follow-up study. In the NFBC 1986 there were altogether 804 SGA children when children were 8 years old (SGA-LBW, n=114, SGA-NBW, n=690). The correspondent numbers at the age of 16 years were 73 SGA-LBW and 445 SGA-NBW children. Information on LLDs was gathered at the age of 8 years and on school performance at the age of 16 through questionnaires completed by the adolescents themselves. In addition, some socio-demographic factors were analysed.

*Results:* Adolescents with SGA-LBW and SGA-NBW who had LLDs at the age of 8 years reported to have problems in Finnish at comprehensive school. In addition, SGA-NBW children experienced problems in mathematics. Additionally, SGA-LBW children repeated grade more often than children in other groups. On the other hand also NBW children born appropriate for gestational age (AGA) and with LLDs had many problems in academic skills at the age of 16 years.

*Conclusion:* SGA together with LLDs at the age of 8 years seem to be a risk factor for problems in academic skills in adolescence especially in NBW group. However, also children in AGA-NBW group with LLDs had problems in academic skills. The effect of SGA and LLDs as well as some socio-demographic factors on later school achievement will be discussed.

## T7.2.1

### The big five personality profiles in relation to health in middle adulthood

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#### Abstract

*Objective:* Personality traits, especially Neuroticism and Conscientiousness, have been related to health. Less is known about how personality traits are combined within adult individuals over years and how these combinations of traits, that is, personality profiles, are associated with health. The present study was designed to fill this void by investigating the links of longitudinal personality profiles to health among 304 middle-aged adults (53% males) from the Finnish Jyväskylä Longitudinal Study of Personality and Social Development.

*Methods:* The personality traits (Neuroticism, Extraversion, Openness, Conscientiousness, Agreeableness) were assessed by the NEO-Personality Inventory at ages 33, 42, and 50. Subjective (self-rated health, psychosomatic symptoms, psychological distress) and objective (body mass index, blood pressure) health were measured at ages 42 and 50.

*Results:* Five longitudinal personality profiles were extracted across 17 years using latent profile analysis. Resilient individuals (n=65, 37 males, 28 females) scored low in Neuroticism and high in the other traits. Overcontrolled individuals (n=40, 23 males, 17 females) scored high in Neuroticism and low in the other traits. Undercontrolled individuals (n=41, 16 males, 25 females) scored high in Extraversion and Openness and low in Conscientiousness. Effortfully Controlled individual (n=25, 21 males, 4 females) had high scores in Conscientiousness but low scores in the other traits. Ordinary individuals (n=133, 65 males, 68 females) had medium scores in all personality traits. Resilient individuals had the best subjective health, and Overcontrolled individuals the poorest subjective health across eight years. Effortfully controlled, Undercontrolled, and Ordinary individuals were in the middle of these extremes in subjective health not differing from each other. No differences were found in objective health.

*Conclusions:* Overcontrol and resilience were the most discriminative in terms of good subjective health. High Extraversion needed a combination with high Conscientiousness (Resilients) to be related to good health; high Extraversion with low Conscientiousness (Undercontrolled) was associated with poorer health. The results revealed a "health dimension" in personality that helps to understand the connections of subjective health to personality whether it is described in terms of single personality traits or personality profiles. However, the personality profiles offer more nuanced associations with health than the single traits.

## T7.2.2

### **A prospective examination of the bidirectional association between physical functioning and depressive symptoms at older ages. The English Longitudinal Study of Ageing**

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#### **Abstract**

**Background:** There is limited longitudinal research on the bidirectional association between depressive symptoms and physical functioning. We examined whether elevated depressive symptoms were related to subsequent physical functioning. We also examined whether poor physical functioning was related to subsequent depressive symptoms.

**Methods:** The sample consisted of 3,704 men and women aged 60 and over from the English Longitudinal Study of Ageing and was followed approximately for a period of four years. The 8-item CES-D was the measurement of self-reported depressive symptoms. Physical functioning was assessed by measured gait speed. GEE and logistic and multinomial logistic and OLS regression models were estimated.

**Results:** Elevated ( $\geq 4$ ) depressive symptoms were related to subsequent gait speed (2-year lagged GEE models) and decrease in gait speed after adjustment for the following covariates: age, sex, marital status, education, total net household wealth, BMI, cardiovascular and non-cardiovascular comorbidities and health behaviours (and time in the GEE models). Persistently elevated depressive symptoms were also associated with subsequent slow gait speed in a model adjusted for the same covariates. Gait speed (2-year lagged GEE models) and decrease in gait speed between baseline and first follow-up were related to subsequent depressive symptoms after adjustment for baseline depressive symptoms and the covariates listed above.

**Conclusions:** The prospective association between elevated depressive symptoms and poor physical functioning appears to be bidirectional.

## T7.2.3

### Psychosocial stress, obesity and risk of type 2 diabetes: evidence for a gender-specific bidirectional effect during a 20-year follow-up in the Whitehall II study

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#### Abstract

*Objectives:* We and others have previously shown a possible gender-specific interaction between stress and obesity in relation to T2DM. Therefore, we aimed to investigate the association between psychosocial work stress and incident T2DM, stratifying by gender and body weight status.

*Methods:* We studied 5895 Caucasian middle-aged men and women in the Whitehall II study, who were free from diabetes at analysis baseline (1991-1993). Type 2 diabetes was ascertained by an oral glucose tolerance test supplemented by self-reports at baseline and 4 consecutive waves of data collection, including 3 clinical examination phases (1991-2009). Cox regression analysis was used to assess the association between job strain (high job demands/low job control) and 20-year incident T2DM, stratifying by gender and body mass index (BMI < 30 kg/m<sup>2</sup> v. BMI ≥ 30 kg/m<sup>2</sup>). These models were adjusted for potential confounders (age, socioeconomic position, height) and mediators (time-varying waist circumference, systolic blood pressure, triglycerides, HDL-cholesterol, C-reactive protein, interleukin-6 and fibrinogen).

*Results:* Overall, work stress was associated with incident T2DM among women (Hazard Ratio 1.41; 95% Confidence Intervals: 1.02; 1.95) but not among men (HR 0.87; 95% CI 0.69; 1.11) (p for gender interaction=0.017). Among men, work stress was associated with a lower risk of T2DM in non-obese (HR 0.70; 0.53; 0.93) but not in obese individuals (p for interaction=0.17). In contrast, among women, work stress was associated with higher risk of T2DM in the obese (HR 2.01; 1.06; 3.92) but not in the non-obese (p for interaction=0.005). Adjustment for other risk factors (waist circumference, blood pressure, blood lipids and inflammatory markers) reduced these associations indicating that cardiometabolic and inflammatory factors are partly driving this gender and body weight-specific association between work stress and incident T2DM.

*Conclusions:* Body weight status and gender play a critical role in determining the direction of the association between psychosocial stress and T2DM. Stress is linked to lower risk of T2DM among non-obese men but higher risk of T2DM among obese women. The potential effect-modifying role of gender and obesity should not be ignored by future studies investigating psychosocial stress in relation to T2DM.

## T7.2.4

### **Obesity and psychological distress as risk factors for disability: A longitudinal community study**

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#### **Abstract**

*Objective:* Recent cross-sectional evidence suggests that co-occurring obesity and psychological problems amplify the risk of disability, but this effect has not been studied in longitudinal data. The aim of the present study was to determine whether recurrent psychological distress interacts with obesity to amplify the incident risk of disability.

*Methods:* A longitudinal cohort followed from 1994-95 to 2006-07 from the Canadian National Population Health Survey (NPHS). Study sample included adults aged 18-65 years old (n=8 062) with initial information on psychological distress and weight status. The outcome measure was disability status derived from the Health Utility Index Mark 3. Covariates of interest were repeated non-specific psychological distress (Kessler K6 scale) and body-mass index. Risk of disability was examined using Cox proportional hazard regression models, adjusted for age, gender, ethnicity, marital status, physical activity level, smoker status, chronic conditions, recent negative life events and social support.

*Results:* Participants with both obesity and repeated distress had approximately double the risk of disability compared to those with obesity or distress alone (hazard ratio of 3.1 (95% confidence interval (CI): 2.0-4.8) compared to 1.5 (CI: 1.1-1.9) and 1.8 (CI:1.4-2.3), respectively), after controlling for socio-demographic and health variables.

*Conclusions:* Recurrent psychological distress, even at moderate levels, interacts with obesity to amplify the risk for future disability. Addressing recurring psychological distress in obese individuals has the potential to reduce the public health burden of comorbid obesity and psychological distress by tackling disability.

## T7.3.1

### **BeLHIS: towards the integration of the longitudinal approach in the Belgian health information system**

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#### **Abstract**

*Objective:* The aim of this presentation is to show the results of BeLHIS (Belgian Longitudinal Health Information System), a Belgian project whose main objective is to promote the integration of a longitudinal perspective into the national Health Information System (HIS) and to illustrate recent developments in the longitudinal approach of health in our country.

*Methods:* Firstly, we have analysed the Belgian privacy-related legal framework on the management of personal (health) data. Secondly, we have compared the origin and specificity of the Belgian statistical system with other statistical models in Europe. Besides, we have studied changes in the application of ICT in health-related tools and programs. Finally, we have conducted case studies on breast cancer, diabetes and arthroplasty in order to illustrate the importance of developing longitudinal indicators and prospective methodologies which can sustain a more dynamic approach of these chronic pathologies.

*Results:* Recent changes in the legal framework seem to have facilitated scientific health research. Since two years, some major health and statistical institutions have independently developed a prospective view on health. Those initiatives represent a significant step towards the set up of a national health information system enriched with a longitudinal component. Nevertheless, these initiatives are mostly focusing on health care consumption, while less attention is devoted to the broader public health field. Finally, the new technology applications launched by the Belgian Administration during the last years have not yet achieved the expected outcomes.

*Conclusion:* The BeLHIS project emphasizes the need of a coordination process and structure in order to provide managers, policy makers and scientists with a broader access to longitudinal health data and public health information.

## T7.3.2

### **Establishing routinely-updateable longitudinal fertility records from national primary care data: A valuable resource for studying the impact of maternal illness on pregnancy and children's health**

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#### **Abstract**

*Objectives:* Ethical sensitivities surrounding the collection of pregnancy outcomes such as stillbirth and congenital anomaly, coupled with the methodological considerations of studying relatively rare outcomes, introduce substantial challenges to the assessment of maternal morbidity and drug safety in pregnancy. Routinely collected general practice data can provide large sample sizes, objective recording of pregnancy history as well as reducing the potential for reporting bias but are limited by the absence of directly obtainable data on timing of pregnancy events, partially due to anonymisation. Our aim was to develop algorithms to obtain the chronological order of pregnancy events for women, including the recovery of a link to the records of their live children.

*Methods:* We obtained longitudinal medical records for women aged 15-45 years registered in general practices in The Health Improvement Network electronic database, representing over 5% of the United Kingdom population. Algorithms were developed to distinguish incident pregnancy events from past events recorded as medical history (e.g. previous miscarriage); to identify live and non-live pregnancy outcome dates; to interpolate conception dates; and to link children's medical records to their mother's. Programming was conducted in SQL Server 2008.

*Results:* We identified 592,267 pregnancy events occurring between 1990 and 2009 in a population of 2,216,297 women (9,228,135 person-years). The majority of these (74.9%) ended in live births resulting in an overall fertility rate of 48 live births per 1,000 person-years and a standard bell-shaped distribution across maternal age with the highest fertility rates in women age 25-30 years. We successfully matched over 90% of live birth events to children's longitudinal medical records and 0.5% of the unmatched were identified as infant deaths. Spontaneous abortions, terminations and stillbirths accounted for 11.9%, 13.0% and 0.3% of pregnancies respectively and all showed the expected inverse bell-shaped distributions across maternal age with younger and older mothers at greatest risk.

*Conclusions:* We have developed procedures which successfully identify women's pregnancies and their matched children's data in a large nationally-representative database which is routinely updated. Comprehensive data on medications and diagnoses within this database make it a valuable resource for epidemiological analyses of pregnancy, delivery and childhood conditions.

### T7.3.3

## Sample selection in longitudinal studies: The case of the Ninfea birth cohort

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#### Abstract

*Objectives:* To assess under which circumstances selection of study subjects from restricted source populations in cohort studies introduces bias in the exposure-disease associations and to quantify the extent of the induced bias. We present the case of the NINFEA web-based birth cohort as an example of study based on a restricted sample.

*Methods:* We used Monte Carlo simulations to quantify the potential bias introduced by sample selection in longitudinal studies in various settings. Through linkage of the NINFEA study to the Piedmont birth registry data – which holds information on both maternal and birth factors of all births from the same region as NINFEA – we assessed the extent of the selection bias affecting NINFEA. We i. investigated whether maternal characteristics were associated with the selection into the cohort; ii. studied two birth outcomes – birth weight for gestational age and type of delivery – and iii. compared the exposure-outcome associations estimated in the birth registry data and in NINFEA, deriving the corresponding relative odds ratios (ROR). To explain RORs different from 1 we explored whether the confounding patterns for the disease-outcome associations differed across the general and the selected populations.

*Results:* Simulations show that when exposure and risk factor are strongly associated with the selection (odds ratios of 4 or 0.25) and the unmeasured risk factor is associated with a disease hazard ratio of 4, the bias in the exposure-disease estimates is  $\pm 0.15$  (log scale).

Smoking, parity, maternal age, maternal education, alcohol consumption and folic acid intake were all directly or inversely associated with participation in the NINFEA cohort and the confounding patterns differed between the NINFEA sample and the birth registry data. However the estimates derived from these two populations were quite consistent, with the more extreme ROR being 0.73 (0.47-1.14).

*Conclusion:* The bias induced by the sample selection in longitudinal studies is usually weak and thus studies based on restricted source population should lead to relatively robust estimates of the exposure-disease associations. The results from the NINFEA cohort support these findings.



## T7.3.4

### Comparison of physical activity questionnaires in a large population based study (The HUNT Study, Norway) and the International Physical Activity Questionnaire (IPAQ), short form

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#### Abstract

**Objective:** To study the comparability of the International Physical Activity Questionnaire (IPAQ) for the assessment of physical activity (PA) with two differently structured PA questionnaires used in one the largest population based health studies ever performed, the Nord-Trøndelag Health Study (HUNT 1 and HUNT 2), Norway.

**Methods:** The questionnaires were administered twice to a random sample of 108 men aged 20-39, and in the same individuals levels of  $VO_{2max}$  (measured on treadmill) and PA and energy expenditure (EE) (measured by ActiReg), were obtained. ActiReg records the main body positions (stand, sit, bent forward and lie) together with the motion of the trunk and/or one leg each second.

**Results:** The HUNT 1 questionnaire on PA showed intraclass correlation coefficients (ICC) ranging from 0.81 to 0.88, indicating very good reliability. In HUNT 2 ICC were 0.08 for light activity and 0.39 for hard activity, showing poor and fair reliability, respectively, while ICC for the IPAQ ranged from low 0.30 for moderate activity hours, to high 0.80 for sitting hours. In all three questionnaires we found moderate, significant correlation between the index based on questionnaire responses and  $VO_{2max}$  (HUNT 1  $r=0.48$  ( $p\leq 0.01$ )) and for hard PA (HUNT 2,  $r=0.46$  ( $p\leq 0.01$ )) and for total vigorous activity IPAQ ( $r=0.41$  ( $p\leq 0.01$ )). In HUNT 1 metabolic equivalent (MET) values of 6 or more estimated from ActiReg and total vigorous activity from IPAQ most strongly correlated with the index  $r=0.39$ ,  $r=0.55$ , respectively and in HUNT 2 with hard PA  $r=0.31$ ,  $r=0.48$  ( $p\leq 0.01$ ) respectively.

**Conclusions:** In young men the HUNT 1 questionnaire on PA showed very good reliability and moderate validity, while HUNT 2 showed poor to fair reliability measuring light and hard PA, and respectively poor and moderate validity. Both questionnaires are very short and compared favorably with much longer instruments for assessment of more vigorous PA. The HUNT 1 questionnaire was best reproducible and yielded the most significant data on PA behaviour, making it useful also in future epidemiological studies.

## **T7.4.1**

### **Secular trends in the prevalence, incidence, and persistence of overweight and obesity among Danish school children**

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#### **Abstract**

*Objective:* To investigate if the secular increase in the prevalence of overweight and obesity among Danish school children is due to an increasing incidence and/or persistence of overweight and obesity.

*Methods:* Data were obtained from The Copenhagen School Health Records Register comprising 115,903 boys and 114,432 girls born 1930-1973 with height and weight measurements at 7 and 10 years of age. Body mass index was calculated. Overweight and obesity were defined by the criteria proposed by the International Obesity Taskforce. The secular trends in the prevalence, incidence, and persistence (percentage who remained overweight and/or obese) from age 7 to 10 years were compared by plotting them against birth cohorts.

*Results:* The prevalence of overweight and obesity increased throughout the entire period with a slight levelling off occurring in birth cohorts from the 1940s to the 1960s. The incidence of overweight among both boys and girls increased from the 1930s to the 1940s birth cohort among whom it reached ~3%. The persistence of overweight increased from 54% to 61% from the 1930s to the 1940s birth cohort among girls and increased sharply from 47% to 72% from the 1930s to the 1950s birth cohort among boys. The incidence of obesity among both boys and girls and the persistence of obesity among girls increased throughout the period, while the persistence of obesity among boys remained stable (~45%).

*Conclusion:* The increased prevalence of overweight among boys and girls and of obesity among girls could be ascribed to both an increased incidence and an increased persistence, i.e. to both more children developing overweight/obesity and fewer children losing weight. The increased prevalence of obesity among boys was, however, mostly due to an increased incidence. In the fight against the obesity epidemic, obesity-initiating factors, determinants of the persistence of overweight and obesity that sustain overweight and obesity as well as factors promoting 'spontaneous' remission of overweight and obesity should be identified.

## T7.4.2

### **Early life predictors of childhood adiposity: The Gateshead Millennium Study**

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#### **Abstract**

*Objective:* With the high prevalence of childhood obesity, there is a need to relate measures of body fat to early risk factors for obesity which could, potentially, be modifiable. The objective of this study was to use the Gateshead Millennium Study (GMS) to identify risk factors for childhood adiposity.

*Methods:* The GMS is a population based cohort of 1029 infants born in 1999-2000 in Gateshead in Northern England. Throughout infancy and early childhood, detailed information was collected using questionnaires and through the Personal Child Health Record completed by health staff and parents. Assessments at age 6-8 years included detailed body composition, objective measures of habitual physical activity, dietary intake and the child's food and physical activity environment. Due to correlations between the traditional measures of adiposity available, an adiposity index (AI) was calculated using factor analysis on fourteen variables; measures of frame size and adiposity (age, height, waist circumference, bone frame measurements of shoulder, elbow, wrist, hip and knee, skinfold measurements of the subscapular, triceps, biceps and suprailliac sites and impedance-based fat and lean mass measurements (expressed as scores). On the basis of the size of the factor analysis loadings, the first component, taken to be the AI, consisted mainly of variables measuring fat-mass.

*Results:* Data were collected on 619 children, aged 6-8 years. In adjusted regression models, differing associations were seen with adiposity by sex. In boys, increased adiposity at 6-8 years was significantly associated with increased weight gain from 6 weeks to 12 months, maternal emotional over-eating, decreased satiety response (at 5 years) and decreased physical activity (at 6-8 years). In girls, increased adiposity at 6-8 years was associated with increased weight gain from 6 weeks to 12 months of age and measures of emotional under-eating and increased desire to drink at age 5 years. Increased adiposity was also associated with decreased satiety response at 5 years and with a low intake of fruit at age 6-8 years.

*Conclusion:* A wide range of factors are independently related to childhood adiposity. A path analysis will be presented displaying the pathways between these factors.

### T7.4.3

## Maternal job stress during pregnancy and body composition in the 5-year-old child

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### Abstract

**Objectives:** Prenatal exposure to maternal stress may program the fetal HPA axis, potentially leading to altered metabolism in later life, associated with adiposity and diabetes. This association is little studied in humans, and thus we aim to explore whether different levels of job strain experienced by the mother during early pregnancy, as well as maternal total serum cortisol levels (also early pregnancy), are associated with increased body mass index (BMI), central adiposity or body fat mass in the child at age five. Additionally, we aim to explore whether these associations are modified by gender or mediated by gestational age and fetal growth restriction.

**Methods:** A cohort of 2,693 pregnant women (ABCD study, Amsterdam, the Netherlands) completed a questionnaire including the Job Content Questionnaire, assessing job strain (combination of high workload and low control). Cortisol was assessed in a subsample (N=1,660). Gestational age, birth weight (standardized for gestational age, gender and parity) and information on many covariates were available. At the age five health check, height, weight (BMI, kg/m<sup>2</sup>) and waist circumference (waist-to-height ratio, WHtR) were measured. Fat Mass Index (FMI, kg/m<sup>2</sup>) was calculated from bioelectrical impedance analysis. Inclusion: gestational age  $\geq$  37 weeks. Associations were tested using regression analyses. Age and gender of the child were added to the models by default. Confounders added: maternal pre-pregnancy BMI; educational level; smoking; ethnicity and exclusive breastfeeding.

**Results:** High job strain, as compared to low job strain, was borderline associated with higher BMI, after adjustment for confounders ( $\beta$  0.3 p=0.08). This association was not mediated by gestational age or fetal growth restriction. High job strain was not associated with WHtR or FMI. Not including smoking as a confounder, because it may be part of the causal chain in the effect of job strain, did not alter the results. Only in girls, high maternal cortisol was independently associated with higher FMI, WHtR and FMI, after adjustment for confounders ( $\beta$  0.4 p=0.06;  $\beta$  1.0 p=0.02;  $\beta$  0.36 p=0.03).

**Conclusions:** Results show that psychosocial stress and cortisol potentially program obesity and adiposity in the next generation in humans, with possible gender differences.

## T7.4.4

### Preschool childcare arrangements and Body Mass Index over 10 years of follow-up in childhood

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#### Abstract

**Objective:** Although childcare has become a normative experience for most children, no study has examined the putative influence of childcare on childhood body mass index (BMI) trajectories. The aim of this study was to determine whether preschool childcare arrangements are associated with BMI trajectories in the first decade of life, among children born 1997 to 1998 in the Canadian province of Quebec.

**Methods:** A population sample of a birth cohort (n=1,274) was followed from 5 months to 10 years. BMI was calculated using weights and heights reported by mothers at ages 5 months, 1.5 years, 2.5, 3.5, 4, and 5 years and measurements were obtained at 6, 7, 8 y, and 10 years. Children receiving childcare arrangements (childcare centre, family childcare or relative) from 5 months to 4 years were compared to children in parental care on their BMIs, using mixed models.

**Results:** We found that BMI trajectories changed as a function of childcare arrangements, after adjusting for confounding factors (p for interaction of child's age by childcare = .011). Compared to those in parental care, children in childcare centre had .49 kg/m<sup>2</sup> higher BMI (p= .010), and those in relative care had .48 kg/m<sup>2</sup> higher BMI (p= .077) at 6 years. A similar pattern of results was observed at 7 years, although significant only at the .10 level. In addition, overweight, during the first years of elementary school, was more frequent among children in childcare centre and relative care than those in parental care. By 10 years of age, childcare participation was no longer associated with BMI.

**Conclusion:** We found BMI differences according to childcare participation during early childhood, but not in the long term. Future studies should (1) examine whether associations emerge in adolescence, and (2) investigate likely explanatory factors responsible for BMI differences in childcare.

## T7.5.1

### Predicting patterns of developmental change: language development into primary school

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#### Abstract

*Objectives:* Although it is possible to examine population subgroups using test cut point it is preferable to examine the performance of such groups across time if measures allow. This analysis will compare the profile of children's language development between three and five years drawing on data (n=11788) in the UK's Millennium Cohort Study.

*Methods:* Following clinical convention, the threshold for caseness was set at -1.5 standard deviations below the mean on the British Ability Scales, a well recognized standardized assessment of language development. We identified four groups based on their profiles across time on the British Abilities Scales. Group 1 comprised those whose scores fell 1.5 SD below the mean at both time points (n=199), Group 2 made up those whose scores deteriorated across time i.e. starting within normal limits and falling outside the normal range at five years (n=234), Group 3 comprised those who appeared to be resilient – i.e. starting below the norm and improving across time (n=257) Group 4 comprised those whose scores remained within normal limits between 3 and 5 (n=11098). Multinomial regression was employed to assess the influence of these variables on the first three groups relative to the fourth. Potential predictors included gender, whether the child was small for dates, whether they had been in a special care baby unit, had long term health conditions, report of parental concern about hearing at nine months, attachment and developmental performance at nine months.

*Conclusion:* The findings will be discussed in terms of their implications for our understanding of developmental change which has tended to emphasise continuities rather than discontinuities in child development. We will also interpret the data in terms of current health and educational policy and the popular desire to implement early screening procedures to identify "at risk" children. We argue that risk itself is not sufficient to warrant universal procedures which tend not to be very strong predictors even across such a narrow age span and using identical measures.

## T7.5.2

### Language development during infancy: associations with pre- and perinatal factors

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#### **Abstract**

*Objective:* The period of infancy is established as one of the most critical periods for language development, yet delay in language development during this period is a condition which remains largely undiagnosed and uncared for. The aim of this study is to: i) further the understanding of the factors during the pre- and perinatal period which influence infant language development, and ii) explore the potential of utilising measures during the pre- and perinatal period to facilitate early identification of infants at risk of developmental delay.

*Methods:* The study is conducted using data from the 1966 Northern Finland birth cohort (NFBC1966), a prospective mother-child birth cohort which included all pregnant women with an expected date of delivery in 1966 as well as their children. The study will exploit the availability of rich birth cohort data to evaluate the association of a wide range of socio-demographic, parental, psychological and health-related factors measured during the pre- and perinatal period with infant language development, both normal and delayed.

*Results:* From the 28 pre- and perinatal factors available in the NFBC1966, only 8 were found to have independent and significant associations with infant language development. These factors predicted infant developmental delay, but explained only a small percentage of the variance (4%).

*Conclusion:* Rich longitudinal birth cohort data provide a useful resource for identifying the effects of early life factors on infant developmental outcomes. Although information on pre- and perinatal factors lacks prediction power and cannot be used alone in performing a reliable risk-assessment, it can be used to enhance the overall developmental surveillance process of the infant. Using measurements collected during this period offers the additional advantage of enriching the surveillance process with risk assessments made as soon as the infant is born, hence providing the opportunity for the earliest possible identification and treatment of developmental delay.

## T7.5.3

### Language development in preschool children: What are predictive factors for language performance at age 2? What are predictive factors for language performance at age 3?

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#### **Abstract**

*Objective:* To identify the predictive value of early childhood factors for language development at age 2 and age 3.

*Methods:* A community-based sample of 2542 children, recruited at 18 months during their routine visit of a child health care centre, were followed at ages 2 and 3 in a prospective, longitudinal study in 6 regions of the Netherlands. Child and family factors recently identified by US Preventive Services Task Force and additional environmental and motor developmental factors were tested as predictors of a) language performance (child-test applied by child health care physician) at age 2, b) receptive language skills (child-test applied by parents) at age 3, and c) parent reported productive language performance at age 3.

*Results:* Multivariate regression models accounted for 25.1%, 10.2% and 13.2% of the variance in the scores for language performance at age 2, and receptive and productive language at age 3, respectively. A higher language score at the age of 2 was significantly associated with an early age of first walking, being a girl, often singing with the child, often reading out books with the child ( $p < .001$ ), low birth order, playing with other children ( $p < .01$ ), high maternal educational level, right hand preference, favourable result of hearing test, mother never having language problems, timely gestation and day care outside the home ( $p < .05$ ). Factors that were significantly associated with better receptive language score at age 3 were young age of first walking, often reading out books with the child ( $p < .001$ ), being a girl, often singing with the child ( $p < .01$ ), good health and small family size ( $P < .05$ ). Factors that were significantly associated with better productive language score were: mother not stammering, often singing with the child ( $p < .001$ ), being a girl, often reading out books with the child, young age of first walking ( $p < .01$ ), not having ear tubes, father never having language problems and small family size ( $p < .05$ ).

*Conclusions:* Consistent with earlier research were the observed predictive value of child factors, neurobiological development and family history. However, these findings support also the importance of environmental factors relating to language stimulation activities in early childhood for language development in pre-school children.



## T7.5.4

### Profiles of language development in pre-school children: a longitudinal latent class analysis of data from the Early Language in Victoria Study (ELVS)

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#### Abstract

*Objective:* Pre-school language impairment is common and greatly reduces educational performance and long-term achievement. Population attempts to identify children who might benefit from early intervention, however, are hampered by variability in language acquisition. This study used latent class analysis to identify the most common developmental pathways to language impairment in the pre-school years.

*Methods:* Longitudinal latent class analysis was applied to language measures across 5 waves (at 8, 12, 24, 36 and 48 months of age) on 1113 children from the population-based Early Language in Victoria Study (ELVS), in order to identify groups (classes) exhibiting distinct profiles of development. The continuous language measures were trichotomised at each wave into the following categories: "impaired" (bottom 7% of scores in the sample), "typical" (middle 85%) and "precocious" (top 8%). Six latent class models were fitted with increasing numbers of classes from 1 to 6 using MPlus software. The distributions of potential risk factors for impairment were compared between the resulting classes.

*Results:* Five substantive classes were identified: Typical, i.e. language development in the typical range at each age; Precocious (late), i.e. typical development in infancy followed by high probabilities of precocity from 24 months onwards; Impaired (early), i.e. high probabilities of impaired language up to 12 months followed by typical language thereafter; Impaired (late), i.e. typical language in infancy but impairment from 24 months on; Precocious (early), i.e. high probabilities of precocity in early life followed by typical language ability by 48 months. High levels of maternal education, socio-economic status and maternal vocabulary were more common in classes with improving language profiles.

*Conclusions:* For some children, pre-school language is characterised by periods of slow development, accelerated development and catch-up growth. The path to language impairment at 4 years is not characterised by poor communication skills in infancy, suggesting that very early identification (by 2 years of age) of children who will show impairment is not straightforward. These study findings could partly explain why population screening efforts in young children have not proved particularly effective to date.

## **T7.6.1**

### **Inequalities in disability-free life expectancy by social class and area type: England, 2001-03**

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#### **Abstract**

*Objective:* To measure the social pattern and scale of inequality in Disability-Free Life Expectancy (DFLE) in England, and determine whether the pattern and scale are consistent in advantaged and disadvantaged local areas.

*Methods:* Census and vital event data available from the ONS Longitudinal Study were used to calculate estimates of DFLE at birth and at age 65 based on limiting long-term illness or disability (LLTID) status for each Registrar General's Social Class (RGSC) in 2001-03, in England as a whole and within the 'Spearhead group' and non-Spearhead local areas using the Sullivan method.

*Results:* The differences observed in DFLE between professionals and the unskilled social classes were statistically significant and substantial, demonstrating a clear social inequality in the amount of life, the functional health status during those years lived, the absolute number of years, and the relative proportion of life spent free from a LLTID. A predominantly linear relationship was present with DFLE increasing with rising social class. Among professionals no statistically significant differences in DFLE at birth were found between advantaged and disadvantaged local areas. However, males and females assigned to the other social classes in the disadvantaged areas had lower DFLE than their counterparts in the advantaged areas. Females assigned to manual social classes living in advantaged areas had comparable DFLE to females assigned to the managerial and technical social class in disadvantaged areas. The magnitude of inequality in DFLE between professionals and the unskilled class in the proportion of life spent free of LLTID was also higher in disadvantaged areas: among males, a 7.7 percentage point difference was present in advantaged areas compared with 13.1 percentage point difference in disadvantaged areas; among females, the equivalent differences were 5.2 and 9.4 per cent.

*Conclusions:* These results confirm that the assumptions made with regard to sex differences in DFLE need to be set in the context of socio-economic position, and assumptions made regarding sex and social differences need to be set in the context of geography. The scale of the inequalities shown is important for policy responses and understanding of differences in service needs.

## T7.6.2

### Socio-economic differences in diabetes mortality: a retrospective cohort study in the Brussels-Capital Region

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#### Abstract

*Objective:* The aim of this study is to identify socio-economic (SE) differences in premature diabetes mortality in men and women aged 25 to 74. To capture the actual burden of diabetes, both death certificates with diabetes as underlying (UCOD) and multiple (MCOD) cause of death (any mention of diabetes) are analysed.

*Methods:* The study population consists of all inhabitants of the Brussels-Capital Region aged 25-74 (N=598,578). Data are derived from record linkage between the Belgian 2001 census and registration records of all deaths and emigrations for the period 2001-2005. The total number of diabetes-related deaths is 720. Indicators of socio-economic status (SES) are educational attainment (immaterial dimension) and housing quality (material dimension). Age-adjusted mortality rates are calculated using direct standardisation. Rate ratios (RR) are obtained by Poisson regression models with diabetes mortality as the dependent variable.

*Results:* Overall, a lower SES is associated with higher diabetes mortality. According to the indicator of SES used and the extraction of diabetes as either UCOD or MCOD, the strength of the association differs. In men, an inverse educational gradient is observed. Men with primary or no formal education have a  $RR_{MCOD}$  of 2.4 (95% CI 1.8-3.3) compared to those who attained higher education. In women, the lowest educated – primary or no formal education – have a 6 times higher RR of dying from diabetes compared to women with higher education ( $RR_{MCOD}=6.0$ ; 95% CI 3.2-11.3). However, the relation between education and diabetes mortality is not linear. Further analyses point in the direction of an exclusion mechanism. A linear gradient between housing quality and diabetes mortality is observed for both men and women. In women, the gradient is steeper than in men. Women with insufficient or basic housing quality have a  $RR_{MCOD}$  of 7.9 (95 % CI 2.9-21.4) compared to those living in very comfortable circumstances.

*Conclusion:* The results of this study show considerable SE differences in diabetes mortality. Health interventions targeting both the gradient and the most disadvantaged groups are necessary to reduce premature diabetes mortality.

## T7.6.3

### Mortality in relation to time since divorce

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#### **Abstract**

*Objective:* Excess mortality of the divorced has been widely observed in different societies, but the mechanisms producing it are not thoroughly understood. This study assessed the relative importance of selective and causal mechanisms in producing excess mortality after divorce, and evaluated the acute stress effects of experiencing divorce in comparison to the chronic effects of being divorced.

*Methods:* The study was based on population register data. The sample covered 11 % of the married Finnish population aged 30-64 years at the end of 1990, with follow-up information on date of divorce. Over-sampling was used to include 80 % of all deaths during 1991-2003. Cox regression models with annually time-varying covariates were used to analyze how the event of divorce related to the risk of death, and how social and economic factors attenuated the observed excess mortality. Alcohol-related and external causes of death were analyzed separately.

*Results:* Social and economic conditions explained about half of the all-cause mortality differences among men and somewhat more among women. The majority of this was due to post-divorce factors. Among men excess all-cause mortality declined in time after divorce, mainly due to the reduction in mortality differences in alcohol-related and external causes of death. However, there were significant mortality differences even after eight years. Whereas excess mortality attributable to alcohol-related and external causes of death was also high immediately after divorce among women, the contribution to all-cause mortality was smaller. Post-divorce excess mortality was larger among men than women regardless of the length of time since the divorce.

*Conclusion:* The effects of divorce on all-cause mortality are highly persistent. Differences in pre-divorce social and economic circumstances seem to explain some of the excess mortality after divorce, but their effect appears minor compared to causation. The pattern of reduction in alcohol-related and external causes of death provides evidence of divorce-induced acute stress leading to changes in health behavior, particularly among men. The loss of social support and inability to cope with stress may explain why excess mortality after divorce is larger among men than women.

## T7.6.4

### Mortality from road traffic accidents in Switzerland: longitudinal and spatial analyses

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#### Abstract

*Objective:* Road traffic accidents (RTA) are an important cause of premature death. We examined socio-demographic and geographical determinants of RTA mortality in Switzerland.

*Methods:* We use data from the Swiss National Cohort, where 2000 census data were linked to RTA mortality records 2000-2005 (ICD-10 codes V00-V99). Data from 5.5 million residents aged 18-94 years, 1744 study areas, and 1620 RTA deaths were analyzed, including 978 deaths (60.4%) in motor vehicle occupants, 254 (15.7%) in motorcyclists, 107 (6.6%) in cyclists, and 259 (16.0%) in pedestrians. Weibull survival models and Bayesian methods were used to calculate hazard ratios (HR), and standardized mortality ratios (SMR) across study areas.

*Results:* Adjusted HR comparing women with men ranged from 0.04 (95% CI 0.02-0.07) in motorcyclists to 0.43 (95% CI 0.32-0.56) in pedestrians. There was a u-shaped relationship with age in motor vehicle occupants and motorcyclists. In cyclists and pedestrians, mortality increased after age 55 years. Mortality was higher in individuals with primary education (HR 1.53; 95% CI 1.29-1.81), and higher in single (HR 1.24; 95% CI 1.05-1.46), widowed (HR 1.31; 95% CI 1.05-1.65) and divorced individuals (HR 1.62; 95% CI 1.33-1.97), compared to persons with tertiary education or married persons. The association with education was particularly strong for pedestrians (HR 1.87; 95% CI 1.20-2.91). RTA mortality increased with decreasing population density of study areas for motor vehicle occupants (test for trend  $p < 0.0001$ ) and motorcyclists ( $p = 0.0021$ ) but not for cyclists ( $p = 0.39$ ) or pedestrians ( $p = 0.29$ ). SMR standardized for socio-demographic and geographical variables ranged from 82 to 190.

*Conclusion:* Prevention efforts should aim to reduce inequities across socio-demographic and educational groups, and across geographical areas, with interventions targeted at high-risk groups and areas, and different traffic users, including pedestrians.

## T8.1.1

### Association between body mass index and 25-hydroxyvitamin D examined using a genetic approach—the 1958 British birth cohort

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#### Abstract

**Objective:** 25-hydroxyvitamin D [25(OH)D] level is associated with body mass index (BMI) but the nature and direction of the association is uncertain. We used single nucleotide polymorphisms (SNPs) identified for their association with BMI to investigate whether elevated BMI is causally related to higher 25(OH)D level.

**Methods:** We tested associations of 20 previously identified obesity-related SNPs with BMI (for validation) and with 25(OH)D (to test the causal association) individually and in combination (using a weighted allele score) in ~5220 individuals from the 1958 British Birth Cohort (1958BC).

**Results:** Of the 20 obesity SNPs, 10 were associated with log transformed BMI [beta (se) ranged from 0.006 (0.003) for the *NEGR1* variant to 0.011 (0.003) for the *FTO* variant] but only one SNP (*KCTD15*) showed an association with log transformed 25(OH)D levels [beta (se): -0.02 (0.009),  $p = 0.024$ ]. The risk allele based on these 10 SNPs were associated with log BMI [score (beta (se): 0.01 (0.002),  $p$  for trend  $<0.0001$ ] explaining 2% of the variance of BMI, which was higher than the *FTO* variant alone, which explained  $<1\%$  of the variance. There was no significant association between the BMI allele score and 25(OH)D concentration ( $p$  for trend=0.222).

**Conclusion:** BMI associated SNPs were not associated with 25(OH)D concentration in this study despite their association with BMI. This might reflect lack of power despite the fact that the allele score improved the strength of the available genetic data as “an instrument” for causal analysis or the absence of a true causal association of BMI with 25(OH)D concentration. Large scale analyses using the same approach, as well exploration of a causal link in the opposite direction, are both warranted.

## T8.1.2

### E-cadherin (CDH1) polymorphisms and airway remodeling, inflammation and FEV<sub>1</sub> decline in asthma patients using inhaled corticosteroids (ICS)

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#### Abstract

**Objective:** Airway epithelium protects the underlying tissue against noxious inhalants. Epithelial integrity is impaired in asthma and can be restored by inhaled corticosteroids (ICS). Loss of epithelial integrity may contribute to airway remodeling and accelerated lung function decline. E-cadherins form intercellular junctions that maintain epithelial integrity. The main aim of the study is to investigate whether single nucleotide polymorphisms (SNPs) in the E-cadherin (*CDH1*) gene are associated with airway remodeling, inflammation and annual FEV<sub>1</sub> decline in asthma.

**Methods:** Epithelial E-cadherin expression, basement membrane (BM) thickness, number of submucosal vessels and inflammatory cells were determined in bronchial biopsies of 138 asthmatics (population 1). Associations between 17 haplotype tagging SNPs and biopsy parameters and FEV<sub>1</sub>/VC were analyzed by multiple linear regression, association with E-cadherin expression by non parametric tests. FEV<sub>1</sub> decline was determined in 281 asthmatics with a 30-year follow-up (population 2). Linear mixed effect models assessed associations of SNPs with FEV<sub>1</sub> decline after the age of 30 including interactions of ICS use and *CDH1* SNPs.

**Results:** Seven of the 17 SNPs associated with airway remodeling, 3 SNPs with CD8+T-cell numbers, 2 with eosinophil counts and 7 SNPs with FEV<sub>1</sub> decline. All associations occurred only in patients using ICS. In general, SNPs associated with less remodeling, correlated with less rapid FEV<sub>1</sub> decline and higher FEV<sub>1</sub>/VC. Decreased epithelial E-cadherin expression was associated with 5 SNPs in no ICS users.

**Conclusions:** *CDH1* gene polymorphisms may play an important role in airway remodeling, inflammation and lung function decline, especially in patients with asthma using ICS.

## T8.1.3

### Genome wide methylation is associated with lipid profiles at age 50

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#### Abstract

*Objective:* DNA methylation is an epigenetic modification which plays a key role in the regulation of gene transcription. Levels of genomic DNA methylation decrease with age in some individuals and these changes are thought to be associated with an increased risk of development of common complex diseases. The objective of this study is to determine the role of global DNA methylation in the pathogenesis of common complex diseases.

*Methods:* DNA samples were obtained from participants in the Newcastle Thousand Families Study, a longitudinal birth cohort, established in 1947, providing extensive clinical information on cardiometabolic biomarkers at age 50 years (n=231). Global DNA methylation in these individuals was assessed using a Pyrosequencing assay covering 3 CpG sites within LINE-1, a retrotransposon found throughout the genome which acts as a surrogate for global DNA methylation. The relationship between DNA methylation and a range of clinical biomarkers of cardiometabolic health was assessed using linear regression. Regression coefficients [95% CI] are provided indicating change in the dependent variable per unit change in methylation.

*Results:* Positive correlations were observed between DNA methylation and levels of fasting glucose (3.68 [0.47,6.89] p=0.025) and c-peptide (3.55 [0.28,6.82] p=0.033). A positive correlation was also observed between DNA methylation and serum lipid biomarkers including total cholesterol (6.12 [1.83, 10.40] p=0.005), and Apolipoprotein B (1.11 [0.50,1.71] p=<0.001) and a negative correlation between DNA methylation and HDL-cholesterol (-1.31 [-2.01,-0.61] p=<0.001).

*Conclusions:* These data demonstrate that global DNA methylation levels at age 50 years are associated with biomarkers for both type 2 diabetes and cardiovascular disease. Age-associated decline in global methylation might be expected to be associated with an adverse metabolic profile (inverse correlation). A positive correlation was observed and further interrogation of the association between metabolic biomarkers and DNA methylation levels is warranted.



## T8.1.4

### The association of 20 adult height SNPs with early growth trajectories (birth to ten years)

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#### Abstract

**Objectives:** Previous genetic studies have identified a number of single nucleotide polymorphisms (SNPs) associated with adult height and have combined 20 of these SNPs into an allelic score which explains 3% of adult height variation. These SNPs have also been studied comparing their association with peak height velocity in infancy and peak height velocity in puberty, with some possible interactions between these SNPs and growth periods suggested by this research. In this study we test the association between these 20 SNPs and early childhood growth using growth trajectories in height from birth to age 10.

**Methods:** We use longitudinal height data to construct growth trajectory models for 7758 children from the Avon Longitudinal Study of Parents and Children (ALSPAC). We test these models for association with 20 of the previously reported adult height SNPs (both individually and using a combined allelic score, where the number of tall alleles are summed for each individual).

**Results:** In our study birth length and growth in the first year of life was only weakly associated with the allelic score. There were stronger associations between the allelic score and growth later in childhood (0.004cm (SE=0.001) per 'tall' allele per month between 11 and 32 months). By age ten the height difference between an individual with 17 'tall' alleles and an individual with 27 tall alleles was estimated to be 2.7cm (0.5SD) in boys and 2.0cm (0.3SD) in girls – roughly half that seen in the adult study (5cm, 0.7SD).

There was some evidence that specific SNPs were associated with growth at particular growth periods; the HHIP SNP (rs2055059) was associated with early growth (up to 32 months in boys, 29 months in girls) and the SOCS2 SNP (rs11107116) with later growth (after 32 or 29 months).

**Conclusions:** This study demonstrates the importance of 20 known adult height SNPs on childhood growth. These SNPs appear to have some influence on birth length and even greater influence on height growth in later childhood. By age ten they appear to have an effect on height that is roughly half the magnitude to that seen in adults.

## T8.2.1

### Age of introduction to lumpy foods and associations with dietary patterns throughout childhood

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#### **Abstract**

*Objectives:* The weaning period is influential for determining later taste and texture preferences. The World Health Organisation recommends that solid foods are introduced after 6 months of age. This may delay the progress to chewy foods. We have previously shown that children introduced to lumpy (chewy) foods late (after 10 months of age) consumed a narrower range of foods and less fruit and vegetables at 15 months and 7 years of age. Here we examine whether age of introduction to lumpy solids is associated with dietary pattern scores obtained from Principal Components Analysis (PCA) in early and middle childhood. Dietary patterns inform us about the types of diet consumed in a population.

*Methods:* Over 7000 children from the Avon Longitudinal Study of Parents and Children (ALSPAC) a UK population-based cohort study were included. Data was collected via self-completion questionnaire on the age at which lumpy solids were first introduced to the child (<6 months, 6-9 months, 10+ months). Dietary pattern scores were obtained using PCA from food frequency questionnaires (FFQs) at 3, 4, 7 and 9 years of age. General liner models were used to estimate the effect of early (<6 months) and late (10+ months) introduction to lumps on each dietary pattern score, taking into account a number of potential confounding factors.

*Results:* Early age of introduction to lumpy solids was associated with increased scores on the 'traditional' dietary pattern (meat, potato and vegetables) at each time point, while late age was negatively associated with this pattern across time (all  $p < 0.005$ ). The 'health conscious' pattern score (vegetarian style foods, salad, rice, pasta, fruit and fish) followed a similar pattern up until the age of 7 years. The 'processed' pattern score (high fat, processed foods) at each time point did not differ according to age of introduction of lumpy solids.

*Conclusions:* The results support our previous findings examining associations between age of introduction to lumpy solids and consumption of individual foods: children who were introduced late to lumps are less likely to consume a diet rich in fruit and vegetables and this persists throughout childhood.

## T8.2.2

### Household composition and individual diet; results from the National Survey of Health and Development 1982 and 1999

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#### Abstract

*Objectives:* Household composition is one of several socio-economic determinants that may have a major effect on nutritional status of individuals. The aim of this study is to compare the intake of key nutrients of members of a UK cohort at 2 stages of their adult lives according to the size and composition of the household.

*Methods:* The MRC National Survey of Health and Development (NSHD) 1946 Birth Cohort is a longitudinal survey which has collected dietary information recorded in 5-day estimated diaries on three occasions during adult life. The current analysis was carried out of the 1982 and 1999 dietary data from 2256 and 1772 individuals aged 36 and 53 years respectively. Details of each household were used to define family categories according to number of adults and children under 16 and /or dependant adults. ANOVA was used to compare intakes of key nutrients by family category with social class included as a co-variate

*Results:* In 1982 significant differences were found between family categories in intakes of protein, calcium, carotene, folate, vitamin C and fibre. Single adults with dependants consistently had the lowest mean intakes. Subjects living alone or with a partner tended to have the highest mean intakes of nutrients. Subjects living with partners and dependent children had lower intakes of nutrients and as numbers of dependants increased, intakes of women were even lower. By 1999 men aged 53 years living alone consistently had the lowest mean nutrient intakes but only carotene intake for this group was significantly lower than other categories. For women aged 53 years there were no significant differences between categories. Being a single adult with dependants was no longer a significant factor for diet quality; women living in a large family had the highest intakes of energy, protein, fibre and vitamin C.

*Conclusion:* Being a single parent or living with a dependant was a risk factor for a poorer quality of diet at age 36 years. Older men and women aged 53 years benefited from living in a family rather than alone or as a couple. This has implications for diet quality in old age.

## **T8.2.3**

### **Family structure and maternal employment in childhood and their influence on young people's eating habits**

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#### **Abstract**

*Objective:* Over the last decades, the increasing obesity rate in Britain entails a rising in individual's health issues, health care costs and social costs. Overweight and obesity are the result of a continuous imbalance between calories consumption and expenditure. Although the possible solutions are easily identified: promotion of diet changes and increase of physical activities, they are difficult to implement because they imply changes in people's preferences and behaviours. Thus, today's public health policy focuses on understanding and correcting the factors responsible for shifts in consumers' food choices – especially those of children. This paper explores the relationship between several eating habit outcomes in early adulthood and maternal employment, parental joblessness and family disruption.

*Methods:* The analysis is performed using the British Household Panel Survey, which since 2004 provides information on weight and height of children, diet characteristics and physical activities. We use conventional binary longitudinal models to investigate the relationship between the propensity to be overweight at the beginning of adulthood life and 1) experiencing family disruption and 2) growing up with a working mother or jobless parent(s). We also look at whether family disruption, parental employment and education influence children's eating (consumption of vegetable and fruit, fast food and junk food) as well as their physical activity habits.

*Results:* Female's participation in the labour market has been related to the rise in obesity through changes in time allocation from food preparation to work as this may cause a large consumption of ready-to-eat meals which are high in calories and fats. Furthermore, living in a single-parent family during childhood is usually associated with disadvantageous outcomes for young adults. So we expect to find that obesity and unhealthy diet are linked to experiencing any of these events.

*Conclusion:* We investigate whether differences in maternal working conditions along with their personal characteristics may affect the weight of their offspring. Understanding the determinants responsible of childhood obesity is important for devising policy. If a working mother is one of the driving forces behind children being overweight, then policies incentivising parental employment (especially that of single parents) may produce undesirable effects from a public health point of view.

## **T8.2.4**

### **Disordered eating attitudes and behaviours in children and adolescents 11-18 years of age in Cyprus: a six year follow up, school-based study**

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#### **Abstract**

*Objective:* The aim of the present study was the re-evaluation of eating attitudes and behaviours in the Cypriot adolescent population.

*Method:* In 2003 a representative sample of children and adolescents aged 10-18 years of age from all over Cyprus, were invited to complete in schools the questionnaires EAT-26 and EDI-2. The same methods were used to collect data in 2009-2010 using the EAT-26 and EDI-3.

*Results:* Concerning the EAT-26, the percentage of participants who scored above cutoff 20, which is indicative of a tendency for eating disorders, has remained on the same high level for both genders over a six year span. The percentage of participants with a score of above normal on the DT and BD subscales of the EDI-3 has also remained consistent between 2003 and 2009. Concerning the B subscale of the EDI, the percentage of participants with a score of above normal was 35% for females and 27.4% for males in 2003. In 2009, 36.4% of females and 36.8% of males scored above normal. Statistical analysis shows that this difference is significant both for females  $t = -3.536$   $p < 0.04$  and for males  $t = -2.588$   $p < 0.01$  highlighting that by 2009 this tendency has increased.

*Conclusion:* Disordered eating attitudes in Cypriot children and adolescents remain common, with a higher tendency for females. Especially with regards to bulimia we find an increasing tendency in both males and females over a six year span. Strategies aimed at decreasing these disordered eating attitudes and behaviours are greatly warranted in our population.

## **T8.3.1**

### **Age period effects in risk factors in adults. The Doetinchem Cohort Study 1987-2007**

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#### **Abstract**

*Objective:* Obesity, hypertension and hypercholesterolemia are modifiable risk factors that deteriorate with ageing. With data from the Doetinchem Cohort Study we analyzed changes in life style and biological risk factors in healthy Dutch adults who were 20-59 years at baseline.

*Methods:* The Doetinchem Cohort Study is a prospective study on life style, biological risk factors and health in the Netherlands. An age-sex stratified random sample of men and women in four age groups of originally 20-29, 30-39, 40-49, 50-59 years were measured up to four times with 5 year intervals (n= ca. 6300). Measurements included questionnaires and a physical examination. The following definitions of biological risk factors were used: Obesity: BMI  $\geq 30$  kg/m<sup>2</sup>; Hypertension (WHO): systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg and/or use of medication; Hypercholesterolemia: total cholesterol  $\geq 6,5$  mmol/l.

*Results:* The levels of body weight, blood pressure and total cholesterol increase with age. Especially for obesity, a strong period effect is observed: each 10-year age group has a higher prevalence of obesity than their predecessors. For smoking, in men each 10-year age group has a higher prevalence of never smokers than their predecessors. Results will be presented for overweight, obesity, hypertension, hypercholesterolemia and smoking, and combinations of lifestyle and risk factors.

*Conclusion:* For smoking, favourable period effects are observed in men. Especially the strong period effect in obesity is of great concern, due to the impact on diabetes, cardiovascular diseases and osteoarthritis.

## T8.3.2

### Incidence and determinants of disability in ADL in older Brazilians: a six years follow up survey in Sao Paulo, Brazil

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#### Abstract

*Objectives:* The objective of this study was to analyze the incidence of disability in activities of daily living (ADL) in six years (2000 – 2006) and analyze their determinants in older Brazilians.

*Methods:* Data comes from two rounds of a longitudinal survey – SABE Study (Health, Well being and Aging). SABE began in 2000 with a sample that included population aged 60 and more living in Sao Paulo/Brazil (n=2,143 from a multi stage clustered sampling). In 2000, were selected for this study 1634 elderly (698 men and 936 women) who didn't have difficulty in ADL (walk across the small room, dressing, bathing, eating, transferring in the bed and using the toilet). In 2006, the same activities were analyzed again and the incidence was calculated based in a sample of 905 elderly (353 men and 552 women). Logistic regression was used for the analysis of the determinants using ADL status in 2006 and in the baseline: age, years of education, marital status, living condition, depressive symptoms, Mini Mental State Exam, body mass index, handgrip and self-report of diabetes, heart disease, stroke and osteoarthritis.

*Results:* The incidence of disability in men was 19,54% and in women 32,73%. The Logistic Regression analyses demonstrated an independent relationship between incidence of disability in men and: age (OR = 1.16 IC 95% 1.11 – 1.21) and self-report of stroke (OR = 8.65 IC 95% 2.43 – 30.72). For women was independently associated to incidence of disability: age (OR = 1.05 IC 95% 1.01 – 1.09), self-report of osteoarthritis (OR = 2.77 IC 95% 1.62 – 4.72), self-report of heart disease (OR = 2.11 IC 95% 1.11 – 4.02), depressive symptoms (OR = 2.95 IC 95% 1.55 – 5.62), body mass index (OR = 1.07 IC 95% 1.02 – 1.12) and handgrip (OR = 0.92 IC 95% 0.87 – 0.97).

*Conclusions:* The incidence of disability in ADL was greater in women than in men in six years of follow up. The age was determining factor for both genders. While stroke was an important factor in men, osteoarthritis, heart disease, depressive symptoms, body mass index and handgrip were important in women.

### T8.3.3

## Mortality patterns in a cohort of Polish elderly individuals: 22-year follow-up Krakow study

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### Abstract

*Objective:* The aim of the study was to assess predictors of all causes mortality in relation to health status, life style and socio-demographic characteristics of older people during baseline study.

*Methods:* A base-line study was performed over 1986/87 in a randomised sample of 2605 individuals (34.6% males and 65.7% females), aged 65 years and over, residents of Krakow city centre. Face to face interviews covered questions on demographic data, information on self-reported chronic diseases, current and previous lifestyle, occupational activity, marital status, living conditions, everyday activities and leisure time activities, self-rated health status, and attitudes towards positive health behaviours. The vital status of all individuals under study was ascertained by monitoring city vital records and general mortality was analyzed. Statistical analysis was performed using Cox proportional hazard model.

*Results:* During the 22 years of observation 81.1% of study population died. In males, the most important predictors of mortality were smoking (HR=1.44 95%CI: 1.20-1.74) and number of chronic diseases (HR=1.10 95%CI: 1.01-1.20). Higher education as well as positive attitudes toward health were predictive factors with hazard ratio 0.71 and 0.79, respectively. The same set of predictors was observed in younger group of males ( $\leq$  75 years of life), but in the older group none of these predictors was statistically significant. Mortality in this group was mainly related to poor self-rated health (HR=1.60 95%CI: 1.11-2.32). In females, also mortality was related to smoking status (HR=1.60 95%CI: 1.29-1.98) and number of chronic diseases (HR=1.08 95%CI: 1.01-1.15). In addition, we observed that diabetes present during the baseline study was risk factor of mortality (HR=1.64 95%CI: 1.33-2.03). In younger women the results were very similar, but in older ones, mortality was related only to diabetes (HR=1.51 95%CI: 1.03 – 2.19).

*Conclusion:* The most important factors influencing mortality were smoking and number of chronic diseases. In addition for older males we have observed impact of poor self-rating health on mortality, and diagnosis of diabetes in females.



## **T8.3.4**

### **Survival analysis and inequities in older Brazilians: a six year follow up survey in São Paulo, Brazil**

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#### **Abstract**

*Objective:* In Brazil, the aging process is frighteningly fast with important consequences for health services. By 2025 they will be more than 30 million people, about 15% of Brazilian population. A large portion of this increase will occur in persons aged 80 and older. This study analyzes inequalities associated with survival of elders in a six year follow-up in Sao Paulo, Brazil.

*Methods:* Data comes from a longitudinal survey – SABE Study (Health, Well being and Aging) that began in 2000 with a sample that included population aged 60 and plus living in São Paulo/Brazil (n=2,143 from a multi stage clustered sampling). A two-stage sampling procedure with probability proportional to the size was carried out using census tracts with replacement. To achieve the desired number of respondents aged 75 or older, additional households close to the selected census tracts were sampled. The second wave was done in 2006 when 1,115 elders were re-interviewed. Descriptive statistics included tests for association using Rao Scott procedure with correction for sample-design. Multi variable analysis was done by adjusting logistic regressions with robust estimation. Kaplan-Meier Survival Analysis was used to approach the results with death after six years. Variables analyzed were: social demographic conditions (sex, schooling, income, early conditions) and health conditions (depression, comorbidities, disability, self-perceived health, falls).

*Results:* Data show an annualized mortality rate of 55.2 per 1000 for males and 34.0 for females. The demographic variables were associated with survival, besides age and gender, greater education ( $p < 0.0000$ ), higher income ( $p < 0.0000$ ) and urban origin for women ( $p = 0.015$ ). The health related variables were self-reported better health ( $p < 0.000$  for women and  $p = 0.016$  for men), no self-reported disease ( $p < 0.000$ ), depression ( $p = 0.035$  for women) and no disability ( $p < 0.000$ ). In the Kaplan-Meier, men with excellent health are close to the women with regular health self-reported. Absence of disability makes the male curve higher than the female.

*Conclusions:* The study results show inequalities associated with lower survival. Public policies should take into account the specific needs of the elderly population to facilitate access to health care services and reduce inequalities.

## T8.4.1

### Social networks and mental health: Evidence from SHARE

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#### **Abstract**

*Objectives:* This study investigates whether social support networks of older Europeans exert a causal influence on their mental health. Late-life depression is common in Europe, and the relationship between social interaction and the mental health of older people is well documented. The theoretical framework underpinning these findings involves two hypotheses. The main effects hypothesis predicts that individuals with strong social support experience higher levels of wellbeing than those with weak social support, while according to the stress-buffering hypothesis, it is only upon exposure to unexpected negative life events that individuals with weaker levels of social support are adversely affected.

*Methods:* This paper tests these hypotheses in relation to mental health using data from two waves of the Survey of Health, Ageing and Retirement in Europe (SHARE 2004 & 2006), which includes the EURO-D scale of depressive mood. Using panel data techniques, including estimators for count data, we account for unobserved factors such as personality, and address concerns about reverse causality with instrumental variables. Using objective differentiating criteria such as proximity of family and social engagement, cluster analysis identifies four distinct social support networks.

*Results:* Cross-country variation in social support and the prevalence of depressive symptoms is evident, emulating previous literature suggesting a North-South gradient in European social and family life. We find a robust result that for women, weak social support networks are associated with higher levels of depressive mood (the main effects hypothesis). The magnitude of this effect is significant, and appears to be mediated through feelings of loneliness. We find no evidence that network membership either exacerbates or mitigates the effect of negative life events on depressive mood for either gender (the buffer hypothesis).

*Conclusions:* We find that social support has an independent, causal, positive effect on mental health for women only. Profiling individuals by their social network type may provide a means of identifying those most at risk of developing depressive symptoms as they age.

## T8.4.2

### **The longitudinal effects of the numbers of relatives and friends in regular contacts on psychological well-being among middle aged adults**

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#### **Abstract**

*Objective:* To examine the longitudinal effect of the numbers of regularly contacting close social ties on subsequent psychological well-being over and above depression, and individual social position and cohabitation status among middle aged adults. .

*Methods:* We used available cases obtained from the age 42, 45 and 50 data of a prospective British cohort study, the National Child Development Study (Born in 1958, Men=3133, Women=3402). The size of regularly contacting close social ties, indicated by the numbers of relatives and friends with whom cohort members saw once month or more, was assessed at age 45. The outcome variable, psychological well-being, was indicated by a total score on the Warwick-Edinburgh Mental Well-being Scale (14 item, range 14-70) administered when cohort members were at age 50.

In this study, depression, cohort members' social position and cohabitation status were treated as confounders. Depression was indicated by the presence or absence of depression (scores over 2 on the depression subscale of the Clinical Interview Schedule-Revised), assessed at age 45. Cohort member's social position indicated by the Registrar General's Social Classes and cohabitation were obtained at age 42. Multiple regression was used to examine independent significant effects of the numbers of relatives and friends in regular contacts on psychological well-being.

*Results:* After accounting for the confounding effects, the number of friend in regular contact decreased, the respondents' psychological well-being decreased. Having friends was more important than having relatives, but both were independently associated with better psychological well-being among men.

*Conclusion:* Overall, well-integrated network of friends of regular contacts is the source of psychological well-being among middle aged men and women. Additionally, having greater numbers of relative of regular contacts is also beneficial for middle aged men's psychological well-being.

### T8.4.3

## Reassessing the long term risk of suicide following a first episode of psychosis

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### Abstract

*Objectives:* Following an influential meta-analysis in the 1970s, the lifetime risk of suicide in schizophrenia has been estimated at 10% and this figure is still routinely quoted in the literature. The long term risk of suicide following a first episode of psychosis has been misjudged, because previous studies have often been based on prevalence cohorts, been biased to more severely ill, hospitalised patients, extrapolated from a short follow-up time and made a distinction between schizophrenia and other psychoses. The aim of this study is to determine the epidemiology of suicide in a clinically representative cohort of first episode psychosis patients.

*Methods:* All 2723 patients who presented for the first time with psychosis in three geographical catchment areas in London (1965-2004;n=2056), Nottingham (1997-1999;n=203) and Dumfries and Galloway (1979-1998;n=464) were traced after a mean follow-up period of 11.5 years. Analysis was by Poisson regression and indirect standardisation was used to calculate Standardised Mortality Ratios (SMRs) for suicide, standardised for age and gender.

*Results:* Case fatality from suicide was considerably lower than expected from previous studies: 1.9% (53/2723); proportionate mortality was 11.9% (53/444). Although the rate of suicide was highest in the first year after presentation, risk persisted late into follow-up, with median time to suicide being 5.6 years. Suicide occurred approximately 12 times more than expected from the general population of England and Wales (SMR 11.65; 95%CI 8.73-15.24), and 49 of the 53 suicides were excess deaths. Even a decade after first presentation, suicide risk remained almost 4 times higher than in the general population (SMR 3.92; 95%CI 2.22-6.89): a time when there may be less intense clinical monitoring of risk.

*Conclusions:* The highest risk of suicide following a psychotic episode occurs soon after presentation, yet clinicians should still be vigilant in assessing risk a decade or more after first contact. The widely held view that "10-15% die from suicide" is misleading as it refers to proportionate mortality, not "lifetime risk". Nonetheless, there is a substantial increase in risk of suicide compared with the general population.

## T8.4.4

### Religion and assisted and non-assisted suicide in Switzerland: national cohort study

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#### Abstract

*Objective:* The association between religion and suicide has been debated ever since in the 19th century suicide rates were found to be higher in the Protestant compared to the Catholic cantons of Switzerland. We examined religious affiliation and suicide in modern Switzerland, where assisted suicide is legal.

*Methods:* The 2000 census records of 1,722,456 (46.0%) Catholics, 1,565,452 (41.8%) Protestants and 454,397 (12.2%) individuals with no affiliation were linked to mortality records for adults aged 35-94 years. Outcomes were all suicides and suicides by poisoning, hanging, drowning, fire arms, fall, vehicle, other means and unknown means (ICD-10 codes X60-X84) that occurred between the date of the census (December 5, 2000) and December 31, 2005. Hazard ratios (HRs) with 95% confidence intervals (CIs) were adjusted for age, sex, marital status, education, type of household, language and degree of urbanization.

*Results:* Suicide rates per 100,000 inhabitants were 19.7 in Catholics (1664 suicides), 28.5 in Protestants (2,158 suicides) and 39.0 in those with no affiliation (882 suicides). Poisoning was the most frequent method in individuals with no affiliation (335; 38.0%), followed by Protestants (620; 28.7%) and Catholics (335; 20.1%). Compared to Protestants, adjusted hazard ratios (95% confidence intervals) for all suicides were 0.82 (0.75-0.89) for Catholics and 1.19 (1.08-1.32) for no affiliation in age group 35-64 years, and 0.65 (0.58-0.72) and 2.08 (1.82-2.37), respectively, in age group 65-94 years ( $p < 0.0001$  from test of interaction). The association was strongest for suicides by poisoning in age group 65-94 years, the majority of which are assisted: compared to Protestants, adjusted hazard ratios were of 0.46 (0.37-0.56) for Catholics and 2.93 (2.42-3.55) for those with no affiliation.

*Conclusions:* In Switzerland the protective effect of a religious affiliation appears to be stronger in Catholics than in Protestants, stronger in older than in younger people and particularly strong for assisted suicides.

## **T8.5.1**

### **Evaluation of the compression expansion and dynamic equilibrium theories using Western Australian linked hospital morbidity and mortality data**

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#### **Abstract**

*Objectives:* Three hypotheses have been advanced to predict changes in population health in countries experiencing low birth and death rates, and increasing expectation of life. These are the compression of morbidity, expansion of morbidity, and dynamic equilibrium theories. Determining which of these best accounts for changing patterns of illness and death is an important step in understanding both the public health and economic impacts of health intervention in an ageing population. The aim of this study was to evaluate the compression, expansion and dynamic equilibrium theories in Western Australia (WA).

*Methods:* Life tables and survival curves for first-time hospital episodes for chronic disabling and activity limiting conditions and all cause mortality in persons aged 15 or more years in WA in 1980-2003 were constructed using data from the WA Data Linkage System. Changes in life expectancy, average age at first-time hospitalisation and time spent in chronic disabling or activity limiting states were used to evaluate the competing hypotheses.

*Results:* Life expectancy increased by 4.0 and 2.6 years over the 24-year study period in males and females respectively. However, average time spent with a diagnosed chronic disabling condition increased by 8.2 and 8.1 years in males and females respectively, while time spent in an activity limiting state remained largely unchanged.

*Conclusions:* This study found evidence to support an expansion of morbidity and some evidence against the dynamic equilibrium theory. Our results suggest that an increase in the 'medicalisation of more serious morbidity' may be in operation rather than an increase in more serious morbidity *per se*. This is consistent with population trends towards higher levels of self-reported ill-health in Australia and portends further challenges for the containment of health care costs in the future.

## **T8.5.2**

### **Health care expenditure in the last years of life for out-of-hospital Medicare Benefits Schedule funded services in Western Australia: A population-based data linkage study**

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#### **Abstract**

*Objectives:* Explore the relationship between time-to-death, age and health care expenditure for government funded out-of-hospital services in last years of life to determine effects of service type and the stability of this relationship over time.

*Methods:* Records of all deaths in Western Australia from 1990 to 2004 extracted from the mortality register and linked to records from the Medicare Benefit Scheme. Claims five years prior to death were identified from all Medicare Benefit Scheme claims originating in Western Australia between 1984 and 2004. Out-of-hospital costs were assigned to all services within five years of death from five major causes using Medicare Benefit Scheme costing information.

*Results:* Out-of-hospital health care expenditure increased for primary care services during last two months of life. A similar trend was observed in specialist services and diagnostic and therapeutic services, however an earlier increase in expenditure occurred during the penultimate year before death.

*Conclusions:* Primary care service cost patterns varied for specialist services and diagnostic and therapeutic services for both time to death and age. Significant differences in relationship between time to death, age and health care expenditure were identified between service types, highlighting potential shortcomings in using single population models to predict future health care expenditure.

### **T8.5.3**

## **Association of mental health with health care utilisation and cost: a population study**

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### **Abstract**

*Objective:* Few studies have used population-based data to examine the health care costs of those who suffer from mental health problems. Using 9 years of physician billing data, we compare the health costs of groups with and without mental health problems.

*Methods:* A dataset containing registration data for all cases receiving tertiary mental health service was constructed and subsequently matched on age and sex in a ratio of 1:8 with health care users who did not receive treatment in the tertiary mental health system. Three groups emerged in the final dataset: Those with mental health problems treated in publicly funded tertiary care (n = 76,677), those with mental health problems treated in their doctors' offices (n = 277,627), and those without mental health problems (n = 329,177). Examining over 52 Million billing records for these individuals, we compare average number of visits and average "health only" billing cost per unique individual over the 9 year study period across these three groups.

*Results:* Among all health care users in the data, the health costs (total costs – mental health costs) were greater for those with problems treated in publicly funded tertiary care (\$3,437 average) and those with mental health problems treated in their doctors' offices (\$3,265 average), as compared to those without mental health problems (\$1,345 average).

*Conclusions:* Having a mental health problem is highly correlated with higher health-related expenditures. This has important policy implications on how mental health resources are constructed and rationed within the health care system.



## T8.5.4

### Evaluating the impact of health insurance for the poor: Evidence from Indonesia

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#### Abstract

*Objective:* One of the key barriers limiting access to health services is financial: people tend not to seek care out of fear they may not be able to afford it. By removing financial barriers to health care, one would expect to find an increase in utilization. Parallel with the efforts to reach the Millennium Development Goals, Indonesia's first steps toward universal health coverage occurred with the introduction of the ASKESKIN Insurance program for the poor in 2005. The main objective of the program is to increase access to basic health services of lower income groups by removing financial barriers that discourage utilization.

*Methods:* This study evaluates the impact of ASKESKIN on behaviour to seek care among targeted groups, the poor and near poor, and the non-poor. The analysis makes use of panel data from the Indonesia Family Life Survey (IFLS). The data allows the analysis of changes in utilization by those who have ASKESKIN insurance and by type of health provider they visited in the last four weeks. The community instrument of the IFLS allows us to avoid bias from endogenous take-up of the program by using information on the availability of Askeskin at the community level. Particularly we use duration of exposure to the program at the community level interacted with some household characteristics to instrument the endogenous take-up of the program. The approach recognizes that it takes time for individuals to learn of a program and for communities to learn how to target and distribute insurance cards. It then exploits heterogeneity in exposure across communities to identify the effects of the program.

*Results:* Our preliminary findings show that the program significantly increases health care service utilization by those who reported ill. But, non-poor individuals appear to be benefited more by the program compared to targeted poor individuals. One possible explanation why the impact deviates from the original design is that while the program removes the financial barrier to access health services, it does not necessarily affect the health seeking behaviour of the poor. Also, as the program targeted the poor communities, it does not improve the problem of supply of health services in those communities.

*Conclusion:* We conclude that the program increase utilization of health care services but not as the way as the program was initially designed. This is consistent with previous findings. But it also differed in term of magnitude of the program effect. We argue that this is because in previous study there is still potential selection that is not sufficiently addressed with only household fixed-effect.

## T8.6.1

### Exposure to statins and risk of common cancers: a series of nested case-control studies

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#### Abstract

*Objective:* Multiple randomised controlled trials have demonstrated the benefits of statins in improving survival for patients with ischaemic heart disease and this has resulted in a substantial increase in statin prescribing. Whilst there are definite benefits of statins in reduction of mortality in high risk patients, uncertainties remain about whether statins might increase or decrease risk of cancer. The aim of this study is to investigate whether there is an association between use of statins and the risk of a number of common cancers.

*Methods:* A series of nested case-control studies were conducted within 574 UK general practices using the QResearch primary care database. Cases with primary cancers were diagnosed between 1998 and 2008. The effect of statin on 21 site-specific cancers was estimated with conditional logistic regression adjusted for co-morbidities, smoking status, socio-economic status and use of non-steroidal anti-inflammatory drugs, cyclo-oxygenase-2 inhibitors and aspirin.

*Results:* A total of 41749 women and 46376 men diagnosed with cancer and 362254 matched controls with at least 6 years of records were analysed. The adjusted odds ratios for any statin use for cancer at any site were 0.98 (95%CI 0.94 to 1.03) in women and 1.03 (95%CI 1.00 to 1.07) in men. Prolonged (more than 4 years) use of statins was associated with a significantly increased risk of colorectal cancer in women (odds ratio 1.42, 95%CI 1.18 to 1.70) and bladder cancer in men (odds ratio 1.32, 95%CI 1.07 to 1.61) and a reduced risk of leukaemia in men (odds ratio 0.71, 95%CI 0.50 to 0.99). There were no significant associations with any other type of cancer.

*Conclusion:* In this large population-based case-control study prolonged use of statins was not associated with an increased risk of cancer at any of the most common sites in either gender except for colorectal cancer in women and bladder cancer in men and there was a reduction of leukaemia risk in men.

## T8.6.2

### Longitudinal patterns of weight in women diagnosed with breast cancer

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#### Abstract

*Objective:* Weight gain is a common concern following breast cancer and is associated with negative health outcomes; hence, prevention of weight gain is of clinical interest. We describe weight fluctuations up to 18-months following a breast cancer diagnosis and explore a range of personal, treatment, and behavioural characteristics for associations with same.

*Methods:* Six-monthly, clinical, assessments of weight were made on a population-based sample of women newly-diagnosed with unilateral breast cancer (n=215). Mean weight gain at 12 and 18 months relative to 6 months were estimated using a linear mixed model. Explanatory variables considered were personal characteristics (age, income, carer of children), treatment characteristics (surgery type, positive nodes excised, exposures to chemotherapy, radiotherapy, or hormone therapy), and behavioural characteristics (physical activity level). Interaction effects considered the time-dependent nature of any identified associations. Mean weight changes of 3 kg or greater were a priori considered to be of substantial potential health detriment.

*Results:* 57% of women were in the unhealthy weight range (defined by body mass index). Overall, women gained minimal weight over time: compared to their 6-month weight, women at 12 months averaged 1.1kg (SE 0.8) heavier, similarly so at 18 months (1.1kg, SE 1.2). This clinically-negligible weight fluctuation overall disguised a significant subgroup-specific pattern. Substantial weight differences at 6 months were noted with positive node excision: women with 1 to 9 nodes were 3kg heavier than those with no positive nodes; those with 10+ nodes were 7kg heavier. At 12 and 18 months, however, only the latter group maintained a substantial weight differential from the others ( $p < 0.001$ ). No further interaction effects were noted. At main effect level (compared to their respective referents), substantially higher weights were seen amongst those insufficiently active (9kg, SE 2.3), those undergoing radiotherapy (6.6kg, SE 3.1) and those earning below-average incomes (3.7kg, SE 2.5).

*Conclusions:* Unhealthy weight is as much of an issue for women with breast cancer as for the general population, and interventions, even generic, that address the importance of achieving and sustaining a healthy body weight, delivered to all women with breast cancer, may have substantial benefit.

### T8.6.3

## Educational differences in breast cancer mortality in the Brussels-Capital Region

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#### Abstract

*Objective:* The aim of this study is to investigate whether there is an inversion of the gradient in breast cancer mortality in the Brussels-Capital Region. Several studies have shown a shift from a positive to a negative relationship between education and breast cancer mortality over time. In this presentation, trends in inequalities in breast cancer mortality are addressed through a comparison of two longitudinal datasets. In addition, the study investigates whether the gradient persists after adjustment for reproductive history.

*Methods:* The study population consists of all women in the Brussels-Capital Region aged 50-79 in 1991 (N=155,481) and in 2001 (N=144,571). The first dataset consists of a linkage of the Belgian 1991 census with registration records of all deaths and emigrations between March 1991 and December 1995. The second dataset consists of a linkage of the Belgian 2001 census with registration records for the period October 2001-December 2004. Rate ratios are calculated through survival analyses with breast cancer mortality as dependent variable and educational attainment as independent variable. Reproductive factors are controlled for through the inclusion of number of children and age at first birth.

*Results:* During 1991-1995, tertiary educated women show a higher rate ratio compared to women with primary education. Control for number of children and for age at first birth reduces the excess mortality of tertiary educated women, but differences remain significant.

In the 2001-2004 period, the educational differences are no longer significant. Rate ratios have become smaller. Even more, inclusion of reproductive factors changes the direction of the gradient, women with secondary education having the highest mortality in breast cancer. Trends in breast cancer mortality between 1991-1995 and 2001-2004 differ significantly by educational attainment. Rates diminish considerably among women with tertiary education, slightly among women with primary education and increase among women with secondary education.

*Conclusions:* The results show that educational differences in breast cancer are changing over time. Highly educated women may have benefited more from screening programs and health interventions. In order to achieve further declines in breast cancer mortality, policy interventions should take this into account. Other hypotheses should be considered as well.

## T8.6.4

### Perineal use of talcum powder and endometrial cancer risk

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#### Abstract

*Objectives:* Several studies have reported a positive association between perineal use of talcum powder among adult women and ovarian cancer risk. However, the relationship between talcum powder use and other gynecologic malignancies such as endometrial cancer has not been examined, and little information is available on non-hormonal risk factors for endometrial cancer.

*Methods:* Perineal use of talcum powder was assessed in 1982 in the Nurses' Health Study. Approximately 40% of women who responded to the questions about perineal use of talcum powder reported ever use. Cox proportional hazards models were used to estimate the incidence rate ratio of endometrial cancer and 95% confidence interval (CI), adjusted for body mass index and other potential confounders. We evaluated the relationship among all women and stratified by menopausal status.

*Results:* Our analysis included 66,028 women with 599 incident cases of invasive endometrial adenocarcinoma diagnosed between 1982 and 2004. Although no association was observed overall, the association varied by menopausal status ( $p$ -interaction=0.02) and a positive association was observed among postmenopausal women; ever use of talcum powder was associated with a 21% increase in risk of endometrial cancer (95% CI: 1.02, 1.44), while regular use (once/week) was associated with a 24% increase in risk (95% CI: 1.03, 1.48). In addition, we observed a borderline increase in risk with increasing frequency of use ( $p$ -trend=0.04).

*Conclusions:* Our results suggest that perineal talcum powder use increases the risk of endometrial cancer, particularly among postmenopausal women. Future and larger studies are needed to confirm this association and investigate potential mechanisms.

## T9.1.1

### The parent – offspring association in Body Mass index: explanations from the 1958 British cohort

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#### Abstract

*Objective:* There is consistent evidence of a positive association between parental and offspring adiposity. Explanations for the association are likely to include genetic predisposition, pre-natal programming and shared environment. We aimed to establish whether associations between parental and offspring BMI in mid-life (i) are explained by offspring lifestyle factors, and (ii) whether intergenerational influences on BMI depend upon socio-economic position (SEP).

*Methods:* Data on adult (45y) BMI of the 1958 British birth cohort and their parents (n=9346) were analysed, with and without adjustment for several offspring lifestyle factors, including diet, physical activity, alcohol consumption and smoking, which were assessed prospectively. In additional analyses, parent –offspring associations were examined separately by SEP and, variation in the association was tested using an interaction term in models of all SEP groups combined.

*Results:* Results from multiple linear regression analyses of parental (mother and father) and offspring (sons and daughters) BMI demonstrate strong associations in both sexes, if parental BMI was 1kg/m<sup>2</sup> higher offspring BMI at 44-45y was higher by between 0.24 and 0.35 kg/m<sup>2</sup>. Adjustment for lifestyle and socioeconomic factors attenuated associations slightly but all associations were maintained in fully adjusted models. Parents and offspring BMI associations varied by social class, with stronger associations for higher (I&II) compared to lower classes (IV&V). This reflected a greater average BMI gain in offspring relative to parents in lower classes (p for interaction<0.05). For example, in classes IV&V the average adult BMI of male cohort members was 3.42 kg/m<sup>2</sup> greater than their fathers, compared to 2.47 kg/m<sup>2</sup> in classes I&II.

*Conclusion:* Parent – offspring BMI associations are evident in mid-adulthood but are not explained in a simple way by offspring lifestyles. That parent – offspring associations vary by SEP suggests that intergenerational transmission of adiposity reflects an inter-play between genes and the obesogenic environment which is likely to contribute to social inequalities in obesity-related disease.

## T9.1.2

### Contribution of environmental factors to intergenerational correlations in size at birth

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#### Abstract

*Objective:* Size at birth is a key health indicator with strong familial associations. We examined birth size data on grandparents and grandchildren and studied (a) whether correlations in size at birth across three generations are consistent with those found across two generations, and (b) the extent to which they are mediated by intergenerational socio-environmental continuities.

*Methods:* The Uppsala Birth Cohort Multigenerational Study includes manually collected archive data on a representative and well-defined cohort of 14,193 males and females born in Uppsala, Sweden 1915-1929 and information on descendants of the cohort obtained through linkage to routine data registers ([www.chess.su.se/ubcosmg](http://www.chess.su.se/ubcosmg)). We analysed data on 7,657 singletons born 1915-1929 (G1) and their grandchildren (G3). A range of socio-demographic variables on G1 participants, their parents and their children were available. Standard regression and biometrical genetic models were used to study the correlations in size at birth of G1-G3 pairs. All analyses were carried out in Stata 11 and Mplus.

*Results:* The correlations between G1 and G3 size at birth varied by size at birth variable, with larger coefficients for birth weight and birth length than for head circumference. They also varied by grandparental groups, with maternal grandmothers and grandfathers generally showing larger values than paternal ones. We found stronger correlations in maternal than paternal pairs for birth weight (0.112 versus 0.081,  $p=0.002$ ) but not for birth length (0.088 versus 0.076,  $p=0.29$ ). These correlations were not reduced by adjustment for socio-demographic factors in linear regression models. In contrast, significant shared environment contributions to the intergenerational correlations were identified in biometrical genetic models, averaging 14% for birth weight and birth length. Correction for missing data bias slightly increased these estimates, while relaxation of model assumptions did not affect the conclusions.

*Conclusion:* Our results show that there is only weak evidence that correlations between the size at birth of grandchildren and their maternal grandparents are stronger than that with their paternal grandparents. Socio-demographic conditions shared by the maternal and paternal G1-G3 pairs moderately – but significantly – contribute to intergenerational correlations.

### T9.1.3

## Intergenerational transmission of overweight among Finnish adolescents and their parents: a 16-year follow-up study

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### Abstract

**Objectives:** The objective of our study was to examine associations of parental pre-pregnancy body mass index (BMI), BMI 16 years after pregnancy, weight change and BMI class transition over the 16-year follow-up period with the BMI of their 16-year-old children.

**Methods:** The study population was derived from the general population-based Northern Finland Birth Cohort 1986. A total of 3678 child-mother-father trios (1885 girls, 1793 boys) were analysed. The weight and height of adolescents were clinically measured whereas in parents, self-reported measurements were used. Childhood overweight and obesity were defined according to the International Obesity Task Force BMI cut-off points. Parental BMI was classified into three categories based on the World Health Organization definitions. Associations of parental BMI status and weight change with offspring BMI were assessed using binary logistic regression analyses stratified by gender and adjusted for parental age and education.

**Results:** Children whose both parents were overweight or obese both before pregnancy and after 16-y follow-up had a strikingly high risk of overweight at 16 y [girls odds ratio (OR) 14.43, 95% confidence interval (CI) 7.11-29.29; boys OR 5.60, 95% CI 3.13-10.04]. Parental pre-pregnancy obesity strongly predicted offspring overweight (mother-son OR 4.79, mother-daughter OR 4.33, father-son OR 3.53, father-daughter OR 5.31). Maternal and paternal long-term weight gain  $\geq 18$  kg moderately increased the risk of overweight in boys and girls (ORs 1.74-2.60).

**Conclusions:** The results established the relationship between parental overweight and offspring overweight in adolescence for which both parents' long-term overweight (BMI  $\geq 25$  kg/m<sup>2</sup> before pregnancy and after 16-y follow-up) was the strongest single predictor. The findings highlight the importance of targeting parents early on to prevent excessive weight gain in youth.



## T9.1.4

### Intergenerational continuity of gestational duration in three generations of Swedish males and females

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#### Abstract

*Objective:* We analysed associations between gestational duration in grandchildren and their grandparents in a Swedish multigenerational cohort. To our best knowledge, this is the first study of continuity in gestational duration across three generations.

*Methods:* The Uppsala Birth Cohort Multigenerational Study includes manually collected archive data on a representative and well-defined cohort of 14,193 males and females born in Uppsala, Sweden 1915-1929 as well as information on descendants of the cohort obtained through linkage to routine data registers ([www.chess.su.se/ubcosmg](http://www.chess.su.se/ubcosmg)). Using a path analysis (Mplus 5.1), we analysed biologically related grandparents and grandchildren, where the grandparent, the grandchild and the intermediate biological relation were all singletons. A total of 26,423 grandchildren and their 7915 grandparents were included in the analysis and each grandparental type – maternal grandmothers, maternal grandfathers, paternal grandmothers and paternal grandfathers – was considered separately. Models were fitted separately for male and female grandchildren due to evidence of effect modification by sex.

*Results:* Gestational duration in grandparents was positively associated with gestational duration in their grandchildren. The observed associations are equivalent to a 0.3-0.4 (0.01≤p≤0.07) day increase in the grandchild's gestational duration for each additional week in the maternal grandparents' gestational duration and 0.1-0.2 (p≥0.2 in all models) day increase in the grandchild's gestational duration for each additional week in the paternal grandparents' gestational duration. We additionally found evidence that birthweight-for-gestational age in maternal grandfathers was positively associated with gestational duration in their grandchildren, and stronger evidence that birthweight-for-gestational age in paternal grandfathers was inversely related to gestational duration in their grandsons. Confounding by socioeconomic factors did not appear to explain the observed relationships. Models provided a good fit to the data.

*Conclusion:* We found gestational duration in maternal grandparents to be positively associated with gestational duration in their grandchildren. We speculate that the negative associations observed between birthweight-for-gestational age in paternal grandfathers and gestational duration in their grandchildren relates to inverse association between father's birthweight and offspring's gestational duration and is a result of rapid foetal growth triggering earlier delivery.

## T9.1.5

### Differential associations between grandparental and parental cardiovascular disease and offspring birth weight. A multigenerational family based study of the Cohort of Norway (CONOR)

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#### Abstract

**Objective:** Earlier studies have reported an inverse and stronger association between parental risk of coronary heart disease and offspring birth weight among mothers than among fathers in an attempt to disentangle intra uterine factors from common genetic and socioenvironmental factors shared between parents. There is sparse evidence adjusting for cardiovascular risk factors and looking at multiple generations. Here we investigated if there is a differential association between fathers' and mothers' risk of coronary heart disease and offspring birth weight before and after adjusting for traditional cardiovascular risk factors in both parents simultaneously. Secondly, we compared the associations in risk of coronary heart disease and smoking related causes of death among all four grandparents and offspring birth weight before and after adjusting for these cardiovascular risk factors.

**Methods:** CONOR was linked to the Medical Birth Registry (MBR) and Cause of Death Registry, and from the full cohort we identified parental offspring trios including grandparental data internally linked within CONOR cohort using multigenerational data base. Blood pressure, s-cholesterol, smoking, physical activity, length of education gestational length were used as covariates. The analysis was run in cox proportional hazards regression. Birthweight was adjusted for gestational length. We used self reported smoking and smoking related deaths in grandparents and parents to assess the role of causal pathways through the maternal and paternal line as the effect of smoking in pregnancy on birth weight is well established.

**Results:** CONOR includes 173,236 subjects. We were able to identify 19,848 parent offspring trios within CONOR. There was a decrease in risk of myocardial infarction among mothers per quintile increase in offspring birthweight, HR=0.87 (0.77-0.98). Among fathers no similar effect was seen, HR=0.94 (0.83-1.08). Adjusting for cardiovascular risk factors in both parents had little impact on the relative parental effects. History of myocardial infarction among mothers mother was related to offspring birth weight, HR=0.92 (0.88-0.97) but there was no effect for the other grandparents.

**Conclusions:** This study adds support to the role of intrauterine programming for the risk of cardiovascular disease in adulthood and demonstrates the value of multigenerational family based studies to elucidate causal pathways.

## **T9.2.1**

### **Mortality and stratification dimensions**

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#### **Abstract**

In many studies of social inequality in health, different dimensions of social stratification have been used more or less interchangeably as measures of the individual's general social standing. However, education, class and income may influence – or be associated with – health through partly different mechanisms. In this presentation I will show that education, class or status and income are associated with mortality also when variation in the other factors is under control. The position of the marital partner is also of importance. The results are based on register data and refer to all Swedish employees in the age range 35-59 years. There are clear gradients in total death risk for all socioeconomic factors except for income from work among women. The size of the independent effects of education, class, status and income differ between men and women. For both sexes, there are clear net associations between education and mortality. Class and income show independent effects on mortality only for men and status shows an independent effect only for women. Women's education and men's social class are associated with the death risk of the partner. While different stratification dimensions – education, social class, income, status – all can be used to show a "social gradient" with mortality, each of them seems to have a specific effect in addition to the general effect related to the stratification of society for either men or women.

## T9.2.2

### Inequity in cancer incidence between occupational categories – a 45 year follow-up study of five Nordic populations

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#### Abstract

**Objectives:** Our giant Nordic Occupational Cancer (NOCCA, <http://astra.cancer.fi/NOCCA>) study covers all 15 million working-aged persons who participated in at least one of the population censuses between 1960 and 1990 in Denmark, Finland, Iceland, Norway and Sweden, and the subsequent 2.8 million incident cancer cases diagnosed in these people in a follow-up until 2005. All Nordic countries have a nation-wide registration of incident cancer cases during the entire study period.

**Methods:** The observed number of cancer cases in 70 diagnostic categories in each group of persons defined by country, sex, age, period and occupation was compared with the expected number calculated from the stratum-specific person years and the incidence rates for the national population. The result was presented as a standardised incidence ratio, SIR, defined as the observed number of cases divided by the expected number.

**Results:** For all cancers combined, the study showed a wide variation among men from an SIR of 0.79 (95% confidence interval 0.66-0.95) in domestic assistants to 1.48 (1.43-1.54) in waiters. The occupations with the highest SIRs also included workers producing beverage and tobacco, seamen and chimney sweeps. Among women, the SIRs varied from 0.58 (0.37-0.87) in seafarers to 1.27 (1.19-1.35) in tobacco workers. Low SIRs were found for farmers, gardeners and forestry workers in both genders. The variation in relative risk across occupational categories varied considerably between cancer types. For mesothelioma, there was a 20-fold variation in risk among plumbers as compared to farmers, while the variation between the lowest and highest occupation-specific incidence of cancers of colon or brain was not even two-fold.

**Conclusions:** The Nordic countries are known for equity and free and equal access to health care for all citizens. The present study shows that the risk of cancer, even under these circumstances, is highly dependent on the person's position in the society. These differences seem not to decrease in recent years. Direct occupational hazards – such as asbestos exposure – seem to explain only a small part of the observed variation, while indirect factors such as lifestyle changes related to longer education and decreasing physical activity become more important. Subsequent studies within the NOCCA project will focus on associations between specific work-related factors and specific cancer diseases with the aim to identify dose-response patterns. These in-depth studies utilise the Nordic Job Exposure Matrix that transforms information about occupational title histories to quantitative estimates of specific exposures. Information of non-occupational co-factors will also be available. Because risk factor information will be partly available on an individual level but partly only on an aggregate level, a methodological development targeted at better interpretation of results is an essential component of NOCCA networking.

## T9.2.3

### Socioeconomic status as a predictor for telomere length: Evidence from the West of Scotland Twenty-07 Study (1987-2007)

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#### Abstract

*Objective:* Telomere length is used as a marker for biological ageing and it has been proposed that poor socioeconomic status (SES) accelerates telomere shortening, leading to reduced life expectancy. However, the evidence for an association between SES and telomere length is inconsistent, and the few studies conducted have been limited by small and unrepresentative samples. This large, community-based longitudinal cohort study investigates if cross-sectional and prospective indicators of SES are associated with telomere length.

*Methods:* Data are taken from the Twenty-07 study, consisting of 2092 study members (1154 women) from three cohorts aged approximately 36, 56 and 76 in 2007/08. Peripheral blood leukocyte telomere length was measured in the most recent wave of the study using Real-Time qPCR. In order to compare the strength of the associations between the indicators of SES and telomere length, we computed a Relative Index of Inequality (RII) for our one area-level and our four individual-level SES markers. RII-adjusted scores for mobility in occupational class and home tenure over a 20 year period (1987/88 – 2007/08) were used for longer-term, prospective measures of SES. Gender and cohort were controlled for in all analyses.

*Results:* Preliminary results showed that females had longer telomeres than males ( $\beta=0.023$ ,  $p=0.002$ ) and older cohort members had shorter telomeres ( $p<0.001$ ). There were trends for associations between poorer SES and shorter telomere length in the cross-sectional SES indicators of employment status and home tenure. However, these associations were weakened after adjusting for known key risk factors (smoking, alcohol consumption and body mass index). For occupational class mobility, those remaining in the non-manual class over the twenty year period did not have significantly longer telomeres than those who remained in the manual class ( $\beta=-0.004$ ,  $p=0.286$ ). A similar result was apparent for mobility in home tenure over the same time period.

*Conclusions:* Results from cross-sectional and prospective analyses suggest limited evidence for an association between SES and telomere length. This adds to growing evidence that the links between SES and biological ageing (at least using telomere length as a marker) may not be strong.

## T9.2.4

### **Breastfeeding habits according to social status and migration background – the case of Germany**

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#### **Abstract**

*Objective:* Scientific research has showed that breastfeeding has numerous undoubted health benefits for infants and mothers. Additionally, the length of the breastfeeding time is also strongly connected to the future health status of children. Some studies show a relation to the emergence of allergies in later life stages. The breastfeeding habits, though, differ in different societies and social circles. In our study we investigate the socio-demographic determinants of the length of the breastfeeding of young parents in Germany.

*Methods:* We use hazard regression model and study the transition towards weaning. We investigate also the decision to start breastfeeding. We take into account different socio-demographic characteristics of the parents and the families that might influence the decision to start and stop breastfeeding. We also pay attention to the healthy life styles of the parents, like smoking and drinking habits, for instance.

We use data from the first wave of the panel study German Health Interview and Examination Survey for Children and Adolescents (KIGGS). The survey was conducted between 2003 and 2006 by Robert Koch Institute and comprises 17 641 children aged 0 to 18 at the time of the interview.

*Results:* Our preliminary results show that the social status of the parents plays a substantial role in the decision to breastfeed. People from the lower social class are less willing to breastfeed their children and if they start breastfeeding, they wean quicker. The migration background of the parents also shows some influence, though not that high as expected. In families with one or two parents with migration background is more often breastfed than in families with no migration background.

*Conclusions:* Breastfeeding promotes health, helps to prevent disease, and reduces health care costs as well as feeding costs. It is very important for the public health policy planning to evaluate the breastfeeding habits of women and identify the factors that influence the early weaning. Our results reveal the necessity of providing more information for the positive effects of breastfeeding particularly to families from the lower social strata of the society and the lower educated mothers.

## T9.3.1

### Association between pre- and perinatal factors and infant height growth velocity in the Northern Finland Birth Cohorts 1966 and 1986

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#### Abstract

**Objective:** The Developmental Origins of Health and Disease (DOHaD) hypothesis suggests that adverse influences during foetal life lead to smaller birth size and increase later chronic disease risk. Previous research indicates that restricted foetal growth is often followed by accelerated infant growth which may independently contribute to higher disease risk. This is the first study to evaluate associations between prenatal maternal factors, birth length (BL) and infant peak height growth velocity (PHV) in two longitudinal population-based birth cohorts born 20 years apart. The aim of the study was to assess the association between BL and PHV, and to explore whether the association between maternal factors and PHV is mediated by BL.

**Methods:** The study consists of singletons from the prospective Northern Finland Birth Cohorts 1966 (NFBC1966, N=3,783) and 1986 (NFBC1986, N=5,577) with frequent height measurements at 0-2 years. Individual height growth curves were estimated using parametric models by sex. PHV was derived as the maximum value of the growth velocity curve. Its association with BL and maternal factors was studied using unadjusted and adjusted regression models by cohort and sex, after replacing missing values using the multiple imputation method.

**Results:** The mean PHV was 53cm/year in both cohorts, 3-4cm/year higher in boys than in girls. We identified an inverse association between BL and PHV, which was much stronger in the NFBC1986 (-1.40cm/year/1 cm in BL) than in the NFBC1966 (-0.17cm/year/1cm in BL), possibly partly due to the improved accuracy of BL measurements over 20 years. Maternal height showed a positive, presumably genetically mediated association with PHV. Parity showed an inverse association with PHV, which was unaffected by the adjustments and not mediated by BL. Pre-eclampsia associated positively with PHV in all except NFBC1966 females, and this association was confounded by maternal factors and partly mediated by BL, particularly in the NFBC1986. Maternal education, smoking or pre-pregnancy BMI were not associated with PHV.

**Conclusion:** This study supports the hypothesis that smaller size at birth is associated with accelerated postnatal growth, independently of other determinants of height growth. Some but not all of the associations between maternal factors and PHV were mediated by BL.

## **T9.3.2**

### **Is parental experience of racism related to early child development in the UK?**

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#### **Abstract**

*Objectives:* Previous work has shown that experience of racism is related to poor health outcomes in adults, but little is known about whether such experiences translate into developmental outcomes in children. In this paper we: 1. examine the relationship between parental experience of racism and markers of child development, and 2. assess whether family socioeconomic position and neighbourhood level disadvantage explain observed relationships.

*Methods:* We used data from the UK Millennium cohort study on ethnic minority participants. Questions on parental interpersonal experience of racism, and the perception of racist attacks in the residential neighbourhood were asked when cohort members were aged 5 years. Markers of child development at age 5 and 7 were obesity and overweight, socioemotional difficulties, and cognitive ability scores.

*Results:* We found that 43% of parents reported any experience of interpersonal racism, and 12% reported that racist attacks or insults were common in their residential neighbourhood. It appeared that parental reports of interpersonal racism were not strongly associated with poor developmental outcomes. Conversely, perception of racism in the area of residence was significantly associated with socioemotional difficulties and spatial ability. Statistical adjustment for socioeconomic factors attenuated associations, but the area measure remained independently associated with socioemotional difficulties and spatial ability. Additional results of longitudinal analysis using newly available data from MCS sweep 4, when cohort members are 7 years of age, will be presented.

*Conclusions:* Parental perceptions of racism in residential neighbourhoods are linked to poor developmental outcomes in children. Economic disadvantage among ethnic minority groups appears to partly explain some of these relationships.



### **T9.3.3**

## **A longitudinal study of developmental delay in children with Williams Syndrome**

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### **Abstract**

*Objective:* Current psychological literature has been scarce in terms of developmental delay in children with WS regarding attainment of major motor, social and linguistic milestones. The current study examines attainment of major developmental milestones in the areas of personal/social development, early linguistic development and gross/fine motor development in 50 children with a confirmed diagnosis of WS from Greece, Hungary and Slovakia over a period of 8 years. The aim is to determine the average age of attainment for social, early language and gross/fine motor milestones in children with WS and compare them with TD controls matched for chronological age. Compile a developmental milestone database.

*Methods:* Data from the children's medical history, Denver Developmental Screening Test (DDST)/Child Development Inventory (CDI) and parents' diaries were used to determine age of milestone attainment.

*Results:* A comprehensive database of 78 milestones was compiled and children with WS were found to be significantly behind in age of attainment of developmental milestones when compared to TD controls matched for chronological age, with gross and fine motor development being most affected.

*Conclusion:* Children with WS present with a significant delay in the age of attainment of personal/social, early language and gross/motor developmental milestones. These delays might have a significant effect on the phenotype in later childhood. Close monitoring of developmental milestones is extremely important for children with the condition.

## **T9.3.4**

### **Dynamics of brain cortical activity in gifted high school seniors developing own creativity: A longitudinal study**

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#### **Abstract**

*Objective:* As a cognitive ability, creativity lies at the core of numerous discoveries. Cerebral interhemispheric interaction is known to be the psychophysiological basis of creativity. The cerebral mechanisms regulating the development of creativity have not yet been practically studied. Therefore, the longitudinal study of creativity and its cerebral mechanisms is necessary. The objective of this study is to examine the dynamics of creativity and of cerebral hemispheric activity in intellectually gifted high school seniors (15-17 years old).

*Methods:* The subjects were 68 intellectually gifted high school seniors divided into two groups – experimental and control. Subjects of the experimental group were taught with the help of a special creativity development program (psychological training of creative thinking, EEG alpha feedback training, etc.) and with the help of the usual school program as well. Subjects of the control group were taught only with the help of the usual school program. We tested the level of creativity and EEG power in subjects of both groups at the beginning (15 years old) and at the end (17 years old) of our longitudinal research. EEG was recorded at a resting state from 21 scalp electrodes according to the 10-20 system.

*Results:* The highly significant creativity increase in the experimental group suggests that it may be possible for a wide range of people to become more creative. The distinguishing characteristics of EEG-patterns in subjects of the experimental group compared to controls at the end of the longitudinal study are: 1) Significantly lower level of the brain cortical activation (at alpha-1 band) and higher level of beta-1 EEG power, 2) Significantly higher level of theta power in frontal and central brain cortical regions that testifies to the fact of actualization of past experience in creative subjects, 3) Activation decrease of the left frontal cortical area provides the situation of defocused attention process.

*Conclusion:* The obtained results received practical application at the educational establishments of Rostov region (Russia) for elaborating methods of teaching, for enhancing teaching high school seniors and organizing a psycho-physiological basis for the development of their creativity.

## **T9.3.5**

### **The development trajectories of health, social wellbeing and learning outcomes of Australian infants and their interrelationships**

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#### **Abstract**

*Objective:* The health, social wellbeing and learning outcomes have been carefully measured and tracked within the Longitudinal Study of Australia Children (LSAC). The development trajectories of these outcomes for Australian infant have not been reported at a national level. Moreover, no study has explored the interrelationships of these development trajectories anywhere in the world at a national level. The aims of this study are four-fold: 1) to explore the individual development trajectory for each of the three major outcomes among Australian infants (0-1 year) over a six year period; 2) to explore the interrelationships among the three development trajectories; 3) to examine the differences of each trajectory between male and female, Aboriginal and non-Aboriginal infants; 4) to explore if such trajectories show different covert classes or clusters.

*Method:* We use the baseline, wave 2 and wave 3 LSAC data for the three outcomes and other relevant variables. We will use the latent growth curve to model individual and conjoint growth trajectories. We will also explore whether these trajectories will be dependent on gender and Aboriginality. We will combine the latent growth curve modeling technique with latent class analysis to explore the potential hidden classes of these trajectories among Australian infants. All analyses will be conducted using Mplus 5.2.

*Results:* Our study will show the nature and the interactions of the three growth trajectories. It will provide evidence if these trajectories and their interrelationship are different between male and female, Aboriginal and non-Aboriginal infants. Furthermore, we will also show if there is hidden heterogeneity and different classes of these trajectories, and the possible determinants of such classes.

*Conclusion:* Our study is the first of its kind in providing a comprehensive analysis of the development trajectories of the three most important outcomes for Australian infants at a national level. The nature and interactions among these trajectories will provide the critical evidence in understanding the infant growth and possible policy intervening points. The possible different classes of the trajectories may also help us in prioritizing the target populations. It will also provide the base for further research in understanding the determinants of such trajectories.

## **T9.4.1**

### **Longitudinal twin studies of anxiety and depression in adult and adolescent twins**

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#### **Abstract**

*Objective:* To search for evidence that different genetic influences on common psychiatric symptoms of anxiety and depression come into play at different stages of life.

*Methods:* Questionnaires containing standard psychiatric symptoms were administered to large samples of MZ and DZ twins longitudinally. Data were analysed by fitting genetic simplex models using full information maximum likelihood (FIML) methods.

*Results:* Most genetic influence was continuous from age to age, but some evidence of genetic innovations was found, particularly for depression in the 60s and older.

*Conclusion:* We found evidence for specific genetic influences on late-onset depression, distinct from genes influencing basal depression at earlier ages, and consistent with a cardiovascular involvement in old-age depression.

## T9.4.2

### Self-esteem development from adolescence to middle age. A prospective cohort study from 16 to 42 years of age

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#### Abstract

*Objectives:* The aim of the study was to investigate the trajectory of self-esteem development from adolescence to middle age and adolescent correlates of this trajectory in a cohort of Finnish school children over a period of 26 years.

*Methods:* Subjects (N=2194) participated at 16 years in a cohort study targeting at all ninth-grade pupils attending secondary school in 1983 in Tampere, Finland. They were followed up using postal questionnaires at 22 (N=1656), 32 (N=1471) and 42 (N=1336) years. Self-esteem was measured at each time point by a seven-item scale. Covariates in adolescence included gender, family background (parental socioeconomic status and divorce), school achievement (mean of school marks) and risky health behaviours (daily smoking, heavy drinking). The trajectory of self-esteem was analysed with latent growth curve models. Missing data due to attrition was dealt with full information maximum likelihood method.

*Results:* The shape of the self-esteem trajectory was non-linear: from 16 to 32 years self-esteem grew linearly, but between 32 and 42 years there was virtually no growth at all. The mean of the slope factor was positive and significant ( $p < .001$ ), indicating true growth in self-esteem from adolescence to middle age. Negative correlation ( $-.32, p < .001$ ) between the initial level and slope factors suggests presence of a ceiling effect. The variances of both the initial level and slope factors were significant ( $p < .001$ ), showing that there is a lot of individual variability in the growth trajectories. Male gender ( $p < .001$ ), school achievement ( $p < .001$ ) and heavy drinking ( $p = .025$ ) associated with higher initial level of self-esteem. Gender was the only significant ( $p = .001$ ) covariate of the slope factor, growth rate being slower among males. However all covariates together explained only 2% of the variance of the slope factor.

*Conclusions:* Self-esteem followed a trajectory which was increasing from adolescence to adulthood but remained stable in adulthood. Individual variability in growth trajectories was large and the studied covariates in adolescence explained only little of this variability.

### **T9.4.3**

## **Inattention, hyperactivity, impulsivity: epidemiology and correlations. A nationwide Greek study from birth to 18 years**

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### **Abstract**

*Objective:* To explore the prevalence of inattention, hyperactivity and impulsivity (ADHD-like symptoms) at the ages of 7 and 18 years and the associated factors in the Greek population.

*Methods:* Information was derived from a population-based representative sample of 11,048 newborn infants, which followed-up at 7 and 18 years of age, through questionnaire surveys. After applying matching procedure, a data set of 2,695 individuals covering all the three time periods was compiled and used in this study. Pearson  $\chi^2$  test and multivariate logistic regression analysis were used to assess associations between ADHD-like symptoms and various perinatal and childhood factors.

*Results:* Hyperactivity was 7%, inattention 9.5 % and impulsivity 7% for children aged 7 years while a substantial decline of these symptoms was observed by 18 years. The male to female ratio was 3 to 1. Adverse perinatal factors, poor academic outcome, co-morbidity, physical punishment and more accidents and fights with peers were found to be associated with ADHD-like symptoms at 7 years. Factors identified to be related at 18 years included gender, smoking during pregnancy, maternal stress and physical punishment.

*Conclusion:* The prevalence of ADHD-like symptoms over time in the Greek population and its associated factors coincided with the international trends of the disorder.

## **T9.4.4**

### **The effects of childhood cognitive ability, teenage self-esteem and school motivation on adult social status and mental health: A life course model**

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#### **Abstract**

*Objective:* This study examines the associations between family social-economic background, childhood cognitive ability, teenage self-esteem and school motivation, and adult social status and mental health in a large representative sample of British population born in 1970.

*Method:* 7,077 participants completed the British Ability Scales at age 10, self-esteem and school motivation scales at age 16, and social status and mental health measures at age 30. A life course model of mental health is tested using Structural Equation Modelling (SEM) to assess the pathways linking early influences to adult outcomes.

*Results:* SEM models show that adulthood mental health (indicated by mental distress and a sense of control over one's life) is directly determined by both early self-esteem and school motivation, and current social status (indicated by educational qualifications and occupational attainments). Social status is strongly influenced by childhood cognitive ability and school motivation. The effects of family social-economic background and childhood cognitive ability on adult mental health are mainly mediated through teenage self-esteem, school motivation, and current social status.

*Conclusion:* Teenage self-esteem, school motivation, and current social status are both predictors and mediators of adult mental health, whereas family background and childhood cognitive ability predicted adult mental health mediating through self-esteem, school motivation, and social status.

## T9.5.1

### Air pollution, foetal growth and the risks of adverse neonatal outcomes. The Generation R Study

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#### Abstract

**Objective:** Maternal exposure to air pollution during pregnancy might have exposure and trimester specific effects on the intrauterine environment, and subsequently adversely affect foetal growth and development. We assessed the associations of maternal exposure to particulate matter (PM<sub>10</sub>) and nitrogen dioxide (NO<sub>2</sub>) with fetal growth characteristics measured in each trimester of pregnancy and the risks of adverse neonatal outcomes.

**Methods:** The study was embedded in a population-based prospective cohort study from pregnancy onwards in the city of Rotterdam, the Netherlands. Associations of maternal air pollution exposure (PM<sub>10</sub> and NO<sub>2</sub> levels, assessed at the home address using dispersion modelling) with fetal growth and neonatal outcomes were examined in 7772 subjects. Fetal length was assessed by ultrasound as crown-rump length in first trimester and as femur length in second and third trimester. Fetal head circumference and weight were assessed in second and third trimester. Information on neonatal outcomes was obtained from midwife and hospital records.

**Results:** Maternal exposure to PM<sub>10</sub> and NO<sub>2</sub> levels was not associated with first trimester fetal crown-rump length. NO<sub>2</sub> levels were inversely associated with fetal femur length in second and third trimester (P for trend < 0.05), while in third trimester higher PM<sub>10</sub> and NO<sub>2</sub> exposure levels were associated with smaller fetal head circumference. PM<sub>10</sub> and NO<sub>2</sub> exposure levels were not associated with neonatal head circumference or length, but higher PM<sub>10</sub> levels were associated with lower birth weight (P for trend < 0.05). Maternal exposure to higher PM<sub>10</sub> levels was associated with an increased risk of preterm birth (P for trend < 0.05). Similar tendencies were observed for the risks of small size for gestational age at birth and low birth weight. No consistent associations were observed for NO<sub>2</sub> exposure levels and the risks of adverse neonatal outcomes.

**Conclusion:** Maternal air pollution exposure was associated with fetal growth retardation from second trimester onwards. In addition, exposure to elevated PM<sub>10</sub> levels was associated with a reduced birth weight and an increased risk for preterm birth.



## T9.5.2

### Aircraft noise, air pollution and mortality from myocardial infarction in Switzerland: national cohort study

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#### Abstract

*Objectives:* Myocardial infarction has been associated with both transportation noise and air pollution. We examined residential exposure to aircraft noise and mortality from myocardial infarction, taking air pollution into account.

*Methods:* We analysed the Swiss National Cohort, which includes geo-coded information on residence. Exposure to aircraft noise and air pollution was determined based on geospatial noise and air pollution (PM<sub>10</sub>) models and distance to major roads. We used Cox proportional hazard models, with age as the timescale, and expressed results as hazard ratios (HR) with 95% confidence intervals (95% CI). We compared the risk of death across categories of A-weighted sound pressure levels (dB(A)) and by duration of living in exposed corridors, adjusting for PM<sub>10</sub> levels, distance to major roads, sex, education and socio-economic position of municipality.

*Results:* We analyzed 4.58 Mio individuals aged >30 years who were followed up 2000 to 2005, and 15,532 deaths from myocardial infarction (ICD-10 I 21, I 22). Mortality increased with increasing level and duration of aircraft noise. The adjusted HR comparing >60 dB(A) with <45 dB(A) was 1.30 (95% CI 0.96-1.76) overall, and 1.48 (1.01-2.18) in persons who had lived at the same place for >15 years. Mortality from all causes, all circulatory disease, cerebrovascular disease, stroke and lung cancer was not associated with aircraft noise.

*Conclusions:* Aircraft noise is associated with mortality from myocardial infarction, with a dose-response relationship for level and duration of exposure. The association does not appear to be explained by exposure to particle matter air pollution, education or the socio-economic status of the municipality.

## T9.5.3

### Prenatal exposure to traffic-related air pollution and neurodevelopment at 1-1.5 years old

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#### Abstract

**Objective:** Air pollution effects on children's neurodevelopment have recently been suggested. However, these studies are based on small samples and confounded by social determinants. Our study aims to assess the effects of traffic-related air pollution exposure during pregnancy in children's neurodevelopment at 1-1.5 years old.

**Methods:** In the Spanish INMA (Environment and Childhood) Project, 2,644 women were recruited at 1<sup>st</sup> trimester of pregnancy. NO<sub>2</sub> and benzene were measured with passive samplers covering the study areas. Land-use regression models were developed for each pollutant using geographic data as predictor variables and then applied to predict outdoor air pollution levels at each women address. Land-use regression estimates were temporally-adjusted using daily levels of the monitoring network stations. We obtained 9-month average exposures in 2,152 pregnant women for NO<sub>2</sub> and in 2,110 for benzene. Information on parental socio-demographic, life-style, and child characteristics was obtained by questionnaire. At 1-1.5 years, mental and psychomotor development with Bayley Scales of Infant Development was assessed.

**Results:** Median exposure during pregnancy was 27.6 µg/m<sup>3</sup> (interquartile range 20.6-35.5) for NO<sub>2</sub> and of 1.3 µg/m<sup>3</sup> (interquartil range 0.9-1.9) for benzene. Air pollution was poorly related with social class determinants and if any in a negative way. Exposure to benzene showed a negative association with mental development score (β=-2.42, 95% Confidence Interval(CI): -5.28, 0.44 and β=-3.36, 95%CI: -6.44, -0.27 for the 3<sup>rd</sup> and the 4<sup>th</sup> quartile of exposure, respectively, in relation to the 1<sup>st</sup> quartile) after adjusting for a large array of potential confounders including maternal smoking during pregnancy and parental social class. A negative relation was also observed with psychomotor development score (β=-1.52, 95%CI: -4.40, 1.37 and β=-1.73, 95%CI: -4.86, 1.40 for the 3<sup>rd</sup> and the 4<sup>th</sup> quartile of exposure, respectively). The effects of NO<sub>2</sub> exposure in both mental and psychomotor development scores were less clear.

**Conclusion:** This study suggests that exposure to vehicle exhaust pollutants during pregnancy has a negative effect in children neurodevelopment at early ages when general cognition is starting to be conformed. Confirmation of these adverse effects in further studies may have large public health implication given the ubiquity of air pollution exposure at population level.

## T9.5.4

### Air pollution and blood pressure in different trimesters of pregnancy. The Generation R Study

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#### Abstract

*Objective:* Exposure to air pollution has been associated with elevated blood pressure and cardiovascular disease. Less is known about the associations of air pollution exposure with blood pressure patterns during pregnancy and the risks of pregnancy hypertensive disorders.

*Methods:* We assessed the associations of air pollution exposure (particulate matter (PM<sub>10</sub>) and nitrogen dioxide (NO<sub>2</sub>), assessed at the home address using dispersion modelling) with repeatedly measured blood pressure and the risks of pregnancy-induced hypertension and preeclampsia in 7117 pregnant women participating in a population-based prospective cohort study in the city of Rotterdam, the Netherlands. Systolic and diastolic blood pressure were assessed by physical examinations in each trimester of pregnancy. Information about pregnancy-induced hypertension and preeclampsia was obtained from medical records.

*Results:* Longitudinal analyses showed that higher PM<sub>10</sub> exposure levels were associated with a steeper increase for systolic blood pressure throughout pregnancy ( $P < 0.05$ ), but not with diastolic blood pressure patterns. Higher NO<sub>2</sub> exposure levels were associated with more gradual increases in systolic and diastolic blood pressure levels ( $P < 0.05$ ). In cross-sectional analyses, higher PM<sub>10</sub> exposure levels were associated with increases in systolic blood pressure in second and third trimester ( $P$  for trend  $< 0.05$ ), and higher NO<sub>2</sub> exposure levels were associated with increases in systolic blood pressure in first and second trimester ( $P$  for trend  $< 0.10$ ). Higher PM<sub>10</sub> exposure levels were associated with an increased risk of developing pregnancy-induced hypertension or preeclampsia ( $P$  for trend  $< 0.05$ ). No associations were observed between NO<sub>2</sub> exposure and the risks of pregnancy hypertensive disorders.

*Conclusion:* Exposure to higher PM<sub>10</sub> levels was associated with a steeper increase for systolic blood pressure throughout pregnancy, and an increased risk for developing pregnancy hypertensive disorders. Our results suggest that air pollution exposure is associated with cardiovascular adaptations during pregnancy.

## T9.6.1

### Work-life imbalance predicts future self-rated health

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#### Abstract

*Objectives:* Several studies have shown that work-life imbalance is associated with poor self-rated health and other negative health outcomes. However, few longitudinal studies have been conducted on this topic. The aim of the study was to investigate how experienced conflict between work and family life is associated with self-rated health measured two years later.

*Methods:* The study is based on the participants in the SLOSH (Swedish Longitudinal Occupational Survey of Health) study (N=11,441). Participants answered all questions twice (2006 and 2008). Work-family conflict (WFC) and general self-rated health were measured by single items with 5 response alternatives at both times. Higher numbers indicate worse health. Work-family conflict was dichotomised into low (very seldom and quite seldom) and moderate (sometimes to very often) in some analyses.

*Results:* Most participants experienced low work-family conflict at both times (86%, n=3125). Five percent (n=200) had low WFC at time 1 and high WFC at time 2. Six percent (n=194) reported high WFC at time 1 and low WFC at time 2. Only 3% (n=120) experienced high conflict at both times. Analysis of variance (ANOVA) showed that the group with stable low WFC had significant better self-rated health (mean=1.88) at follow-up than the remaining three groups (mean 2.15 to 2.37; p=0.002).

Linear regression models showed that higher conflict between work and family life was associated with an increased risk for poor self-rated health (OR=1.41; 95% CI: 1.33-1.50). Controlling for age and sex did not alter the results. Controlling for self-rated health in 2006 attenuated the risk, which however remained significant (OR 1.13; 95% CI: 1.06-1.21).

*Conclusions:* We conclude that work-family conflict is associated to an increased risk for poor self-rated health.

## T9.6.2

### A prospective longitudinal investigation of work-related health determinants of an ageing workforce in Germany – The lidA Study

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#### Abstract

*Objectives:* The demographic transformation of industrial nations like Germany causes an ageing workforce. Future work-related challenges (higher and rapidly changing job demands, willingness to retire later) can be met by healthy and motivated employees, only. Consequently, concepts for the maintenance of work ability, health and motivation of older employees are required. The lidA study investigates factors related to healthy and motivated ageing at work including work environment, socioeconomic status and gender. Specific problems to be considered in the study design, sampling methods and data analysis of this investigation will be presented.

*Methods:* lidA is the largest longitudinal study on the relationship between work, ageing and health in Germany. The study incorporates a cohort sequential design to control for effects of age, cohort and time. Representative, nationwide cohorts of 6,000 employees in two age groups will be followed up in three-year-intervals for a planned period of 12 years. Data on work characteristics, individual factors and health data collected by CAPI will be linked with data of the social security registry and statutory health insurance providers. Statistical analyses will comprise multiple regression and multilevel analyses.

*Results:* We expect the following working environment factors to be strong predictors for healthy ageing at work and the acceptance of late retirement: A good relationship between job demands, rewards, control, social support, career opportunities and health promotion measures. Additionally, adequate individual coping strategies, health behaviour and work-life balance might be predictive.

*Conclusions:* Large, long-time cohort studies have to be designed and planned carefully, ideally taking future developments into account. Sample size calculation including aspects of cluster design and multiple analyses, sample composition over time (loss to follow-up, changes in employment status) and measures to deal with confounding, have to be considered from the outset. Selection of items has to include considerations of comparability with other studies on this topic and reference data. Tackling these problems adequately will offer the unique possibility of analysing factors associated with health in an ageing workforce. The study's results will provide the basis for the political improvement of future working environments with respect to healthy ageing at work.

### **T9.6.3**

## **Conflict between work and family, emotional exhaustion and performance-based self-esteem: reciprocal relationships**

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### **Abstract**

*Objectives:* The purpose of this study was (a) to investigate if an experienced conflict between work and family has a negative effect on emotional exhaustion and (b) if emotional exhaustion and performance-based self-esteem has an effect on the experienced conflict between work and family over a period of two years.

*Methods:* The study is based on the participants in the SLOSH (Swedish Longitudinal Occupational Survey of Health) study. Participants answered all questions twice (2006 and 2008). 1556 persons had complete data on all variables examined here. The conflict between work and family demands (WFC) was measured with a single question (Does your job requirements of your home and family in a negative way?). Performance-based self-esteem (PBS) was measured with four questions. Emotional exhaustion was measured with five questions from the Maslach Burnout Inventory (MBI-GS). Four different models were tested using structural equation models. (A) A stability model without cross-lagged structural paths but with temporal stabilities. (B) A causality model with paths between T1 PBS and T2 WFC and T1 WFC to T2 emotional exhaustion. (C) A model with reverse causality included paths from T1 emotional exhaustion to T2 WFC, and structural paths from T1 emotional exhaustion and T1 WFC to T2 PBS. (D) A reciprocal model included all paths from previous models.

*Results:* All models had good and very similar fit indices. However, the findings support the idea of cross-lagged effects between emotional exhaustion and work family conflict over time. The direct effects of the reciprocal model are significant but quite small (T1 emotional exhaustion → T2 WFC 0.10, T1 WFC → T2 PBS 0.06, T1 PBS → T2 emotional exhaustion 0.05).

*Conclusions:* We conclude that all three variables (WFC, emotional exhaustion and PBS) are quite stable over a time period of two years and that emotional exhaustion has an impact on experienced conflict between work and family life two years later.

## T9.6.4

### Workplace bullying and sleep problems: a follow-up study

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#### **Abstract**

*Objective:* To examine consequences of workplace bullying to sleep problems.

*Methods:* The data were derived from the Helsinki Health Study baseline (in 2000-2002, n=8960, response rate 67%) and follow-up (in 2007, n=7332, response rate 83%) questionnaire surveys among ageing employees of the City of Helsinki, Finland. Participants were 40-60 years old at baseline. The 4-item Jenkins sleep questionnaire was included at baseline and follow-up. Two measures of workplace bullying enquired whether the respondent had been a victim of bullying (currently or previously) or observing bullying. Logistic regression models were adjusted for age, childhood bullying, baseline sleep problems, sociodemographic factors, working conditions, obesity, and physical and mental health.

*Results:* At baseline 5% of women and men were victims of bullying and 19% of women and 13% of men reported previous bullying. Of women 9% and of men 7% reported frequently been observing bullying, whereas 51% of women and 44% of men were least sometimes observing bullying at their workplace. Among women 21% and among men 17% reported frequent sleep problems at baseline and the corresponding figures at follow-up were 26% and 21%. Adjusting for age, victims of bullying were more likely to report sleep problems at follow-up among women (OR 1.70, CI 95% 1.31-2.21) and men (OR 3.16; CI 95% 1.85-5.42). Also those reporting previous bullying were more likely to report sleep problems at follow-up among both women (OR 1.46, CI 95% 1.25-1.71) and men (OR 1.60, CI 95% 1.07-2.39). After adjustment for baseline sleep problems, the associations remained for victims of bullying among men and previous bullying among women. Further adjustments had negligible effects on the associations. Additionally, women who reported frequently observing bullying were more likely to report sleep problems after full adjustments (OR 1.31 CI 95% 1.03 -1.66).

*Conclusions:* Workplace bullying is likely to contribute to subsequent sleep problems. To prevent sleep problems, bullying at workplaces needs to be considered.

## T9.6.5

### Social adversity in adolescence increases the physiological vulnerability to job strain in adulthood: A Swedish prospective population-based study

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#### Abstract

*Objectives:* Social conditions during childhood have been mentioned as a possible confounder in the relationship between job strain and myocardial infarction risk. However, stress theory also suggests that early experiences may modify the individual's vulnerability to later stress, for instance through learned helplessness or hopelessness. We aimed to test if social disadvantage in childhood and adolescence increases the physiological vulnerability to stress, specifically job strain, in adulthood. As outcome, we chose allostatic load, in accordance with Bruce McEwen, as a measure of the cumulative physiological cost of adaptation to stress.

*Methods:* In a prospective population-based cohort (effective n=771; 72%), we examined the association between on the one hand exposure to an adverse social environment in adolescence, measured at age 16, and job strain measured with the Demand-Control Questionnaire (DCQ) at age 43, and on the other hand allostatic load at age 43. Adversity in adolescence was operationalised as an index comprising residential mobility and crowding, parental loss, parental unemployment, and parental physical and mental illness (including substance abuse). Allostatic load was operationalised as an index comprising body fat, blood pressure, inflammatory markers, glucose metabolism, blood lipids, and cortisol area under curve.

*Results:* Adversity in adolescence was associated with higher adult allostatic load in women ( $\beta = 0.170$ ,  $p = 0.001$ ). There was also a significant interaction between adversity in adolescence and job strain in the whole cohort ( $\beta = 0.081$ ,  $p = 0.026$ ), indicating that the ability to cope with the demands in working life may be negatively affected by exposures in early life.

*Conclusions:* Exposure to an adverse social environment in adolescence was associated with an increased level of biological stress indicators among those reporting job strain in mid-life, indicating increased vulnerability to environmental stressors. This suggests that socioeconomic inequalities in health may be exacerbated by a synergistic effect of work stress and early life adversities acting through biological programming, behaviours, or psychological factors.



## T10.1.1

### Associations of gestational weight gain with BMI, waist circumference and blood pressure measured 16 years post-pregnancy: the Avon longitudinal study of parents and children

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#### Abstract

*Objective:* To examine associations of pre-pregnancy weight and gestational weight gain (GWG) with the mothers' body mass index (BMI) waist circumference (WC), systolic (SBP) and diastolic blood pressure (DBP) measured 16 years post-pregnancy.

*Methods:* Data from 2,518 mothers from the Avon Longitudinal Study of Parents and Children, a UK prospective pregnancy cohort were used. Inadequate, adequate and excess GWG were defined according to the 2009 IOM guidelines. Pre-pregnancy weight and GWG were also modelled using random effects multilevel models of incremental GWG (median and range of repeat weight measures per woman: 10 (1, 17)).

*Results:* Women with inadequate GWG had lower mean BMI (-1.38kg/m<sup>2</sup>; 95%CI: -1.93, -0.82) and WC (-2.95cm; -4.45, -1.44) compared to women who gained adequately; women with excess GWG had a greater mean BMI (3.26kg/m<sup>2</sup>; 2.66, 3.86), WC (6.29cm; 4.63, 7.95) and SBP (2.45mmHg; 0.88, 4.03), when adjusting for maternal age at outcome assessment, offspring sex, head of household social class, parity, smoking in pregnancy, mode of delivery, duration of breastfeeding and current smoking. Using estimates from random effects multilevel models of incremental GWG we found that pre-pregnancy weight was positively associated with BMI, WC, SBP and DBP 16 years post-pregnancy. Early pregnancy (0-14 weeks) GWG was positively associated with BMI and WC even after adjustment for confounders, pre-pregnancy weight and previous GWG. Mid pregnancy (15-36 weeks) GWG was positively associated with BMI, WC, and DBP amongst normal weight women but not amongst overweight women. GWG in late pregnancy (37+ weeks) was not associated with maternal outcomes.

*Conclusion:* Long term adiposity and BP are positively associated with pre-pregnancy weight and GWG. Findings support initiatives aimed at optimising pre-conceptual weight. However, the lack of a large detrimental effect of mid pregnancy GWG in overweight women, combined with our observations that inadequate GWG is associated with lower measures of adiposity and BP in mothers and with a reduced risk of obesity and adverse cardiovascular risk profile in offspring, suggests that interventions to facilitate adherence to IOM criteria will require substantive evidence of short and long term benefit to both mother and offspring prior to being adopted.

## T10.1.2

### Pregnancy: A risk factor for social inequalities in overweight and obesity?

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#### Abstract

*Objectives:* Obesity and overweight are not randomly distributed in the population, and strong disparities according to socioeconomic status and racial/ethnic origin exist. In the search for the causes of this epidemic, pregnancy-related weight gain has begun to receive growing attention. The aims of the study are: 1. Estimate the average time to return to pre-pregnancy BMI, and/or reach a "healthy" BMI (18.5-24.9) post-pregnancy. 2. Identify socioeconomic and ethnic characteristics placing women at risk of not returning to a healthy and/or their pre-pregnancy BMI.

*Methods:* Data come from the National Longitudinal Survey of Youth (NLSY79). This prospective cohort is nationally representative of the U.S. population of individuals aged 14 to 22 years in 1979. Having followed for 23 cycles of data collection and over 27 years these respondents' lives, it constitutes one of the richest sources for repeated, prospective information on socioeconomic, fertility and pregnancy-related weight dynamics. Indeed, out of the 4926 women aged 14-22 included in the sample in 1979, we considered 1890 parous women (excluding adolescent mothers and births with information collected retrospectively prior to 1983) who were followed over the bulk of their reproductive lives.

*Results:* Following their first birth, 68.6% of women returned to their pre-pregnancy BMI after 1.9 years on average, and more broadly, 89.9% returned to their pre-pregnancy BMI category after 1.5 years on average. Similarly, we found that 81.2% were able to reach a healthy BMI after 1.7 years on average. However, given that 18.8% of women who returned to their pre-pregnancy BMI were overweight or obese, this suggests that the high proportion of women reaching a "healthy" BMI post-partum is due in part to underweight women transitioning into this "healthy" category. Moreover, the proportion of women who returned to their pre-pregnancy BMI was higher among Whites (70.0%) than Blacks (62.1%) or Hispanics (57.4%) and increased with these women's mothers' education.

*Conclusions:* These analyses highlight the existence of social disparities in the likelihood of returning to pre-pregnancy and/or healthy BMI. Next, we will rely on multivariate survival analysis to estimate this likelihood according to socioeconomic status and ethnicity, controlling for parity, psychosocial factors and prenatal care service use.

## T10.1.3

### Change in abdominal obesity and risk of coronary calcification

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#### **Abstract**

*Objectives:* The objective of this study was to examine the relation between 9 years change in abdominal obesity and risk of coronary artery calcification (CAC).

*Methods:* The study population comprised 573 postmenopausal women selected from a population based cohort study. Data on coronary risk factors were collected at baseline (1993-1997) and follow-up (2002-2004). At follow-up, the women underwent a multi-detector computed tomography (MDCT) (Philips Mx 8000 IDT 16) to assess coronary calcium. The Agatston score was used to quantify coronary calcium. Logistic regression models were used to evaluate the relations under study. Change in markers of abdominal obesity (Waist and hip circumferences, waist to hip ratio and body mass index) was categorized into four groups: low at baseline-low at follow-up (low was defined as below the median); high-low; low-high; and high-high.

*Results:* CAC was related to increase in waist circumference (WC) 2.15 [95% CI; 1.09 – 4.23] and not to decrease in hip circumference (HC) (lose of muscular mass). Compared to subjects whose waist to hip ratio (WHR) remained below the median of the distribution at both occasions, those with a WHR above the median at both occasions had a 2.7 [95% CI; 1.8-4.0] fold increased risk of CAC. Women whose WHR rose over the 9 year period from below the median to above the median had a 2.5 [95%CI 1.4-4.5] fold increased risk of CAC, whereas the women whose WHR became lower had a non-significant 1.6 fold increased risk of CAC [95% CI; 0.8-3,2]. In contrast, change in body mass index (BMI) was not related to risk of CAC.

*Conclusion:* This observational study among healthy postmenopausal women supports the existing evidence that persistent abdominal obesity as well as an increase in abdominal fat over time relates to an increased risk of coronary atherosclerosis.

## T10.1.4

### Octachlorodibenzo-p-dioxin (OCDD) levels in serum could predict the increase in waist circumference over 5 years in an elderly cohort

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#### Abstract

*Objective:* Recently organic pollutants have been suggested to be involved in the pathogenesis of obesity, so called "obesogens". The hypothesis tested in the present was to evaluate if octachlorodibenzo-p-dioxin (OCDD), a marker of dioxin exposure, could predict the change in waist circumference over 5 years in the Prospective Study of the Vasculature in Uppsala Seniors (PIVUS) study.

*Methods:* In the population-based PIVUS study (1016 subjects all aged 70 at baseline) waist circumference was measured at baseline and in 826 subjects at the 5 years follow-up. OCDD was measured by high resolution GC/MS analysis in serum at baseline.

*Results:* The mean increase in waist circumference over 5 years was 3.0 cm. A positive relationship was found between OCDD levels at baseline and the increase in waist circumference after 5 years ( $p=0.009$ ). No interaction was seen between OCDD levels and gender regarding the change in waist circumference after 5 years ( $p=0.88$ ).

*Conclusion:* OCDD levels in serum, a marker of exposure of the persistent organic pollutant dioxin, could predict the increase in waist circumference over 5 years in an elderly cohort, giving further evidence that organic pollutants could be involved in obesity development.

## T10.1.5

### Lifecourse changes in adiposity and the relationship to household income

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#### **Abstract**

*Objective:* Contemporary levels of overweight and obesity are an urgent public health priority. Information on recent increases is based primarily on cross-sectional data, whilst explanations have focussed on physical activity and diet. Other factors, like income, are relatively under-researched. The objective of this study is to examine the changes in adiposity through adulthood and assess the impact of changes in household income.

*Methods:* This study is a longitudinal study of three age cohorts in the West of Scotland assessed up to five times over 20 years. The population consist of three randomly sampled cohorts (N~1,000 each) of community dwelling adults aged around 15, 35 and 55 at first contact in 1987/8. Data for the youngest cohort are included from the third wave when their mean age was 24. The overall age range covered was 23 to 79. Participants were interviewed in their homes by trained nurses who also measured height, weight, waist and hip circumference. Net household income was ascertained and adjusted for household composition and inflation. Descriptive results are presented for BMI, waist circumference and waist-hip ratio. Random and fixed effects models were both used to estimate the effects of changes in income and the likely effect of confounding by time invariant factors.

*Results:* BMI and waist circumference increased with age in all cohorts but there were marked cohort differences with younger cohorts increasing more rapidly and reaching high levels at earlier ages. Waist hip ratio also increased with age, but the cohort differences were less marked. Effects of income were evident for all three measures (all  $p < .001$ ) although interactions with gender evident in cross-sectional analyses were not significant. When stable background characteristics were controlled for in the fixed effects analysis, effects were weaker still and none were significant ( $p = .08$ , for BMI and waist,  $.24$  for waist-hip ratio).

*Conclusions:* Overweight and obesity increase with age and there may be cohort or generational differences in the rate of increase. Household income is associated with adiposity longitudinally, but less so once stable background characteristics are controlled for. It is possible that factors which control an individual's weight trajectory are set earlier in life.

## T10.2.1

### Using longitudinal studies to monitor equity in uptake of screening programmes

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#### **Abstract**

*Objective:* There is a recognised dearth of information about variation in uptake rates of screening programmes in the UK. The few available studies have significant limitations either because they have used ecological measures of socio-economic status (SES) or have been based on surveys. The main objective of the study is to demonstrate the utility of record linkage studies as a tool for monitoring variations in screening uptake by undertaking a study to determine and quantify the socio-demographic and socio-economic factors influencing uptake of breast screening in Northern Ireland.

*Methods:* Record linkage study combining data from the National Breast Screening System and the Northern Ireland Longitudinal Study (NILS) with cohort attributes as per their 2001 census return. NILS is a representative 28% of the population constituted at the time of the 2001 census.

*Participants:* 37,059 women aged 48-64 at the time of the census invited for routine breast cancer screening during the three years following the census. The main outcome measure is the attendance for routine breast cancer screening in the three years following the census.

*Results:* Overall uptake for the linkage cohort was 75% (74% from National Breast Screening System). In the fully adjusted model, uptake was lower amongst women aged 60 and over, those who were not currently married and amongst women whose general health was 'not good' in the year before the census. Uptake was strongly related to car ownership and housing tenure but not to educational status or social-class. Even after adjustment for all other demographic and SES factors there was significant variation in uptake amongst Health Boards responsible for the organisation and promotion of the service; uptake was lowest around Belfast the largest city (OR=0.49, 95% CI=0.45, 0.53, compared to the largest Board). The reduction in Belfast was evident across most social strata and was confirmed by use of different definitions of 'city'.

*Conclusions:* Linkage of screening data to census-based longitudinal studies is an efficient and powerful way to increase the evidence base on sources of variation in uptake and for monitoring equity of utilisation. The findings presented here apply to other screening programmes and to other parts of the UK.

## T10.2.2

### **Unequal healthcare needs and SES over the lifecourse: The role of health insurance in a national health system**

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#### **Abstract**

**Background:** The Canada Health Act guarantees universal public coverage of all “services provided by hospitals, medical practitioners or dentists”. Yet, gaps exist notably in the coverage of prescription drugs, dental and eye care, and a supplementary private insurance market has developed to bridge them. We assess the contribution of supplementary private health insurance (SPHI) to social inequalities in health through a proxy of health care utilization, namely unmet health care needs because of cost.

**Methods:** Data come from the National Population Health Survey conducted by Statistics Canada. We examine these associations among three groups of working age (25-34; 35-44; 45-54 year olds) over a ten-year period, or from 1994/95 to 2004/05. Path analyses were estimated using Mplus® v4.0.

**Results:** First, no significant impact was found among the 25-34 year olds. Second, health insurance coverage among the 35-44 year olds appeared to mitigate health inequalities and to decrease the probability of reporting poor self-rated health (SRH), but only when barriers to health care utilization occur ( $-0.226 \times 1.435 = -0.324$ ). Third, among the 45-54 year olds, health insurance tended to exacerbate health inequalities and to decrease the probability of reporting poor SRH both directly ( $-0.126$  (0.090),  $p < 0.25$ ) and indirectly through unmet needs because of cost ( $-0.385 \times 0.756 = -0.291$ ). All direct, indirect and total effects lead to the same conclusion: increasing years of supplementary health insurance coverage seem to protect against poor SRH.

**Conclusion:** We show here that health inequalities exist and persist even within a national health system, particularly through unequal access to supplementary private health insurance. In the context of the growing reliance on private health insurance coverage to the expense of public coverage, the surveillance of these trajectories is necessary for the development of evidence-based health policies.

## T10.2.3

### **Socioeconomic inequalities in hospital use in women from the Renfrew/Paisley prospective cohort study**

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#### **Abstract**

*Objectives:* To investigate whether women from lower socioeconomic groups have more admissions and bed-days in acute and mental health hospitals than women in higher groups.

*Methods:* The Renfrew/Paisley prospective cohort study was conducted between 1972 and 1976 on residents aged 45-64 of the towns of Renfrew and Paisley, Scotland. 7049 men and 8353 women took part, this large number of women being unusual at the time. Participants completed a questionnaire and attended a screening examination at a specially set-up clinic. Responses to the questionnaire included occupation, home address, age, smoking, being diabetic, bronchitis and angina. Height, weight, blood pressure and lung function were measured at the screening examination, cholesterol was measured and an ECG was made. Carstairs deprivation category was obtained from the home address.

Dates of death are routinely supplied, and information on acute and mental health hospital discharges was provided from computerised linkage with the Scottish Morbidity Records data to 31/12/2008. Number of admissions and total bed-days were calculated for each participant, for all causes and specific causes. Rate ratios by deprivation category were calculated using negative binomial regression analysis. Analyses were first adjusted for age and then for the above risk factors.

*Results:* After exclusions for missing deprivation category, there were 8328 women with 46,715 admissions (mean 5.6, mean bed-days 14.0), with maximum follow-up 36.8 years. There were increasing rate ratios (RRs) with deprivation for admissions and bed-days (RR=1.16 (95% confidence interval 1.03-1.31), RR=1.75 (1.45-2.10) respectively for the most deprived compared with the least deprived) from all causes, which were attenuated somewhat after adjustment for other risk factors. There were similar increasing relationships for cardiovascular disease, coronary heart disease, stroke and respiratory diseases, with no clear pattern for cancers. Mental health admissions were higher in women in the three most deprived categories, but there was no evidence of socioeconomic differences for bed-days.

*Conclusions:* Women living in more deprived areas had a higher number of admissions and bed-days than women in more affluent areas, with stronger relationships seen with bed-days. Some of the differences could be accounted for by risk factors at baseline.



## T10.2.4

### **Inequalities in reported oral health and dental service utilization of Australian children aged 2-3 and 6-7 years**

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#### **Abstract**

*Objectives:* The extent to which the oral health of young Australian children varies according to different indicators of social disadvantage is unclear, making it difficult to identify the most appropriate distribution of oral health interventions. To assess inequalities in the oral health of young Australian children, we examined the associations between early childhood oral health and socioeconomic position (SEP), geographical remoteness, Indigenous status and non-English speaking background (NESB) using data from the Longitudinal Study of Australian Children (LSAC).

*Methods:* Two nationally representative cohorts of around 5000 children each, aged 2-3 and 6-7 years, were used to explore associations between reported oral health and four indicators of social disadvantage (socio-economic position, rurality, Indigenous status and non-English speaking background). The oral health outcomes examined were accidents causing tooth damage, reported experience of caries, frequency of toothbrushing and use of dental services in the last 12 months.

*Results:* Reported caries experience was strongly associated with SEP. The most disadvantaged 2-3 year olds had a three-fold increased odds of caries compared to their advantaged peers. Indigenous status for the older cohort and non-English speaking background for the younger cohort were associated with a two-fold increased odds of caries. Infrequent toothbrushing was more common among low SEP children and Indigenous children. Dental service use was less common among low SEP children, Indigenous children and NESB children aged 6-7 years.

*Conclusions:* Significant disparities in oral health were evident from a very early age. Interventions or policies aiming to reduce such disparities should commence before children reach school age. These interventions should focus on financially or socially disadvantaged children and their parents.

## T10.2.5

### **Compression of morbidity and socioeconomic deprivation in New Zealand: An analysis of hospital use in the last few months of life, 1990-2006**

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#### **Abstract**

*Objectives:* The compression of morbidity hypothesis is usually explored at a country level, yet there are inequalities in health and life expectancy by socioeconomic deprivation within countries. This paper aims to assess the compression of morbidity hypothesis through the use of New Zealand mortality and hospital discharge data, and identify if the process of compression / expansion of morbidity varies by socioeconomic deprivation. This is achieved by examining differences in hospital utilisation prior to death for individuals in New Zealand who died between 1990 and 2006. Utilisation of health services is an underused indicator in this field, a secondary aim is to assess the relevance of using hospital bed days as a proxy for morbidity in different settings.

*Methods:* NMDS records on deaths and public hospital discharges between 1988 and 2006. NZdep deprivation deciles are used. Individual linkage between mortality and hospital records allows examination of hospital use in a window preceding death. Hospital bed day rates are used in preference to discharge rates, in order to weight by severity of the hospital episode, and are filtered to represent ill health (excluding obstetrics etc.). Reference point models provide a visual display of the patterns of hospital bed days in the last few weeks and months of life, allowing comparison by age of death, deprivation decile, gender, and cause of death. Cox proportional hazards models provide a statistical, rather than visual comparison of hospital use prior to death for different groups.

*Results:* The majority of excess hospital use prior to death (compared to individuals who did not die) occurs in the last two years of life. Preliminary results suggest that individuals in both more and less deprived areas are experiencing compression of morbidity, but that this process is more advanced for less deprived areas. In health systems with universal, free health care hospital bed day rates are found to be an acceptable indicator of morbidity after filtering to exclude events not related to ill health, closely following trends in mortality rates.

*Conclusions:* Compression of morbidity seems to be occurring in New Zealand, but there are socioeconomic variations in the pace of this process. Use of health care services is a valuable and underutilised indicator of morbidity in health research.

## T10.3.1

### **Prevalence and overlap of mental illnesses in and around pregnancy: a United Kingdom population-based study**

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#### **Abstract**

*Objectives:* Previous research has shown a high prevalence of depressive disorder and anxiety in women postpartum. No large-scale studies, however, have yet quantified the prevalence comprehensively in terms of the primary care burden in the UK as well as for more severe psychiatric illnesses (e.g. psychosis) and for the potential overlap between mental illnesses across the perinatal period.

*Methods:* We randomly selected one pregnancy ending in a live birth from each woman age 15-45 years registered in The Health Improvement Network nationally representative electronic primary care database. The prevalence of mental illness was calculated within nine months before pregnancy, during pregnancy and within nine months after delivery. McNemar's tests were used to examine whether there were differences in prevalence before or during pregnancy compared with after delivery.

*Results:* In 106,571 women with pregnancies ending in live births, we identified diagnoses of depressive disorders or anxiety in 4.7% (95% confidence interval [CI] 4.5-4.8%) during the nine months before pregnancy, 2.6% (95% CI 2.5-2.7%) during pregnancy and 9.5% (95% CI 9.3-9.7%) during the nine months after delivery. The prevalence of more severe mental illnesses (bipolar disorder and/or psychosis) was 0.11% (95% CI 0.10-0.14%), 0.07% (95% CI 0.06-0.09%) and 0.22% (95% CI 0.19-0.25%) in the three time periods, respectively. Of women with mental illnesses, 12.0% (95% CI 11.1-12.9%) of women had at least two different diagnoses before pregnancy, 10.3% (95% CI 9.2-11.5%) during pregnancy and 10.0% (95% CI 9.4-10.6%) after delivery. The overlap was mainly between depressive disorder and anxiety. The prevalence of mental illness was higher ( $p < 0.001$ ) after delivery than before or during pregnancy. These differences remained ( $p < 0.001$ ) after stratifying women according to whether or not they had a history of mental illness and after restricting to only women's first diagnoses within the study period.

*Conclusions:* Prevalence of general practice diagnoses for all mental illnesses appears higher postpartum than before or during pregnancy and concurrent diagnoses are not uncommon. Maternal mental health should be actively monitored postpartum to enable timely interventions.

## T10.3.2

### Parenting practices and child mental health outcomes

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#### **Abstract**

*Objectives:* Families are central in children's lives and parental practices often influence their development. This study examined the link between three major parenting practices: physical punishment, monitoring of child activities and extensive offering of material goods, and child's mental health.

*Methods:* It used longitudinal and cross-sectional data from the Greek Birth Cohort (1983), which followed-up participants from birth to the age of 18 years. Logistic regression models were conducted to test the unadjusted and adjusted odds of scoring above cut-off point on the mental health problem scales (outcome) for the variables studied. Possible indicators of a supportive or not familiar setting, such as family structure, family extension and maternal education, were also employed as main independent variables.

*Results:* In our study, frequent use of physical punishment was found to be associated with emotional and total problems at 7 years and behavioral deviation at 7 and 18 years of age. Lack of parental monitoring was associated with behavioral and total problems at 7 years and various forms of problem behavior at 18 years. Finally, adolescent's economic experiences were also associated with their psychological status.

*Conclusions:* Our results suggest that parental practices are important correlates of child's mental health. Therefore, attempts to assist families to function well and meet the needs of their children are necessary.

### T10.3.3

## Effects of maternal lifetime and pregnancy eating disorders on childhood psychopathology at age 3 ½: a general population cohort study

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#### Abstract

*Objective:* We aimed to investigate psychopathology, i.e. levels of emotional, conduct, hyperactivity and total psychiatric problems, in children of women with lifetime eating disorders (ED) at age 3 ½ compared to children of women without other psychiatric disorders in a large prospective general population cohort-Avon Longitudinal Study of Parents and Children (ALSPAC). We were interested in the specific effect of lifetime Anorexia Nervosa (AN) vs. Bulimia Nervosa (BN) and the effect of pregnancy ED symptoms.

*Methods:* Women with a lifetime ED (441; of which 193 had lifetime AN and 158 lifetime BN), women without (10461) lifetime other psychiatric disorders and their children were investigated longitudinally. Data on child psychiatric disturbance was obtained using the Strengths and Difficulties Questionnaire (SDQ) for parents.

*Results:* Children of women with lifetime ED had higher scores on emotional (b coefficient: 0.3,  $p < 0.01$ ), conduct (b coefficient: 0.4,  $p < 0.01$ ) and total psychiatric problems (b coefficient: 1.2,  $p < 0.001$ ) compared to children of control women. These differences persisted after controlling for relevant confounders. Children of women with AN had higher levels of emotional problems compared to controls (b coefficient: 0.4,  $p < 0.01$ ); children of women with lifetime BN had a higher conduct problem score (b coefficient: 0.6,  $p = 0.003$ ).

Maternal ED symptoms in pregnancy predicted psychopathology across genders; however with a differential effect on emotional problems (stronger effect for boys).

*Conclusions:* Maternal lifetime ED increases the risk of childhood psychiatric problems at an early age. Different psychopathological features in the offspring of women with AN and BN were highlighted. An effect of pregnancy ED symptoms was highlighted, possibly suggesting in utero effects. These findings have important implications for the prevention of childhood psychiatric disturbance and help increase our understanding of risk mechanisms.

## T10.3.4

### Childhood asthma precedes ADHD in adolescence – a prospective population-based Swedish twin study

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#### Abstract

*Objective:* Cross-sectional studies report a relationship between childhood asthma and symptoms of ADHD. The mechanisms underlying this association and how these disorders evolve in relationship to each other and over time are yet unclear.

Our objective was to investigate the prospective and longitudinal link between childhood asthma and ADHD symptoms (hyperactivity-impulsivity, HI and inattention, IN) in early adolescence. We also aimed to explore the contribution of genetic and environmental factors and the impact of asthma medication.

*Methods:* Parents of 1,480 Swedish twin pairs born between 1985- 1986 were asked to participate in a longitudinal study. Data on asthma and symptoms of ADHD along with sex, socioeconomic status, zygosity and medication was collected through parental questionnaires at ages 8-9 and 13-14 years. Data on birth weight was obtained through linkage with the Swedish Medical Birth Register. We performed generalized estimating equations to investigate whether asthma at age 8-9 precedes ADHD symptoms at age 13-14. Secondly, basic twin methods were used to assess the genetic or environmental contribution to the association.

*Results:* After adjusting for confounders and previous symptoms of ADHD (HI and IN), the children with asthma at age 8-9 had an almost twofold increased risk of having one or more symptom of HI (OR 1.88, 95% CI 1.18-3.00) and a more than two-fold increased risk to have three symptoms or more of HI (OR 2.73, 95% CI 1.49-5.00) at age 13-14. For IN, no significant relationship was seen.

For both asthma and HI, monozygotic twin correlations were consistently higher than dizygotic correlations, suggesting substantial genetic influences. In addition, the results from twin modelling indicate that 60% of the phenotypic correlation between asthma and HI ( $r=0.24$ , 0.07-0.40) was due to genetic influences.

*Conclusions:* Our findings suggest that childhood asthma is associated with subsequent development of symptoms of ADHD in early adolescence. Results from the twin analyses indicates that the association between asthma and ADHD is mostly explained by shared genetic influences and to a lesser extent by shared environmental factors. Early strategies to identify children at risk may reduce the burden of asthma and ADHD in adolescence.

## T10.3.5

### **Mother's psychological distress and conduct behaviour in boys and girls aged 5 years old: findings from the UK Millennium Cohort Study**

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#### **Abstract**

*Objective:* The objective of this paper is to examine the relationship between maternal psychological distress and conduct problems in boys and girls in early childhood and the potential pathways via socio-economic circumstance and parenting behaviour.

*Methods:* Data used was collected as part of the UK Millennium Cohort Study (MCS) consisting of a sample of 18,552 families recruited between 2000-2001 when the cohort child was aged 9 months old, with follow ups at aged 3 years old (n=15,590) and 5 years old (n=15246). Multivariate logistic regression was used for the analysis and sampling weights applied.

*Results:* At aged 5 years old 12% of boys (n=6,366) and 9% of girls (n=6,307) had a high conduct score indicative of a problem. Boys of mother's with high psychological distress at either one, two or three time points during their child's early years, compared to none, showed a step wise increasing odds (unadjusted) of having a conduct problem at aged 5 years old with a 2.5 times, 4 times and 7.5 times higher odds, respectively. Girls had a similar pattern of increasing odds (unadjusted) of conduct problems in relation to the number of time points at which maternal psychological distress was present although the effect appeared stronger in girls at 5 years old who had 3 times, 5 times and 8.5 times higher odds, respectively. After controlling for child, mother and family characteristics, socio-economic position and parenting behaviour the odds of boys having a conduct problem were particularly attenuated in those of mother's with high psychological distress at three time points during their child's early years, reducing from 7.5 to 5 fold higher odds. The odds of girls having a conduct problem were particularly attenuated in those of mother's with high psychological distress at two time points during their child's early years reducing from 5 to 3 fold higher odds.

*Conclusion:* The results suggest there remains a significant independent relationship between maternal psychological distress and conduct problems in 5 year old boys and girls and that pathways via socio-economic position and parenting behaviour may operate differently by gender of child. Further investigation is required.

## T10.4.1

### Birth weight and early socio-economic disadvantage as predictors of sex hormones and sex hormone binding globulin in men at age 49-51 years

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#### Abstract

*Objective:* A number of associations have been shown between early growth and later sex hormone levels in women, but less is known about this relationship in men. This study investigated lifecourse predictors of sex hormones in men in the Newcastle Thousand Families birth cohort.

*Methods:* The Newcastle Thousand Families Study is a prospective study initiated in 1947 when all 1142 births to mothers resident in the city of Newcastle upon Tyne were recruited. Detailed information on many aspects of their lives was collected prospectively during childhood, including early growth and socio-economic conditions. At age 49-51, 574 study members returned detailed self-completion questionnaires and 412 attended for clinical examination, including 172 men in whom the following reproductive factors were measured: oestradiol, follicle stimulating hormone (FSH), luteinising hormone (LH), testosterone and sex hormone binding globulin (SHBG). Measures of free testosterone and the free oestrogen index (FOI) were also calculated. These data were analysed in relation to a range of factors from across the lifecourse.

*Results:* Social class at birth independently predicted FSH and LH, with higher levels with increasing socio-economic disadvantage. SHBG was higher with increasing standardised birth weight and lower with increasing BMI ( $r=-2.05$ , 95% CI -3.39, -0.71,  $p=0.003$ ). BMI also significantly predicted LH, SHBG and testosterone. None of the variables included within this analysis were significant predictors of oestradiol. No other associations were seen with any of the variables included from across the lifecourse.

*Conclusion:* Our findings suggest that birth weight and early socio-economic status may be positively associated with levels of sex hormones and SHBG in men. These novel findings are independent of contemporary BMI. Given the associations between early life and the sex hormone and related outcomes in this study, it is possible that sex hormones may play a mediating role in the associations between circumstances in early life and later risk of chronic disease.



## T10.4.2

### Reproductive factors and postmenopausal hormone use in relation to endometrial cancer risk in the Nurses' Health Study cohort 1976-2004

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#### Abstract

*Objectives:* Endometrial cancer is a disease primarily driven by cumulative exposure to estrogen unopposed by progesterone. Reproductive factors associated with changes in endogenous hormone levels and use of exogenous hormones such as postmenopausal hormones (PMH) influence the risk of disease.

*Methods:* The authors used the Nurses' Health Study (NHS), comprised of 121,700 nurses, to assess the above associations. Over 28 years of follow-up, 778 adenocarcinoma cases were diagnosed and 1,850,078 person-years were accumulated. Cox proportional hazards models were used to estimate relative risks (RR) and 95% confidence intervals (CI).

*Results:* A late age at menarche decreased the risk independent of body mass index (BMI) (P-trend=0.02). A late age at menopause increased cancer risk (P-trend=0.0003). An advanced age at last birth reduced the risk (P-trend <0.0001), however, an inverse association with age at first birth and parity diminished after adjustment for age at last birth. Compared with never users, an increased risk was observed among long-term (≥5 years) users of both estrogen (E) (RR=7.67, 95% CI: 5.57, 10.57) and combined estrogen plus progesterone (E+P) (RR=1.52, 95% CI: 1.03, 2.23). Normal-weight (BMI<25) women had the highest risk following E or E+P use (P-interaction-E=0.0008, P-interaction-E+P=0.02).

*Conclusions:* The findings from this study underscore the importance of hormonal mechanisms in endometrial carcinogenesis.

### T10.4.3

## Maternal CRP levels in pregnancy are associated with wheezing and lower respiratory tract infections in the offspring

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### Abstract

**Objective:** Increased C-reactive protein (CRP) serum levels have been associated with reduced lung function and asthma in adults. Although elevated levels of maternal CRP have been related to adverse pregnancy outcomes, it remains unknown whether they may affect respiratory health of the offspring. We assessed whether maternal CRP serum levels during pregnancy and variations in CRP gene are associated with wheezing and lower respiratory tract infections (LRTIs) in the offspring.

**Methods:** A prospective, population-based birth cohort was set up in Sabadell, Spain (n=657). Information on wheezing and LRTIs in the offspring was obtained at 6 and 14 months of age. CRP assay and genotyping was performed in the mothers. Adjusted odds ratio (OR) and 95% confidence intervals (CI) were estimated using multinomial logistic regression models.

**Results:** A total of 63 (12.5%) children experienced recurrent wheezing and 61 (12.4%) recurrent diagnosis of LRTIs. Elevated maternal CRP levels during pregnancy were related to age, parity, obesity before pregnancy, higher levels of IgE, and lack of physical activity. Children in the highest tertile of maternal CRP levels had an increased risk of experiencing recurrent wheezing (adjusted OR=2.87; 95% CI, 1.23-6.71) and being diagnosed with recurrent LRTIs (adj. OR=2.37; 95% CI, 1.01-5.55), as compared with children in the lowest tertile. Rs1205 polymorphism influenced maternal serum CRP levels but not the risk of wheezing or LRTIs in the offspring.

**Conclusion:** Increased CRP serum levels in pregnancy are associated with wheezing and LRTIs in offspring at early age. However, genetic variation in CRP influencing maternal serum levels is not related to these offspring phenotypes.

## T10.4.4

### Hyperemesis gravidarum: maternal characteristics and perinatal outcome in the Perinatal Registry Netherlands 2000 – 2006

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#### Abstract

*Objective:* To describe the characteristics of women and their infants who suffer from hyperemesis gravidarum in a large observational study of 1,199,218 pregnant women, and explore the independent effect of hyperemesis gravidarum on neonatal outcomes.

*Methods:* From the Perinatal Registry Netherlands, we selected all singleton pregnancies of at least 24 weeks without congenital anomalies in the years 2000 to 2006. We examined the characteristics of women who suffered from hyperemesis gravidarum (and were admitted to hospital for that reason) and their children.

*Results:* During the period 2000 – 2006 the percentage of women with hyperemesis gravidarum decreased in the Netherlands (from 0.15% to 0.10%). Women who suffered from hyperemesis gravidarum were younger, more often primiparous, of lower socio-economic status, more often of non-Western descent and had more often conceived through assisted reproduction techniques ( $p$  always  $< 0.001$ ). Also, they more often carried a female fetus.

Women who suffered from hyperemesis gravidarum more often delivered prematurely (9% vs 6%,  $p < 0.001$ ) and were more likely to have an adverse outcome (defined as SGA, NICU admission or death, 16% versus 11%,  $p < 0.001$ ). These differences were only partly explained by maternal characteristics (parity, ethnicity, duration of pregnancy).

*Conclusion:* Hyperemesis gravidarum is associated with an increased risk of adverse neonatal outcomes. Studies to examine the effectiveness of treatment for hyperemesis gravidarum are needed urgently.

## T10.4.5

### Association of C-reactive protein levels in early pregnancy with maternal blood pressure and the risks of hypertensive complications

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#### Abstract

*Objectives:* Hypertensive disorders are a major complication of pregnancy, constituting an important cause of maternal and foetal morbidity and mortality. Aim of this study was to investigate the association of high sensitivity C-reactive protein, as a marker of low grade inflammation, with maternal blood pressure development in pregnancy.

*Methods:* In 6,016 mothers participating in a population-based prospective cohort study in the Netherlands, we measured high sensitivity C-reactive protein levels in early pregnancy (median 13.2 weeks, 95% range 9.6 to 17.6). Maternal blood pressure measurements were performed in each trimester of pregnancy. Information on pregnancy induced hypertension and preeclampsia was retrieved from delivery records and detailed reviews of the hospital charts of the women.

*Results:* Multivariate linear regression models showed that compared to low maternal C-reactive protein (<2.5 mg/L), elevated levels (≥2.5 mg/L) were significantly associated with an increase in maternal systolic and diastolic blood pressure in every trimester of pregnancy. Elevated C-reactive protein levels in early pregnancy were also associated with the risks of pregnancy induced hypertension and preeclampsia. All associations attenuated after adjustment for maternal body mass index.

*Conclusions:* Elevated C-reactive protein levels in early pregnancy are associated with maternal blood pressure and the risks of hypertensive pregnancy complications, but these associations can largely be explained by maternal body mass index. Further studies are needed to explore the mechanisms underlying the associations of maternal body mass index, elevated C-reactive protein levels and blood pressure development during pregnancy.

## T10.5.1

### **Patterns of alcohol use among adolescents in the ALSPAC study, socioeconomic position and the role of prior substance use: a latent variable approach**

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#### **Abstract**

*Objective:* To investigate the different patterns of alcohol use among boys and girls at age fifteen in a birth cohort (ALSPAC, UK) and their associations with early measures of socioeconomic position (SEP) and prior substance use.

*Methods:* 2475 boys and 2771 girls attended a clinical assessment at age 15.5 years (5th-95th percentile: 15.2-16.3). Measures of alcohol included age at first drink, drinking occasions in the past six months, drinking five or more drinks on any single day (binge drinking) and experiencing any alcohol problems in the past two years. Socioeconomic position was assessed with the highest parental social class, maternal education at pregnancy and average household disposable income during the preschool period. The reported drinking habits constituted our primary outcomes and were further investigated by latent class analysis. The association between current patterns of alcohol use and multiple SEP indicators and the role of previous alcohol, tobacco and cannabis use were assessed in two-steps logistic regressions (generalized ordered logistic for latent classes). The influence of missing data was assessed by multiple imputation.

*Results:* Having drunk at or before age twelve and drinking twenty or more times in the past six months, were positively associated with increasing levels of income. Experiencing alcohol problems had an inverse relationship with social class. Latent class analysis suggested four groups in both boys and girls: "non drinkers", "infrequent drinkers", "moderate binge drinkers" and "heavy drinkers". Girls were more common in the infrequent drinking and moderate binge drinking groups. Adolescents in the highest quintile of income households were more likely to be in relatively higher drinking categories as compared to people in the lowest quintile (OR 1.23, 95%CI 1.02-1.49). Previous alcohol, tobacco and cannabis use were consistently more common in the heavier drinking groups and independently predicted the outcome. Adjustment for previous substance use did not alter the associations with SEP. Analysis after multiple imputation did not substantially alter the results.

*Conclusion:* There were similar patterns of alcohol use in boys and girls aged 15 in a British birth cohort. We found that boys and girls of higher income households were more likely to consume alcohol and to do so in different modalities. This might reflect the greater accessibility to alcohol in higher income households. Policies to tackle adolescent alcohol misuse should particularly focus on wealthier families and early substance use.

## T10.5.2

### **Alcohol consumption among 14-17 year olds and its relationship with other outcomes and behaviour**

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#### **Abstract**

*Objective:* To look at the prevalence and frequency of alcohol consumption among young people in England, as well as the characteristics of young people who drink to different frequencies and the relationship between alcohol consumption, other risky behaviours and educational outcomes at the age of 16.

*Methods:* Using a cohort of young people in English schools who had been followed from the age of 14 and interviewed annually, we used multilevel models to explore relationships between alcohol consumption and individual and school characteristics. We also used causal models to look at uptake and increased prevalence of alcohol consumption and other risky behaviours.

*Results:* We found a number of characteristics that were associated with having tried alcohol, including being female, white, non-religious and having been bullied in the previous year. Characteristics associated with not having tried alcohol included having a special educational need or disability, having unemployed parents and having a mother with no UK qualifications. In our causal models, we found links in both directions between trying alcohol and taking up or increasing frequency of other risky behaviours, including smoking, trying cannabis, truancy and criminal behaviour. However, the relationships where alcohol use preceded other risky behaviours tended to be stronger than those in the reverse direction. Finally, we found that drinking was associated with a greater likelihood of being NEET, leaving full-time education at 16 and having lower GCSE results. However, these relationships were largely explained by the links between drinking and other behaviours, especially truancy and being suspended from school, and by reduced educational aspirations, more negative attitudes to education and poor family cohesion among young people who had tried alcohol.

*Conclusions:* We have identified a number of groups of young people who may be particularly likely to try alcohol at a young age, as well as a number of possible negative consequences of this. Our causal models show that trying alcohol is strongly related to taking up other risky behaviours, but that after adjustment for other behaviours, attitudes and aspirations it does not seem to be the driver of negative educational outcomes.

## T10.5.3

### **Binge drinking in midlife as a risk factor for developing depression during 24 years of follow-up**

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#### **Abstract**

*Objective:* To examine the relationship between binge drinking at baseline and the onset of new depression during 24 years of follow-up after adjustment for age, socioeconomic status, education and marital status.

*Methods:* Data from phases 1 (1985-88) to 9 (2007-09) of the Whitehall II prospective cohort were used. The final sample consisted of a total of 5985 (male n=4161, female n=1824) British civil servants aged 35-55 years who were non-depressed at baseline. Cohort members were grouped, at phase 1, according to their self-reported usual and maximum number of drinks consumed in a single sitting – abstainers, non-bingers (reference category) and bingers. Alcohol consumption was divided into two categories and number of drinks consumed was converted to units for analysis: wine and spirits (1 unit per drink), and beer (2 units per drink). For usual drinking sessions those who reported consuming 5+ units of wine/spirits and 10+ units of beer were categorised as bingers, those consuming 1-4 units of wine/spirits or 1-9 units of beer were classified as non-bingers. For maximum drinking sessions, participants were defined as bingers following the Department of Health guidelines as those consuming 8+ or 6+ units of alcohol for males and females respectively for both categories of consumption. Those who reported consuming no drinks were classified as abstainers. Depression cases (scores  $\geq 4$ ) were identified using the depression subscale of the General Health Questionnaire.

*Results:* Adjusted Hazard Ratios (HR) and 95% Confidence Intervals (CI) were estimated using Cox proportional hazard models fitted in the total cohort and stratified by gender. Usual drinking session spirit/wine bingers had an increased risk of depression (HR 1.28, CI 1.02-1.60) compared to non-bingers in the total sample. Maximum drinking session spirit/wine bingers had a greater risk of depression in the total (HR 1.23, CI 1.04-1.44) and male (HR 1.27, CI 1.03-1.56) samples. There were no statistically significant effects when using beer exposures or for abstainers after adjustment for confounders.

*Conclusion:* Binge drinking on wine and spirits, but not beer, in midlife increases the risk of having a depressive episode over the course of the following 22-24 year period.

## **T10.5.4**

### **Predicting treatment demand in Cyprus for heroin and other narcotics**

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#### **Abstract**

*Objectives:* The primary objective of this study is to estimate the incidence (occurrence of new cases) of heroin and other narcotics treatment demand in Cyprus for a given year, based on data from previous years. A secondary objective is to examine the influence of covariates, such as gender, age at first use and route of administration, on latency period (temporal distance between first use and first treatment request).

*Methods:* The data are obtained from forms kept by all treatment centres in Cyprus and are updated every year to include all new cases. The data for the 2010 analysis come from the years 2003-2009. Based on latency period distribution, a back calculation – forward estimation procedure is used to obtain an estimate of incidence for the following year. Cox Regression is used to explore the influence of covariates on latency period.

*Results:* Statistical analysis for the year 2010 will be performed in September after all data will have been collected. The results are expected to be similar to those of 2009. For 2009, the estimate was 71 and it was found that being male increases latency time, the later one starts to use narcotics in one's life, the longer it takes until seeking treatment and the later in history (calendar year) one has sought treatment, the shorter one's latency period is. Route of drug administration (injecting or not) does not seem to matter.

*Conclusion:* Estimates have so far been conservative due to the incompleteness of the data. As data accumulate, estimates seem to become more valid.



## T10.6.1

### Lipid metabolism at age 16 years: association with maternal pre-pregnancy overweight and gestational diabetes mellitus

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#### Abstract

**Objective:** Foetal programming of disease is an established concept. Prenatal exposure to gestational diabetes (GDM) is a recognized risk factor for overweight and aberrant glucose metabolism. However, some recent studies, including our own, indicate maternal overweight as an essential determinant of these risks. Little is known on the effects of foetal programming on lipid metabolism in humans.

**Methods:** Data is based on the Northern Finland Birth Cohort 1986, including all children born in 1985-1986, in the two northernmost provinces of Finland, examined at the age of 16 years. The study population (n=4,168) was allocated in groups: Children of (1) normal-weight women with GDM (n=49); (2) overweight women with GDM (n=35); (3) normal-weight (n=503) and (4) overweight (n=154) women with risk factors for GDM, normal OGTT results; and (5) women with no risk factors for GDM (n=3,427). Lipido, epidemiologically validated software available at <http://www.computationalmedicine.fi/software>, was used to extract detailed information from the basic lipids. Statistical analyses were performed stratified by gender. The risk of dyslipidemia (values above/below the International Diabetes Federation paediatric, metabolic syndrome diagnostic criteria for triglyceride/HDL-cholesterol concentration) associated with maternal overweight and GDM was estimated using logistic regression analysis.

**Results:** Boys born to mothers with pre-pregnancy overweight had higher total and low-density lipoprotein cholesterol, and triglyceride concentrations than those born to normal weight mothers. They also had higher very low density lipoprotein triglyceride, intermediate density cholesterol and apolipoprotein B concentration, and total/high-density lipoprotein cholesterol ratio. In girls, study groups differed only in apolipoprotein B concentration. In boys, concomitant prenatal exposure to maternal overweight and GDM associated with increased risk for dyslipidemia (OR 2.0, 95% confidence interval 1.2 to 3.3). This risk persisted after adjustment for birth size, maternal education, paternal body mass index, and maternal and paternal smoking but attenuated after adjustment for current overweight. GDM per se did not associate with increased risk for dyslipidemia.

**Conclusion:** Differences between study groups in lipid metabolism were more evident in boys. Concomitant prenatal exposure to maternal overweight and GDM associated with elevated apolipoprotein B concentration in both genders, and may predispose boys to dyslipidemia already in adolescence.

## T10.6.2

### Farming environment and prevalence of atopy at age 31 – Prospective birth cohort study in Finland

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#### Abstract

*Objective:* Cross-sectional studies have shown an association between farming environment and decreased risk of atopic sensitization, mainly related to contact with farm animals in the childhood. Objective of our study was to investigate the association of farming environment, especially farm animal contact, during infancy, with atopic sensitization and allergic diseases at the age of 31.

*Methods:* In a prospective birth cohort study, 5509 subjects born in northern Finland in 1966 were followed up at the age of 31. Prenatal exposure to the farming environment was documented prior to or at birth. At age 31, information on health status and childhood exposure to pets was collected by questionnaire and skin prick tests were performed.

*Results:* Farm animal contact in infancy was associated with decreased risk of any atopic sensitization [odds ratio (OR) 0.67; 95% confidence interval (CI) 0.56-0.80], allergic eczema (OR 0.77; 95% CI 0.66-0.91), doctor-diagnosed asthma (OR 0.74; 95% CI 0.55-1.00) and also with allergic rhinitis (OR 0.87; 95% CI 0.73-1.03) and conjunctivitis (OR 0.86; 95% CI 0.72-1.02). There was a suggestion that reduced risk of allergic sensitization was particularly evident among the subjects whose mothers worked with farm animals during pregnancy, and that the reduced risk of above diseases by animal exposure was largely explained by reduced risk of atopy. Having cats and dogs in childhood revealed similar associations as farm animals with atopic sensitization.

*Conclusions:* Contact with farm animals in infancy reduces the risk of atopic sensitization, doctor-diagnosed asthma and allergic diseases at age 31.

## T10.6.3

### Association between symptoms of temporomandibular disorders and pain in other areas in young adults

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#### **Abstract**

*Objective:* Temporomandibular disorders (TMD) consist a number of clinical problems involving the masticatory muscles, the temporomandibular joint (TMJ) and associated structures. Studies have shown that especially myogenous TMD can be linked with other pain conditions in the body. The aim of the present study was to evaluate the association between TMD symptoms and pain reports in other areas in a large population sample of young adults.

*Methods:* The study was a part of the 31-year follow-up study of the Northern Finland Birth Cohort. Questionnaire information concerning TMD symptoms (facial pain, TMJ pain at jaw rest and on jaw movement, TMJ sounds and difficulties in mouth opening) and other pain conditions (neck-occipital pain, shoulder pain, lower back pain, sciatica pain) was collected from subsample of 5,696 subjects. The associations between TMD symptoms and other pain conditions were evaluated using chi-square tests. The effect of confounders was controlled in the multivariate analysis.

*Results:* Pain related TMD symptoms and TMJ sounds associated significantly with other pain conditions. On general, women had stronger associations than men. Among women, the strongest associations were found between neck-occipital pain and facial pain (OR 3.6, 95% CI 2.5-5.1), TMJ pain at jaw rest (OR 2.2, 95% CI 1.5-3.0) and TMJ pain on jaw movement (OR 2.5, 95% CI 1.8-3.6).

*Conclusion:* Pain related TMD symptoms associate with other pain conditions. Pain outside the facial area should be assessed in TMD patients and should be taken into account in the treatment scheme.

## **T10.6.4**

### **Adolescence risk factors for unemployment in early adulthood: A 16-year prospective follow-up study**

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#### **Abstract**

*Objectives:* The life-course approach emphasises the contribution of circumstances in childhood and youth to adult well-being. Regarding the adult disadvantage, there is still a lot to know of the social, health-related and economic predictors of unemployment, and the pathways leading from adolescence to early adult unemployment. The aims of the study were a) to examine the associations of various social, health-related and economic problems in adolescence (at 16 years of age) with unemployment at age 32 and b) to find out whether this association is mediated through the respondent's education and family formation paths.

*Methods:* In a 16-year follow-up of an urban Finnish community cohort (547 males and 714 females) from age 16 years, risk factors for unemployment and long-term unemployment were studied. Data were collected with a classroom questionnaire at 16 years and a postal questionnaire at 22 and 32 years. Logistic regression analysis was used as the main statistical tool.

*Results:* According to the preliminary results, there are several adolescence predictors of unemployment in early adulthood. The associations are partly mediated through the respondent's educational path.

*Conclusions:* Improving the living conditions of families with children is a necessary basis to prevent the unfortunate trajectories leading to early adult unemployment.

## P01

### Assessment of serum leptin and thyroid hormones levels in depressed women

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#### Abstract

*Objective:* There is substantial amount of evidence to suggest that alteration in some hormones is associated with depression and assess serum level of thyroid hormones and leptin in patients with depression.

*Methods:* In a case-control study a total of 62 patients with different degrees of depression and 69 healthy, age and sex matched control subjects were selected. The Beck Depression Inventory was used to classify the degree of depression into mild, moderate, and severe. Leptin, thyrotropin (TSH), thyroxine (T4), tri-iodothyronine (T3) were estimated using commercially available kits and Free T4 index was calculated.

*Results:* The leptin and T3 levels were found to be significantly decreased and T4 raised in the depressed women as compared to the healthy control ( $p < 0.05$ ,  $p < 0.001$ , and  $p < 0.001$  respectively). Furthermore, serum level of leptin was significantly lower and T4 was significantly higher in severe depressed women compared to moderate or mild depressed women ( $p < 0.001$  and  $p < 0.01$  respectively).

*Conclusion:* This study showed that thyroid and leptin hormones dysfunction among depressed women. Thus inclusion of thyroid and leptin screening test in depressed patients be needed in proper management schedules and this study of women will form a basis for further longitudinal observations.

## P02

### Maternal postpartum distress and childhood overweight

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#### Abstract

*Objective:* We investigated associations between maternal postpartum distress covering anxiety, depression and stress and childhood overweight.

*Methods:* We performed a prospective cohort study, including 21 121 mother-child-dyads from the Danish National Birth Cohort (DNBC). Maternal distress was measured 6 months postpartum by 9 items covering anxiety, depression and stress. Outcome was childhood overweight at 7-years-of age. Multiple logistic regression analyses were performed and information on maternal age, socioeconomic status, pre-pregnancy BMI, gestational weight gain, parity, smoking during pregnancy, paternal BMI, birth weight, gestational age at birth, sex, breastfeeding and finally infant weight at 5 and 12 month were included in the analyses.

*Results:* We found, that postpartum distress was not associated with childhood risk of overweight, OR 1.00, 95%CI [0.98-1.02]. Neither was anxiety, depression, or stress exposure, separately. There were no significant differences between the genders. Adjustment for potential confounders did not alter the results.

*Conclusion:* Maternal postpartum distress is apparently not an independent risk factor for childhood overweight at 7-years-of-age. However, we can confirm previous findings of perinatal determinants as high maternal pre-pregnancy BMI, and smoking during pregnancy being risk factors for childhood overweight.

**P03**

## **Childhood origins of adult chronic kidney disease**

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### **Abstract**

*Objective:* The purpose of this review was to find out how strong childhood influences were on the development of adult chronic kidney disease (CKD)

*Methods:* A medline search was conducted from 1980 to 2010.

*Results:* An unknown number of adult CKD has its origins not only in childhood, but also during intrauterine life. Insults to the growing kidney may be congenital, acquired, or combined. Some cases may be diagnosed early and progress to CKD during childhood, while others escape detection, only to present later in life as adult end stage renal disease (ESRD) of unknown etiology. The most common causes of ESRD in childhood are: i) Congenital anomalies of the kidney and urinary tract (CAKUT), and tubular, cystic, and other hereditary and metabolic nephropathies (CONGEN), and ii)

Acquired etiologies, which include acute kidney injury (AKI), that progressed to CKD. Causes of AKI include acute tubular, tubulointerstitial, glomerular, and vascular insults. Fetal programming (insults at a critical time of development) with resultant low birth weight and intrauterine growth retardation may have an influence on the development of adult CKD, and hypertension, as shown by human epidemiological studies and animal experiments. Fetal exposure to maternal low protein diet induced hypertension in adult rats. The mechanism appears to be multifactorial leading to abnormal handling of sodium in the kidney. Increased salt intake during childhood and adulthood maintains the rise in blood pressure.

*Conclusion:* Adult CKD may have its origins in childhood and intrauterine life. Reduced nephron endowment is an important red flag. An acquired renal insult superimposed on congenital decreased number of nephrons is more likely to result in long term renal sequelae. Future directions would be that by identifying high risk patients may help in halting or delaying the onset of end stage renal failure (ESRF).

## P04

### Self-reported oral health and health behaviour in young adults – an epidemiological study of the Northern Finland 1966 Birth Cohort

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#### Abstract

*Objectives:* The aim of the study was to evaluate the association between self-reported oral health and health behavior in young adults.

*Methods:* The sample of the study included subjects from the Northern Finland 1966 Birth Cohort. In 1997, the members of the cohort were sent a postal questionnaire and they were invited for a general health examination.

*Results:* The number of eligible replies was 8,690 and the response rate was 75.3%. Less than half (46%) of the respondents reported having good oral health; 35% reported dental caries lesions; 24% bleeding gums while tooth brushing and 16% tooth ache or other oral symptoms. Men reported poorer oral health than women ( $p < 0.001$ ). About half (54%) of the respondents reported brushing their teeth more than once a day; 42% used xylitol products almost daily or more often and 21% used sweetened soft drinks more than once a week. Mean body mass index (BMI) was 24.4 (SD 4.9) ( $n = 8,444$ ). The logistic regression analysis showed a statistically significant association between respondents' subjective oral health and their self-reported general health, amount of active physical exercise and level of education. The frequency of tooth brushing, drinking sweetened soft drinks and using xylitol products were associated with the oral health as well. Self-reported oral health improved when the BMI increased ( $p < 0.001$ ).

*Conclusion:* It can be concluded that only half of the young Finnish adults reported having good oral health. Oral health was associated with general health and health behavior including physical activity, tooth brushing and some dietary habits.



## P05

### A potential rat model for the impact of prenatal stress (food restriction) during pregnancy on striatal gene expression among adult offspring

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#### Abstract

*Objectives:* We set out to use a rat model to investigate the effects of prenatal exposure to nicotine on striatal gene expression patterns in adolescent offspring, while controlling for nutritional status using controls matched for dietary intake.

*Methods:* We used microarrays to investigate striatal mRNA profiles of adolescent Lister-hooded rats prenatally exposed to nicotine, compared to non-exposed controls and a group of pair-fed (PF) controls that were matched to the reduced dietary consumption found between the nicotine-exposed and non-exposed groups.

*Results:* There were no significant differences in gene expression profiles between the nicotine exposed and either of the two control groups. Specifically, there were no significant findings at an FDR q-value <0.1, although a number of genes were significantly differentially expressed when less stringent criteria were used. In contrast we found significant changes in multiple probe-sets between the PF compared to both the nicotine exposed and non-exposed controls. This included a large proportion of immediate early genes (IEGs) including, c-fos, fosb, arc and jun.

*Conclusions:* There appear to be no major direct effects of prenatal nicotine exposure on striatal gene expression during adolescence, in this model; although some interesting genes were identified with less stringent criteria, including Snord115, which encodes a small nucleolar RNA involved in HTR2C mRNA editing. We did however find significant findings in the comparison between the PF controls and the other two groups. Ingenuity Pathways Analysis revealed that these genes belong to a network of functionally related genes that may have relevance in stress responses. These data indicate the impact of the prenatal environment on offspring striatal gene expression during adolescence. More specifically, our data suggest that prenatal exposure to maternal stress resulting from food restriction leads to changes in baseline genetic expression patterns in adolescent offspring, potentially related to the stress response.

## P06

### Respiratory infections in McMaster University undergraduates: A cross-sectional survey and The McFlu Cohort Study

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#### Abstract

*Objectives:* Upper respiratory tract infections (URTI) and influenza-like illness (ILI) occur frequently in university students. We undertook a cross-sectional survey, followed by a cohort study, to measure respiratory illness and its sequelae.

*Methods:* We surveyed 1069 McMaster University students using a 1-page anonymous paper questionnaire to assess respiratory illness. Students living in residence were invited to enroll in the prospective McFlu cohort study involving weekly email-based surveys and self-collected nasal swabs for diagnosis, with 122 students participating. URTI was defined as cough, sore throat, or stuffy nose. ILI was defined as fever with cough or sore throat.

*Results:* Of 1069 survey participants, 596 (55.9%) were female with median age of 18 years (range: 17-32). Seasonal influenza vaccination in 2008/09 was reported by 289 (27.1%) and 436 (40.9%) indicated an intention to vaccinate against H1N1 upon availability. From weeks 37 to 40 (Sept-Oct 2009), URTI and ILI affected 332 (31.1%) and 42 (3.9%) students, respectively. Only 52 of 332 (15.7%) URTI affected students sought medical attention. Within the McFlu cohort study, vaccine coverage for seasonal and H1N1 influenza included 9 (7.4%) and 19 (15.6%) students as of week 4 (Jan 2010). In total, 167 cases of URTI and 22 cases of ILI affected 91.8% and 18.0% of the cohort sample from weeks 38 to 9. Viral infections were diagnosed in 49 of 95 unique submitted symptomatic swabs. Of 9 pandemic influenza A diagnoses, 6 presented as ILI while 3 presented without fever.

*Conclusions:* Respiratory infections were very common in the university population, but influenza A was uncommon despite low vaccination coverage for pandemic influenza.

**P07**

## **Changes in physical activity and ischemic heart disease in a Danish cohort**

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### **Abstract**

*Objectives:* Physical activity has a positive effect on health. Most studies documenting this association are based on a single measure of physical activity. However, the health effects of changes in physical activity are less studied. The aim of this study was to investigate the association between changes in leisure time physical activity and subsequent risk of ischemic heart disease.

*Methods:* In the longitudinal Copenhagen City Heart Study we examined the risk of ischemic heart disease after changes in physical activity among 3,408 men and 4,317 women who participated in health examinations carried out in 1976-78 and 1981-1983. Leisure time physical activity was measured by a self administered questionnaire. Information of ischemic heart disease was obtained from The Danish National Hospital Register updated until January 2009. Relative risks associated with changes in physical activity on the risk of ischemic heart disease were estimated by Cox regression analysis adjusting for potential confounding factors.

*Results:* 1,106 men and 1,040 women developed ischemic heart disease. The preliminary results showed that individuals who were physically active in leisure time at both examinations had the lowest risk of ischemic heart disease. . Physically active women who became inactive had a higher risk of ischemic heart disease compared to women who remained physically active (hazard ratio (HR)=1.27, 95% confidence interval (CI): 1.04-1.55). The same tendency was observed in men although not statistically significant.

*Conclusion:* Individual changes in physical activity were followed by changes in the risk of ischemic heart disease. Thus, this study strengthens the causal understanding of physical activity and cardiovascular health and thereby underlines the importance of a stable physically active life style.

**P08**

## **GLOMMS I – Longitudinal laboratory outcome, dialysis, mortality and morbidity at six years in a cohort with Chronic Kidney Disease**

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### **Abstract**

*Objective:* To investigate longitudinal outcome in a cohort labelled as having chronic kidney disease (CKD).

*Methods:* The GLOMMS I cohort consists of patients identified in 2003 with abnormal renal function tests (creatinine above 150micromol/l for males and 130micromol/l for women) and case note review to determine both the presence of CKD and baseline comorbidity. Follow up is complete to June 2009 (6 years). The dates of starting renal replacement therapy (RRT, dialysis or transplantation) or death were collected and event rates calculated. Data-linkage to the Scottish Morbidity Record (SMR01) has been undertaken to determine other important health events including myocardial infarction, revascularisation procedures and amputation. All creatinine measurements for this cohort since 2003 are available, and change in renal function over time is being mapped to identify whether long-term outcome can be predicted.

*Results:* Amongst 3430 individuals with CKD (1916 females, 1514 males), median age in 2003 was 78.5years. There was a high level of comorbidity, 40% had ischaemic heart disease, 17% congestive cardiac failure, 23% type 2 diabetes, and only 1.6% had no comorbidity at baseline. By follow up (June 2009), 2100 (61%) had died; those with a given comorbidity having higher mortality than those without. Age had an important effect on outcome. At follow up 171 (5%) had started RRT (77 had subsequently died). 1236 (36%) had neither died nor started dialysis at follow up. For these people currently not on RRT, data on progression of their renal disease is currently in preparation.

*Conclusions:* For a typically elderly cohort of patients with chronic kidney disease, after at least 6 years a significant number 1235 (36%) did not progress to starting RRT, or die. More knowledge of outcomes other than mortality and need for starting RRT is essential for appropriate patient management and service planning.

**P09**

## **Health and biomeasure data in Understanding Society**

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### **Abstract**

*Objective:* This paper will summarize the health measures for adults and youth from Understanding Society – the new UK Household Longitudinal Survey.

*Methods:* There are several varieties of health-related data. In the main or self-completed surveys, health data is collected from each adult in the household annually or in rotating modules. A self-completed youth questionnaire collects information about health status and health behaviours from youth aged 10-15 years. Nurse collection of objective biomeasures was recently introduced for adults successfully interviewed in Wave 2. Consents to link administrative health records have been requested.

*Results:* The paper will summarize health related data for adults and children. The battery of biosocial measures includes anthropometric measures, blood pressure, lung function, and the collection of whole blood through venipuncture. Data linkage will be used to examine health care use, diagnoses, and mortality. Descriptive results on self-reported health measures from the first wave will be presented.

*Conclusions:* The strength of the health data of Understanding Society stems from the ability to examine health in connection to other areas of social variation and in being able to examine individuals in the context of family, community and the larger social structure. Understanding Society is a useful data source for epidemiologists wishing to relate objective and subjective health measures to diverse social and psychological factors.

## P10

### Frailty impact on survival analysis in older Brazilians: a three year follow up survey in Sao Paulo, Brazil

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#### Abstract

**Objectives:** The number of Brazilian older adults is expected to grow dramatically over the next decades. By 2,025 they will be more than 30 million people, about 15% of Brazilian population. A large portion of this increase will occur in persons aged 80 and older were frailty in frequently observed. Frailty is an important health problem associated with high risk for adverse health outcomes including mortality, institutionalization, falls, decrease of functional capacity and hospitalization. Implications of these public health problem demand increasing attention, particularly because frailty has been documented as avoidable and, if installed, is reversible by active intervention strategies. In this study we will analyze the survival curve of older Brazilians (? 75 years) according frailty categories – not frail or robust, intermediate, frail – in a large, well-defined sample of older Brazilian in three years follow up.

**Methods:** Data comes from a longitudinal survey – SABE Study (Health, Well being and Aging). SABE began in 2000 with a sample that included population aged 60 and living in São Paulo/Brazil (n=2,143 from a multi stage clustered sampling). Frailty components (Fried's model) were not included at this wave. The second wave was done in 2006 (n= 1,115 re-interviewed) when the frailty analysis began. Frailty follow up were analyzed with data from four waves, two by phone and two by home visit, on 2008 and 2009. Survival analysis was done based on data of 2006 (687 very old people with 75 years and plus), up to 2009 (death analyses). Kaplan-Meier Survival Analysis was used to analyze the results considering frailty categories in baseline. Losses occurred during the follow-up where considered with the half time of the period. Cox proportional hazards model was tested using social demographic conditions (sex, income) and health conditions (cognitive decline, disability, self-perceived health).

**Results:** Of the 687 elders at baseline, there were 134 deaths and 116 follow-up losses. In survival analysis, the 3 strata (not frail, intermediate and frail) did not reach the median survival; only frail elders reached 25% survival time, with 17.2 months, so frail elders presented the worst prognosis. The hazard ratio for intermediate is 1.94 and 5.47 for frail, in relation to robust (p trend=0.000). The hazard adjusted model showed a hazard ratio 1.6 for pre-frail and 2.9 for frail (p<0.01; p trend=0.003).

**Conclusions:** Frailty is associated with mortality in Brazilian elders. Recognition of variables involved in frailty may help to perform active prevention and intervention actions and, consequently, maximize survival.

## P11

### Influence of breakfast habits on weight status and nutrient intake in adolescents

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#### Abstract

*Objective:* Skipping breakfast skipping is common, especially in adolescent girls, with increasing evidence linking breakfast consumption to body weight.

*Methods:* Data was available from 3321 individuals who completed 3-day diet records at both age 10 and 13-years participating in the Avon (UK) Longitudinal Study of Parents and Children. Only those who completed 3 complete diet records at both ages were included. Height and weight were measured during the research clinics. Breakfast skippers were defined as consuming less than 100kcal on average before 10am over 3 days. Individuals were grouped according to eating/not eating breakfast at each age (4 groups). Analyses were performed separately for sex; with primary outcomes being growth and nutrient intake.

*Results:* At age 13-years, skipping breakfast was almost 3 times higher than at 10-years for both sexes and more likely in girls (18%), than boys (9%). In boys, the eating/not eating group were shorter than other breakfast groups by 2cm at 10-years and 3cm at 13-years ( $p=0.004$ ). There was evidence of an independent association between breakfast consumption and waist circumference in girls, with a higher waist circumference in those not eating breakfast at 13-years (66.2cm (SE 0.55)) compared to those eating breakfast at both ages (64.4cm (SE 0.31)  $p=0.005$ ). However, breakfast eaters consumed, on average, more energy and macro-nutrients compared to breakfast skippers for both ages and sexes.

*Conclusion:* There was a different effect of breakfast skipping between girls and boys; boys were shorter and girls fatter in the eating/not eating group. Breakfast habits may be important in determining growth and weight status in adolescents.

## P12

### Impact of physical activity in pregnancy on BMI, waist circumference, and blood pressure in adult offspring

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#### Abstract

**Objectives:** It is well documented that physical activity (PA) has a protective effect on risk of metabolic syndrome and diabetes, and that gestational diabetes mellitus and metabolic syndrome in pregnancy increases the risk of obesity and metabolic syndrome in the offspring. To our knowledge, no previous human or animal studies have investigated the association between PA during pregnancy and the potential effects on offspring BMI and blood pressure. We hypothesize that PA during pregnancy reduces weight gain and risk of gestational diabetes mellitus, thereby protecting against the metabolic syndrome in the offspring. The objective of the project was to explore the potential association between PA during pregnancy and BMI and blood pressure (BP) in the 20y old offspring.

**Methods:** PA in mid-pregnancy was assessed by questionnaires among 965 women who delivered during 1988-1989. PA was assessed as PA at work and in leisure time and as participation in sport activities using established metabolic equivalent task (MET) scores and MET-hours. At the age of 20 years, 656 offspring completed a web-based questionnaire (information on anthropometry) and 443 participated in clinical examinations (blood pressure). Data were analysed using multivariable linear regression and analyses were adjusted for maternal smoking, height, BMI, parity and age.

**Results:** For work-related PA, 178, 235, 190, and 16 women were categorized 'Low', 'Low – moderate', 'Moderate – high', and 'High', respectively. For leisure-time PA, 186, 538, and 43 women were categorized 'Low', 'Moderate', and 'High', respectively. Around 20% of the women reported to participate in one, two or three sport activities for at least one hour pr. week. Offspring BMI, waist circumference, systolic BP, and diastolic BP [mean (st.d.)] were 22.0 (2.85) kg/m<sup>2</sup>, 80.9 (6.99) cm, 109.9 (10.63) mmHG, and 65.7 (6.70) mmHG, respectively. These outcomes did not differ statistically across various groups defined by PA measures, not even after adjusting for confounding variables, e.g., by maternal smoking or BMI.

**Conclusions:** There was no effect of PA in pregnancy on offspring BMI, waist circumference or blood pressure. Further studies are needed to explore the potential effect(s) of PA in pregnancy on other variables related to the metabolic syndrome.



## P13

### C-reactive protein levels in early pregnancy and the risks of fetal and maternal complications

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#### Abstract

**Objectives:** Low grade systemic maternal inflammation during pregnancy might adversely affect early placental development and subsequently lead to pregnancy complications. The objective of this study was to determine the associations of maternal C-reactive protein levels with foetal growth and the risks of pregnancy complications.

**Methods:** We examined the associations of maternal high-sensitivity C-reactive protein levels measured in early pregnancy (median 13.2 weeks, 95% range 9.6 to 17.6) with foetal growth measured by ultrasound in each trimester and the risks of pregnancy complications. We used data from 6,016 mothers participating in population-based prospective cohort study in the Netherlands.

**Results:** As compared to low maternal C-reactive protein levels (<2.5 mg/L), elevated levels (≥10 mg/L) were associated with smaller first trimester foetal crown to rump length (difference -0.76 mm, 95% confidence interval [CI] -1.33 to -0.18). Elevated maternal C-reactive protein levels were not associated with foetal head circumference, femur length or estimated weight in second and third trimester, but with smaller head circumference and lower weight at birth (differences compared to low levels -1.57 mm, 95% CI -2.94 to -0.21 and -66.30 grams, 95% CI -101.98 to -30.62, respectively). Mothers with elevated C-reactive protein levels in early pregnancy had increased risks of delivering preterm, low birth weight or small size for gestational age children (odds ratio 1.61, 95% CI 1.21 to 2.12, compared to low levels). After adjustment for body mass index, C-reactive protein levels were not associated with the risks of pregnancy induced hypertensive complications or gestational diabetes.

**Conclusions:** Elevated maternal C-reactive protein levels (≥10 mg/L) in early pregnancy were associated with early foetal growth restriction and increased risks of neonatal complications.

## **P14**

### **Preventive child health care in dialogue with data on developmental outcome. Understanding pathways of adaptation: MOMKNOWSBEST**

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#### **Abstract**

Our MOM cohort study aims to study the association between (early) signs of behavioural and developmental problems (at age 3, 4 and 5/6 years), and successful adaptation to (pre)school. The MOM study is part of a research programme in the field of Public Health Genomics.

Early (partial) drop out of education is associated with a decrease in social participation during adult life. Children with learning disabilities often also have behavioural, social and emotional problems. In general, Dutch preventive child health care guidelines are specific but are not sufficiently sensitive to detect psychosocial difficulties and, therefore, cannot judge the mental and physical fitness necessary for successful adaptation to school.

The possible continuation of childhood problems into adulthood argues for a prospective developmental approach. Therefore, our cohort study started in September 2009, and follows children from the age of 3 years to 5/6 years. Parents' concerns and determinants of child development are systematically elicited and addressed, taking into account the changing nature of development, risk and protective factors.

Information is obtained from parents, day-care, kindergarten, school and preventive health care professional settings in order to create health profiles. Outcome is measured by the degree of successful adaptation to (pre)school. The main screening instrument is the Parents' Evaluation of Developmental Status (PEDS), a parental report tool to facilitate ongoing developmental surveillance.

## P15

### Frailty in older Brazilians: determinants and evolution – a two year follow up survey in Sao Paulo, Brazil

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#### Abstract

**Objectives:** In Brazil, the aging process is frighteningly fast with important consequences for health services. Previous analyses have shown a high prevalence of frailty among Brazilian older population and it is considered an important issue in Public Health. The purpose of this study is to provide a systematic examination of frailty categories – no frail, pre-frail, frail – in a well-defined sample of older Brazilian adults in 2006, an evolution of this condition and their adverse outcomes in two year follow up.

**Methods:** Data comes from two rounds of a longitudinal survey – SABE Study (Health, Well being and Aging). SABE began in 2000 with a sample that included population aged 60 and plus living in São Paulo/Brazil (n=2,143 from a multi stage clustered sampling). Frailty components (Fried's model) were not included at this wave. The second wave was done in 2006 (n= 1,115 re-interviewed) when the frailty follow up began. Frailty follow up was analyzed with data from four waves, two by phone and two by home visit on 2008 and 2009, only with very old persons (? 75 years, n=687). Frailty determinants and adverse outcomes were analyzed in this study using data from 2006 and 2008. Variables analyzed were: social demographic and health conditions. Descriptive statistics included tests for associations using Rao Scott procedure with correction for sample-design. Multi variable analysis was done by adjusting logistic regressions with robust estimation.

**Results:** In 2006, frailty prevalence among very old people was 48.8% pre-frail and 14.0% frail. After two years, the prevalence changed to 46.3% pre-frail and 35.1% frail. Univariate analysis of frailty determinants indicated association with cognitive decline (p<0,030), comorbidities (p=0.008), disability (p=0.001) and self perceived health (p=0.000). Adverse outcomes associated with frailty were hospitalization (OR=5.5; p=0.040) and disability (OR=6.0; p=0.021). Multiple logistic regression (adjusted for sex, education, comorbidities and cognitive decline) showed association with disability (OR=6.2; p=0.024) and self perceived health as regular or poor (OR=3.9; p=0,003).

**Conclusions:** Frailty is an important health problem associated with high risk for adverse health outcomes. Public policies should take into account the specific needs of the elderly population with high risk to develop frailty.

## P16

### The 11-year follow-up of the CCC2000 birth cohort study: Developmental pathways of psychopathology and identification of 'at risk' mental states in children

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#### Abstract

*Objectives:* The natural history of mental health disorders in childhood is still largely uncovered. There is a lack of data on early developmental psychopathology in unselected populations, which leaves a missing link in the current understanding of how, when and why psychopathology develops early in life. The Copenhagen Child Cohort CCC 2000 was established in Denmark in year 2000 to study developmental pathways of mental disorders prospectively from birth in a general population. Results from investigations of the CCC 2000 at child age 0-10 months, 1? years and 5-7 years have provided new knowledge on mental health and psychopathology in the first 7 years of life, and with the coming 11-year follow-up study (CC11) we will expand this knowledge to an age where neuro-developmental disorders are manifest and where early symptoms of adolescent psychopathology appear. The aim of this study is: i) to describe prevalence, comorbidity, and early life determinants of mental health disorders in pre-puberty, ii) to describe developmental pathways from birth regarding 1) Attention Deficit Hyperactivity Disorder (ADHD), 2) psychosis-like symptoms, 3) functional somatic symptoms and health anxiety, and 4) eating behaviours and eating disorders and iii) to characterize early 'at risk' mental states based on early signs and symptoms and associated risk factors.

*Methods:* The CCC2000 birth cohort, which consists of 6090 children born in the area of Copenhagen, Denmark in 2000, will be investigated again at age 11 years in 2011. The key measures of the CC11 study are questionnaires filled in electronically by child, parent and teacher. The general psychopathology will be assessed by Strength and Difficulties Questionnaire (SDQ) and Development and Well Being Assessment (DAWBA), which were both used in the 5-7 year follow-up. Functional somatic symptoms and eating behaviours will be assessed by Children's Somatization Inventory (CSI-24), Childhood Illness Attitude Scales (CIA), Childhood Eating Assessment Questionnaire (CEAQ), The Eating Pattern Inventory for Children (EPI-C), Children's figure rating scale and Mc Knight Risk Factor Interview. Additionally, a hands-on health examination will be carried out at the school and there will be a case-control study on cognition. Finally, the database will link to several Danish registers.

*Results:* Data analyses and presentation of the first results will take place in 2012-2013.

## P17

### How should changes in measurements over time be handled?

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#### Abstract

*Objective:* Sometimes measurements have to be changed over time in longitudinal research, either due to cheer improvement, new knowledge gained, or practical circumstances. Due to space restrictions, all instruments of interest can sometimes not be included at each time point. These circumstances raise the issue of how to handle data in longitudinal analyses. The current aim was to investigate what happened to the mean values of the Swedish Parenting Stress Questionnaire (SPSQ) when it had to be shortened at later follow-ups.

*Methods:* All parents to be during 1997-99 were invited to participate in the population-based prospective longitudinal ABIS-study (All Babies In southeast Sweden). ABIS aims to investigate the associations between different factors (genetic, environmental, nutritional, demographic, and stress) and poor child health (esp. type 1 diabetes, obesity, and allergy). Questionnaire data and biological samples have been collected at child birth, and at age 1, 2, 5, and 8. ABIS is an extensive study trying to cover different areas, which means comprehensive questionnaires where different interests compete. Due to space restriction, some stress instruments has only been used at one time points and others (such as the Swedish version of the parenting stress index) have been shortened with time. At age 1 and age 2 parenting stress was assessed with the full 34-item version of the SPSQ, and at age 5 and age 8 with 23 of the 34 items, excluding the dimensions for social isolation and health.

*Results:* Correlations between means based on 34 and 23 items at age 1 and age 2, respectively, were significant, age 1 and age 2:  $r = .96$ ,  $p < .001$ , but means based on 23 items were higher, age 1: mean difference =  $.15$ ,  $t(10736) = 75.8$ ,  $p < .001$ , and age 2: mean difference =  $.14$ ,  $t(8641) = 64.3$ ,  $p < .001$ . Correlations for parenting stress based on 34 or 23 items did not change between follow-ups.

*Conclusion:* A shorter version of the SPSQ could be used. However, it is important to discuss whether to stick to the original measurements in order to ensure methodological consistency or allowing measurements to change over time.

P18

## Socio-economic position and prognostic factors of non-Hodgkin lymphoma

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### Abstract

*Objective:* There seems to be social inequality in survival in most cancers, with most deprived patients having the worst prognosis. Few studies have documented also such inequalities in survival in non-Hodgkin lymphoma (NHL) patients. As the survival of NHL patients strongly depends on a range of prognostic factors, like stage at diagnosis and performance status, the association between these prognostic factors and socioeconomic position (SEP) is of particular relevance in order to explain social differences in prognosis.

*Methods:* The data were derived from a nationwide clinical database of NHL patients diagnosed in Denmark in 2000-2008. These data were linked to data from several central registries providing information on highest attained education, cohabiting status, and income, as well as comorbidity from previous hospitalizations. A total of 6,234 patients were included in the study. Multivariate logistic regression models were used to analyse the association between socioeconomic factors and comorbidity, and a range of prognostic factors; namely three indicators with relation to the progression of the disease; the Ann Arbor stage, the presence of extranodal involvement of the cancer, and elevated levels of lactate dehydrogenase (LDH), two indicators more closely related to the general condition and the symptoms of the patient; the Cooperative Oncology Group performance status and the presence of b-symptoms (fever, night sweats, weight loss), and one composite measure The International Prognostic Index (IPI).

*Results:* The risk of being diagnosed with advanced disease, as expressed by six prognostic markers, increased with decreasing level of education, and in patients living alone. For instance, patients with a higher education had an odds of being diagnosed with advanced stage of 0.85 (0.74-0.99), and an odds of having elevated levels of LDH of 0.83 (0.74-0.93), as compared to those with short education. This difference in risk seemed not to be mediated by differences in histological subgroups reflecting aggressiveness of disease among the social groups. Also, men were diagnosed with more advanced disease compared to women.

*Conclusions:* Low levels of education are associated with a higher risk of having advanced disease at the time of diagnosis. Possible explanations include patients' awareness of their symptoms, an appropriate health behaviour (i.e. visiting the general practitioner for relevant symptoms), and good communication with health staff, which might be more predominant among higher education.

**P19**

## **Anxiety disorders and quality of life over the life span**

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### **Abstract**

*Objectives:* European epidemiological studies have shown a concerning amount of anxiety disorders within the general population. The prevalence of anxiety disorders is related to quality of life, which are both, reported at different levels over the life span. The present study measures the prevalence and correlates of anxiety disorders in Cyprus within the general population, a community sample and a sample of University students from the University of Cyprus. This study also looks at the relationship between anxiety disorders and quality of life in different age cohorts.

*Methods:* The sample consists of Cypriot adults (18 to 65 years), 229 from the general population selected through stratified random sampling, 60 from the community who presented themselves as volunteers, and 342 students from the University of Cyprus. Participants were asked to complete a packet of questionnaires, including Greek versions of the Anxiety Sensitivity Index (ASI), the Perceived Stress Scale (PSS), the Fear Survey Schedule (FSS) and the World Health Organization's Quality of Life Questionnaire (WHO-QOL-BREF). The presence of other forms of psychopathology was screened using an adapted paper version of the Psychiatric Diagnostic Screening Questionnaire (PDSQ).

*Results:* Questionnaires have been analyzed for 631 participants (448 women, 183 men,  $M_{age} = 30.58$ ). Anxiety symptoms are frequently reported at similar levels for both men and women across the ages, although contextual differences abound, with women reporting more symptoms of panic and men reporting more symptoms of paranoia. Quality of Life is negatively correlated with age, however, this relationship becomes null when we separate age into cohorts. Age cohort does, however, reveal a significant negative relationship with Social Phobia, which is consistent with findings that Social Phobia tends to be more frequent among younger ages.

*Conclusions:* These initial results indicate that although the prevalence of anxiety disorders seems high, life span correlates such as age, age cohort and Quality of Life provide contextual information that is important for intervention and the development of a theoretical framework for dealing with anxiety. These initial results should be interpreted with caution due to the uneven sex distribution.

## P20

### Non-shared environmental effects of birth weight on ADHD symptoms persist into early adolescence. A 10-year longitudinal twin study

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#### Abstract

*Objective:* Markers of poor fetal development, especially low birth weight, have been associated with attention-deficit hyperactivity disorder (ADHD). However, genetic factors may underlie this association. This study examined whether birth weight was associated with ADHD symptoms using a monozygotic twin differences design to isolate non-shared environmental influences from genetic and shared environmental factors.

*Methods:* ADHD symptoms in up to 5,000 twin pairs from the U.K. population-representative Twins Early Development Study were rated by parents (ages: 2, 3, 4, 7, 8, 9, 12 years) and teachers (ages: 7, 9, 12 years). Twin birth weight was obtained via parent report when the twins were 18-24 months old.

*Results:* Birth weight and ADHD symptoms were negatively associated. Within MZ pair comparisons revealed that the lighter twin in a pair had, on average, more ADHD symptoms than the heavier co-twin, suggesting that the association between birth weight and ADHD symptoms was non-shared environmentally mediated. Neither gestational age, gender, nor socio-economic status, moderated this non-shared environmental association. Effect sizes were generally stronger for more discordant twins and for parent than teacher rated ADHD symptoms. Although effect sizes were small, the magnitude of the associations was consistent over a 10-year period spanning ages 2 to 12 years.

*Conclusions:* Results suggest that birth weight is a non-shared environmental risk factor for ADHD symptoms with persistent impact across development.



## P21

### Comparison of predispositional factors of chronic illnesses of deterioration in all age groups (2-102 years of age). Osteoporosis an underhanded enemy

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#### Abstract

*Objective:* the scope of the present study was the exploration of factors which predispose persons to chronic diseases of deterioration in all age groups. Children 3-10 years of age, adults 20-60 years of age and elderly people above 60 years of age were studied.

Anthropometric measurements (weight, height, waist circumference, BMI), arterial blood pressure, 3-day food diary and measurement of osteoporosis with ultrasounds were taken.

*Results:* the results of the study indicate that there is a steady increase in the number of overweight and obese persons with increasing age, ranging from 22.2% in kindergarten to 39.8% in primary schools, to 50% in the adult population and 82% in the elderly. As far as waist circumference is concerned, this was found to be high in 29% of girls and 25.7% of boys in kindergarten and 23.6% of children, both boys and girls, in primary school. In adults an increased waist circumference  $WC > 98\text{cm}$  was found in 35% of men and  $WC > 85$  was found in 37% of women. In the elderly, the percentages with a high WC were 70% for men and 92% for women.

With regards to systolic arterial pressure (SAP) 10% of kindergarten children have high SAP and in primary schools 13.6% have high SAP. In adults  $SAP > 135\text{mm Hg}$  was 32% and in the elderly  $SAP > 135\text{mm Hg}$  was 64%. Diastolic arterial pressure (DAP) was increased in 23.9% of children in kindergarten and 11.5% in primary school children. Adults with  $DAP > 85\text{mm Hg}$  was 20% and in the elderly 25%.

The dietary habits of children showed an increased consumption of fats, simple sugars, salt, and a decreased intake of vitamins A, C, trace-elements Fe, Ca, Mg, Se, natural fibers and omega3 polyunsaturated fatty acids.

Adults consume above normal levels of fat, simple sugars, too much salt, and few natural fibers, fruit and omega3 fatty acids. They do not eat enough fish, fruit, vegetables but over-consume meat, cold meats, sweets and salty foods. They do not follow the traditional Mediterranean diet that we have inherited.

Osteoporosis was studied by way of echo measurement of bone density in the heel of the foot. It was found that at the ankle, a considerable number of people have an increased risk for bone fracture, especially women. 37.2% of females 20-60 years of age have an increased danger for fractures and 5.2% have a very high risk for bone fractures. Elderly men above 60 years of age, 50% have a high risk for fractures and 15% a very high risk. For elderly females above 60 years of age, the corresponding results are 71% and 16% accordingly.

*Conclusions:* The factors which predispose people to chronic diseases can be detected from childhood and become worse in adult life and worsen still more by old age.

Prevention is fundamental for the preservation of good standards of health and should begin from the endometrial-infantile age. Nutrition has stopped being Mediterranean and has become the western type unhealthy diet. Furthermore, a significant number of middle-aged women have the tendency for or already suffer from osteoporosis; by old age both men and women are at high risks.

## P22

### Maternal fish consumption, foetal growth and the risks of neonatal complications. The Generation R Study

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#### Abstract

*Objectives:* Maternal fish consumption during pregnancy is suggested to affect birth outcomes, yet results remain contradictory. Previous studies mainly focused on birth outcomes and did not study foetal growth during pregnancy.

*Methods:* In a prospective cohort study from early pregnancy onwards in the Netherlands, we assessed the associations of maternal total, lean, fatty and shellfish intake in early pregnancy with foetal growth characteristics in second and third trimester and the risk of neonatal complications encompassing preterm birth, low birth weight, and being small for gestational age at birth. In total, 3,398 pregnant women were enrolled and completed a 293-items semi quantitative food frequency questionnaire to obtain information about fish consumption during early pregnancy. Head circumference, femur length and foetal weight were estimated in the second and third trimester by ultrasound. Information about neonatal complications was available from hospital and midwife registries.

*Results:* Maternal characteristics associated with high levels of fish consumption include a higher average age, higher level of education, and are more frequently non-smoking and user of folic acid during pregnancy ( $P < 0.001$ ). We observed no associations between maternal total fish consumption or specific consumption of lean fish, fatty fish or shellfish and foetal growth characteristics in second and third trimester. Likewise, total fish consumption or specific consumption of any type of fish was not associated with the risk of neonatal complications.

*Conclusions:* These findings show that in a population which is relatively low in exposure to fish consumption, consumption of lean, fatty or shellfish in early pregnancy is not associated with foetal growth or with the risks of neonatal complications.

## P23

### Automated segmentation of the hippocampus in The Disconnected Mind Study: Preliminary findings

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#### Abstract

*Objective:* Assessing atrophy of the hippocampus as a potential biomarker for neurodegenerative disorders such as Alzheimer's disease can be achieved through MRI, but it is also important to look at normal changes to whole and regional brain structures, to more fully understand and evaluate subtle age-related changes.

The usual method of assessing hippocampal volume is to manually delineate the hippocampus in a T1-weighted MRI, which is time consuming making it inefficient for large scale studies. Automated methods are often faster and reduce human error but have not been reliably applied to ageing brains.

*Methods:* A sample of 32 participants MR scans from the LBC 1936 cohort, chosen to represent a range of atrophy, underwent segmentation of the hippocampus using FSL\_FIRST: a freely available automated software developed by the FMRI group at the University of Oxford. We used a shape modelling tool that utilises the Montreal Neurological Institute 152 (MNI) brain template to segment structures. This template was derived from a sample of young healthy adults. As it was not considered representative of the changes that occur in healthy ageing, such as enlarged ventricles and white matter lesions, a template derived from an ageing cohort of 65-70 yr old men was also applied to the sample. The results were visually assessed independently by two experienced radiologists.

*Results:* 14 of 64 hippocampi were delineated with a high degree of accuracy (22%), with significant errors found in 12 (19%) for both templates. The errors were localised in the posterior and anterior boundaries, where the method seemed to over-estimate the size of the hippocampus, though commonly omitted to include the uncinata process. The segmentation visually improved when the template derived from an ageing cohort was used.

*Conclusion:* FSL\_FIRST did not perform a reliable segmentation of the hippocampus. Improving the registration process by using non-linear methods and an improved hippocampal mask from a template based on older individuals may improve the accuracy of the technique, which could then be confidently used in place of manual segmentation.

## P24

### Trajectories of psychosomatic symptoms from adolescence to adulthood

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#### Abstract

*Objectives:* The aim of the study is to investigate the trajectories of psychosomatic symptoms from adolescence to adulthood in a cohort of Finnish school children over a period of 16 years.

*Methods:* The original study population included all ninth-grade pupils attending secondary school in 1983 in Tampere, Finland (n=2269). They were studied at 16, 22 and 32 years of age by self-administered questionnaires. The psychosomatic symptoms scale covered 17 somatic and mental complaints. The symptom profiles were modelled as linear latent growth curve models, allowing both the intercepts and slopes of the profile curves to vary individually.

*Results:* The mean profiles of psychosomatic symptom scores of both sexes were increasing by age. The symptom scores were constantly higher for females than for males but the growth patterns were different; in males, the mean symptom level was slightly decreasing by the age of 22, following then a sharper incline than in females, for whom the mean symptom level was increasing more by the age of 22 than by the age of 32. There was also considerable variability in the growth profiles between the individuals. The baseline effect was negative; the higher the initial symptom level, the lower the subsequent symptom level both for mental and somatic symptoms. We divided the individuals to groups according to the baseline symptoms scores ("low-scorers") and ("high-scorers") at age 16. The profiles in the high-scorers show a decline by age 22 for both sexes, more clearly for males, whereas in the low-scorers the symptom pattern is increasing throughout the follow-up. Between the sexes, the largest difference in reporting psychosomatic symptoms is in early adulthood (age 22) and although the mean symptom levels increase in both sexes, the differences attenuate in both low-scorers and high-scorers.

*Conclusions:* The variability in the growth patterns in psychosomatic symptoms seemed to be large not only among the sexes but also among individuals in general.

**P25**

## **The impact of stress on semen quality**

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### **Abstract**

*Objective:* Stress is one the most important health and social problems. Psychological stress has long been suspected as having important impact on infertility. Studies on the effects of psychological stress on male fertility, especially semen quality have so far yielded equivocal findings.

*Methods:* The study population consists of 179 men register to infertility clinic in purpose of diagnosis with normal fertility (semen total concentration 15-300 mln/ml) or with little oligozoospermia (semen total concentration 10 do 15 mln/ml).

The semen samples was analysed in one laboratory according to the WHO manual for basic semen analysis. The main semen parameters were assessed: volume, motility, % atypical, % of progressive spermatozoa.

To asses the occupational stress the General Health Questionnaire 28 (GHQ-28) was used. As a results of this questionnaire we used sum of the points obtain by man taking part in the study and the number of stressful events at work (if the stressful events or situation appeared) announced by studied subjects.

*Results:* The level of stress measured by General Health Questionnaire 28 (GHQ-28) taking into account the number of stressful events, such situations affect semen volume and % of progressive spermatozoa after controlling factor that can have impact on semen quality like: time of couple infertility, abstinence and diseases in the past that can affect fertility.

*Conclusion:* The study confirms that occupational stress can affect male semen quality, but as there are few studies in those directions the results need to be confirmed. The cohort assembled for this study will form a basis for further longitudinal observations.

P26

## Work during pregnancy based on prospective cohort study in Lodz region

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### Abstract

*Objective:* Maternal work during pregnancy, especially with high work-related physical exertion, is still considered one of the most prevalent risk factors of negative pregnancy outcome. Heavy work is thought to reduce the blood volume available to the fetus and, consequently, the amount of oxygen and nutrients. The aim of the study was to evaluate the work during pregnancy based on prospective cohort study in Lodz region.

*Methods:* The study population consisted of 203 women (16-45 years old) before 22 weeks of pregnancy recruited in 7 Maternity Units in Lodz. The women were interviewed three times during pregnancy (interview A, B, C) and one after delivery (interview D) to evaluate the pregnancy outcome. The cohort was established in years 2006-2008.

*Results:* 70% of studied women work before pregnancy. About 17,8 % of study population were unemployed and it was about 68% not working women. Most of pregnant women quit work about 9 week of pregnancy (50%). Quite big group of pregnant women quit work about 23 week of pregnancy (22% of working women). Mostly at the beginning of pregnancy quit work women working in production sector, shop assistants and seamstresses than women working in the office. About 15 week of pregnancy quit work 73% women working in production sector, and about 54% shop assistants and 56% seamstresses and 33% women working in the office. When women's work was associated with lifting heavy objects (> 5kg) they earlier quit work.

*Conclusions:* On one hand we can assume that women during pregnancy know about hazards associated with some type of work and in early pregnancy quit work. On the other hand the ideal situation will be when women can change their work position on safer during pregnancy. This cohort of mothers being assembled will form a basis for further longitudinal observations.

**P27**

## **Prevalence of obesity and its effective agents in women of childbearing age**

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### **Abstract**

*Objectives:* An epidemic of obesity is taking place in the world. This important hygienic problem is the risk factor of some diseases. For determination of obesity risk factors, estimation of odds ratio (OR) through a logistic regression is usual. The purpose of this study is to determine the prevalence of obesity and its risk factors in rural women. In spite of the importance of the matter, a few studies have been done in the rural areas.

*Methods:* Through a cross-sectional study in 2009, 920 women in childbearing age from rural areas of Fars province were selected by random-multi stage sampling. The relationship between BMI and explanatory variables of interest including years of education of woman and her husband, number of children, age of woman and her husband, socio-economic status and mean duration of breast feeding for each child was checked by calculating odds ratio, using the logistic regression approach. Over-weight or obesity was defined as BMI of 25 or higher and data were analyzed using SPSS13.

*Results:* In this study all studied women aged 17-47 years old and the prevalence of over-weight ( $25 < \text{BMI} < 30$ ) and obesity ( $\text{BMI} \geq 30$ ) was respectively 30% and 14%. A significant association was found among husbands education, number of children, socio-economic status and increasing risk of obesity (P-VALUE  $< 0.05$ ).

*Conclusion:* Because of high prevalence of obesity in rural areas (similar to urban areas) and its side effects on health, this study of women will form a basis for further longitudinal studies and prevention and controlling of obesity should be in the priority of health programs.

## P28

### **Association of in utero exposure to glucocorticoids on birth size: a systematic review**

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#### **Abstract**

*Objective:* Synthetic glucocorticoids are routinely used in threatened preterm delivery for stimulating foetal lung maturation. Animal studies have reported reductions in birth weight in offspring exposed to glucocorticoids in utero. With smaller birth size being associated to diseases in adulthood, a systematic review was undertaken to evaluate current literature on human studies examining the associating of in utero exposure to glucocorticoids on birth size (i.e. birth weight, birth length, head circumference, ponderal index).

*Methods:* Inclusion/exclusion criteria and key search words were decided a priori. A checklist designed for observational studies by Tooth et al was chosen to evaluate the quality of the studies. To make the comparison more stringent and specific to the outcome of interest, a second checklist (the DAC score) was created by the authors to examine specific quality differences between the studies in relation to the outcome of interest. A literature search was performed using Medline, EMBASE, PubMed, Cochrane, Google scholar and Institute of Life Science databases, for studies published between 1978 and 2009. Bibliographies of studies chosen were checked.

*Results:* Of 1,101 studies found seventeen met the inclusion criteria. The average DAC score for birth weight was 7.5, head circumference 8.5 and birth length 7.5. Of the seventeen studies examining birth weight, nine reported a reduction in birth weight (12g - 332g); five of these scored above average with three attaining the highest scoring. Five out of nine studies reported a reduction in head circumference (0.31-1.02 cm); with one being the highest scoring study (DAC 22). Two of four studies reported a reduction in birth length (0.8cm) (DAC 9 and 10).

*Conclusion:* The methodological inconsistencies made a quantitative analysis such as meta-analysis or even a weighted means impossible. Due to the limitations and low quality of the studies a firm conclusion cannot be drawn. The evidence suggests an association between in utero exposure to glucocorticoids and a reduction in birth size, however further studies are indicated.



**P29**

## **The Jyväskylä Longitudinal Study of Personality and Social Development: Midlife development**

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### **Abstract**

The JYLS was started in 1968 by Lea Pulkkinen with a random sample of 369 (53% males) second-grade school children in the town of Jyväskylä, Finland. Since then, the originally eight-year-old (born 1959) participants have been followed at ages 14, 20, 27, 36, 42, and 50 (in 2009). The study is specific in terms of its long duration, low attrition rate, and participants' representativeness. The main methods of data collection include teacher ratings and peer nominations in childhood and adolescence and psychological interviews, self-reports, and medical examinations in adulthood. Furthermore, registered information has been collected over the years. The main areas of study have been psychological functioning (e.g., socio-emotional behavior, personality, well-being), social functioning (e.g., education, work, adjustment to society), family life (e.g., own family and family of origin), and health (e.g., health behavior, subjective and objective measures of health). Their developmental continuity from mid-childhood to mid-adulthood as well as their mutual links have been examined. Also risk and protective factors have been of interest. Considering that the participants have faced midlife, the particular focus of the research group is on midlife development which is not well understood in the previous literature. Areas of study include personality adjustment vs. growth, work ability and plans for retirement, caring roles, and health issues. Particular attention is paid, first, in studying associations between these different areas and, second, using a lifespan perspective.

## P30

### **Need for treatment during a 5-year follow-up among patients receiving short- or long-term psychotherapy**

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#### **Abstract**

*Objectives:* Need for treatment is a scarcely used measure of effectiveness in psychotherapy trials. It is, however, a good measure of public health importance of the disorder considered. This study aims to consider changes in need for auxiliary psychiatric treatment after starting short and long-term psychotherapy.

*Methods:* A total of 326 psychiatric outpatients, with mood or anxiety disorder were randomly assigned to solution-focused therapy (SFT), short-term psychodynamic psychotherapy (SPP), or long-term psychodynamic psychotherapy (LPP). The patients were followed for use of auxiliary treatment during a 5-year follow-up from start of treatment. Primary outcome measures were use of psychotherapy and psychotropic medication and hospitalization due to psychiatric reasons.

*Results:* About 60% of the patients used auxiliary treatment during follow-up. Auxiliary treatment was most common in the brief therapy groups and the incidence of auxiliary treatment was highest during the first year after start of therapy. The average number of all therapy sessions among patients starting the therapy were 60, 70, and 240 in SFT, SPP, and LPP, respectively, whereas the average number of therapy sessions given according to study protocol (study treatment) were 10 in the SFT, 19 in the SPP, and 232 in the LPP group. More than 50% of the patients receiving short-term therapy received in average 5 times more therapy sessions than given as study treatment.

*Conclusion:* Auxiliary treatment might be usual especially among patients receiving short-term therapies. It is of importance to consider auxiliary treatment when interpreting results of therapy effectiveness studies.

## P31

### The relative importance of modifiable risk factors of type 2 diabetes in high- and low-risk populations: meta-analysis of two cohort studies

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#### Abstract

**Objective:** Lifestyle factors predict occurrence of type 2 diabetes, but their effect in high- and low-risk populations is poorly known. The presence of the metabolic syndrome helps to identify individuals at high risk for type 2 diabetes. This study determines the prediction and relative importance of lifestyle factors on type 2 diabetes incidence in those with and without metabolic syndrome using a new Population Attributable Fraction measure, which indicates the proportion of cases attributable to a given exposure.

**Methods:** Two representative Finnish cohorts, the Mini-Finland Health Survey (MFH) collected in 1978-1980 and the Health 2000 Survey collected in 2000-2001, including altogether 8,627 men and women, aged 40-79 years, and free of diabetes and cardiovascular disease at baseline were pooled. A low-risk lifestyle was defined as a body mass index (BMI) < 25.0 kg/m<sup>2</sup>, occasional or regular exercise, moderate alcohol consumption, not smoking, and serum vitamin D level above median. The metabolic syndrome was defined according to the International Diabetes Federation criteria including obesity, blood pressure, serum HDL cholesterol, serum triglycerides, and fasting glucose. During a maximum 10-year follow-up, altogether 226 type 2 diabetes cases occurred. Adjusted study-specific and pooled relative risks (RR) and Population Attributable Fractions (PAF) for lifestyle factors and components of metabolic syndrome were estimated. Possible modification by metabolic syndrome on the prediction of the lifestyle factors on type 2 diabetes incidence was studied.

**Results:** Overweight was the strongest predictor of type 2 diabetes (PAF = 77%, 95% confidence interval (CI): 53%, 88%). Together with lack of exercise, unsatisfactory alcohol consumption, smoking, and low vitamin D level it explained 82% of the cases. Altogether 62% (CI: 47%, 73%) of the cases were attributable to the metabolic syndrome and 92% (CI: 67%, 98%) to the most unfavourable combination of its components. The metabolic syndrome did not modify the prediction of lifestyle factors but persons with normal blood pressure benefited more from positive changes in exercise, alcohol consumption, and smoking than those with elevated blood pressure (P for interaction = 0.01).

**Conclusions:** Modification of lifestyle factors could apparently reduce type 2 diabetes risk, especially in persons with normal blood pressure.

## P32

### Mediterranean diet and children: Perspectives for research – a new proposed field for longitudinal studies

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#### Abstract

*Objective:* There is a growing body of literature during past years in reference to the Mediterranean Diet's (MD) health benefits in adults, but relevant research data are scarce in children. To present available research evidence with regards to the health benefits of the MD in children and examine research perspectives.

*Methods:* A literature search in the online databases of PubMed, Scopus, Google and Heal-Link was conducted during the year 2008 to identify relevant studies.

*Results:* Twenty three publications were identified; 21 were derived from cross-sectional studies, one from a prospective study, and one from an intervention study. Of these publications, 8 report on the nutritional adequacy of the MD in meeting children's needs, four report on the association between adherence to the MD and lipid profiles, and 14 on the association between adherence to the MD and disease indices. Of the latter, 7 refer to MD's relationship to childhood asthma, 6 on MD's relationship to childhood obesity, and one on its association with blood pressure levels.

Data on the association between the MD, diet quality and morbidity indices in children are scarce. However, the available data support the notion that this dietary pattern effects on the risk for asthma symptoms. A negative correlation between the degree of adherence to the MD and obesity has been shown, but in virtually all studies, did not retain its significance after the adjustment for confounding factors. Finally, studies on the relation between adherence to the MD and blood lipid concentrations are very few and limited by their failure to appropriately state how the MD was defined.

*Conclusion:* Further investigation on the correlation between the degree of adherence to the MD and various health or morbidity indices in children of different ages and nationalities is needed. Longitudinal studies that will examine the overall effect of MD from early childhood into adulthood will give definite answers on the influence of this dietary prototype in several health and disease indices. Secondary analyses in present longitudinal studies could give useful insights into the above research data gaps.

(Financial support: This work was supported by a grant by NESTLE HELLAS.)

## **P33**

### **Relationships between children's and their parent's dental fear during 3.5-year period**

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#### **Abstract**

*Objectives:* The aim was to study relationships between children's and their parent's dental fear during a 3.5-year period.

*Methods:* The study group consisted of all 5th and 6th graders (11- to 12-year-olds), except for mentally disabled and handicapped children attending special schools, in the beginning of the 2001–2002 school year in the town of Pori, Finland, and their parents (n=1691). Children filled out the questionnaires at school and took parents' questionnaires home to one of their parents to be filled out in Fall 2001, Spring 2003 and Spring 2005. All three children's and parent's questionnaires were returned properly filled by 934 children. In 579 cases the responding parent was the same in every time point. Children's and parents' dental fear was evaluated with a single item question with 5 reply alternatives (not afraid, a little afraid, afraid to some degree, quite afraid or very afraid). Those who reported being quite or very afraid of dental treatment were considered fearful. We studied the relationship between children's and their parent's dental fear and the stability of that relationship among all dyads and dyads with fearful participant at baseline.

*Results:* At baseline, in 75% of the child-parent dyads both participants were non-fearful, in 3% both were fearful, and in 22% other participant was fearful and other was not. In the follow-up, in 61% of the child-parent dyads both participants had similar dental fear status in all three time points. Of these similarly fearful dyads, 97% were non-fearful at all time points. When following up dyads with fearful participant at baseline, we found no statistically significant relationship between children's and parent's dental fear in later time points.

*Conclusions:* Relationship between children's and their parent's dental fear may be based on the low prevalence of dental fear. In fluctuation of fear among dyads with fearful participant at baseline, no connection between participants' dental fear was found.

## P34

### Diagnostic errors and health inequalities: results from a six-year autopsy cohort study

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#### Abstract

*Objective:* Patient safety and reducing health inequalities are becoming priorities for healthcare systems worldwide. While the impact of socioeconomic factors on health has largely been demonstrated, the relationship between social status and medical errors has been explored only partially.

The aim of this study was to determine whether socioeconomic factors can be associated with diagnostic errors in subjects who died in hospital.

*Methods:* An historical cohort was analyzed through 2003-2008, including all the consecutive in-hospital deaths followed by autopsy. Diagnostic errors were defined as the presence of clinically missed diagnosis involving a principal underlying disease or primary cause of death. The discrepancy between clinical and postmortem diagnosis gave the measure of diagnostic error for each patient.

The clinical and socioeconomic information was collected for each patient (length of stay, reason for admission and death, comorbidity, age, sex, educational level, marital status, occupational status, deprivation level according to the Italian deprivation index).

Univariate and multivariate stepwise forward logistic regression models were used in order to determine the independent association between diagnostic errors and socioeconomic variables.

*Results:* The sample included 397 cases. The rate of diagnostic errors was 45.6% (95%CI 40.5-50.5), with 58.6% (95%CI 51.3-65.8) of unexpected findings contributing to patient's death. Diagnostic error rate increased in patients of deprived/very deprived areas, even after adjusting for confounding factors (OR 1.8, 95%CI 1.1-3.2;  $p=0.047$ ).

*Conclusion:* The results showed that errors can be related to living in a deprived area. Despite the possible limitations (small sample size, single centre study, etc.), these findings suggest that social factors and errors are not independent. Moreover these results emerged in a context where advanced diagnostic technologies, academic competence and social policies are available. Therefore new integrated healthcare strategies could be necessary to face both problems.

## P35

### Evaluation of oxidative stress markers in pathogenesis of primary open-angle glaucoma in elderly patients

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#### Abstract

**Objective:** Primary open-angle glaucoma (POAG) is the leading cause of blindness in most industrialized countries. Findings from epidemiological studies indicate that apart from high intraocular pressure and age, oxidative stress might be associated risk factors in pathogenesis of POAG.

**Methods:** Peripheral blood samples from forty subjects over sixty years of age including 20 patients with open angle glaucoma and 20 controls without glaucoma symptoms were enrolled in our study. In our work the activity of antioxidant enzymes: catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPX) as well as a total antioxidant status (TAS) were estimated. An alkaline comet assay was used to measure the DNA damage levels of strand breaks (SB), oxidized purines as glycosylo-formamido-glycosyalse (Fpg) sites, and oxidized pirimidines as endonuclease III (Nth) sites.

**Results:** We measured endogenous as well as exogenous DNA damage after 10  $\mu$ M hydrogen peroxide treatment (H<sub>2</sub>O<sub>2</sub>). We did not observe any statistical changes in strand breaks lesion of DNA in examined POAG patients according to healthy subjects ( $P > 0.05$ ). However, either endogenous ( $P < 0.01$ ) or exogenous ( $P < 0.001$ ) level of oxidative DNA damage in POAG patients was found to be statistically higher than controls. It was also indicated a significant decrease of antioxidant enzymes CAT ( $P < 0.001$ ); SOD ( $P < 0.05$ ), GPX ( $P < 0.001$ ) and non-statistical decrease of TAS status ( $P > 0.05$ ) in glaucoma patients according to controls.

**Conclusion:** In conclusion our data revealed that oxidative stress have a pathogenic role of primary open-angle glaucoma in elderly patients. Therefore, we suggested that the modulation of a pro-oxidant/antioxidant status might be a relevant target for both prevention and therapy. This evaluation of oxidative stress markers will also form a basis for further longitudinal observations of glaucoma development in elderly patients.

(This work was supported by grant N N402 375838 from Polish Ministry of Science and Higher Education.)

## P36

### **Current adult ADHD symptoms predict parenting stress in Swedish mothers: A longitudinal population study**

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#### **Abstract**

*Objective:* To examine whether retrospectively recalled childhood and current adult symptoms of attention-deficit hyperactivity disorder (ADHD) were associated with maternal parenting stress, and whether this relationship was mediated by other variables including perceived stress, depression, and socio-economic background.

*Method:* Participants were recruited from the Swedish Women's Experience of Pregnancy and Delivery Follow-up project (KUBU); a cohort study of mothers recruited during pregnancy and followed longitudinally until child age of 5 years. Parenting stress, childhood and current ADHD symptoms, depression, social support and perceived stress were measured in 652 mothers when their children were aged two years. A subset of 214 mothers was followed-up when their children were aged four, when the assessments were repeated.

*Results:* Reports of parenting stress correlated moderately over time,  $r = 0.66$ . Hierarchical regression analysis revealed that higher perceived stress, less social support, higher depression and higher adult symptoms of ADHD were significantly associated with higher levels of parenting stress for mothers of children aged two. Adult ADHD continued to make a significant contribution to parenting stress even when perceived stress and depression were controlled for. The analysis was repeated for the subset of mothers when children were aged four years, and revealed that perceived stress, social support and adult symptoms of ADHD continued to be associated with parenting stress two years later. In addition, maternal ratings of paternal ADHD were also associated with parenting stress at age four. Neither retrospectively reported childhood symptoms of ADHD or socio-economic status, measured via maternal education level, showed significant association with parenting stress at either time point; however, lower maternal education level was associated with greater childhood symptoms of ADHD and less social support following pregnancy.

*Conclusion:* Results suggest that adult symptoms of ADHD are significantly associated with parenting stress, independent of symptoms of depression and life stress. These associations remain stable over time.



P37

## Parenting stress and adult attachment among parents to toddlers

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### Abstract

*Objective:* The aim of the current study was to investigate to which extent self-rated adult attachment style contributes to parenting stress in a large population-based sample of mothers and fathers to toddlers.

*Method:* The current study is part of the ABIS-project (All Babies In Southeast Sweden), which is a large longitudinal cohort study aiming to investigate factors associated with poor child health where all families expecting a child in southeast Sweden 1997-99 were invited. The data used in the current study was collected by questionnaires (mothers  $n=7852$ , fathers  $n=270$ ) when the children were 2-3 years old. Self rated attachment style was measured by the 18-item version of the Relationship Scale Questionnaire (RSQ) which was reconstructed by exploratory factor analysis to fit our sample. Three dimensions of RSQ were revealed: (1) Important with independence, (2) Attachment related anxiety, and (3) Uncomfortable with closeness. Parenting stress was measured by Swedish Parenting Stress Questionnaire (SPSQ), which is a translation and reconstruction of the Parenting Stress Index validated for Swedish conditions. Associations were examined by multivariate linear regression where the new RSQ factors were set to independent variables and SPSQ scales to dependent variables. Gender-effects were modelled in interaction-variables for each RSQ-dimension.

*Results:* Together the three dimensions of adult attachment showed significant associations with parenting stress (R-square change=0.214,  $F(3, 7717)=723.56$ ,  $p<0.001$ ) after adjusting for demographic factors (parental gender, age, education, foreign origin, cohabit status, number of children). Parenting stress was most affected by attachment related anxiety ( $b=0.20$ ,  $t=38.96$ ,  $p<0.001$ ), where more anxiety implied higher parenting stress. Weaker associations were found between parenting stress and the attachment dimensions capturing avoidance: Important with independence ( $b=0.07$ ,  $t=13.40$ ,  $p<0.001$ ) and Uncomfortable with closeness ( $b=0.07$ ,  $t=12.04$ ,  $p<0.001$ ). No gender-effects were found (R-square change=0.000,  $F(3, 7714)=0.98$ ,  $p=0.401$ ).

*Conclusion:* Parenting stress was associated with dimensions of adult attachment. Thus it may be meaningful to assess adult attachment in epidemiological studies investigating how stress in the family affects child health.

## P38

### Twins versus singletons – morbidity and mortality across the lifespan

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#### Abstract

*Objective:* To investigate whether twins differ from singletons with respect to overall mortality and morbidity from cardiovascular disease and cancer. Twins are on average born earlier and smaller than singletons. While there are several reports of associations between foetal growth and adult disease among twins (similar to those in singletons) few studies have been able to show any difference in adult morbidity and mortality comparing twins and singletons. This may indicate that the general growth constraint in twins has no adverse effects on adult health, but if twinning shares common causes with adult health a negative effect of twin-growth constraint could be confounded. Most previous comparisons have been between twins and the general population, with little ability to adjust for potential confounders. We propose an alternative design to contrast morbidity and mortality in twins and singletons.

*Methods:* Twins born between 1932 and 1958 will be followed with respect to overall mortality and morbidity of cardiovascular disease and cancer from 1971 (when the cohort was established) to 2006 (identifying ICD-codes in National Registries for hospital admissions, cancer and causes of death, and including information on migration to ensure time-at-risk). The twin experience will be contrasted to that of all their single-born siblings who will be followed from the same age (provided they are at-risk). Then in a final step, the singletons from twin families will be compared to singletons in the general population (represented by an age and sex matched sample). The morbidity and mortality in these three cohorts will be described and compared using failure time analysis methods, with appropriate accounting for the dependence within families, using SAS 9.2 software.

*Results:* Analyses are still ongoing.

*Conclusion:* According to the null hypothesis twins do not differ from singletons with respect to adult morbidity and mortality. In the alternative, the unique experience of twinning does lead to increased morbidity and mortality (potentially through foetal programming) and this would result in twins faring worse than their singleton siblings. Further, if this effect is offset by other (familial) factors leading to better health, we would expect singletons from twin families to be on average healthier than the general population.

## P39

### Neurological anomalies in the Born in Bradford cohort study: Preliminary findings

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#### Abstract

*Objective:* The Born in Bradford Study is a prospective birth cohort study tracking the health outcomes of 13,000 babies booked for delivery at the Bradford Royal Infirmary. As part of the study, we actively ascertained congenital anomalies encountered in the cohort, with the aim of deriving prevalence and classifying anomalies by system affected. We present descriptive preliminary data on babies with neurological anomalies.

*Methods:* We recorded cases of congenital anomalies in babies in the cohort born between 2007-2010. We collected data retrospectively from clinic letters from specialist neonatal care, lists of children affected by neurosensory deficits, children referred for genetic testing, and speciality clinic lists. We also organised passive surveillance on a multiple ascertainment model. Clinicians reported babies with suspected anomalies through a notification card. Clinical records were reviewed by principal investigators and all anomalies present were coded to ICD-10. Clinically recorded ethnicity and consanguinity data were also collected.

*Results:* During this period 18,184 babies were born in the hospital, of which 57% (n=10,382) were recruited to the cohort study. Within the cohort 242 (2 %) were found to have congenital anomalies; 26 (11%) babies had neurological anomalies; of which 2 had more than one neurological anomaly. Of these 26 babies, 88% (n=23) were of South Asian ancestry, 12% (n=3) were of White British ancestry; 54% (n=14) were male and 46% (n=12) were female. Of these 38% (n=10) have died. Neurological anomalies included microcephaly (n=14), hydrocephalus (n=1), lissencephaly (n=2), ventriculomegaly (n=2), plagiocephaly (n=2), Dandy Walker syndrome (n=2), nemaline rod myopathy (n=1), congenital myopathy (n=1), congenital muscular dystrophy (n=1), congenital muscular weakness (n=1) and Leigh's disease (n=1). Where data on family structure was available, 14 (54%), were born to consanguineous parents; 9 (64%) of which were first cousin unions.

*Conclusion:* These preliminary findings suggest a higher number of neurological disorders in the South Asian population included in the Born in Bradford cohort. Although the numbers are small and represent a preliminary subset of this cohort study, these findings indicate the potential burden caused by neurological birth defects and impact on infant mortality and morbidity.

P40

## Night shift work and risk factors for breast, colon and prostate cancers – two ongoing studies in Poland

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### Abstract

*Objectives:* Night shift work has been recently classified by IARC as a probable carcinogen (group 2a) with the suggestion of the increased breast cancer risk in long term night shift female workers (nurses) but also potentially increased risk of colon and prostate cancer in male night shift workers. Two studies have been undertaken in Poland in order to evaluate associations between night shift work and well established risk factors for these cancers.

*Methods:* Study I: Cross-sectional study in nurses included 356 nurses currently working on rotating night-shifts and 369 nurses working only during the day. Data on breast cancer risk factors and occupational history were collected during in-person interviews; body weight and height were measured. Blood and urinary samples were collected, mammographic examinations performed. Study II: A cohort of six thousand employees of enterprises in Łódź having shift work schedule (including night shifts) is being set up. Both women and men of age >35 will be eligible for the inclusion into the study. Information on the established risk factors for breast, colon and prostate cancer will be collected through a self administered questionnaire.

*Results:* Preliminary analyses of the cross-sectional study in nurses showed no associations between current rotating night shifts or night shift duration and such selected breast cancer risk factors as nulliparity, delayed menopause, number of full term births, OC/HRT use or mammographic density. In postmenopausal nurses borderline significant associations ( $0.1 > p > 0.05$ ) were found between current rotating night shift work and BMI and estradiol(E2), and statistically significant increased estradiol levels in nurses with more than 15 years of night shift work duration ( $p = 0.001$ ). As many as 64 enterprises (apart from health care sector) with 18 thousand employees were identified in Łódź as a source population for the planned cohort study.

*Conclusion:* The preliminary results of the cross-sectional study suggest that increased BMI and estradiol in postmenopausal nurses working rotating night shifts might contribute to the elevated breast cancer risk observed in nurses. The cohort of night shift workers being assembled will form a basis for further longitudinal observations.

## P41

### Sex differences in infant response to maternal cortisol during pregnancy

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#### Abstract

*Objectives:* Effects of prenatal stress on behaviour and physiology in offspring have been widely demonstrated in animal studies. These may be explained, at least in part, by alterations in the HPA axis of the developing foetus, caused by elevated maternal corticosteroids, and mediated via effects on gene expression. There is limited evidence regarding the role of the maternal HPA axis in humans. Sex differences in the effects of prenatal stress on physiology and behaviours have been reported in animals and these may have implications for understanding of sex differences in psychopathology in humans. We examined sex differences in prenatal stress and negative emotionality in human infants.

*Methods:* As part of the Wirral Child Health & Development Study, a birth cohort recruited in pregnancy, measures of psychosocial risk from a general population sample of 1289 first time mothers recruited at 20 weeks gestation, were used to generate a stratified sample of 213 who provided diurnal cortisol at 34 weeks. Their infants were assessed at age 5 weeks using the Neonatal Behavioral Assessment (NBAS; Brazelton). Assessments were video recorded, and the number of times the infant went from calm to crying in response to a mildly aversive manoeuvre, provided the measure of negative emotionality.

*Results:* All analyses controlled for infant gestational age at birth and age at NBAS. There were no associations between maternal anxiety or depression at 20 or 24 weeks and infant negative emotionality. Mean waking cortisol (square root transformation) across two days predicted infant negative emotionality in interaction with sex. Increasing maternal cortisol was associated with a greater probability of high negative emotionality in girls, and of low negative emotionality in boys.

*Conclusions:* Elevated emotional reactivity in female offspring of mothers with higher waking cortisol may, in combination with later stresses, create vulnerability to depression. Decreased emotional reactivity in male offspring may represent early precursors of fearlessness and externalising problems. Repeated assessments over time in this study will examine conditions under which negative emotionality confers resilience or vulnerability.

## P42

### The role of paid maternal employment in childhood on adolescent health and health behaviours in BHPS study

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#### Abstract

*Objective:* Maternal employment has been shown to influence number of child and adolescent outcomes such as cognitive outcomes, educational achievement, behavioural problems, overweight and obesity, self-rated health or child fatalities. There is, however, only limited number of UK studies using health measures as study outcomes. The aim of this study is to help filling this gap by looking at influence of maternal employment in three periods of childhood on health outcomes among young people aged 16-21 years in British Household Panel Survey (BHPS).

*Methods:* BHPS is annual panel survey that has started in 1991. Response rate to wave 1 was 74%, and response between waves 2 and 17 varied between 84%-89%. There are 3,696 individuals for whom at least one measurement of self-rated health and/or GHQ-12 and/or smoking at age 16-21 and maternal employment data prior to age 16 years are available. Other variables, such as gender, maternal age, maternal education and marital status, household income or maternal smoking were used as additional explanatory variables. Logistic regression modelling (using clustering of measurements within individuals) was used to estimate the associations between dichotomized study outcomes and maternal employment.

*Results:* 19% of young adults aged 16-21 reported poor self-rated health. 29% of young adults reported being current smoker. Approximately 40% of mothers worked at some point during age 0-4 of their child. This proportion increased to 59% at age 5-11 and 68% at age 12-16. Children of mothers who were not employed reported OR of poor SRH 1.41, 1.00 and 1.24 for 3 periods of exposure, however these effects were partly explained when adjusted for maternal education and household income. The differences in GHQ-12 by maternal employment were limited. Children of mothers who were not employed were more likely to smoke with the strongest effect of last period of exposure (OR 1.40, 95% 1.21-1.64).

*Conclusions:* The associations between maternal employment in childhood and young adults' health and smoking exist at least partly because of the generally higher social position and more stable family structure of households with working mothers. Maternal education and household income seem to be stronger social predictors of study outcomes than maternal employment status.

## P43

### Multi-center all-Polish health survey – Wobasz project. Predictive values of classical factors of cardiovascular mortality in Polish population

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#### Abstract

*Objective:* Description of predictive values of classical factors of CVD mortality in Polish population.

*Methods:* The Project WOBASZ was undertaken in 2003-2005. The survey covered the whole territory of Poland. A sample of 19200 men and women aged 20-74 was drawn and 14769 peoples were scined. The individual record contains many variables based on measurements and information collected during interview. In this paper the following were used: age in day of interview, level of total cholesterol, HDL-cholesterol, triglicerides, glucose, CRP, homocysteine, BMI, DBP, SBP, and depression factors. The proportional hazards models (Cox model) were used to estimate predictive values of selected factors by uni- and multivariate analysis. In 2009 the longitudinal observation was made of this cohort on the end of year 2008. The cardiovascular deaths were recorded and their time.

*Results:* The mean follow-up was  $4.42 \pm 0.76$  yrs in men and  $4.49 \pm 0.61$  yrs in women. In 2004-2008 period were observed 507 incidences; in this – 144 CVD deaths in men and 52 in women. The most often reason of death was CHD in men and stroke in women. In the univariate analysis the significant predictors of CVD mortality were: age (HR=1.089), total cholesterol (1.234), glucose (1.134), CRP (1.435), homocysteine (1.070), SBP (1.014), depression (1.081) in men and age (1.131), HDL (0.332), triglicerides (1.150), glucose (1.235), CRP (1.780), homocysteine (1.066), BMI (1.064), DBP (1.038), SBP (1.029), depression in women.

In multivariate analysis only age, total cholesterol, homocysteine and depression were as independent predictors of CVD mortality in men and age, glucose, CRP and homocysteine in women.

*Conclusions:* In the Polish population the selected classical risk factors of CVD mortality confirmed important predictive value. The significant role of these factors must be applied to modify its levels in order to reduce of CVD mortality ratios.

**P44**

## **Environmental tobacco smoke exposure and psychomotor child development**

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### **Abstract**

*Objective:* The aim of the study was to assess children's ETS exposure during prenatal period and within first 2 years of life and to evaluate the influence of prenatal and postnatal ETS exposure on children's neurodevelopment

*Method:* The study population consisted of children with well assessed prenatal exposure to environmental tobacco smoke (three times analysis of cotinine level in saliva of pregnant women). Assessment of child ETS exposure after birth was based on questionnaires conducted with mothers, confirmed by biochemical verification of cotinine level in child urine. The cotinine level in biological samples was analyzed using Liquid Chromatography (HPLC) with Tandem Mass Spectrometry (MSMS). The Bayley Scale for Infant and Toddler Development (BESID-III) was used for the evaluation of child neurodevelopment.

*Results:* Multivariate analysis (including gender, birth order of the child and parental educational status) indicated the statistically significant association between child prenatal ETS exposure and cognitive development ( $b=-4,0$ ;  $p=0,04$ ). ETS exposure has also negative impact on motor ( $b=-2,7$ ;  $p=0,2$ ) and language ( $b=-3,4$ ;  $p=0,08$ ) abilities of the child although the results were not statistically significant. The same association was observed for child exposure within 2 years of life.

*Conclusions:* Maternal smoking was found to be related to a decrease in child neurodevelopment although it impossible to separate the prenatal from postnatal exposure. All effort should be taken to eliminate the child ETS exposure.



**P45**

## **Multicenter, Polish National Mother and Child cohort study**

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### **Abstract**

*Objective:* The aim of the study is to evaluate the impact of exposure to different environmental factors during pregnancy on pregnancy outcome and children's health. Specific research hypotheses refer to the role of heavy metals, exposure to polycyclic aromatic hydrocarbons (PAHs) and environmental tobacco smoke (ETS) in the aetiology of SGA and PD. It is also intended to explain the role of oxidative stress and nutritional status of the pregnant women. The impact of occupational exposures and stressful situations will be evaluated from questionnaire data.

*Method:* Polish Mother and Child Cohort Study (REPRO\_PL) is multicenter prospective cohort study conducted in 8 different regions of Poland. The final cohort is intended to comprise 1300 mother-child pairs to be recruited within 4-year period (2007–2011). The recruitment and all scheduled visits are conducted in maternity units or clinics in the districts included in the study. We include into the study women between 8-12 weeks of single pregnancy, not assisted with reproductive technology, and not expected to be finished as spontaneous abortion. All women with the serious chronic diseases specified in study protocol are excluded from the study. The women are followed-up 3 times in pregnancy (once in each trimester) and after delivery for the notification of pregnancy outcome. During each visit, detailed questionnaire and biological samples are collected including saliva, urine, hair, maternal blood and cord blood. About 6 weeks postpartum, breast milk from part of the women is collected.

*Results:* Up today the cohort comprise of 1000 recruited pregnant women. All planned biological samples were collected from 600 women, and from 100 women breast milk was collected.

*Conclusions:* The results of the study will become available within the next few years and will help to determine levels of child prenatal exposure in several areas of Poland and its impact on course and outcome of pregnancy.

**P46**

## **The Canadian Longitudinal Study on Aging (CLSA)**

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### **Abstract**

*Objectives:* The Canadian Longitudinal Study of Aging (CLSA) is a 20-year prospective cohort study of the Canadian population. The overall aim of the CLSA is to examine aging as a dynamic process.

*Methods:* The CLSA is a Canada-wide study of 50,000 people between the ages of 45 and 85 years at baseline. Twenty thousand of the 50,000 will provide the core CLSA information through questionnaires only. Recruitment of the first 20,000 participant providing questionnaire information only began in early-2010. The remaining 30,000 will also be asked to provide in-depth information through physical examinations and biological specimen collection. The recruitment of these participants will begin in mid-2011.

The CLSA program of research will allow examination the relationships among precursors (e.g. gene variants or nutrition), changes in quantitative traits (e.g. cognition or inflammatory biomarkers), and the consequences of the changing phenotype on the development or prevention of disease (e.g. dementia or depression), disability (e.g. frailty or physical limitations), and psychosocial outcomes (e.g. emotional distress or social isolation). The depth and breadth of data collected will allow this program of research to address questions such as: i) What are the determinants of changes in biological, physical, psychological and social function over time and across ages?, ii) How important are genetic and epigenetic factors in the aging process?, iii) Why do some individuals experience healthy aging while others do not?, iv) Are there identifiable patterns of cognitive functioning in midlife that predict onset of dementia in later life?, v) How do work and family transitions intersect with negative/positive changes in social networks and support and how do these transitions influence overall health?

*Conclusion:* Through the CLSA we will investigate the interrelationships among intrinsic and extrinsic factors influencing health from mid-life to older age. This will allow us to capture transitions, trajectories and profiles of aging, elucidate the concept of successful aging, and identify modifiable factors that could be used to develop interventions to improve the health of older populations. Once in place, the CLSA will also provide infrastructure and enhance capacity for sustained high quality longitudinal research on aging in Canada.

P47

## The Canadian Longitudinal Study on Aging (CLSA): Validation of disease ascertainment algorithms

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### Abstract

*Objective:* Standard clinical diagnostic procedures are often inappropriate and frequently not feasible to apply in population-based studies, yet ascertaining accurate disease status is essential. Many longitudinal studies have developed and/or used disease-specific algorithms to identify the presence or absence of major chronic diseases and conditions. These algorithms combine different types of information such as self-reported diagnoses, questionnaires, medical records, anthropometric measures, physician examination, medications, and laboratory and clinical tests to determine an individual's disease status. The objective of this study was to develop and test disease ascertainment algorithms for the Canadian Longitudinal Study of Aging (CLSA).

*Methods:* We conducted a systematic review to identify algorithms, criteria, and tools used to ascertain 17 chronic diseases, and assessed the feasibility of developing algorithms for the CLSA. The CLSA clinical working group used the results of the systematic review to develop 13 disease ascertainment algorithms for diabetes mellitus type 2, osteoarthritis [hand, hip, knee], parkinsonism, ischemic heart disease, chronic airway obstruction, stroke, high blood pressure, depression, hypothyroidism, osteoporosis, and dementia/cognitive impairment. The sensitivity and specificity for seven algorithms (diabetes, osteoarthritis [hand, hip, knee], parkinsonism, ischemic heart disease, and chronic airflow obstruction) were tested in patients with and without the conditions in question.

*Results:* Of the 29,616 citations screened, 668 papers met all inclusion criteria. The diagnosis of some symptomatic conditions, such as osteoarthritis and arthritis, will require substantiation by clinical criteria (e.g., x-rays, bone density measurement) while other conditions, such as depression, can be assessed solely by self-report. Preliminary results from our validation study indicate that the seven algorithms tested all have sensitivity and specificity above 0.7.

*Conclusion:* Our preliminary results suggest that the disease ascertainment algorithms work well to distinguish between disease positive and disease negative individuals. Further examination will be required to assess their measurement properties in a general population sample.

P48

## Survival rate in patients with Mucormycosis during 8 years (Iran – Isfahan 2001 -2009)

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### Abstract

*Objectives:* Although any status of immunodeficiency can provide a background, diabetes mellitus and leucopenia are two major settings for invasive Mucormycosis. This fungal infection is almost always dangerous and accompanied with high mortality and morbidity. The main purpose of this study was to assess the survival rate after treatment and management of patients with Mucormycosis during 8 years in Iran (Isfahan referral center Al-zahra hospital).

*Methods:* The study was performed as cross sectional and retrospective. From January 2001 to August 2009 all the data in 17 records labeled mucormycosis was extracted. Data was analyzed by SPSS and Fisher exact test.

*Results:* The overall survival rate was 64%. Specifically, the survival rate was 66.7%, 60%, 50%, 66% respectively for diabetes mellitus, hematologic malignancies, patients undergoing dialysis, and those taking immunosuppressive drugs. Survival rate was 75% for those with infection limited to the eyes. Those who received Amphotricine B had a survival rate of 66.7%, those who were treated with Azols 60%, and in leukopenic patients treated with each drug plus GCsF the rate was 50%. Patients who received medication plus extensive or limited surgery had a survival rate of 71%, while in those without surgery it was 72%. The mean age of patients was 55.47 years. The majority of patients were male (63.6%). Adverse effect of drugs and renal involvement (doubling in creatinin) overall was 35%.

*Conclusion:* Mucormycosis is an opportunistic infection in hospitalized patients with more prevalence in diabetes mellitus after a DKA episode and patients with leucopenia. Survival rate in our patients was higher in comparison with other studies, even though it was not significantly meaningful between different groups. Although survival rate with surgery didn't increase, we believe that renal toxicity has decreased due to diminished dose of drug administration after surgery.

**P49**

## **Finnish Health in Teens study – plans for a new prospective cohort study**

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### **Abstract**

*Objectives:* To start a new prospective cohort study among Finnish preadolescents: the Finnish Health in Teens – Fin-HIT – study. This will be a multipurpose cohort with the initial objective of studying the role of childhood growth environment and genetic factors, as well as gene-environmental and gene-gene interactions, on the development of overweight, obesity and disordered eating.

*Methods:* All children in Finland turning 11 years, starting from the beginning of year 2011, will be invited to the study together with one of their parents or legal guardians. The enrolment will continue until a cohort of 40,000 children is enrolled.

Questionnaire information will be obtained on exposures, mediating factors and outcomes. Children will have the option to fill in the questionnaire via Internet or in paper format, with minimal assistance from an adult. Follow up questionnaires are planned to be sent out every 2-5 years.

Information will be collected on the children's height, weight, waist circumference, symptoms of disordered eating, family environment, use of media (TV, computer, magazines), sense of coherence, puberty, lifestyle related health behaviour (e.g. diet, physical activity and sleep), and mental health (e.g. depression, anxiety, self esteem). The parents are also expected to answer a separate questionnaire about their socioeconomic status, and health related issues of themselves and their children.

Saliva samples will be collected from the children using Oragene kits. DNA will be extracted from saliva for genotyping. Some information on exposures (e.g. birth weight) and outcomes (e.g. hospitalizations for eating disorders) will be obtained using Finnish nationwide registers.

*Results:* The outcomes of the study will be extensive information on children's physical and mental health on a population level, with initial focus on the prevalence, and risk and protective factors of overweight, obesity, and disordered eating. The results are expected to provide information that may substantiate public health professionals on the establishments of recommendations on specific strategies to prevent or limit the impact of health inequalities on future adult health.

## P50

### Delayed childbearing: pregnancy and maternal outcomes in Iran

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#### Abstract

*Objective:* Women have greater control over their reproductive lives than before. The reasons might be social changes in the structure of the family, with more late and second marriages, the necessity for many family women to work, and a revolution in the availability of safe, effective contraception. Pregnancy in older women is associated with many other risk factors, such as pre-existing diabetes mellitus, hypertension, and other chronic disorders which should be into account. To clarify these issues, the aim of this study was to investigate the association of maternal age with risk of adverse pregnancy and mother outcomes in Tehran, Iran.

*Methods:* We conducted the study in years 2001-2006 in Akbar-abadi teaching hospital, the largest maternity hospital in the capital city of Tehran, Iran. This hospital covered >80% of all deliveries in the south and south west of Tehran with a population of ?2.7million. In this retrospective hospital-based study, data of nulliparous women aged 35 years or older (n=245) were compared to data of nulliparous women aged 18-34 years old (n=293). We used univariate analysis to assess the association of maternal age with pregnancy and neonatal outcomes. By using multiple logistic regression, the effect of confounding factors (education of mother, occupation, hypertension and diabetes in pregnancy) were adjusted.

*Results:* We studied 538 nulliparous women who gave birth during the study period. 54% (n=293) of the women were 18-34 years of age, and 46% (n=245) were 35 years or more. Women aged 35 years or older had increased percentages of gestational hypertension (18.8% vs 19.6%; P=0.02) and diabetes in pregnancy (3.7% vs 1.4%; P=0.08) compared with women younger than 35 years. Some obstetric complications were also increased, including cesarean delivery, malposition, low birth weight, small for gestational age, NICU admission, and congenital anomalies in women aged 35 years and older, compared to younger women. Advanced maternal age was independently associated with low birth weight (1.08; CI:1.03-1.13), preterm labor (1.04; CI: 1.01-1.07), and rate of cesarean delivery (1.21; CI: 1.17-1.25).

*Conclusion:* Women aged 35 years or more are at higher risk of preterm labour, cesarean delivery, and low birth weight compared with younger women.

## P51

### Serum 25(OH)D concentration and subsequent risk of type 2 diabetes

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#### Abstract

*Objectives:* The objective was to prospectively investigate the association between serum 25(OH)D concentration and the incidence of type 2 diabetes. To our knowledge, this is the first cohort study on this topic.

*Methods:* A study of 4,097 Finnish men and women, aged 40–69 years, and free of diabetes at baseline, was carried out in 1978–80. Data on education, smoking, and leisure time exercise were collected in a health examination. Height and weight were measured, and blood samples were collected and stored at -20°C. In 2003–2004, radioimmunoassay (125I RIA Kit, DiaSorin, Minnesota) was used to assess serum 25(OH)D in thawed samples.

During 17 years of follow-up, 187 incident type 2 diabetes cases were identified from a nationwide registry of patients receiving medication reimbursement and these cases were linked to the study population by the unique social security numbers assigned to Finnish citizens.

Relative risks of type 2 diabetes between quartiles of serum 25(OH)D, adjusted for confounding factors, were estimated using Cox's model.

*Results:* The mean concentration of serum 25(OH)D was 43.6 nmol/l (SD=19.5). After adjustment for age, sex, and the month when the blood samples were collected, a statistically significant inverse association was observed between serum 25(OH)D concentration and the incidence of type 2 diabetes. The relative risk between the highest and lowest serum 25(OH)D quartile was 0.60 (95% CI=0.36–0.98; ptrend=0.01). This association was attenuated after further adjustments for BMI, leisure time exercise, smoking, and education (RR=0.70, 95% CI=0.42–1.16; ptrend=0.07).

*Conclusions:* These results suggest a reduction in type 2 diabetes risk for people with higher serum 25(OH)D concentration. The strengths of this study include its longitudinal design and the use of serum 25(OH)D concentration as an indicator of vitamin D status, reflecting the vitamin D obtained from both diet, supplements and cutaneous synthesis. Further research is needed to confirm the association, and to distinguish between the independent role of vitamin D and the role of healthy dietary and lifestyle patterns in reducing the risk of type 2 diabetes.

P52

## Time trends of socio-demographic and risk factors of artificial reproduction techniques 1994 – 2008

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### Abstract

**Objectives:** The population based active Mainz Birth Registry was established in 1990 covering the region of Rheinhesse (approx. 400,000 inhabitants). More than 63,000 births have been registered till 2008 (90% according to the federal birth statistics). The major goal of this registry is to record morphogenetic defects of newborn and possibly underlying risk factors.

**Methods:** Prior to birth all mothers were routinely asked about their socio-demographic data and the use of artificial reproduction techniques (ART: in-vitro-fertilization (IVF), intracytoplasmatic sperm injection (ICSI)) by the midwives. All newborn were screened for malformations at birth by especially trained paediatricians. Time trends were analysed with linear/non-linear regression using SAS and displayed as 3-years moving proportions or odds ratios.

**Results:** While in 1994 (first in vitro fertilization in the monitored region) 3,705 pregnancies were recorded this number decreased to 3,281 in 2007 (- 11.4%). The lowest number of pregnancies, 2,862, was in 1999 (-22.8%). In the same period the use of ART raised from 0.1% to 1.7% (peak 2.8% in 2006), many of these being multiple pregnancies (21.1%). In the same time span the proportion of mothers with non-migrant background decreased continuously from 77% in 1994 to 66% in 2007 and relevant changes of socio-economic class took place in this sub group. The proportion of mothers  $\geq 35$  years rose from 11.6% to 25.7% mainly accounting for mothers with a non-migrant background. The usage of ART is influenced by these socio-demographic changes and is described in detail. In the first years the ICSI technique showed a considerable risk of birth defects in the offspring, (odds ratio = 6.1) which decreased continuously to expected values in untreated spontaneous pregnancies until 2005, but slightly increasing since then.

**Conclusion:** The use of ART is highly correlated with maternal age and associated factors, also on social class and migration status. The high number of primipara in this group lies within the method itself. A lack of information about the discussed techniques in the lower social class and/or migrant families seems obvious. The increase malformation prevalence in the ICSI sub group can not be explained by the underlying maternal background risk solely.



## P53

### Longitudinal care pathways of the use of residential or outpatient services in dementia

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#### Abstracts

**Objective:** To evaluate social, clinical and welfare state in demented patients in charge of outpatient centres for dementia of Lazio Region (U.V.A.) as predictive of the use of residential or outpatients health and social services.

**Methods:** A longitudinal retrospective study, financed by the Italian Ministry of Health, was conducted in 2008 on 1.010 patients belonging to five UVA of Rome and Lazio Region. We collected information about stage of dementia, cognitive, functional and behavioural status, caregiving, use of social/health services. The use of services, as well as sociodemographic and clinical data in the previous 12 months, were collected. Two models of logistic regression were applied to investigate factors associated with the use of different social/health services, classified as residential or outpatient services (dependent variable).

**Results:** Mean age: 80 yrs(SD=10); women: 71,7%. Most frequent diagnosis were AD(60,3%), mixed forms(19,4%), vascular dementia(10,8%). A caregiver was present in 97% of cases (son:42,4%). Moderate cognitive impairment ( $11 \leq \text{MMSE} \leq 17$ ): 40,7%; severe cognitive impairment ( $0 \leq \text{MMSE} \leq 10$ ): 28,7%. Sixty-nine% presented 2 or more Basic Activity of Daily Living(BADL) lost; ninety-one% presented 4 or more Instrumental Activity of Daily Living (IADL) lost. The 37,9% used a residential or outpatient services. The use of outpatient services is more probable in presence of: caregiver (OR=4,05; IC95%=0,94-17,42); severe (OR=6,37; IC95%=1,92-21,15) or moderate(OR=3,74; IC95%=1,14-12,27) dementia; sleep disorders (OR=1,59; IC95%=1,11-2,27), while it is less probable in presence of depression(OR=0,64; IC95%=0,45-0,92).

The use of residential services was more probable for women (OR=1,65; IC95%=1,08-2,54) and in presence of: euphoria(OR=4,43; IC95%=1,45-13,59), antipsychotic (OR=1,79; IC95%=1,19-2,69), analgesic (OR=2,78; IC95%=0,92-8,40) and antiepileptic drugs (OR=2,19; IC95%=1,02-4,69), while it is less probable in presence of caregiver (OR=0,08; IC95%0,03-0,25), less than 2 BADL lost (OR=0,39; IC95%=0,24-0,64), less than 4 IADL lost(OR=0,3; IC95%0,12-0,74), two OR=0,49; IC95%=0,29-0,81) or more(OR=0,44; IC95%=0,26-0,75) comorbidities; AChEI (OR=0,64; IC95%=0,43-0,96); memantine (OR=0,29; IC95%=0,11-0,74) and psychomotor agitation(OR=0,59; IC95%=0,31-1,11).

**Conclusion:** Our study shows that the use of any social/health services is related to moderate-severe dementia, while preserved functional abilities (BADL, IADL) reduce the use. The presence of a caregiver is related to the use of outpatient services, but reduces the use of residential services, suggesting a better care/attention from the family. Sixty-two% never used any kind of services. Further studies are needed to evaluate the role played by type of caregiver, unmet needs of families, presence of a social net, differences in the offer of services among districts, that could favour/compromise the access.

## **P54**

### **Early risk factors for mental health disorders in Danish children 5-7 years of age. The CCC2000 birth cohort**

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#### **Abstract**

*Objective:* General population studies of mental disorders in younger children are few, and the prevalence and associates of psychopathology in Danish pre-school children is unknown. The main objective of the study is to investigate socio-demographic and perinatal risk factors of mental health disorders in 5-7 year-old children in a general population and in children hospitalized in the first 7 year of life.

*Methods:* The study is a 5-7 years follow-up of the Danish birth cohort The Copenhagen Child Cohort, CCC2000, including 6,090 children from the general population. The cohort was screened for mental health problems by questionnaires to parents and pre-school teachers (Strengths and Difficulties Questionnaire, SDQ). Screen positive children and a random sample of 1330 children were diagnostically assessed after parent interviews and questionnaires to pre-schoolteachers (Developmental and Well-being Assessment, DAWBA). Data on peri-natal adversities, socio-demographic risk factors and hospital admissions were obtained from Danish National Registers.

*Results:* The overall prevalence of mental health disorders in 5-7 years-old children was 4.4% (95%CI: 3.3-5.5). Emotional disorders were found in 2.0% children, behavioural disorders in 1.5% (95%CI: 0.9-2.2) and hyperkinetic disorder in 0.9% (95%CI: 0.4-1.4). The prevalence of pervasive developmental disorders was 1.0 (95%CI: 0.5-1.5). Nearly a third had co-occurrence of mental health diagnoses and the relative risk of having a mental health disorder was significantly higher in boys compared to girls:1.8 (95%CI:1.1 – 3.1).

*Conclusion:* Preliminary results on early risk factors, predictors and the longitudinal course of mental health problems between birth and 7 years in CCC 2000 will be presented at the congress.

**P55**

## **Maternal effects for preterm birth: a genetic epidemiologic study of 630,000 families**

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### **Abstract**

*Objective:* This study was undertaken to disentangle the maternal genetic from the fetal genetic effects for preterm birth and to study the possibility of these effects being explained by known risk factors.

*Methods:* By cross-linking of the population-based Swedish Multi-Generation and Medical Birth registers, 989,027 births between 1992 and 2004 were identified. Alternating logistic regression was applied to model the familial clustering with pairwise odds ratios (PORs), and covariates were included to evaluate if the familial aggregation was explained by exposure to shared risk factors. Generalized linear mixed models were used to estimate the contribution of genetic and environmental effects.

*Results:* Sisters of women who had a preterm delivery had themselves an increased odds of having a preterm delivery (POR = 1.8, 95% confidence interval: 1.5, 2.1), while there was no corresponding increase in odds in families joined by brothers (POR = 1.1, 95% confidence interval: 0.9, 1.4). Twenty-five percent of the variation in preterm birth was explained by maternal genetic factors, whereas fetal genetic factors only marginally influenced the variation in liability.

*Conclusion:* The increased odds ratio between offspring of sisters was independent of maternal risk factors for preterm birth, suggesting that the relative importance of maternal effects is not explained by these well known risk factors.

**P56**

## **Respondents' private theories of change and stability of alcohol habits**

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### **Abstract**

*Objective:* The aim of this study is to describe private theories of change and stability of alcohol habits among individuals with a history of alcohol abuse or alcohol dependence. The meta-theory under examination is Blomqvist's theory of spontaneous recovery with focus on the changing process from addiction.

*Methods:* Data were based on xx subjects from the PART-study. Alcohol habits were measured by the Alcohol Use Disorders Identification Test (AUDIT) at the three phases and some of the respondents, with a cut-off by >11 on AUDIT in the first phase questionnaire, were subject to a SCAN-interview to test for an alcohol diagnosis (current or in remission at the baseline SCAN interview).

*Results:* Results on subjective factor for change and stability in alcohol habits are presented.

*Conclusions:* This pilot study will generate the design for four forthcoming longitudinal studies. The findings of the planned studies may develop and deepen the available knowledge about changing and foremost maintaining factors that affect people's alcohol habits.

P57

## Do psychiatric disorders influence intra-generational social mobility?

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### Abstract

*Objective:* The aim of this study is to investigate the extent to which psychiatric inpatient hospitalization influences intra-generational social mobility.

*Methods:* The data were extracted from the Social Mobility Database, a linkage of several Swedish registries. We selected individuals born 1939-1949 encompassing manual and non-manual classes in the 1980 Census, a total of 906, 868 individuals. During the follow-up period 1973-1979, 19,748 psychiatric hospitalizations occurred due to 1) schizophrenia, 2) alcohol and substance dependency, 3) mood and affective disorders, and 4) neurotic and stress related disorders. Occupational class in 1990 was categorized into high- and low manual, high- and low non-manual, self-employed and unclassifiable. Intra-generational social mobility was measured by the occupational class changes between 1980 -1990. The influence of psychiatric hospitalization on intra-generational social mobility was, so far, analyzed by descriptive methods.

*Results:* In 1980, 44% of the non-hospitalized and 64% of the hospitalized subjects belonged to the manual classes. The non-manual classes constituted 64% of the non-hospitalized and 36 % of the hospitalized subjects. Social stability was common, with 40% of the non-hospitalized and 54% of the hospitalized subjects having the same class in 1980 and 1990. About 40% of the non-hospitalized and 54% of the hospitalized subjects were intra-generationally mobile between 1980-1990. Downwards mobility among manual and non-manual classes was experienced by 8% of the non-hospitalized and 8% of the hospitalized subjects. Upward mobility was more common, with 19% of the non-hospitalized and 14% of the hospitalized subjects. About 9% of the non-hospitalized and 30% of the hospitalized subjects ended up in the unclassifiable group in 1990. Mobility to self-employed occupations was experienced by 3% of the non-hospitalized and 2% of the hospitalized subjects.

*Conclusions:* About 40% of the non-hospitalized and 54% of the hospitalized subjects changed occupational class between 1980 -1990. Social stability was more common among the non-hospitalized (60%) than among the hospitalized subjects (46%). Downward mobility between manual and non-manual classes was similar (8%) among non-hospitalized and hospitalized subjects. While upwards mobility was experienced by 19% of the non-hospitalized and 14% of the hospitalized subjects.

P58

## 25-hydroxyvitamin D and parent-reported depressive symptoms in childhood – a prospective study of a contemporary birth cohort

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### Abstract

**Objective:** Depression affects 1-6% of children or adolescents worldwide and early onset often predicts more serious disease manifestation in later life. Anxiety and depression have a clear seasonal pattern, which suggests a risk factor that is associated with length of photoperiod, such as vitamin D status. Vitamin D deficiency has been shown to affect behaviour, cognitive phenotypes and brain development and morphology in rodents. With respect to humans, evidence from a small number of randomised controlled trials and cross-sectional studies has been inconsistent. To date only studies of human adults have been completed.

**Methods:** A prospective cohort study examining the association of variation in serum total 25-hydroxyvitamin D [25(OH)D], parathyroid hormone (PTH) and albumin-adjusted calcium with parent-reported symptoms of depression in childhood was undertaken. Data were used from the Avon Longitudinal Study of Parents and Children (ALSPAC). Serum 25(OH)D, PTH and albumin-adjusted calcium were measured at mean age 10.3 years. The prevalence of depressive symptoms was defined as scoring in the highest tertile of the Mood and Feelings Questionnaire at the age of 11.7 years (n=3959).

**Results:** In the age, ethnicity, season of blood sampling and gender adjusted model for a 1 standard deviation (SD) greater 25(OH)D the odds ratio of depressive symptoms was 0.97 (95%CI:0.89-1.05), with equivalent results for PTH and calcium being 1.02 (95%CI: 0.96, 1.10 and 0.99 (95%CI: 0.92, 1.06), respectively. With further adjustment for recent traumatic experiences, regular sleeping pattern, family history of psychiatric problems, maternal smoking during pregnancy, child IQ at the age of 8.5 years and socioeconomic and demographic characteristics, these results were unchanged.

**Conclusion:** Our results suggest that in these children variation in 25-hydroxyvitamin D, PTH and calcium are not related to parent-reported symptoms of depression. However, parent-reported scores do not reveal depressive symptoms as early as self-reported measures.

**P59**

## **Changes in adult dental fear during 3.5-year period**

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### **Abstract**

*Objective:* The aim was to study changes in adults' dental fear during a 3.5-year period.

*Methods:* The study group consisted of parents of all 5th and 6th graders (11- to 12-year-olds), except for mentally disabled and handicapped children attending special schools, in the beginning of the 2001-2002 school year in the town of Pori, Finland (n=1691). Children took the questionnaires home in Fall 2001, in Spring 2003 and in Spring 2005, and gave it to one of their parents to be filled out. All three parent's questionnaires were returned by 934 children. In 616 cases the responding parent was the same in every time point. Of the parents, 586 were mothers and 30 were fathers. Their dental fear was evaluated with a single item question with 5 reply alternatives (not afraid, a little afraid, afraid to some degree, quite afraid or very afraid). Those parents who reported being quite or very afraid of dental treatment were considered fearful. The individual stability of dental fear was studied.

*Results:* Of the mothers, 18% had dental fear in 2001, 22% in 2003, and 20% in 2005. For the fathers, corresponding numbers were 7%, 17%, and 10%, respectively. In general, dental fear fluctuated in individual level ( $p=0.018$ ). Of the mothers, 13% responded to be fearful in every time point and 72% responded not to be fearful in every time point. Among 15% of the mothers, dental fear fluctuated. Of the fathers, 7% responded to be fearful in every time point and 80% responded not to be fearful in every time point. Among 13% of the fathers, dental fear fluctuated.

*Conclusion:* There are changes in dental fear over time both in terms of recovery from and development of fear.

## P60

### Postpartum depression and prepregnancy BMI: the HBC Study

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#### Abstract

*Objective:* Postpartum depression (PDD) is a common psychiatric illness seen among women after childbirth. Its prevalence reported from Western countries ranges from 10 to 20%, although it is suggested to amount to 60% in some cultural settings. Such diversity may be accounted for by culture-bound factors, or by the cross-nationally differing prevalence of socio-psychological or environmental risk factors that remain to be undetected. In Japan, the proportion of women with low body mass index (BMI) has been dramatically increasing among women at the reproductive age of 20s and 30s, which arouses concern about maternal health in the pre-, peri-, and ante-natal period. One of the possible adverse effects includes mental problems in mothers, who undergo pregnancy and delivery, with physically handicapped status of low BMI. This study thus investigated whether low BMI prior to pregnancy is a risk factor for PPD by employing data on a prospective follow-up of a birth cohort in Japan: the Hamamatsu Birth Cohort for Mothers and Children (HBC).

*Methods:* We contacted a consecutive series of 522 pregnant women who gave consent to participate in this study and were expected to give birth at our two research sites. Four hundred eighty (92%) of 522 parturients gave birth between 20 December, 2007 and 30 September, 2009, and were assessed for PPD during 3 months after childbirth. Assessment of PPD was made using the Edinburgh Postnatal Depression Scale. We defined PPD as those women with a score of 9 points or over. Statistical analysis was conducted with logistic regression analysis using Stata SE version 10.1. Institutional ethics committee approval was obtained.

*Results:* Low prepregnancy BMI was associated with an elevated risk for PPD (OR for a one-unit decrease in BMI = 1.11, 95%CI 1.00 to 1.21). Other risk factors included lack of social support (OR for no emotional support from anyone = 3.46, 95%CI 1.73 to 6.93), and advanced age in the parturients (OR for 35 years or over = 2.07, 95%CI 1.13 to 3.81).

*Conclusion:* We found that, in Japan, low prepregnancy BMI confers risk to PPD. Searching for the mechanism underlying such an association is required.



## P61

### Mother's unintended pregnancy associated with lower ponderal index at 4 months of the infant: the HBC Study

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#### Abstract

**Objective:** Unintended pregnancy has been reported to be associated with ill health in children in developing as well as developed countries. The reported frequency of unintended pregnancy ranges from 30 to 50%. However, little is known about the outcomes and public health impacts of unintended pregnancy on the infant's health. The present study determines whether unintended pregnancy exerts a detrimental effect on physical growth of the infant.

**Methods:** We enrolled a consecutive series of 389 pregnant women who gave consent to participate in an ongoing prospective study, the Hamamatsu Birth Cohort for Mothers and Children (HBC). We followed them until the infants born to the participating women become 4 months of age. Our interview team asked each woman the intention of pregnancy during mid-gestation, which was categorised as "intended", "mistimed" and "unwanted" under the definition by previous studies. Then, following previous studies, we amalgamated "mistimed" and "unwanted" pregnancy into "unintended" pregnancy. We also collected information on parity, socioeconomic status and life styles (e.g. smoking habit) of the participating family, as well as gestational age and birthweight. As an outcome measure of child growth, we chose the ponderal index (PI) of the infants at 4 months ( $100 \times \text{weight}[\text{g}] / \text{height}[\text{cm}]^3$ ). Mean PI was compared among infants born from two categories of pregnancy intention using t-test, and then ANCOVA was adopted for multivariate analysis with adjustment for covariates (maternal education, paternal education).

**Results:** Parturients with "unintended pregnancy" was 123 (31.6%). Mean PI at 4 months of infants with "unintended pregnancy" was 2.68, whilst that with "intended pregnancy" was 2.74. After controlling for covariates (maternal education, paternal education), the difference was statistically significant ( $p=0.02$ ); mean PI at 4 month for infants of "unintended pregnancy" was 0.06 point lower than that of "intended pregnancy".

**Conclusion:** Unintended pregnancy is a common phenomenon in a representative sample of Japanese women, and has a detrimental effect on physical growth in their offspring.

## P62

### Early- and late-onset of postpartum depression and the associated risk factors: the HBC Study

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#### Abstract

*Objective:* The time frame for postpartum depression (PPD) differs among studies – either 4 weeks or 3 months after childbirth. To address potential difference in PPD in relation to onset of the illness, we investigated risk factors for early- and late-onset PPD using a representative birth cohort in Japan.

*Methods:* We evaluated 504 women who completed the Edinburgh Postnatal Depression Scale (EPDS) for two to three times within 3 months after childbirth. Mothers with an onset of PPD (≥9 points on EPDS) within 4 weeks after childbirth were classified as having early-onset PPD, and those with PPD that occurred during the period of the 5th to 12th week after childbirth were classified as having late-onset PPD. We adopted multinomial logistic regression to investigate risk factors associated with each of early- and late-onset PPD, while simultaneously allowing for all risk factors a priori selected in the model.

*Results:* We evaluated 504 women who completed the Edinburgh Postnatal Depression Scale (EPDS) for two to three times within 3 months after childbirth. Mothers with an onset of PPD (≥9 points on EPDS) within 4 weeks after childbirth were classified as having early-onset PPD, and those with PPD that occurred during the period of the 5th to 12th week after childbirth were classified as having late-onset PPD. We adopted multinomial logistic regression to investigate risk factors associated with each of early- and late-onset PPD, while simultaneously allowing for all risk factors a priori selected in the model.

*Conclusion:* The finding that risk sets for early- and late-onset PPD differ suggests that these two types may have different aetiology.

## P63

### Methods for assessing white matter lesion progression in longitudinal studies: preliminary findings from The Mild Stroke Study

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#### Abstract

*Objective:* We investigate how to assess white matter lesion (WML) progression, as segmentation results are known to be sensitive to the different intensity distributions in longitudinally acquired MRI scans and there exists a lack of consensus in a methodology to segment these features reliably.

*Methods:* We conducted a study in a sample of 10 patients (mean age 72 years) with ischaemic lacunar or minor cortical stroke that had MR scans at the time of onset and 27 months later, who agreed to participate in The Mild Stroke Study. They underwent structural MRI, specifically T2-, T2\*-, T1- and FLAIR-weighted sequences on a GE Signa LX 1.5T scanner. The MR images were pre-processed using FSL tools and the WMLs were segmented by thresholding FLAIR images using an optimized slice dependent threshold and a novel multispectral method developed in-house (MCMxxxVI), each using two different approaches to image intensity normalization. The difference in total WML volume after 27 months was calculated as the difference between follow-up and baseline measurements. We analysed this result in each case and calculated the mean difference across the sample.

*Results:* When the intensity of all images is automatically adjusted (1% of the data saturated at low and high intensities) the results by both methods are similar (mean differences in the longitudinal results: 5.798 cm<sup>3</sup> for the thresholding method and 6.323 cm<sup>3</sup> for MCMxxxVI), whereas visual intensity adjustment results in large differences between the outcomes (mean differences of 3.031 cm<sup>3</sup> and 9,198 cm<sup>3</sup> respectively). For the thresholding method, the intensity inhomogeneities generally lead to an overestimation of WML volume, particularly when dirty white matter areas are prominent which reduces the longitudinal differences.

*Conclusions:* Preliminary results indicate that both methods are highly sensitive to intensity changes, and suggest that great care is required when performing automated serial measurements of WML volumes. More extensive validation in a wider sample is needed, with a variety of white matter lesion extents.

## P64

### ENRIECO: Environmental Health Risks in European Birth Cohorts

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#### Abstract

**Objective:** ENRIECO is a project funded by the European Community 7th Framework Programme that brings together more than 30 European birth cohorts. Its overall aim is to advance knowledge on specific environment and health causal relationships in pregnancy and birth cohorts by providing support to exploitation of the wealth of data generated by past or ongoing studies funded by the European Community and national programmes. Specific objectives are: to make inventories of existing cohorts including a searchable database; to evaluate existing environmental exposure information, methods and tools, including assurance of quality and interoperability, and data access, analysis and validation, and make recommendations; to evaluate existing health information, methods and tools, including assurance of quality and interoperability, data access and validation, and make recommendations; the evaluation of the existing environmental exposure response data, methods and tools, including assurance of quality and interoperability, and data access and validation, and make recommendations; to build databases, and conduct assurance of quality and interoperability, data access, analysis and validation; and to disseminate the knowledge.

**Methods:** ENRIECO is creating an inventory of all existing pregnancy and birth cohorts in Europe with data on environmental exposures. This inventory will be available as a web-based searchable database to other researchers and policy makers. Working groups are evaluating European birth cohort research in specific exposure areas such as air and water pollution, heavy metals, pesticides, persistent organic pollutants, and chemicals of emerging concern, and in specific outcome areas such as reproductive outcomes, childhood respiratory health, neurodevelopment, cancer, growth and obesity. Further, case studies examine areas in which pooling of data across cohorts may be feasible (for example PCBs and birth outcomes).

**Results:** The work of the ENRIECO working groups will be presented.

**Conclusion:** The social relevance of this project is significant as there is an urgent need to evaluate and combine the existing data, methods and tools from European birth cohort studies so as to help identify causal links between environmental exposures and health and provide recommendations for effective policy decisions.

P65

## Long term outcome of pregnancies complicated by hyperemesis gravidarum. A systematic review

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### Abstract

*Objective:* There is evidence that HG is associated with a predominance of female fetuses, lower birth weight and shorter gestational age, but the evidence has not been reviewed systematically. As the adverse effects of prematurity and low birth weight on disease risk in later life have become clear, the repercussions of HG might not be limited to pregnancy alone. The aim of this review was to summarize the available evidence on fetal and neonatal outcome of pregnancies complicated by HG and long term health effects of the offspring.

*Methods:* A literature search was conducted in the electronic databases PubMed and Embase (November 2009). Studies were included that reported on the fetal, neonatal and long term outcome of pregnancies complicated by HG. Furthermore, we tracked references.

*Results:* The search resulted in 204 studies, of these; twenty-four suitable studies were identified. The quality of reporting of most studies was limited. All studies confirmed the higher female/male ratio in pregnancies complicated by HG (OR female fetus 1.28 [1.22, 1.35]). Results on birth weight and gestational age were too heterogeneous to be pooled. One study reported an association of HG and testicular cancer.

*Conclusion:* HG is associated with a higher female/male ratio of the offspring. No estimation can be made about the effect on birth weight and gestational age.

P66

## Long-term (10 year) associations between physical load and chronic low back pain. The Doetinchem Cohort Study

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### Abstract

*Objective:* One of the few risk factors that is consistently associated with low back pain (LBP) is physical load in work or daily life, however, most studies on physical load are cross-sectional or do have a limited follow-up period. Using long-term large scale population-based data we explored the long-term associations between physical load and chronic LBP.

*Method:* Between 1993 and 2007, around 5,700 randomly selected men and women of originally 20-59 years were measured three times with 5 year intervals. Physical load in daily activities (9 items) was assessed by questionnaire at the first two measurements and chronic LBP was measured three times. Multivariate generalized estimating equation models were used to study the longitudinal association between physical load and chronic LBP and the association between time patterns of physical load and chronic LBP. All analyses were adjusted for gender, age, education, work status, body mass index, physical activity and smoking. Multiple imputations were applied to account for missing data.

*Results:* Only awkward postures was associated with chronic LBP in the analyses including all physical load variables (prevalence ratio (PR) = 1.3 (1.1 1.6)). About 7.9% of the participants reported awkward postures at both measurements, 7.8% at the first measurement only and 6.9% at the second measurement only. The association with chronic LBP was identical for awkward postures at both measurements (PR = 1.5 (1.3 1.8)), awkward postures at the first measurement (PR = 1.6 (1.4 1.9)) or awkward postures at the second measurement (PR = 1.5 (1.3 1.8)).

*Conclusion:* Among several physical load factors, awkward postures were most predictive for chronic LBP in the general population, even if awkward postures were only reported at one instance. The avoidance of awkward postures in work or daily life seems still a relevant element of the prevention of chronic LBP.

## **P67**

### **Does a weight loss episode during school-age have any impact on final height?**

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#### **Abstract**

*Objective:* To examine if there is, for schoolchildren during age 7y to 18y, any impact of weight loss episodes, independent of cause, on final height.

*Methods:* Samples from two Swedish national birth cohorts, 1973 and 1981 (all children born on the 15th day of every month), with few missing cases (4.5% and 1.6%, respectively), were studied. Data (height and weight) were collected from school health records and analyzed longitudinally. Episodes of more than 10% reduction in BMI for 1836 boys and 1694% girls born in 1973 and 1512 boys and 1529 girls born in 1981 are described and compared to height at age 18.5y for girls and boys, here considered as final height.

*Results:* For 5,5% boys and 4.8% girls born in 1973 and 4.7% boys and 7.6% girls all with at least an episode of 10% or greater reduction of BMI height at age 18.5 are presented.

*Conclusion:* Severe weight reductions during school-ages have impact on final height for both boys and girls.

**P68**

## **Gene-environment interaction in 7-9-year-old children with depression**

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### **Abstract**

*Objectives:* The aim is to identify environmental risk- and resilience factors, genetic markers and the interaction of these parameters in depressed 7-9-year-old children.

*Methods:* This is a genetic epidemiological study of Major Depressive Disorder (MDD) in children. The study runs in three phases, I: Pilot study, II: Study of risk- and resilience factors in the environment, III: Study of genetic markers and gene-environment interaction. The Danish National Birth Cohort (DNBC) included 100.000 pregnant women in the period from 1996-2002. DNBC supplies questionnaire data and DNA. Registries will supply demographic data. The DNBC 7-year follow up survey included the psychiatric screening interview 'The Strength and Difficulties Questionnaire' (SDQ). On the basis of the SDQ data from children born in 2001-2003 (N~24.000), emotional disorder high-risk groups and control groups are created. Mothers of the selected children will be asked to perform the online diagnostic interview 'The Development and Well-being Assessment' (DAWBA). The purpose of the pilot study is to clarify the best selection criteria for identifying children with MDD by DAWBA.

*Results:* Preliminary results from the pilot study will be presented.

*Conclusions:* There is a need for further knowledge about the genetic and environmental aetiology of early onset MDD. Gene-environment studies require high numbers of cases, and cooperation between research groups is often needed, in order to establish sufficient sample sizes. The results from this project can be an important part of this cooperation, and contribute to larger international studies in a significant matter.



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