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konferanse.

## DEN SEKSTENDE NORSKE EPIDEMIOLOGIKONFERANSEN

SAS-BRYGGEN, BERGEN,

11.-12. NOVEMBER 2008

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## THE 4TH CONFERENCE OF EPIDEMIOLOGICAL LONGITUDINAL STUDIES IN EUROPE (CELSE)

SAS-BRYGGEN, BERGEN,

12.-14. NOVEMBER 2008

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## **Den 16. norske epidemiologikonferansen Bergen 11.-12. november 2008, med forkurs 10. november**

Årets NOFE-konferanse arrangeres i Bergen i regi av Institutt for samfunnsmedisinske fag, medisinsk fødselsregister (Nasjonalt folkehelseinstitutt) og Universitetsforskning i Bergen (Unifob helse). Konferansen er lagt til SAS-hotellet på Bryggen i Bergen.

Mandag 10. november innledes konferansen med forkurset – "Usikkerhet og sannsynlighet. En filosofisk tilnærming", ledet av professor i vitenskapsfilosofi Roger Strand. Kurset holdes i Kalfarveien 31 i lokalene til Institutt for samfunnsmedisinske fag, UiB.

Konferansen har i år som tidligere et bredt spekter av aktuelle tema, som sikkert vil treffe mangfoldet av norske epidemiologer.

Tirsdag 12. november vil konferansens hovedforedragsholder, Holger Ursin, holde foredraget; "Muskel-skjelett epidemien – vår tids største folkesykdom". Muskel-skjelett diagnoser utgjør cirka 50% av alle sykemeldingsperioder og er således en utfordring for folkehelsen.

Sist på tirsdagen blir det utnevning av et nytt æresmedlem i foreningen, før kåring av årets epidemiologiske artikkel. NOFEs årsmøte er som vanlig siste post på det faglige programmet. Om kvelden blir det den tradisjonsrike NOFE-middagen, som i år avholdes på Fløyen, med god utsikt over Bergen.

Vi ønsker dere alle hjertelig velkommen til den 16. norske epidemiologikonferansen. Vi vet det blir et lærerikt kurs og en innholdsrik konferanse, og håper alle får hyggelige dager i Bergen.

I etterkant av årets konferanse vil konferansen "The 4th Conference of Epidemiological Longitudinal Studies in Europe (CELSE)" avholdes fra onsdag 12. november etter lunsj til fredag 14. november. For de som har interesse av denne konferansen finner man et eget program lenger bak i heftet.

### ***Med hilsen fra arrangementkomiteen for NOFE-konferansen 2008***

*Stein Atle Lie, leder (Unifob helse), Astrid Lunde (Institutt for samfunnsmedisinske fag, UiB), Kari Klungsøyr (Medisinsk fødselsregister), Patricia Schreuder (Medisinsk fødselsregister), Rolv Skjærven (Institutt for samfunnsmedisinske fag, UiB), Lorentz M. Irgens (Institutt for samfunnsmedisinske fag, UiB)*

**Den 16. norske epidemiologikonferansen  
Bergen 11.-12. november 2008,  
med forkurs 10. november**

## Program

### **Mandag 10. november, 13:00-17:00**

**Kurs:** Usikkerhet og sannsynlighet. En filosofisk tilnærming.

**Kursansvarlig:** Roger Strand, professor i vitenskapsfilosofi, UiB

**Sted:** Kalfarveien 31, Bergen, Institutt for samfunnsmedisinske fag

**17:00:** *Get-together* (Kalfarveien 31)

### **Tirsdag 11. november**

#### **Den 16. norske epidemiologikonferansen, SAS-Bryggen, Bergen**

10:00-10:25 Registrering og kaffe

#### **Plenumsesjon**

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10:25-10:30	Velkommen	
10:30-11:30	Holger Ursin	Muskel-skjelett epidemien – vår tids største folkesykdom
11:30-11:45	<b>Pause</b>	

#### **Parallellsesjon A1-A2**

##### **Tema: Kvinnehelse**

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11:45-12:00	A1	Anne-Sofie Furberg	Glutathione S-transferase M1 genotype influences salivary 17- $\beta$ estradiol levels in women without adiposity. A study based on hormonal profiles from entire menstrual cycles
12:00-12:15	A2	Lilian Leistad	Prevensjonsvaner blant kvinner 20-24 år

#### **Parallellsesjon B1-B2**

##### **Tema: Perinatal**

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11:45-12:00	B1	Christian Madsen	Ambient air pollution exposure, residential mobility and term birth weight in Oslo, Norway
12:00-12:15	B2	Cecilie Dahl	Early initiation of breastfeeding and prevalence of diarrhea in Rwandan children less than 12 months of age

12:15-13:00 **Lunsj**

#### **Parallellsesjon A3-A5**

##### **Tema: Dødelighet**

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13:00-13:15	A3	Ellen M. Hagen	Mortalitet og dødsårsaker etter traumatisk ryggmargsskade på Vestlandet 1952-2001
13:15-13:30	A4	Hans Magne Gravseth	Suicide in young Norwegians in a life course perspective
13:30-13:45	A5	Kristin Holvik	Male gender and cardiovascular disease are independent positive predictors of 1-year mortality in elderly hip fracture patients

**Parallellsesjon A6-A8****Tema: Muskel-skjelett**

13:45-14:00	A6	Anne Johanne Søgaard	Er det sammenheng mellom psykologisk distress og underarmsbrudd? Osloundersøkelsene 1972/73 og 2000
14:00-14:15	A7	Anne M. Fenstad	The nordic arthroplasty register association – The first report from a unique collaboration
14:15-14:30	A8	Helene Devold	Prescription of anti-osteoporotic drugs during 2004-2007 – A nationwide register study in Norway

**Parallellsesjon A9-A11****Tema: Kosthold/diabetes**

14:30-14:45	A9	Svetlana Skurtveit	Road traffic accident risk in patients with diabetes mellitus, receiving blood glucose-lowering drugs. Prospective follow-up study
14:45-15:00	A10	Magritt Brustad	Dietary patterns in areas with both Sami and Norwegian populations – the SAMINOR-study
15:00-15:15	A11	Tove Nystad	Prevalence of obesity and self-reported type 2 diabetes among Sami, Kvens and Norwegians – the SAMINOR study
15:15-15:30	<b>Pause</b>		

**Parallellsesjon B3-B6****Tema: Metode**

13:00-13:15	B3	Geir Aamodt	A comparison of different methods for spatial prediction
13:15-13:30	B4	Eystein Glattre	For the fun of it: testing the climatologic CO <sub>2</sub> -hypothesis by methods of fractal epidemiology
13:30-13:45	B5	Nina Gunnes	Assessing quality of life among lung cancer patients in a randomized clinical trial: Correcting for missing data
13:45-14:00	B6	Per-Henrik Zahl	Bias in observational studies of the association between hormone replacement therapy and breast cancer

**Parallellsesjon B7-B9****Tema: Metode**

14:00-14:15	B7	Jon Michael Gran	Estimating the causal effect of treatment on survival from HIV – a sequential Cox approach
14:15-14:30	B8	Milada Cvancarova Småstuen	Weighted Cox regression applied to a large dataset of testicular cancer survivors
14:30-14:45	B9	Tron A. Moger	Frailty modeling of bimodal age-incidence curves of nasopharyngeal carcinoma in low-risk populations

**Parallellsesjon B10-B11****Tema: Diverse**

14:45-15:00	B10	Rune Johansen	Har den psykiske helsen i Norge blitt bedre de siste 10 årene?
15:00-15:15	B11	Ruhina T. Biswas	Can long-term exposure to traffic noise increase the risk of cardiovascular diseases? –A follow up of ‘The Oslo Health Study’ by questionnaire
15:15-15:30	<b>Pause</b>		

**Plenumsesjon**

15:30-16:00	<b>Æresmedlem i NOFE (2008), utnevnelse og foredrag</b>		
16:00-16:30	<b>Beste artikkel 2007, kåring og foredrag</b>		
16:30-17:30	<b>Årsmøte i NOFE</b>		
20:00→	<b>Festmiddag</b>		

**Onsdag 12. november****Den 16. norske epidemiologikonferansen, SAS-Bryggen, Bergen****Plenumsesjon A12-A16****Tema: Cancer**

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10:00-10:15	A12	Ragnhild Sørum	Trends in incidence of ductal carcinoma in situ: the effect of a population based screening program
10:15-10:30	A13	Pål Suhrke	Breast cancer incidence and postmenopausal hormone therapy in Norway
10:30-10:45	A14	Paula Berstad	Body mass index and risk of breast cancer in white and African American women: a case-control study
10:45-11:00	A15	Anita Iversen	Timing of menarche and first full-term birth in relation to 17- $\beta$ estradiol levels in premenopausal women. The EBBA-I study
11:00-11:15	A16	Eiliv Lund	Systems epidemiology in cancer
11:15-11:25		Magritt Brustad	Neste års konferanse i Tromsø
11:25-11:30		<b>Avslutning</b>	
12:00-13:00		<b>Lunsj</b>	

## A1

**Glutathione S-transferase M1 genotype influences salivary 17- $\beta$  estradiol levels in women without adiposity. A study based on hormonal profiles from entire menstrual cycles**

Anne-Sofie Furberg<sup>1,2</sup>, Anne McTiernan<sup>3</sup>, Peter T. Ellison<sup>4</sup>, Karen W. Makar<sup>3</sup>, Anita Iversen<sup>2</sup>, Grazyna Jasienska<sup>5</sup> and Inger Thune<sup>6</sup>

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2) Institute of Community Medicine, Faculty of Medicine, University of Tromsø, Tromsø, Norway

3) Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

4) Department of Anthropology, Harvard University, Cambridge, MA, USA

5) Department of Epidemiology and Population Studies, Jagiellonian University, Krakow, Poland

6) The Cancer Center, Ullevål University Hospital, Oslo, Norway

**Objective:** Studies suggest that enzymes involved in the estrogen metabolic pathway are susceptibility factors for breast cancer; however, there is limited direct evidence in relation to estradiol levels. The glutathione-S-transferase M1 enzyme (GSTM1) enzyme is involved in estrogen peroxidation, and a shortage seems to enhance estrogen exposure. A homozygous deletion of the GSTM1 gene leads to total absence of enzyme activity, and studies indicate that an association with breast cancer risk may be modified by body mass. So far, parallel studies on intermediate biomarkers (i.e. estradiol) are largely missing. Thus, in the present study, we assessed the association between a GSTM1 genetic polymorphism (null/rs1065411) and daily salivary levels of 17- $\beta$  estradiol throughout one entire menstrual cycle and evaluated modification of genotype effects according to metabolic profile in 190 premenopausal women aged 25-35 years.

**Material and methods:** The women participated in the Energy Balance and Breast Cancer Aspects study (EBBA-I, 2000-2002) in Tromsø, North Norway (inclusion criteria: healthy, non-pregnant, non-lactating, no current use of exogenous hormones). Salivary levels of 17- $\beta$  estradiol were assessed by radioimmunoassay (The Reproductive Ecology Laboratory, Harvard University). Height and weight were measured. Genomic DNA was extracted from EDTA whole blood. GSTM1 genotyping was done on the ABI PRISM® 3100 Genetic Analyzer (Fred Hutchinson Cancer Research Center). The GSTM1 assay distinguishes between the GSTM1\*A allele (G nucleotide, Lys at aminoacid 173), the GSTM1\*B allele (C nucleotide, Asn at aminoacid 173), and the homozygous gene deletion. Regression models were used to study the relation between genetic (null genotype versus all other alleles combined) and metabolic susceptibility factors, and levels of 17- $\beta$  estradiol.

**Results:** Mean body mass index (BMI) was 24.4 kg/m<sup>2</sup>. The homozygous gene deletion of GSTM1 had a prevalence of 52%, and the frequency of the null genotype was similar in heavy women (BMI  $\geq$  26.3 kg/m<sup>2</sup>, upper quartile) as compared to other women ( $p = .18$ ). The null genotype was associated with lower levels of 17- $\beta$  estradiol by cycle day compared to other alleles ( $p = .04$ ). However, the association was confined to women that were normal weight to slightly overweight ( $p$  for interaction = .01). In women with BMI < 26.3 kg/m<sup>2</sup>, the null genotype was associated with significantly lower levels of 17- $\beta$  estradiol by cycle day compared to other alleles ( $p = .02$ ) and an 18% reduction in overall average level of 17- $\beta$  estradiol throughout the cycle ( $p = .02$ ), while in heavy women no association with estradiol levels was observed.

**Conclusion:** In our study, GSTM1 genotype was a significant determinant of circulating estradiol levels in premenopausal women without marked adiposity. Thus, interestingly our results strongly support that the effect of body mass on estradiol levels and subsequent breast cancer development may be modified by GSTM1 genotype.

## A2

### Prevensjonsvaner blant kvinner 20-24 år

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**Formål:** Antall selvvalgte svangerskapsavbrudd er høyest blant kvinner i alderen 20-24 år. Dette gjelder i Norge så vel som i de øvrige nordiske landene. Foreløpige tall fra Nasjonalt folkehelseinstitutt, Avdeling for Medisinsk fødselsregister, viser at det i 2007 ble utført 29,3 aborter per 1 000 kvinner i denne aldersgruppen. Dette er en økning på 5% fra 2006. På bakgrunn av dette ønsket vi å kartlegge prevensjonsvanene til kvinner i denne aldersgruppen.

**Materiale og metode:** Våren 2008 ble kvinner født i perioden 1. april 1984 - 31. mars 1988 (alder 20-24 år) og som var bosatt og/eller studerte i kommunene Tromsø, Bodø, Hamar og Porsgrunn, invitert til å delta i en spørreundersøkelse om prevensjonsvaner omhandlende tidligere og nåværende bruk av prevensjon. I tillegg ble informasjon om spørreundersøkelsen offentliggjort i lokalmedier, og ved oppslag på universitet - og høyskoler, apotek og legekontor. Etter en purring hadde totalt 1435 kvinner i målgruppen respondert. SPSS ble benyttet i analyser av datamaterialet.

**Resultater:** I alt 93% av kvinnene i dette utvalget oppga at de hadde brukt hormonell prevensjon noen gang, 3,5% hadde kun brukt ikke-hormonell prevensjon, mens de resterende aldri hadde brukt prevensjon. Når det gjaldt de siste 30 dagene, hadde 67% brukt hormonell prevensjon, 9% hadde kun brukt ikke-hormonell prevensjon og 24% hadde ikke brukt noen form for prevensjon. I alt 90% hadde noen gang brukt kondom, hvorav 18% hadde brukt kondom ved siste samleie. Av de som oppga at de ikke hadde brukt prevensjon de siste 30 dagene, oppga 39% at de ikke var seksuelt aktive. Ved spørsmål om kvinnene i hele utvalget følte de hadde nok kjennskap til hormonelle prevensjonsmidler svart 57% ja, men 67% ønsket også mer informasjon om mulige bivirkninger ved bruk av hormonell prevensjon. Over halvparten av kvinner i alderen 20-24 år som brukte hormonell prevensjon ønsket både å regulere smerter/blødninger ved menstruasjon og å forhindre graviditet. Av de som brukte ikke-hormonell prevensjon, oppga omtrent en tredjedel at engstelse for bivirkninger eller ønske om ikke å tilføre ekstra hormoner til kroppen, som grunner til at de ikke brukte hormonell prevensjon. Videre oppga en fjerdedel av kvinnene i denne gruppen at de brukte kondom for å beskytte seg mot seksuelt overførbare sykdommer.

**Konklusjon:** Studien viser at kvinner i alderen 20-24 år generelt sett har et bevisst forhold til prevensjonsbruk, men at de generelt sett ønsker mer informasjon om ulike typer prevensjonsmidler. Videre viser foreløpige tall at abortraten i dette utvalget er noe lavere enn forventet.

Prosjektet er finansiert av Helsedirektoratet.

## A3

**Mortalitet og dødsårsaker etter traumatisk ryggmargsskade på Vestlandet 1952-2001**E.M. Hagen<sup>1,2</sup>, S.A. Lie<sup>3</sup>, T. Rekand<sup>1</sup>, N.E. Gilhus<sup>1,2</sup> og M. Gronning<sup>1,2</sup>

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**Bakgrunn:** Formålet med undersøkelsen var å identifisere de faktorene som har størst betydning for dødeligheten etter en traumatisk ryggmargsskade (RMS) hos pasienter bosatt på Vestlandet og som ble skadet 1952-2001.

**Metode:** Pasienter ble identifisert fra sykehusregistre, og diagnosen ble verifisert ved personlig gjennomgang av journal. Fra journalen ble det hentet opplysninger om skadenivå (cervikalt versus thoracolumbosakralt), og pasientens ryggmargsskade ble klassifisert som komplett eller inkomplett. Ved komplett klinisk skade er det ingen motorisk eller sensorisk funksjon nedenfor skadenivået. Ved inkomplett skade er det i varierende grad motorisk og, eller sensorisk funksjon nedenfor skadenivået. Standardized Mortality Ratio (SMR) ble beregnet ut fra det observerte antall døde sammenholdt med det forventet antall i Norges befolkning, alders- og kjønnsmatchet. Relativ Mortality Ratio (RMR) ble beregnet for kombinasjoner av skadenivå og klinikk, justert for alder, kjønn og skadeperioder. Dødsårsakene (både hovedårsak og underliggende årsaker) ble hentet fra dødsattestene og kodet i henhold til "The European shortlist for causes of death".

**Resultater:** Totalt 401 pasienter (70 kvinner og 331 menn) ble identifisert. Per 31.08.08 var 173 pasienter døde, 143 menn og 30 kvinner. Gjennomsnittlig alder ved skade var 42,6 år (2,6-96,6 år). Gjennomsnittlig alder for menn var 42,0 år og kvinner 46,2 år. Gjennomsnittlig tid fra skade til død var 10,7 år (0,0-45,1 år). Gjennomsnittlig alder for menn var 11,5 år og kvinner 7,6 år. Pasienter med traumatisk RMS hadde signifikant redusert forventet levetid SMR=1,85. Størst reduksjon hadde kvinnene; SMR=2,88 versus menn SMR=1,72. Pasienter med komplett RMS hadde signifikant redusert forventet levetid SMR=4,19. Størst reduksjon hadde pasienter med komplette cervikale skader SMR=6,54 og de med komplette thoracolumbosakrale (TLS) skader SMR=3,08. Pasienter med inkomplette skader uavhengig av skadenivå hadde kun lett redusert forventet levetid SMR=1,26 for cervikale og SMR=1,14 for TLS. Korrigert for alder, kjønn og skadeperiode hadde pasienter med komplett TLS skade en signifikant økt relativ mortalitets risiko RMR=4,56, og komplette cervikale skader RMR=2,49 i forhold til inkomplette cervikale skader. Kvinnene hadde i forhold til menn en signifikant økt RMR på 1,96 (korrigert for alder, skadenivå, klinikk og skadeperiode). De vanligste årsakene til død var hjertesykdom, lungesykdom og kreft. Psykisk sykdom, selvmord/ forgiftning, lungesykdom og reumatologisk sykdom var hyppigere dødsårsak i siste del av observasjonsperioden (1977-2001) enn i første (1952-1976). Urogenitale sykdommer som årsak til død var klart sjeldnere i siste periode sammenlignet med første del av observasjonsperioden. Tretten prosent kvinner var død som følge av selvmord/ forgiftning mot 4% menn, dette var dog ikke statistisk signifikant.

**Konklusjon:** Komplett RMS gir redusert forventet levetid uavhengig av skadenivå. Kvinner har redusert forventet levetid i forhold til menn korrigert for andre faktorer. De viktigste årsakene til død etter traumatisk RMS er hjertesykdom, lungesykdom og kreft.



## A4

### Suicide in young Norwegians in a life course perspective

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**Background:** Suicide is a leading cause of death in young adults. Several risk factors are well known, especially those related to adult mental health. However, some risk factors may have their origin in the very beginning of life. This study examines suicide in the general Norwegian population in a life course perspective, with a main focus on early life factors.

**Methods:** We linked several national registers, supplying personal data on biological and social variables from childhood to young adult age. Participants were all Norwegians live born during the period 1967-1976, followed up through 2004. Persons who died or emigrated before the year of their 19<sup>th</sup> birthday, at which age follow-up started, were excluded. Thus, the study population comprised 610 359 persons, and the study outcome was completed suicide.

**Results:** 1406 suicides (0.23%) were recorded, the risk being four times higher in males than in females. Suicide risk factors included: not being first born (adjusted HR in males and females (95% confidence intervals): 1.22 (1.07 to 1.39) and 1.42 (1.08 to 1.88)), instability of maternal marital status during childhood, parental suicide (mainly in females), low BMI (only investigated in males), low education, and indications of severe mental illness.

**Conclusions:** Suicide in young adults may be rooted in early childhood, and the effect is likely to act through several mechanisms, some of which may be linked to the composition and stability of the parental home. A life course perspective may add to our understanding of suicide.

**A5****Male gender and cardiovascular disease are independent positive predictors of 1-year mortality in elderly hip fracture patients**

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**Background:** In 2004 a unit for elderly with fractures was established in Diakonhjemmet hospital, aiming to reduce delay in operation for hip fracture patients in Oslo, as well as to offer a multi-disciplinary treatment scheme providing orthopaedic and geriatric care for the frail elderly. Around 600 hip fracture patients >65 years residing in eight districts in Oslo are treated annually, constituting about half of all hip fracture patients in Oslo.

**Objectives:** (1) To describe the patient population in the unit for elderly with hip fractures; (2) to study the relationship between delay in operation and postoperative complications; (3) to study whether characteristics relating to the patients as well as to the treatment may predict 1-year mortality after hip fracture surgery.

**Material and methods:** The quality database for elderly with fractures in Diakonhjemmet Hospital include data from medical records regarding age, gender, place of residence, date of fracture, date of admission, type of fracture, type of surgical procedure, blood sample data, length of stay, height and weight, functional data, calcaneal bone mineral density, comorbidity, and postoperative complications for patients admitted to the unit. Per September 2008, the database included 476 patients >65 years with a primary operation for hip fracture during December 2006-August 2008. Of these, 253 patients had been followed up one year after surgery.

**Results:** (1) The proportion of women was 77% (367 of 476). Women were older than men (mean 85.5 vs. 83.2 years,  $p=0.003$ ). Mean body mass index (BMI) at admission was 22 kg/m<sup>2</sup> for both genders (range 14-34 kg/m<sup>2</sup>), implying malnutrition in half of the patients. In those who had two weight measurements ( $n=183$ ), BMI decreased by 0.4 kg/m<sup>2</sup> during the stay ( $p<0.001$ ). Almost half of the patients (48.5%) had cardiovascular disease, and there was no gender difference. Median (25,75-percentile) length of stay was 10 days (4, 16), and time from admission to surgery was 10 hours (5, 19). Thirty-four percent waited <6 hours, and in total 90% waited <24 hours. Eighty-six percent of the falls happened indoors. Older age was a significant predictor for falling indoors.

(2) We observed no association between delay in operation and urinary tract infection, respiratory infection, heart failure, or postoperative wound infection. There was a tendency to a positive association between delay in operation and risk of delirium.

(3) Overall 1-year mortality was 39.5% (100 of 253). Mortality was higher in men than women (47% vs. 37%). Men had almost threefold the odds of dying (OR 2.9; 95% CI 1.1-7.6;  $p=0.033$ ) when adjusting for age, type of fracture, district of residence, BMI, falling indoors or outdoors, delay in operation, cardiovascular disease, and blood transfusion. Having cardiovascular disease was associated with 2.6 times higher odds of dying when adjusting for the same factors including gender (OR 2.6; 95% CI 1.1-6.2;  $p=0.034$ ). None of the other variables in this logistic regression model were significantly associated with mortality.

**Discussion:** Our patient database provides the opportunity to study predictors of outcome after hip fracture in the elderly in order to optimise treatment and care. We found that this is a frail group with high risk of dying. Indoor fallers constituted the majority of the patients, and falling indoors was an indicator of high age and higher mortality. Significant predictors of 1-year mortality after surgery for hip fracture in this group were male gender and cardiovascular disease.

## A6

**Er det sammenheng mellom psykologisk distress og underarmsbrudd?  
Osloundersøkelsene 1972/73 og 2000**

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**Formål:** Det er tidligere påvist en sammenheng mellom lettere psykiske plager og osteoporotiske brudd blant kvinner, men ingen longitudinell studie har funnet tilsvarende sammenheng blant menn. Formålet med denne studien var å se på sammenhengen mellom psykologisk distress registrert blant unge og middelaldrende menn i Oslo i 1972/73 – og underarmsbrudd rapportert retrospektivt ved Andre runde av Oslo-undersøkelsen i 2000.

**Materiale og metode:** Alle menn bosatt i Oslo 40-49 år (n=25,915) og et 7% utvalg av menn 20-39 år (n=4,110) ble invitert til en hjerte-kar undersøkelse i 1972/73. I alt deltok 17,972 (60%). Alle som ble invitert i 1972/73 og som fortsatt bodde i Oslo/Akershus i år 2000, ble invitert til Andre runde av Oslo-undersøkelsen/Oslo II. Totalt deltok 7,393 av dem som deltok første gang. Ved den første undersøkelsen ble mennene foruten opplysninger om symptomer på hjerte-kar sykdom og livsstil, stilt spørsmål: 1) om de hadde vært mer anspent og irritert siste år enn før, 2) om det hadde vært mer enn vanlig press på jobben og 3) om de regnet seg som en person som presser seg selv og velger et høyt tempo. Spørsmålene ble valgt ut for å kartlegge ansenhet/irritabilitet, arbeidsstress og type A-atferd. På grunnlag av faktor analyse, ble det laget en sum-score av disse tre spørsmålene (range 0-3) – kalt psykologisk distress. Ved Andre runde av Oslo-undersøkelsen 28 år senere ble mennene stilt spørsmål om de noen gang hadde hatt brudd i håndledd/underarm – og alder siste gang.

**Resultater:** I alt 6886 av de mennene som deltok begge ganger, besvarte spørsmålet om underarmsbrudd. Det var statistisk signifikant positiv sammenheng mellom underarmsbrudd og arbeidsstress (p=0.026), men noe svakere sammenheng med type A atferd og ansenhet/irritabilitet. Justert for alder var det signifikant sammenheng mellom underarmsbrudd og sum-scoren psykologisk distress (p=0.042). Andelen som rapporterte underarmsbrudd økte jevnt fra 16.3% blant dem som ikke rapporterte noe psykologisk distress, til 20.4% blant dem som svarte ja på alle spørsmålene. Justert for alder, fysisk aktivitet, høyde og alkohol hadde de med score 3 en OR=1.32 (KI 1.07-1.61) (Test for trend p=0.007). Ytterligere justering for sivilstatus, utdanning, KMI, fysisk aktivitet i arbeid, røyking og kronisk sykdom endret ikke på resultatene. Det var ingen statistisk signifikant sammenheng mellom psykologisk distress og underarmsbrudd etter 50 år.

**Konklusjon:** De som rapporterte ansenhet/irritabilitet, høyt stressnivå på jobben og type A atferd i alderen 20-49 år hadde økt risiko for underarmsbrudd. Resultatene må sees i lys av at bruddene er selvrapportert og at de kan ha skjedd langt tilbake i tid, også før opplysningene om psykologisk distress ble innhentet.

## A7

**The Nordic Arthroplasty Register Association: The first report from a unique collaboration**

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**Hensikt:** Datautdrag fra hofteproteseregistrene i de tre skandinaviske landene er blitt samlet i en analysefil. Hensikten er å lage en felles nordisk analysefil slik at epidemiologi, demografi og resultater for spesielle pasientgrupper i landene kunne sammenlignes direkte. Dette gir en unik mulighet til å studere resultater i pasientgrupper som er for små i hvert enkelt land. På grunn av forskjeller i systemene har det hittil vært begrensede muligheter for å sammenligne resultater og for samarbeid mellom registrene i de nordiske landene.

**Materialer og metode:** Registrene hadde i utgangspunktet ulike kodesystem og de registrerte parametre var ulike. Det ble derfor etablert et nytt kodesystem. Det ble kun inkludert parametre som samtlige registre kunne levere data på. Primære totale hofteproteser fra 1995-2006 ble selektert for studien. Danmark, Sverige og Norge leverte data etter at disse var blitt anonymisert og konvertert til det nye kodesystemet. Cox multipl regressjon, med justering for alder, diagnose og kjønn ble brukt til overlevelsesanalyser, med revisjon uansett årsak som endepunkt.

**Resultater:** Totalt 280201 primær operasjoner ble inkludert i studien; 69242 fra Danmark, 140821 fra Sverige og 70138 fra Norge. I Danmark og Sverige var 58% og 60% av pasientene kvinner, mens det i Norge var hele 70% kvinner. Hoftesykdom i barndommen var årsak til operasjon hos 3,1% i Danmark, 1,8% i Sverige og 8,7% i Norge. Det er stor forskjell i valg av protesetyper mellom landene. Bare tre protesetyper (Charnley (DePuy), Exeter (Stryker) og Lubinus IP /SPII (Link)) var blant de ti vanligste i alle tre land. Sementerte proteser ble brukt i 46% av pasientene i Danmark, 89% i Sverige og i 79% i Norge. Også operasjonsteknikk er forskjellig. Bakre tilgang var brukt ved 91% i Danmark, 60% i Sverige og 24% i Norge. Av de totalt 280201 primær operasjonene hadde 9596 blitt revidert. Samlet for alle proteser i de respektive land var 10-års overlevelse 92,0% (95% KI: 91,6 – 92,4) i Danmark, 93,9% (95% KI: 93,6-94,1) i Sverige og 92,7% (95% KI: 92,3-93,0) i Norge. I Danmark var 34% av revisjonene gjort på grunn av luksasjon sammenlignet med 23% i både Sverige og Norge. Utskifting av bare kopp eller liner ble gjort ved 44% av revisjonene i Danmark, 29% i Sverige og 33% i Norge.

**Konklusjon:** Dette unike samarbeidet er nå i funksjon og vi har påvist forskjeller mellom landene på kjønnsfordeling, diagnoser, protesevalg, fiksasjonsmetoder og revisjonsårsaker. Det store antallet pasienter i denne analysefilen vil forbedre våre muligheter i fremtidig forskning.

**A8****Prescription of anti-osteoporotic drugs during 2004-2007 – a nationwide register study in Norway**

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**Objective:** The incidence of osteoporotic fractures in the Norwegian population is among the highest ever reported. Prevention of these fractures could save the society for expenses to hospital stays and nursing homes, and patients for pain, loss of quality of life and premature death. However, over-treatment may burden patients with side-effects and the society with unnecessary expenses. The aim of this study was to assess the annual prevalence and incidence of the prescription of anti-osteoporosis drugs by age, gender and place of living during 2004-2007.

**Material and methods:** Data from patients aged  $\geq 40$  years receiving bisphosphonates (alendronate with or without cholecalciferole, risedronate, ibandronate, etidronate with or without calcium), raloxifene or teriparatide in 2004-2007 were retrieved from the Norwegian Prescription Database (NorPD). The NorPD covers the total population in Norway. Key measurements were prevalence, resident county of bisphosphonate users, incidence and prescription refill. Prescription refill represent patients dispensed at least one prescription of osteoporosis drugs in both 2005 and 2007.

**Results:** Totally 81 943 persons (89% women and 11% men) were dispensed at least one prescription on osteoporosis medicine during 2004-2007, which corresponds to 3.8% of the Norwegian population  $\geq 40$  years of age. Of all prescribed anti-osteoporosis drugs dispensed in 2007, bisphosphonates constitute 97%. The prevalence of overall bisphosphonate use among women increased from 40.4 in 2004 to 44.5 per 1000 in 2006, but did not increase further in 2007. The same pattern was seen in men. The use of alendronate, which represented 91% of all the bisphosphonate-use in 2007, increased from 2004 to 2007 while the use of the other bisphosphonates decreased. The counties with highest overall bisphosphonate use were Møre og Romsdal and Sogn og Fjordane, whereas the lowest were seen in Finnmark, Vestfold and Vest-Agder. The incidence rate of overall bisphosphonate use decreased from 2005 to 2007. Among those dispensed a bisphosphonate in 2005, 74% refilled at least one prescription in 2007.

**Conclusion:** The prevalence did not increased from 2006 to 2007 in the same extent as the previous years, and the incidence rate for overall bisphosphonate use decreased during the study period. Almost 3/4 of those dispensed a bisphosphonate in 2005 refilled their prescription in 2007.

**A9****Road traffic accident risk in patients with diabetes mellitus, receiving blood glucose-lowering drugs. Prospective follow-up study**

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**Background:** Studies have shown that patients with diabetes mellitus may have a slightly increased risk of road traffic accidents as a driver, but results are inconsistent. Management of diabetic patients is progressively aiming at near normoglycemia, and new data are needed.

**Objectives:** We wanted to investigate, at a national level, whether patients using insulin or oral anti-diabetics had an increased risk of road traffic accidents compared to those not using these drugs.

**Methods:** All Norwegians 18-69 years (3.1 million) were followed from April 1<sup>st</sup> 2004 until the end of September 2006. Information on prescriptions, road traffic accidents and emigration/death was obtained from the following population-based registries: the Norwegian Prescription Database, the Road Accident Registry and the Central Population Registry. The exposure period was after the first insulin or oral antidiabetics prescription received during this period had been dispensed. Standardized incidence ratios (SIRs) were calculated by comparing the incidence of accidents in the exposed person-time to the incidence of accidents in the unexposed person-time.

**Results:** A total of 20,494 road traffic accidents with personal injuries were registered in Norway in this period. 183 accidents were registered for insulin users without antidiabetics and 219 for users of oral blood glucose-lowering drugs without insulin. The SIR (95% CI) for all ages and both genders combined were: insulin 1.4; 1.2-1.6, oral antidiabetics 1.2; 1.0-1.3 and users of selective beta-2-adrenoreceptor agonists (i.e. anti-asthmatics) 1.3; 1.2-1.3. The highest SIRs were found among the youngest insulin users (18-34 years old).

**Conclusions:** A slightly increased risk of being involved in a road traffic accident was observed for drivers prescribed insulin, while no increased risk was observed for drivers prescribed oral antidiabetics. The increased risk observed for insulin users was similar to that observed for users of anti-asthmatics.

## A10

### Dietary patterns in areas with both Sami and Norwegian populations – the SAMINOR-study

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**Objectives:** To identify dietary patterns and to investigate their association with selected lifestyle and demographic factors, ethnicity and self perceived health.

**Study design and methods:** Population-based cross-sectional design, using food frequency questionnaires. A total of 12 811 subjects aged 36-79 years participated from the municipalities in Norway where more than 5% of the population reported to be Sámi in the 1970 Census, in addition to some selected districts. The data were collected during 2003-2004. A principal component analysis was utilised to assess the associations among food variables. Seven principal components were then used as input in a cluster analysis.

**Results:** Five dietary patterns were identified and labelled “reindeer”, “fish”, “average”, “fruit and vegetables”, and “Westernized, traditional marine”. The reindeer pattern was highly represented by subjects with three generations of Sámi language (Sámi I), obese subjects and those with low physical activity level. The fish pattern was dominated by women and had the largest proportion reporting their health as being “not so good” (35%). However, this pattern had the largest proportion of subjects in the highest age category. The fruit and vegetable pattern was characterised by a health-conscious life-style, included more women than men, and had the largest proportion reporting “very good” health. Ethnicity did not play a major role in predicting dietary patterns except for the reindeer pattern, especially in the inland areas.

**Conclusion:** In the dietary cluster analysis we identified five distinct dietary patterns that were also characterised by additional life-style factors.

## A11

### Prevalence of obesity and self-reported type 2 diabetes among Sami, Kvens and Norwegians – the SAMINOR study

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**Objectives:** To estimate the prevalence of obesity and self-reported type 2 diabetes and to study the association between obesity and self-reported diabetes in different ethnic groups in northern Norway.

**Design:** Cross-sectional population-based study carried out in 2003-4 in an area with mixed Sami, Kvens and Norwegian populations, called the SAMINOR study. The attendance rate was 60.6%.

**Subjects:** A total of 7064 men and 7543 women, aged 36-79 years.

**Measurements:** Height, weight, waist circumference and blood pressure were measured and body mass index (BMI) calculated. Self-reported diabetes and lifestyle information were collected by questionnaire and blood lipids were analysed.

**Results:** The prevalence of obesity ( $\text{BMI} \geq 30$ ) was 38% and 25% in Sami- and Norwegian women and 27% and 24% in the men, respectively. More than 40% of women in all ethnic groups have excess abdominal fat, whereas for men the highest prevalence was for the Norwegian population (25%). The prevalence of obesity increased with increasing age. Prevalence of diabetes was 4.1%, with no gender and ethnic differences. Age, abdominal obesity, BMI, family history of diabetes, hypertension and dyslipidaemia were all associated with increased diabetes. Drinking more than four cups of coffee a day had a protective effect on diabetes in women.

**Conclusion:** The prevalence of obesity is high in this population, particularly among women. However, gender and ethnic differences in the prevalence of diabetes were not observed. Our findings suggested a need for attention to be turned to this obesity epidemic in all ethnic groups.



## A12

### Trends in incidence of ductal carcinoma in situ: the effect of a population based screening program

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**Objective:** The Norwegian Breast Cancer Screening Program (NBCSP), a nationwide organised breast cancer screening program for women aged 50-69 years has gradually been implemented by county in the period 1995-2004. Studies in other counties have indicated associations between implementation of screening and increased incidence of pre-invasive breast cancer (Ductal carcinoma in situ, DCIS) in women attending screening. So far, such an association has not been shown in Norway, where detailed data of high quality is available. The aim is to study the effect of organised screening on trends in incidence of DCIS in Norway.

**Material and methods:** Data were obtained from the incidence database of the Cancer Registry of Norway and the screening database of the NBCSP. All new pure primary cases of DCIS in the period 1993-2006 were retrieved as the basis of the study, n=2862. Information about invitation and attendance to organised screening were given for the underlying female population, n~2.5 mill, of which 24% of the women have been invited at least once to screening. To analyse the trends in incidence descriptive analysis were used.

**Preliminary results:** The age-adjusted incidence of DCIS increased from 4/100 000 women-years before the implementation of organised screening (1993-4) to 12/100 000 women-years in the last period after implementation (2005-6). Correspondingly, the mean annual number of DCIS increased from 91 to 279 cases. Among women in the age-group of screening (50-69 years) the incidence increased from 9 to 43/100 000 women-years. The proportion of DCIS detected by screening was 44% overall in the study period, and 64% among women aged 50-69 years.

**Conclusion:** The incidence of DCIS has risen dramatically the last decades in Norway. The implementation of organised mammography screening can be considered as the main contributor to this increase.

## A13

### Breast cancer incidence and postmenopausal hormone therapy in Norway

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**Background:** In the randomized Women's Health Initiative (WHI) trial, the breast cancer incidence was raised by 24% after a mean exposure of six years to estrogen plus progestin<sup>1</sup> while there was no increase for estrogen alone<sup>2</sup>. In contrast, substantially higher over-risks have been reported in observational studies like the British Million Women Study<sup>3</sup> and two Norwegian studies<sup>4,5</sup>. After 2002 postmenopausal hormone therapy (HT) use has plummeted and this has been suggested as the causal factor behind a recent incidence decline in breast cancer in some countries. We have tested whether this may be the case in Norway by comparing the fluctuations of HT use and incidence of breast cancer in four Norwegian counties.

**Material and methods:** In Akershus, Oslo, Rogaland and Hordaland (AORH) mammography service screening started in 1996, and the attendance rates have been stable for the last decade. We obtained breast cancer numbers from the Cancer Registry of Norway and total HT sales from the data reported by wholesalers to the Norwegian Institute of Public Health. Defined Daily Doses (DDD) are used as units of measurement. We compared sales data and breast cancer incidence rates in a first period (2000-1) and a second period (2005-6) assuming that all of the HT influence occurred in the age group 50-69. We have used power analysis to calculate the probabilities to observe a reduced breast cancer incidence for different risk estimates obtained from observational studies and the WHI trial.

**Results:** Total sales figures of HT decreased by almost 50% from 209 000 DDD/day (2000-1) to 111 000 DDD/day (2005-6). The sales of estrogen plus progestin combinations fell by more than 60%, from 115 000 DDD/day (2000-1) to 44 000 DDD/day (2005-6). In the thirteen years from 1994 to 2006 the numbers of new breast cancer cases in the AORH counties in the age group 50-69 were 312, 318, 518, 589, 504, 479, 490, 529, 497, 570, 540, 598 and 550. There is no statistically significant trend downwards in incidence rates from 2001 ( $p = 0.75$ ). The 8% incidence reduction from 2005 to 2006 is not statistically significant either ( $p=0.07$ ). Power analysis shows that given a 60% decline in the use of estrogen plus progestin, the population of the AORH counties is too small to observe the corresponding decline in breast cancer incidence if users of combined hormone preparations have a 24% increased risk for breast cancer (WHI trial) while the power is above 80% to observe the estimated effect in the observational studies.

**Conclusion:** The marked decrease in HT-use after 2001 was not followed by any significant decrease in breast cancer incidence in the AORH-counties. It is unlikely that the marked increase in HT-use during the 1990ies is a major cause for the contemporary increase in breast cancer incidence in Norway.

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**A14****Body mass index and risk of breast cancer in white and African American women: a case-control study**

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**Objective:** Large body size has been associated with decreased premenopausal breast cancer risk and increased postmenopausal risk, although the data are not completely consistent. To what extent these associations differ between white and African-American (AA) women is largely unknown.

**Material and methods:** We analyzed data from the Women's Contraceptive and Reproductive Experiences Study (Women's CARE) in 4082 white and AA breast cancer case patients and 4177 control subjects aged 35 to 64 years. We used multivariate regression analysis to determine odds ratios (ORs) as measures of relative risk of breast cancer associated with self-reported body mass index (BMI) at age 18 and 5 years prior to diagnosis (recent BMI). We analyzed these associations by menopausal status and ethnicity.

**Results:** BMI at both time points was inversely associated with breast cancer risk in both pre- and postmenopausal women. This inverse association was strongest for BMI at age 18, where women reporting BMI  $\geq 25$  kg/m<sup>2</sup> were at 24% and 32% lower risk of pre- and postmenopausal breast cancer than women reporting BMI  $< 20$  kg/m<sup>2</sup> ( $P_{\text{trend}} = 0.09$  and  $0.001$ ). The inverse association between recent BMI and premenopausal breast cancer risk was of borderline statistical significance ( $P_{\text{trend}} = 0.05$ ). Recent BMI was inversely associated with postmenopausal breast cancer only among white women (OR in women with recent BMI  $\geq 35$  kg/m<sup>2</sup> vs.  $< 25$  kg/m<sup>2</sup> was 0.63, 95% CI 0.45-0.89,  $P_{\text{trend}} = 0.007$ ,  $P_{\text{effect modification by ethnicity}} = 0.02$ ). Recent BMI was not associated with risk of postmenopausal breast cancer among AA women. These inverse associations among postmenopausal white women were stronger for estrogen and progesterone receptor (ERPR) negative cancer ( $P_{\text{effect modification by ERPR}} = 0.04$  for BMI at age 18 and  $P_{\text{effect modification by ERPR}} = 0.004$  for recent BMI). Among postmenopausal AA women, we observed a positive association between recent BMI and ERPR positive cancer (OR in women with BMI  $\geq 35$  kg/m<sup>2</sup> vs.  $< 25$  kg/m<sup>2</sup> was 1.81, 95% CI 1.07-3.08,  $P_{\text{trend}} = 0.03$ ). We observed no effect modification by hormone therapy history among postmenopausal women.

**Conclusion:** Our results suggest that large body size at age 18 may be inversely associated with breast cancer risk in pre- and postmenopausal white and AA women below age 64. In premenopausal women, recent large body size may also be protective. Among postmenopausal women, the association between recent BMI and breast cancer risk may differ by ethnicity and by ERPR status of tumor.

## A15

### Timing of menarche and first full-term birth in relation to 17- $\beta$ estradiol levels in premenopausal women. The EBBA-I study

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**Objective:** Breast cancer is the most common cancer among women in Norway as well as worldwide; a total of 2,673 new cases were diagnosed in Norway in 2006. Experimental, epidemiologic and clinical studies indicate that the ovarian hormones, estradiol and progesterone, represent key exposures related to risk of breast cancer. In Norway there is a trend towards early age of menarche and having children later in life. Age at menarche and age at first full-term birth are established risk factors for breast cancer. Interestingly, the interval between these milestones of female reproductive history is associated with risk of breast cancer. We therefore hypothesize that the level of free 17- $\beta$ -estradiol throughout an entire menstrual cycle, is associated with the timing of menarche and first full-term birth.

**Material and methods:** In 2000-2002 healthy women in the Tromsø region were invited to participate in the Norwegian Energy Balance and Breast cancer Aspects (EBBA-I) study at the Department of Clinical Research, University Hospital North Norway. A total of 204 women were recruited and met the following inclusion criteria: age 25-35 years, regular menstrual cycles, no fertility problems or gynaecological disorders, not taking any hormonal contraception, and not being pregnant or lactating for 6 months before recruitment. Data on reproductive history was assessed by questionnaire and by interview. The women collected daily morning saliva samples throughout one entire menstrual cycle. The salivary level of 17- $\beta$ -estradiol was assessed by radioimmunoassay (RIA) at The Reproductive Ecology laboratory; Harvard University, USA. Data on possible confounders were collected by measurements, questionnaires, daily logs on diet and physical activity, clinical examinations, and serum samples. We used regression modelling in Stata SE 10.0 to test whether timing of menarche and first full term birth is associated with circulating level of estradiol.

**Results:** The 204 EBBA women were in average 30.7 years with a mean BMI of 24.4 kg/m<sup>2</sup>. Mean age at menarche was 13.1 years and mean cycle length was 28 days for the 98 parous women. The mean age at first full-term birth was 24.5 years. Preliminary results indicate that a long interval between age at menarche and age at first birth is associated with lower salivary levels of 17- $\beta$ -estradiol throughout an entire menstrual cycle.

**Conclusion:** Our results indicate that timing of menarche and first full-term birth is associated with premenopausal levels of estradiol, a major biomarker of breast cancer risk.

## A16

### Systems epidemiology in cancer

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Prospective studies in cancer epidemiology have conserved their study design over the last decades. In this context, current epidemiological studies investigating gene-environment interactions are based on biobank for analysis of genetic variation and biomarkers, using notified cancer as outcome. These studies result rather from the use of high-throughput technologies than from the development of novel design strategies. Here we propose the globolomic design in order to run integrated analysis of cancer risk covering the major -omics in blood and (tumor) tissue. We defined this design as an extension of the existing prospective design by collecting tissue and blood samples at time of diagnosis including biological material suitable for transcriptome analysis. The globolomic design opens up for several new analytical strategies and where gene expression profiles could be used to verify mechanistic information from experimental biology adding a new dimension to causality in epidemiology. This could improve, for example, the interpretation of risk estimates related to single nucleotide polymorphisms in gene-environment studies by changing the criterion of biological plausibility from a subjective discussion of *in-vitro* information, till observational data of human *in-vivo* gene expression. This ambitious design should consider the complexity of the multistage carcinogenic process, the latency time, and the changing lifestyle of the cohort members. This design could open the new research discipline of systems epidemiology defined in this article as a counterpart to systems biology. Systems epidemiology with a focus on gene functions challenges the current concept of biobanking which focuses mainly on DNA analyses.

**B1****Ambient air pollution exposure, residential mobility and term birth weight in Oslo, Norway**

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**Background:** Epidemiological studies have shown a relationship between particle exposure and community health effects. Birth weight is associated with higher risk of infant and childhood mortality and adult health. Several studies have examined possible associations between birth outcomes and exposure to environmental factors such as tobacco smoking, ambient and indoor air pollution.

**Methods:** We used a population-based approach by using information obtained from a national birth registry to examine associations between ambient environmental exposure, residential mobility and term birth weight. A dispersion model was used to capture spatial and temporal variation in ambient air pollution by linking residential address history and work address for a total of 25 229 pregnancies in Oslo in the period of 1999 to 2002.

**Results:** Ambient air pollution was associated with birth weight in both crude and adjusted models. The association was statistical significant at 0.05 level for those women who did not change residential address during pregnancy and for the highest exposed pregnancies. The dispersion model gave better spatial variation in exposure compared to only using a central monitoring station. The observed association was modified and not statistical significant after adjusting for parity. Still, the main association between birth weight and air pollution was observed for parity>1.

**Conclusions:** The results indicate that residential mobility during pregnancy could introduce noise in any possible association between ambient air pollution and term birth weight. Furthermore, factors such as parity could be a confounder due to differences in mobility and maternal ethnicity.

## B2

### Early initiation of breastfeeding and prevalence of diarrhea in Rwandan children less than 12 months of age

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**Background and significance:** According to data from the Demographic and Health Survey (2005) in Rwanda, 9% of children less than 6 months of age and 24% of those between 6-12 months of age suffered from diarrhea in the two weeks before the mother's interview. Breastfeeding is widespread in Rwanda, but contrary to international recommendations (adopted by the Rwandan government), some infants are not being put to the breast within one hour after birth, and may therefore not receive the protective effects of colostrum. This feeding practice may increase children and infants' risk of diarrheal diseases.

**Methods:** The Demographic and Health Survey (2005) is an observational study conducted for the third time in the Rwandan population. Among mothers of children 0-12 months of age, we analyzed the association between putting the child to the breast within one hour after birth, and whether the child had had diarrhea in the last 14 days before the survey. Children who had suffered from diarrhea were compared to those who had not, within two age strata, 0-6 months and 6-12 months. Multiple logistic regression models were constructed, taking potential confounders into account. Odds ratios were used to determine the association between the main predictor variable (whether the child was put to the breast within one hour after birth), and the main outcome variable (whether the child reportedly had an episode of diarrhea in the last 14 days before the survey), in both univariate and adjusted models.

**Results:** Children less than 12 months who were put to the breast within one hour after birth had a 40-50% lower odds (unadjusted) of having had an episode of diarrhea in the last 14 days before the survey, compared to children who were not put to the breast within one hour after birth, 0-6 months: OR = 0.48, (95% CI: 0.28, 0.84) and 6-12 months: OR = 0.57 (95% CI: 0.37, 0.88). This estimate remained unchanged in the adjusted model for the younger age group. In the older age group, when adjusting for significant variables, this relationship disappeared. Two adjusted models were developed for the older age group: Model 1: OR = 0.84 (95% CI: 0.2, 2.8), and Model 2: OR = 0.49 (95% CI: 0.12, 1.95).

**Conclusion:** There is a protective effect of initiating breast feeding within one hour after birth on diarrhea prevalence before 6 months of age, but this effect diminishes after 6 months.

## B3

### A comparison of different methods for spatial prediction

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**Objective:** In geostatistics, there is a need for methods to predict the value of some attribute, such as exposure intensity, at a new location given a set of measurements. The methods must accommodate a latent spatial process governing the dependencies between the locations. Prediction problems are also often multivariate, with more than one variable observed at each location. In air-pollution studies, different gases and particulates of different sizes are observed at each monitoring station. In this article we compare different prediction methods and we evaluate their appropriateness. We include different Kriging methods and a smoothing splines method using thin plate splines. Our aim is two-fold: First we wish to compare univariate and multivariate methods. Multivariate Kriging includes fitting a large set of variogram and cross-variogram functions, so it is of interest to study if single models for each variable will perform better than a larger battery of cross-variogram functions. The second aim is to investigate performance when there is uncertainty not only in the predictions, but also in the parameters of the model (Bayesian and empirical Bayes methods).

**Materials and methods:** We used air-pollution data from Los Angeles to compare the different methods, using cross-validation as our strategy to compare the different methods. We fitted separate models for 12 different communities in Los Angeles. The following gases were the multivariate response variables: NO<sub>x</sub>, NO<sub>2</sub>, and O<sub>3</sub>, while traffic density and distance to the nearest main road were explanatory variables.

**Results and conclusions:** We conclude that Bayesian methods show better performance than maximum likelihood methods (or weighted least squares). The difference between fitting multivariate and univariate models was not significant.



**B4****For the fun of it: testing the climatologic CO<sub>2</sub>-hypothesis by methods of fractal epidemiology**Eystein Glattre<sup>1,2</sup> and Jan F. Nygård<sup>2</sup>

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One of the tentative explanations of global warming is the CO<sub>2</sub>-hypothesis saying that there exists a cause-effect relationship between global CO<sub>2</sub> air concentration and global surface air temperature. We have for fun tested this hypothesis using principles and methods of fractal epidemiology and annual, global data published by the databanks HadCRUT3gl (1850-2008) for temperature and NOAA ESRL, Mauna Loa (1959-2007) for CO<sub>2</sub>. The annual, global CO<sub>2</sub> values for 1851-1899 were computed by linear interpolation based on ice core estimates of the annual, global CO<sub>2</sub> concentration for the years 1847, 1854, 1869, 1874, 1878, 1887, and 1899.

With CO<sub>2</sub> and temperature values for 1851-99 as reference our analysis showed that the series of annual, global CO<sub>2</sub> from 1959 through 2007 is non-fractal while the series of annual, global air temperatures for the same period is fractal – implying that global temperature is influenced by a complexity of causal factors. Analysis also showed that the annual, global temperature is a 1/f signal or noise that reflects a background in self-organized criticality. Finally, analysis showed that there exists a law-like, moderately correlated, complexity-association of annual, global CO<sub>2</sub> and annual, global temperature. If CO<sub>2</sub> is the cause and temperature the effect (as the hypothesis contends), this means *inter alia* that a change in global CO<sub>2</sub> will not by necessity be succeeded by any noticeable change in global temperature and a change in the latter will not by necessity have been preceded by any noticeable change in the former.

**B5****Assessing quality of life among lung cancer patients in a randomized clinical trial: Correcting for missing data**

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**Objective:** The concept of self-reported health-related quality of life has been an area of research over the past 20 years, and international validated questionnaires have been developed in this regard. We consider a randomized phase III study of radiation therapy with concurrent docetaxel versus radiation therapy alone in non-small cell lung cancer stage IIIA/B. In order to assess the quality of life, the EORTC QLQ-C30 questionnaire was administered to the patients at scheduled control weeks after inclusion in the study. During follow-up, subjects occasionally failed to fill in the questionnaire at one or several of the control weeks, resulting in missing data. Our objective is to estimate the score means of discrete longitudinal quality-of-life measures in the presence of monotone missingness.

**Material and methods:** We have analysed a monotone (in terms of missingness) subset of the data as regards estimation of the mean score of two different quality-of-life measures in a hypothetical drop-out-free population. The employed methodology includes three newly developed methods for estimating the mean score of discrete longitudinal data subjected to monotone missingness: the linear-increments method, the inverse-probability-weighting method, and the Markov-process method.

**Results:** Results from the data analyses show that the calculated mean of all the valid (with respect to monotone missingness) observed score measurements at a certain time is larger compared to the estimated score means. Thus, unless we adjust for the missing data using appropriate methods, the mean score is easily overestimated, indicating higher quality of life among the patients than in reality.

**Conclusion:** The mean score estimators corresponding to the three methods mentioned above are able to correct for the bias in the unadjusted observed mean score, induced by the missing data.

## B6

### Bias in observational studies of the association between hormone replacement therapy and breast cancer

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**Objective:** The association between hormone replacement therapy (HRT) and the breast cancer risk is much stronger in observational studies than in the randomized Women Health Initiative (WHI) trial. Here we study how much of the difference that may be explained by bias in the observational study design and explore the possible sources of the bias.

**Data and Methods:** We used data from the WHI trial to construct a data set which could be analyzed as an observational cohort study with 3 year follow-up and where women were categorized with respect to how long they had used hormones at entry (less than one year and 1-4 years, respectively). The main outcome measure was the relative risk of breast cancer.

**Results:** The observational study resulted in a relative risk for breast cancer of 1.48 for women who had used HRT for 1-4 years at study entry and were followed up for 3 years (on average these women had used HRT for six years), compared with non-users. This is substantially higher than the relative risk of 1.10 after the 6 years follow-up in the originally randomized WHI trial. The observation studies are also sensitive to recall bias – women are asked retrospectively about how long they have used HRT when they are included in the study. If women who had used HRT prior to randomization were included, the relative risk was 1.68 compared to 1.24 after 6 years follow-up in the WHI trial. Recall bias may increase the risk from 1.48 to 1.68. Alternatively, one may argue that reduced sensitivity and new HRT users among those initially reporting no use in the observational studies may increase the relative risk from 1.24 to 1.68.

**Conclusion:** The association between HRT and the breast cancer risk is seriously overestimated in some important observational studies. The sources of bias are i) a temporary decline in the breast cancer risk when women start using HRT (because of reduced sensitivity at mammography) ii) many women reporting not using HRT at start of an observational later start using HRT and iii) recall bias in the observational study design.

**B7****Estimating the causal effect of treatment on survival from HIV – a sequential Cox approach**

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**Objective:** Estimating treatment effects in the presence of time dependent confounding has been addressed using marginal structural models (MSMs) by Robins et al. These models give an appropriate adjustment for confounding using inverse probability of treatment weights (IPTW). In this paper we study a more regression based approach to the same problem, avoiding IPTW weighting, fitting standard Cox models to subsets of the data valid for comparison. Combining many such subanalyses, we get an overall effect estimate.

**Material and methods:** The method is based on constructing subsets going from a certain time point with individuals starting treatment at that time (cases), and comparing them to the individuals not yet on treatment by the same time, for as long as they do not start treatment (controls). For each possible time point, a standard Cox analysis can be carried through on such a constructed subset of the real data. Composite likelihood inference is then used to combine these subanalyses and give an overall effect estimate. We apply our method to data from the Swiss HIV Cohort Study (SHCS), studying the effect of treatment with Highly Active Antiretroviral Therapy (HAART) on the survival from HIV. The data used goes from 1996, when HAART became available in Switzerland, to September 2003. The same dataset has been studied using MSMs by Sterne et al.

**Results:** The estimated hazard ratio for HAART versus no HAART was 0.189 (0.109-0.327). The covariates used corresponded to those in Sterne et al., who estimated the effect of HAART to be 0.140 (0.066-0.299). Separate analyses on subgroups, for instance for IDU (injecting drug users) and non-IDU, have also been carried through.

**Conclusion:** For the SHCS data, the MSMs and the sequential Cox models give similar but not identical effect estimates. Though, the two methods do not estimate exactly the same effect measure, and the interpretation may not be exactly the same. The method of sequential Cox models avoids using IPTW weights. These weights can sometimes be unstable, and are in that sense more vulnerable than the more usual inverse probability of censor weights. The sequential Cox analysis can easily be carried through using a stratified Cox model, found in most standard statistical software, once the different subsets of the real data are constructed.

**B8****Weighted Cox regression applied to a large dataset of testicular cancer survivors**

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**Objective:** Cox regression (CR) provides hazard ratio estimates which describe the effect of prognostic factors on survival times in a well-communicable way. However, CR's assumption of proportional hazards (PH) is violated if a factor's effect depends on time, and then interactions of prognostic factors with functions of time would have to be included in the model. Weighted estimation in Cox regression (WCR; Schemper, *The Statistician*, 1992 ; Sasieni, *JASA*, 1993) is a parsimonious alternative that provides valid average hazard ratio(AHR) estimates irrespective of PH.

**Material and methods:** We exemplified the usefulness of WCR on a material based on a linkage between Cancer Registry of Norway and Medical Birth Registry on 3574 cancer survivors and 17 865 age-and gender- matched individuals from the general population (cancer free at inclusion). All subjects were born after 1950 and diagnosed with cancer between 1967-2002. The median age at diagnosis was 29 years, range 16-45. The study aims at comparing time from diagnosis to subsequent parenthood between patients and healthy controls. Since early post-diagnosis reproduction rates are influenced by treatment (for patients), pre-diagnosis parenthood and age, the 'hazard ratio' of parenthood comparing patients and controls strongly depends on time, pre-diagnosis parity, birth-decade and on several other factors. Modelling interactions of patient/control status with both time and co-factors would adequately account for the complex situation but the results are difficult to present in a simple manner. As an alternative we used WCR to avoid presenting time-dependent hazard ratios. The Average Hazard Ratio (AHR) estimate obtained by weighted estimation is mathematically close to the definition of the '*odds of concordance*' which also does not require proportional hazards and gives equal weight to all individuals (by pairwise comparisons of all times T0 and T1). This interpretation is not possible when using Cox model in case of non-proportional hazards.

**Conclusion:** Results can now be clearly arranged in a meta-analysis-type plot, depicting average hazard ratios and confidence intervals for all relevant subgroups. Applying weighted Cox regression instead of Cox regression in case of PH could lead to larger variances, which in our study was not an issue given the large sample size. Weighted estimation allowed us to reduce a potential time dependent effect into a single AHR estimate and is a parsimonious alternative to modeling time-dependency. WCR is particularly useful for describing interactions or comparing effects across many subgroups.

**B9****Frailty modeling of bimodal age-incidence curves of nasopharyngeal carcinoma in low-risk populations**

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**Objective:** The incidence of nasopharyngeal carcinoma (NPC) varies widely according to age at diagnosis, geographic location and ethnic background. On a global scale, NPC incidence is common among specific populations primarily living in Southern and Eastern Asia and Northern Africa, but in most areas, including almost all western countries, it remains a relatively uncommon malignancy. Specific to these low-risk populations, is a general observation of possible bimodality in the observed age-incidence curves. We wanted to construct a model for time-to-event data that enabled us to test if the observed bimodality is statistically significant or not, while also looking at the effects of covariates such as gender, geographic area and diagnosis period.

**Material and methods:** The Cancer Incidence in Five Continents (CI5) Vol. I to VIII ADDS database was used to extract incident cases of nasopharyngeal cancer (ICD-10 C11) for 23 population-based cancer registries covering the low-risk populations, together with the corresponding population data by year of diagnosis (covering three 5-year periods), sex and age. The data were aggregated into five geographic regions. In survival analysis, frailty models account for individual variation in disease susceptibility at the population level. By using a model where we add two independent compound Poisson distributed frailties, we can model bimodal age-incidence curves. We then implicitly assume that the cancers causing the first peak of the age-incidence curve has a different aetiology than the cancers causing the second peak, and this fits with the biological knowledge on NPC. We may also estimate the proportion of individuals susceptible to NPC in the populations.

**Results:** By comparing the new model to a standard unimodal frailty model, we find that the observed bimodality in the age-incidence curves for NPC is statistically significant (p-value<0.001, likelihood ratio test). The new model yields a good fit to the observed data. There was no significant effect of diagnosis period, but the effects of sex and area were significant. For the first peak, the proportion of individuals susceptible to NPC varies from around 1 per 100000 person years for North American women, to 5 per 100000 for Indian men. For the second peak, the estimates range from 25 per 100000 for North/Western European women to 150 per 100000 for Australian men.

**Conclusion:** We have demonstrated that it is possible to construct a regression model for bimodal age-incidence curves in time-to-event data.

**B10****Har den psykiske helsen i Norge blitt bedre de siste 10 årene?**

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**Mål:** Å gjøre rede for hvordan den psykiske helsen endrer seg over tid i den norske befolkningen, og hvilke faktorer som er sterkest assosiert med den observerte utviklingen.

**Materiale og metoder:** Dataene er hentet fra Statistisk sentralbyrå sine levekårsundersøkelser med tema helse i hhv 1998, 2002 og 2005. Av et landsrepresentativt utvalg på 10 000 individer svarte hhv 70% i 1998, 64% i 2002 og 57% i 2005 på det postale vedlegget med spørsmål om psykisk helse. Vi har begrenset analysene til aldersgruppen 25-64 år som totalt utgjorde 16196 individer i alle tre undersøkelsene. Hopkins System Check List (HSCL) med 25 spørsmål er brukt til å måle graden av psykisk plager. Skalaen fanger opp vanlige symptomer på depresjon og angst, og skårer over 1,75 blir regnet som betydelige psykiske plager. Ved hjelp av regresjonsanalyser har vi undersøkt forhold som kan bidra til å forklare observerte endringer i psykiske plager.

**Resultater:** I materialet er det en tydelig nedadgående trend i andel med betydelige psykiske plager i aldersgruppe 25-64 år, fra 10,5% i 1998 til 9,7% i 2002 til 8,7% i 2005, og nivået i 2005 er signifikant lavere enn i 1998. I den grad disse tallene er representative for befolkningen, tilsier dette en reduksjon på 50 000 mennesker i Norge med betydelige psykiske plager i den aktuelle aldersgruppen og i det aktuelle tidsrommet. HSCL-skåren påvirkes i større eller mindre grad av de fleste av de variablene som er inkludert i analysene, men bare to av faktorene som er inkludert i analysene kan forklare tidstrenden; nemlig økt fysisk aktivitet og reduserte økonomiske problemer.

**Diskusjon – har økonomiske oppgangstider og økt fysisk aktivitet gitt bedre psykisk helse?** Vi kan ikke utelukke dette, men det er likevel grunn til å mane til forsiktighet med å godta at nedgangen i HSCL-skåre som vi finner i vårt datamateriale representerer en reell forandring i befolkningen. Svarprosenten har falt betydelig fra 1998 til 2005, og nedgangen er skjevt fordelt i forhold til ulike undergrupper. Vi finner imidlertid ikke noe konkret bevis for at det økende frafallet forklarer nedgangen i HSCL-skåre.

**B11****Can long-term exposure to traffic noise increase the risk of cardiovascular diseases? –A follow up of ‘The Oslo Health Study’ by questionnaire**Ruhina Tasmin Biswas<sup>1</sup>, Bente Oftedal<sup>1,2</sup>, Gunn Marit Aasvang<sup>1</sup> and Per Schwarze<sup>1</sup>

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**Background:** Though mortality from cardiovascular diseases has decreased, it still causes about 40% of the deaths in Norway. Incidence of ischemic heart disease has been pathogenically linked with exposure to high noise levels based on a general stress model. Long-term exposure to road traffic and aircraft noise has been reported to be associated with increased risk of ischemic heart disease and hypertension in the last decades. In Norway about 1.5 million people are exposed to environmental noise above recommended level at their home address of whom more than 10% are highly annoyed by noise. Road traffic is the main source of both noise and air pollution in Norway. Air pollution has also been linked to cardiovascular morbidity and mortality. Thus, it is important to disentangle the health effects of the two different types of traffic-related exposures.

**Objectives:** The main aim is to gain more knowledge on the relationship between road traffic noise at home and the risk of cardiovascular morbidity and mortality, by simultaneously controlling for air pollution at home address. In addition, we will study the changes in cardiovascular diseases over time.

**Material and Methods:** Participants from “The Oslo Health Study” (HUBRO) (N=18,770) and participants from a follow-up questionnaire survey “Health and environment in Oslo” will be included in this project. From HUBRO the following outcomes will be examined: blood pressure, serum cholesterol, self-reported cardiovascular disease and symptoms and cardiovascular mortality using the mortality register. In the “Health and environment in Oslo” study about 29,000 subjects who were invited to take part in HUBRO and live in Oslo will be asked to participate. This questionnaire survey will collect updated information on cardiovascular diseases and symptoms including potential confounders. In addition, the questionnaire comprises noise-related issues such as noise annoyance, noise sensitivity, sleep disturbances and occupational noise exposure. The Municipality of Oslo and the Norwegian Institute of Air Research will provide measures of noise levels ( $L_{den}$  (day-evening-night level) and  $L_{night}$ ) and of air pollution levels ( $PM_{10}$ ,  $PM_{2.5}$ , and  $NO_2$ ) for each home address from 1992 to 2006.

**Results:** Not available

**Conclusion:** Not available



## The 4th Conference of Epidemiological Studies in Europe (CELSE), Bergen November 12<sup>th</sup> to 14<sup>th</sup> 2008

We are happy to welcome you to the CELSE conference for 2008. The conference has a wide range of internationally recognised presenters which together with the submitted papers gives an interesting and high quality program. In addition to the invited speakers there will be both oral and poster sessions. The main programme consists of different topics within a broad field using longitudinal data to study life-course epidemiology. In particular we look forward to listen to the invited speakers. On Wednesday Gita Mishra will talk about *Recent developments in life course epidemiology: from across cohorts to across generations*, while Lars Vatten will discuss *Breast cancer in a life course perspective*. On Thursday Øysten Kravdal starts with his presentation *Lifetime parity and total mortality*, while Rolv Skjærven will give a presentation on *Lifetime parity, preeclampsia and survival*, and Pauline Emmet presents *Controversial issues in Nutritional Epidemiology*. The last day of the conference L.H. Lumey discusses *Long term effects of a famine. An overview of research based on the Dutch famine 1944-45* and Dag Moster presents *Long-term medical and social consequences of preterm birth*.

The venue for the conference is the SAS-Royal hotel at the harbour-front (Bryggen). Bryggen has a history back to the 13th century and is on the UNESCO heritage list. This year's conference is supported by The Department of Public Health and Primary Health Care at the University of Bergen, The Medical Birth Registry of Norway (at the National Institute of Public Health), and Unifob Health (University Research Bergen).

The city of Bergen is known for its hospitality and warm atmosphere. Bergeners are known for their good humour and quick and witty remarks. Bergen is surrounded by 7 mountains and is the main tourist harbour in Norway, also known as the "gateway to the fjords". We wish you all welcome to the 4th Conference of Epidemiological Studies in Europe and hope you will have some enjoyable and pleasant days in Bergen.

On Wednesday evening the Mayor of Bergen arranges a reception in the Bergen Art Galleries in the centre of Bergen, by the city park. The conference gala dinner on Thursday evening is held at the Bellevue restaurant, which has a magnificent view over Bergen.

### ***Best regards from the local organizing committee***

*Rolv Skjaerven, Astrid Lunde, Lorentz M. Irgens  
(Department of Public Health and Primary Health Care, UiB),  
Kari Klungsøyr, Patricia Schreuder (The Medical Birth Registry of Norway),  
Stein Atle Lie (Unifob Health)*

### ***Conference scientific committee:***

*Pauline Emmett, Marja-Riitta Järvelin, Camilla Stoltenberg  
Anne-Marie Nybo Andersen, Tine Brink Henriksen  
George Davey Smith, Rolv Skjaerven*

# The 4<sup>th</sup> Conference of Epidemiological Longitudinal Studies in Europe (CELSE), Bergen, Norway, November 12-14, 2008

## Programme

Oral presentations should leave 5 minutes for discussion

### Wednesday November 12<sup>th</sup>

*The 4th Conference of Epidemiological Longitudinal Studies in Europe (CELSE)*

12:00-14:00	Registration		
14:00-14:30	Opening		
<b>Plenary session</b>			
14:30-15:00	Gita Mishra	Recent developments in life course epidemiology: from across cohorts to across generations	
15:00-15:30	Lars Vatten	Breast cancer in a life course perspective	
15:30-15:45	Heijmans, BT	Persistent epigenetic differences associated with prenatal famine exposure in humans	O01
<b>Poster session</b>			
15:45-16:15	Posters and coffee		
<b>Plenary session</b>			
16:15-16:30	Henriksen, TB	<i>Symposium in Mental health</i> Gestational age at birth and hyperkinetic disorder – a sibling design	O02
16:30-16:45	Järvelin, M-R	Are ADHD symptoms related to growth and metabolic outcomes?	O03
16:45-17:00	Lundervold, AJ	Developmental pathways of behavioural problems. The Bergen Child Study	O04
17:00-17:15	Moilanen, I	Do ADHD-symptoms in childhood predict substance abuse in adolescence?	O05
17:15-17:30	Break		
17:30-17:45	Pillas, D	Maternal factors as predictors of infant developmental delay in the 1966 Northern Finland Birth Cohort	O06
17:45-18:00	Rodriguez, A	Pre-pregnancy maternal obesity is related to ADHD symptoms in children	O07
18:00-18:15	Taanila, A	Learning difficulties as a risk for marginalization	O08
19:30→		Mayor's reception, Bergen Art Galleries	

### Thursday November 13<sup>th</sup>

*The 4th Conference of Epidemiological Longitudinal Studies in Europe (CELSE)*

<b>Plenary session</b>			
09:00-09:30	Øysten Kravdal	Lifetime parity and total mortality	
09:30-10:00	Rolv Skjærven	Lifetime parity, preeclampsia and survival	
10:00-10:30	Pauline Emmett	Controversial issues in Nutritional Epidemiology	

Thursday November 13<sup>th</sup> (cont.)**Poster session**

10:30-11:00 Posters and coffee

**Plenary session**

11:00-11:15	Bhattacharya, S	<b><i>Siblings and generations</i></b> The effect of parity on inherited risk of pre-eclampsia	O09
11:15-11:30	de Moira, AP	Influences on childhood obesity in two generations of the 1958 British birth cohort	O10
11:30-11:45	Hart, C	Alcohol consumption behaviours and social mobility in men and women of the Midspan Family Study	O11
11:45-12:00	Veenendaal, M	Transgenerational effects of the Dutch Famine: An epigenetic study	O12
12:00-12:15	Øyen, N	Premature deaths cluster in families – A population-wide study	O13

12:15-13:15 **Lunch****Parallel session A**

13:15-13:30	Christensson, A	<b><i>Mental health</i></b> Depressive symptoms in nursing students and newly qualified nurses	O14
13:30-13:45	Colman, I	The association between birth weight and depression: The mediating effect of age	O15
13:45-14:00	Haukka, J	Analysing multiple time scales using Bayesian intensity estimator	O16
14:00-14:15	Lie, KK	Sex ratio at birth – association with maternal eating disorders	O17

**Parallel session A**

14:15-14:30	Kelly, Y	<b><i>Social epidemiology</i></b> Born black, brown or white, why do ethnic inequalities in early childhood health and development exist?	O18
14:30-14:45	Lager, A	Childhood IQ does not explain adult health inequalities: A 65-year follow-up of children in Malmö, Sweden	O19
14:45-15:00	Tiikkaja, S	Intergenerational social mobility and cardiovascular mortality among siblings	O20

**Parallel session B**

13:15-13:30	Cribb, V	<b><i>Diet</i></b> Does maternal education affect diet in 10-year-old children?	O21
13:30-13:45	Emmett, P	Diet throughout childhood and age at menarche in a Contemporary cohort of British girls	O22
13:45-14:00	Erkkola, M	Vitamin D intake during pregnancy: asthma and allergic rhinitis in 5-year-old children	O23
14:00-14:15	Haugen, M	Vitamin D supplementation is associated with reduced risk of preeclampsia in nulliparous pregnant women	O24
14:15-14:30	Lumey, LH	Lipid profiles in middle-aged men and women after prenatal famine exposure: the 1944-45 Dutch famine	O25
14:30-14:45	Robinson, S	Patterns of diet in community-dwelling older men and women in UK: the Hertfordshire Cohort Study	O26
14:45-15:00	Snijder, MB	Life course dairy consumption and arterial stiffness at adult age: The Amsterdam Study	O27

**Poster session**

15:00-15:45 Posters and coffee

Thursday November 13<sup>th</sup> (cont.)**Parallel session C**

15:45-16:00	Furberg, A-S	<b>Cohorts</b> Opportunities for molecular cancer research in the Tromsø Study	O28
16:00-16:15	Pittet, V	The Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS): founding and first observations	O29
16:15-16:30	van Eijsden, M	Follow-up measurements in a longitudinal study: the Amsterdam Born Children and their Development cohort	O30

**Parallel session C**

16:30-16:45	Mamun, AA	<b>Obesity</b> Do maternal weight gains during pregnancy link with offspring body mass index and blood pressure at 21 years?	O31
16:45-17:00	Hoekstra, T	Distinct life course developmental patterns of body fatness as predictors for metabolic syndrome components	O32
17:00-17:15	Li, L	Intergenerational influences on childhood BMI: the effect of parental BMI trajectories	O33
17:15-17:30	McGrother, CW	Aetiology of overactive bladder: evaluation of a diet and lifestyle model involving diabetes and obesity in women	O34
17:30-17:45	Schouten, F	Changes in trunk fat mass and peripheral lean mass are associated with changes in carotid arterial stiffness in a healthy population	O35

**Parallel session D**

15:45-16:00	Birmingham, K	<b>Health systems/Ethics</b> Ethical Dilemmas: solutions from the Avon Longitudinal Study of Parents And Children (ALSPAC) Ethics and Law Committee	O36
16:00-16:15	Ingenbleek, A	Input of longitudinal data in the health information system	O37
16:15-16:30	Zahl, P-H	Estimating the proportion of sub-clinical breast cancers that would go in regression if not detected at mammography	O38
16:30-16:45	González-Izquierdo, A	Predicting the risk of hospitalisations from a longitudinal perspective	O39
16:45-17:00	Colman, I	Outcomes of teacher-rated externalizing behaviour in adolescence	O53
17:45	Close of session		
19:00→	Gala dinner	Lyststedet Bellevue	

**Friday November 14<sup>th</sup>*****The 4th Conference of Epidemiological Longitudinal Studies in Europe (CELSE)*****Plenary session**

09:00-09:30	L.H. Lumey	Long term effects of a famine. An overview of research based on the Dutch famine 1944-45
09:30-10:00	Dag Moster	Long-term medical and social consequences of preterm birth

Friday November 14<sup>th</sup> (cont.)**Plenary session**

10:00-10:15	Roseboom, TJ	<b>Frailty</b> Transgenerational effects of prenatal exposure to the Dutch famine on neonatal adiposity and health in later life	O40
10:15-10:30	Savva, GM	Frailty as an index of deficit accumulation in the MRC Cognitive Function and Ageing Study	O41

**Poster session**

10:30-11:00 Posters and coffee

**Plenary session**

11:00-11:15	Gallo, V	<b>Lifestyle</b> NeuroEPIC: Principles, study design, and an example of cigarette smoking associated with amyotrophic lateral sclerosis incidence	O42
11:15-11:30	Kelly, Y	Light drinking in pregnancy, a risk for behavioural problems and cognitive deficits at 3 years of age?	O43
11:30-11:45	Koupil, I	Who continues to smoke in pregnancy? Great-grandparental and grandparental influences on women's smoking in pregnancy	O44
11:45-12:00	Kurtze, N	Reliability and validity of the International Physical Activity Questionnaire in the Nord-Trøndelag Health Study (HUNT) population of men	O45
12:00-12:15	Owe, KM	The association between maternal exercise and excessive birth weight of the infant – the MoBa Study	O46

12:15-13:15 **Lunch****Plenary session**

13:15-13:30	Din, Z-u	<b>Growth</b> Anthropometric outcomes at age 7 years of slow weight gain in infancy	O47
13:30-13:45	Koupil, I	Mother's smoking in pregnancy modifies the effects of preterm birth and concurrent body mass index on blood pressure and hypertension in adolescents	O48
13:45-14:00	Mortensen, LH	Time is on whose side? Time trends in the association between maternal social disadvantage and offspring fetal growth	O49

**Plenary session**

14:00-14:15	Crozier, S	<b>Pregnancy</b> Longitudinal changes in weight and fat mass through pregnancy: the Southampton Women's Survey	O50
14:15-14:30	Goedhart, G	Maternal cortisol and birth weight at term	O51
14:30-14:45	Di Lallo, D	Hospital readmission in very premature infants: an Italian area based follow-up study	O52
14:45-15:00	Closing		

## Posters

### *The 4th Conference of Epidemiological Longitudinal Studies in Europe (CELSE)*

Allami, M	Assessment of the quality of life and its influencing factors in infertile women	P01
Eide, J	Child abuse and fear of pregnancy in the Mother and Child Cohort Study	P03
Engebretsen, IMS	Comparing infant feeding practices among Ugandan infants with a prospective and retrospective study design	P04
Fleten, C	Associations between maternal pre-pregnancy BMI, exercise during pregnancy and birth weight	P05
Furberg, A-S	The Tromsø Staph and Skin Study (TSSS)	P06
Gailute, B	Coronary care among middle-age inhabitants with acute myocardial infarction in Kaunas in 1996 and 2003-2004	P07
Hanif, A	Identification of life threatening factors associated with pregnancies	P08
Heeren, GA	The influence of communication in a family on adolescents' risk behaviour	P09
Iversen, A	EPINOR- A ph.d. school for epidemiologic research in the High North	P10
Luksiene, DI	HAPIEE study: prevalence of obesity and increased waist-hip ratios in Lithuanian urban population	P11
Luksiene, DI	Influence of risk factors and their combination on risk of mortality from stroke in Kaunas elderly men	P12
Nadav, O	Associations between effects of multi years climate changes and morbidity and mortality rates in the south of Israel	P13
Nordtveit, T	Mothers' and fathers' birth characteristics and perinatal mortality in their offspring: a population based cohort study	P14
Radisauskas, R	Morbidity of first and recurrent acute myocardial infarction in Kaunas (Lithuania) population during 1983-2004	P15
Radisauskas, R	Mortality trends of cardiovascular diseases in the middle-aged Kaunas (Lithuania) population during 2001 to 2006	P16
Meinlschmidt, G	Maternal stress during pregnancy and infectious diseases in the offspring	P17
Tegethoff, M	Prenatal stress and respiratory diseases during childhood	P18
Tvinnereim, HM	A biobank of primary teeth connected to the Norwegian Mother and Child Cohort Study	P19
van Eijdsen, M	Ethnic differences in early pregnancy maternal n-3 and n-6 fatty acid concentrations: the ABCD cohort study	P20

## O01

**Persistent epigenetic differences associated with prenatal famine exposure in humans**

B.T. Heijmans<sup>1</sup>, Elmar Tobi<sup>1</sup>, A.D. Stein<sup>2</sup>, H. Putter<sup>3</sup>, G.J. Blauw<sup>4</sup>, E.S. Susser<sup>5,6</sup>, P. Slagboom<sup>1</sup> and L.H. Lumey<sup>5</sup>

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**Background:** Early development is a key period for late-life health. Animal models have shown that transient environmental conditions can induce permanent epigenetic changes with phenotypic consequences. To successfully study this in humans one needs individuals with a well defined and clearly timed environmental exposure to differentiate between environmental effects and normal variation. The Dutch Hunger Winter of 1944-45, a severe famine in the Western part of the Netherlands during German occupation towards the end of World War II provides such an opportunity.

**Methods:** To establish as a first proof-of-principle that adverse conditions in utero can lead to permanent epigenetic changes in humans we studied DNA methylation at the imprinted insulin-like growth factor 2 (*IGF2*) gene. Using mass spectrometry we quantified the amount of DNA methylation of *IGF2* in genomic DNA from whole blood. *IGF2* regulates embryonic development and its imprinting status is set during the early blastocyte stage and is thereafter faithfully maintained.

**Results:** We first measured 60 individuals exposed to famine around the time of conception and an unexposed same-sex sibling for each as controls. There was a decrease from 51.5% to 48.8% (0.6 standard deviations) in *IGF2* methylation comparing the exposed with the controls ( $P=1.2 \times 10^{-4}$ ). We then measured 62 individuals with famine exposure limited to the last trimester of pregnancy and an unexposed same-sex sibling for each. There was no difference in methylation status between these two groups (51.9% vs. 51.4%,  $P=0.5$ ). As expected from previous studies, there was no decline in birth weight among individuals exposed around conception but a 400 gram decline among individuals exposed late in pregnancy. *IGF2* methylation was not associated with birth weight in this study.

**Discussion:** We believe this study is the first report in humans to show a) that DNA methylation is sensitive to environmental conditions in pregnancy, b) that the timing of exposure appears to be critical, and c) that prenatal changes in methylation can persist through adult life. The study shows that exposure to famine in early pregnancy can induce epigenetic differences in *IGF2* in the absence of any changes in birth weight, a measure currently used as a marker for adverse conditions *in utero*. Further study will be required to see if *IGF2* methylation can indeed be used as a marker for adverse conditions during early development and if changes in DNA methylation are wide-spread, or adaptive and locus specific effects of undernutrition.

**O02****Gestational age at birth and hyperkinetic disorder – a sibling design based on complete follow up of all children born in Finland 1987-2001**

Tine Brink Henriksen, Carsten Obel, Alina Rodriquez, Karen Markussen Linnet, Jørn Olsen, Marjo-Riita Järvelin and Mika Gissler for the Nordic Network of Longitudinal Studies of ADHD

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National Research and Development Centre for Welfare and Health (STAKES), Helsinki, Finland

**Background:** Strong associations between very low gestational age (< 28 completed weeks) at birth and Hyperkinetic Disorder (HKD) have been found. Few studies exist on the association between less extreme prematurity and HKD. Some of the explanation of the association may be due to confounding since gestational age at birth and HKD may share common genetic, social, and lifestyle determinants. In this study we adjust, at least partly, for these factors by comparing children who were born preterm with their term siblings.

**Methods:** We studied gestational age and HKD in all singletons born 1987-2001 in Finland (N=894 494). Within this cohort we identified 7 367 siblings from families where at least one of the siblings had HKD and tested the association by use of conditional logistic regression analyses.

**Results:** Compared to children born at term (gestational age of 37 to 41 weeks) children born preterm (< 37 completed weeks) were at increased risk of HKD in the entire unmatched cohort (OR 1.9, 95% CI: 1.7-2.1), with a dose response like pattern of increasing risk with more extreme prematurity. Among siblings we still found a statistically significant but weaker association between prematurity and HKD also when gender of the child, parity and year of birth was adjusted for (OR=1.7, 95% CI 1.2-2.2).

**Conclusion:** Our findings suggest that at least part of the association found between preterm birth and HKD in the offspring is due to confounding.



**O03****Are ADHD symptoms related to growth and metabolic outcomes?**

Marjo-Riitta Järvelin<sup>1,2</sup>, Irma Moilanen<sup>3</sup>, Anja Taanila<sup>1</sup>, Marika Kaakinen<sup>1</sup>, Hanna Ebeling<sup>3</sup>, Carsten Obel<sup>4</sup>, Jørn Olsen<sup>5</sup>, Tine Brink Henriksen<sup>6</sup>, Karen Markussen Linnet<sup>6</sup>, Einar Heiervang<sup>7</sup>, Sandra Loo<sup>8</sup>, James McGough<sup>8</sup>, Susan Smalley<sup>8</sup> and Alina Rodriguez<sup>9</sup>

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**Objective:** The motivation for the current study was that previous work links (i) Attention Deficit Hyperactivity Disorder (ADHD) to overweight and obesity, (ii) some studies suggest that children with hyperactive behaviours may be shorter due to disorder itself or neuro-stimulants used to treat ADHD, (iii) hypothalamic-pituitary-axis malfunction may lead to changes in very early development and birth weight, and (iv) finally that foetal and childhood growth associates with various later outcomes including developmental and metabolic cardiovascular disorders. We studied here whether growth and metabolic outcomes were related to hyperactivity and inattention symptoms evaluated by teachers and parents in childhood and adolescence.

**Material and methods:** In a prospective Northern Finland Birth Cohort 1986, teachers rated the behaviour of 8525 children with Rutter's Child Behavioural Questionnaire (RutterB2) at age 8 years. At 16, parents of 6985 adolescents completed the Strengths and Weaknesses of ADHD-symptoms and Normal-Behavior (SWAN). The children were defined as high scorers for hyperactivity/inattention at age 8 years if they scored in three RutterB items describing symptoms of hyperactivity and inattention equal or over 3 (items 1,3,16; scored originally 0=does not apply, 1=applies partly, 3=applies well). At age 16 years we used 18 items from SWAN describing symptoms of ADHD (1-9 inattentive, 10-18 hyperactive-impulsive and 1-18 combined) to define high scorers as those who exceeded the upper 95%percentile on either combined, inattentive or hyperactive-impulsive scales ("likely ADHD cases"). Height and weight were self-reported at age 7 years but measured at age 16. Metabolic outcomes at age 16 included total cholesterol, HDL, LDL, triglycerides, systolic and diastolic blood pressure (SBP,DBP), waist-hip ratio and body mass index (BMI).

**Results:** Persons with high hyperactivity-inattention score rated by their teachers were slightly shorter at birth and at 7 years than those scoring normal. The odds for scoring high was smaller for taller persons at 7 years even after adjustment for child gender, maternal age, maternal height and SES (OR 0.98; 95% CI 0.97-0.995). Weight and BMI were not associated with high hyperactivity-inattention score. Similar associations were found with parent evaluations at child's age 16 years; the strongest being those between height at 16 years and SWAN score (OR 0.97 for taller persons scoring high; 95% CI 0.95-0.99). No associations were found between weight, BMI and SWAN score. High hyperactivity-inattention score at age 8 and/or 16 were associated with metabolic outcomes at 16 years such as higher waist-hip ratio, BMI (with RutterB only) and serum triglycerides but contrary to expectation lower SBP and DBP with some variation between girls and boys.

**Conclusions:** Children and adolescents with high scores on hyperactivity-inattention scales were shorter at birth and at 7 and 16 years and had some more adverse metabolic outcomes.

## O04

**Developmental pathways of behavioural problems. The Bergen Child Study**Astri J. Lundervold<sup>1,2</sup>

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**Objective:** Investigate the stability of behavioural symptoms from childhood through adolescence in children participating in the Bergen Child Study (BCS).

**Material and methods:** The target population of the BCS included all 7 – 9 year-old children in any school in the municipality of Bergen and Sund during the academic year 2002/2003. In the first wave, all parents and teachers were asked to fill in a screening questionnaire including the Strengths and Difficulties Questionnaire (SDQ). A second stage included the Development and Well-Being Assessment (DAWBA), and a third stage a more comprehensive evaluation of a subsample (329 children). The third stage included a diagnostic interview (Kiddie-Sads-PL) and tests of motor and cognitive function. A second wave, including the instruments used in the first two stages in wave 1, was conducted in 2006/2007 (n = 5196). In the present study we will present preliminary follow-up data from a small subgroup selected from children with symptoms of behavioural disorders (i.e. Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Behaviour (ODD) and Conduct Disorder (CD)) according to the Kiddie-Sads-PL (n = 38).

**Results:** There were 27 boys and 11 girls in the sample, with a mean total IQ score = 79.5 (SD = 20.2). The total mean SDQ score in 2002 was 14.0 (SD = 7.4) for parents and 13.1 (SD = 6.7) for teachers. The correlations between SDQ scores from parents and teachers in 2002 and the IQ score in 2004 were statistically significant; parents  $r = -.435$ ,  $p = .006$ ; teachers  $r = -.405$ ,  $p = .013$ . The correlations between the SDQ scores in 2002 and a letter-number sequencing test in 2007 were also statistically significant; parents  $r = .659$ ,  $p < .001$ ; teachers  $r = .364$ ,  $p = .032$ . Most of the children had an ADHD diagnosis in 2004 (n = 32, n = 25 with only ADHD). The percentage of children with ODD decreased from 18.8 in 2004 to 5.3 in 2007, and overall 18% of the children did no longer fulfill any of the three diagnoses in 2007.

**Conclusion:** The Bergen Child study has a design appropriate for studies of developmental pathways in a whole population as well as in subgroups of children. Preliminary analyses from a follow-up study of children with ADHD, ODD and/or CD demonstrate strong correlations between parent and teacher reports on SDQ and cognitive test performance, but also different pathways with respect to symptoms of behavioural disorders. Results from analyses of potentially risk and resilience factors will be presented at the conference.

## O05

### Do ADHD-symptoms in childhood predict substance abuse in adolescence?

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**Background:** Knowledge of predictive value of different childhood behaviours on adolescent health is important.

**Objective:** To study, if childhood hyperactivity-impulsivity (HI) and inattention (IA) symptoms, as reported by the teachers, predict adolescent substance abuse (SUB-AB).

**Methods:** In the prospective Northern Finland Birth Cohort 1986, 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 15-16 years age 6439 adolescents reported of health habits, including initiation and frequency of smoking, and use of alcohol and drugs.

**Results:** Adolescents had begun smoking at an earlier age and smoked more frequently if they had been scored by their teachers as HI and IA at age 8, when compared with those without HI or IA. IA showed higher predictive value than HI, and the prediction was stronger for girls. The frequencies of use of alcohol and drugs, and frequency of having been drunk in adolescence were higher among those scored high in HI and IA at age 8. The predictive value of IA was a bit higher than HI.

**Conclusions:** The present analyses confirmed the previous knowledge of higher risk for SUB-AB in ADHD, possibly because of common genetic basis. The higher predictive value of IA (vs HI) is surprising and might be explained by the many difficulties that the inattentive children encounter both in academic achievements and in hobbies. Prevention of SUB-AB might include special attention to children and adolescents with HI and IA.

## O06

## Maternal factors as predictors of infant developmental delay in the 1966 Northern Finland Birth Cohort

Demetris Pillas<sup>1,2</sup>, Gopalakrishnan Netuveli<sup>2,3</sup>, David Blane<sup>2,3</sup>, Ulla Sovio<sup>1</sup>, Arturo Gonzalez-Izquierdo<sup>1</sup>, Clive Hoggart<sup>1</sup>, Sarianna Vaara<sup>6</sup>, Markku Koironen<sup>4</sup>, Ioanna Tzoulaki<sup>1</sup>, Anna-Liisa Hartikainen<sup>5</sup>, Anneli Pouta<sup>6</sup>, Anja Taanila<sup>4,7</sup>, Marika Kaakinen<sup>4,8</sup> and Marjo-Riitta Järvelin<sup>1,4,8</sup>

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**Objective:** The timing and achievement of developmental milestones are the most important indicators of the infant's neurological, psychomotor, and socio-emotional integrity and development. Failure to achieve a developmental milestone at the expected age is an indicator of consequent problems, such as long-term disability and abnormal behaviours. Despite the 10 percent prevalence of the various forms of infant developmental delay, the early identification of such problems remains challenging. Although severe disorders can be recognized in infancy, it is unusual to diagnose speech impairments, hyperactivity, or emotional disorders before the age of three or four years, and learning disabilities are rarely identified before children start school, making more research in this area necessary. Evidence suggests that particular maternal factors, such as alcohol abuse, are predictive of infant developmental delay, but a comprehensive exploration of the association between maternal factors and infant developmental delay has yet to be performed. The aim of this study is to utilise the rich set of information/data collected through a Nordic longitudinal birth cohort to identify and explore a wide range of maternal factors in order to identify new factors which would make good predictors of infant developmental delay.

**Material and methods:** We used the data from the 1966 Northern Finland Birth Cohort, a prospective mother-child birth cohort which included all pregnant women with an expected date of delivery in 1966 and their children (n=12,058). Data during pregnancy were collected by a questionnaire administered during the 6<sup>th</sup> to 7<sup>th</sup> month of pregnancy, with the course of pregnancy prospectively recorded in maternity records and transferred by midwives onto study forms. Information on development was gathered during infants' visits to child welfare centres (an average of 10 visits during the first year). The analysis focused on three domains of infant development: neuromotor, linguistic, and bowel/bladder control development. Delayed achievement was defined as achievement within the bottom 25<sup>th</sup> percentiles of scores (last 25% of infants to achieve a specific milestone). Using a systematic statistical exploratory analysis, predictors were grouped in seven categories: socioeconomic, psychological, pharmacological, indicators of health, indicators of hardship, indicators of support received, and delivery-related factors. We used binary logistic regression to assess the association between the various predictors and of infant developmental delay.

**Results:** Preliminary results indicate that associations exist between infant developmental delay and a large number of predictors from all categories explored. Certain predictors are associated with overall developmental delay whereas others appear to be associated with a delay in only one specific domain. Maternal depression, wantedness of pregnancy, educational attainment, strenuous occupation, length of maternity leave, learning about childcare, age, parity and number of previous miscarriages were identified as being good predictors of developmental delay.

**Conclusion:** A large number of maternal factors, many of which are not taken into account when evaluating an infant's development by physicians / child psychologists, can be predictive of infant developmental delay. A better prediction of delay during this critical stage can be achieved if the evaluation of the infant's development takes a holistic approach, taking into account the full set of clinical and non-clinical information that may be available on the mothers and families.

**O07****Pre-pregnancy maternal obesity is related to ADHD symptoms in children: Replication and extension of Nordic findings**

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**Objective:** Nutrient availability defined as maternal weight during pregnancy is important for offspring health at birth and over the lifecourse; however, less is known about psychiatric outcomes during childhood. The Nordic Network on Attention Deficit Hyperactivity Disorder (ADHD) previously reported a novel connection between maternal adiposity at the time of pregnancy and ADHD symptoms in children. The aim of the present study is to replicate and extend this finding in a new and younger cohort from Sweden by examining the possibility of causality more closely.

**Methods:** Women ( $N \approx 3000$ ) were recruited during early pregnancy from nearly all prenatal healthcare clinics in Sweden, data were collected prospectively via medical records and self-report. Child symptoms at the age of five years were assessed by mothers and preschool teachers. Several causal pathways that may explain the association between maternal pre-pregnancy BMI and child behavior problems are explored, including maternal depression and stress during pregnancy.

**Results:** Maternal pre-pregnancy overweight and obesity predicted high inattention symptom scores and obesity was associated with a two-fold increase in risk of difficulties with emotion intensity and emotion regulation according to teacher reports. Presence and duration of problems were associated with both maternal over and underweight according to teachers.

**Conclusions:** Despite discrepancy between maternal and teacher reports, these results provide further evidence that maternal pre-pregnancy overweight and obesity are associated with child inattention symptoms and extend previous work by establishing a link between obesity and emotional difficulties. Maternal adiposity at the time of conception may be instrumental in programming child mental health possibly via disturbed metabolic function. If the associations are causal, the potential for prevention is great.

## O08

**Learning difficulties as a risk for marginalization**

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**Objective:** Many previous studies have shown an association between learning difficulties (LDs) and emotional and behavioural problems in children and adolescents. The negative effect of LDs on adolescents' school performance and educational plans has also been shown. Our aim was to investigate the association between LDs and both emotional and behavioural problems and hyperactive behaviour among 8-year-old children. Secondly we wanted to study the association between LDs assessed at the age of 8 years and self-reported school performance and educational plans at the age of 15/16 years.

**Material and methods:** In the Northern Finland Birth Cohort 1986, when the children were 8 years old (n=9357), teachers assessed children's behaviour by Rutter's Child Behavioural Questionnaire (RB2) and LDs with questions whether a child had difficulties in reading, spelling or mathematics (response rate 92%, n=8525) and parent evaluated children's psychomotor development (response rate 90%, n=8370). At the age of 15/16 years adolescents (n=9340) filled in a postal questionnaire by which they assessed their school performance in Finnish language and mathematics and also reported their educational plans. 78% (n=7182) of them returned the questionnaire and gave permission to use their data.

**Results:** The study indicated that 21.3% (n=1774) of the 8-year old children had one or more LD and; of them 12.3% (n=1026) were verbal (reading and/or spelling), 3.0% (n=248) mathematical and 6.0% (n=500) combined LDs. A child's younger age, problems with fine and gross motor skills, divorced or reconstructed family types, the family's lower socio-economic status and mother's lower education were risk factors for LDs. For boys with LDs, an adjusted risk to have behavioural problems was 2.7 (95% CI 2.2-3.3), emotional problems 3.3 (2.4-4.6) and hyperactivity problems 3.2 (2.7-3.9). The corresponding figures for girls were 3.2 (2.2-4.5), 5.2 (3.7-7.4) and 4.0 (2.9-5.5). At the age of 15/16, most of the adolescents attended comprehensive or upper secondary school, but adolescents with LDs more commonly attended a vocational school (17% vs. 8%) and they had also repeated a grade more often than those without LDs (7.1% vs. 0.6%). Most of the adolescents thought that they managed at school quite well, but the adolescents with LDs thought that they managed poorly compared to their class mates without LDs (in Finnish 19.3% vs. 6.1%, in mathematics 35.5% vs. 20.0%). As to educational plans, most of those with LDs preferred vocational education (43.2% vs. 22.2%), but nearly one third were uncertain about their future plans. The differences between groups were statistically significant and the results were quite similar for boys and girls.

**Conclusion:** This study confirms the earlier findings of the association between LDs and behavioural/emotional problems. Because learning difficulties can have effects on adolescents' later life and academic achievements and through it on their educational plans, choice of a profession and work possibilities, teachers should, as early as possible, pay close attention to children's LDs and especially mathematical LD and emotional problems among girls.

## O09

**The effect of parity on inherited risk of pre-eclampsia**Sohinee Bhattacharya<sup>1</sup>, Amalraj Raja<sup>2</sup>, Doris Campbell<sup>3</sup> and Amanda Lee<sup>2</sup>

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**Objective:** To assess the magnitude of genetic predisposition to pre-eclampsia with reference to other risk factors.

**Material and method:** The Aberdeen Maternity and Neonatal Databank records all pregnancy and delivery details occurring in Aberdeen, Scotland since 1950. It has now become possible to link pregnancy records of mothers and grandmothers to those of the daughters. Using a nested case control design within this intergenerational cohort, statistical modelling was done with known risk/protective factors for pre-eclampsia, separately for nulliparous and parous women. Conditional logistic regression was used to compare characteristics between parous pre-eclamptics and year and parity matched normotensive controls.

**Results:** There were 34,970 mother-daughter pairs. Of the daughters, there were 1,248 nulliparous and 448 parous pre-eclamptics. For nulliparous women, the risk factors remaining in the stepwise model were mother's history of pre-eclampsia {O.R. 2.13 (95% C.I. 1.57, 2.89)}, booking BMI >30Kg/m<sup>2</sup> {O.R. 2.06 (95% C.I. 1.68, 2.52)}, age, gestation period, and booking diastolic blood pressure. Smoking  $\geq 10$  cigarettes a day was protective against pre-eclampsia {O.R. 0.52 (95% C.I. 0.44, 0.62)}. For multiparae, the risk factors included pre-eclampsia in the initial pregnancy {O.R. 8.80 (95% C.I. 1.54, 50.23)}, advanced age at delivery {O.R. 3.09 (95% C.I. 1.69, 5.66)} and BMI >30 Kg/m<sup>2</sup> {O.R. 2.61 (95% C.I. 1.62, 4.20)}. Smoking 10 or more cigarettes per day was protective {O.R. 0.57 (95% C.I. 0.35, 0.94)}. A history of maternal pre-eclampsia was not independently associated with an increased risk of development of pre-eclampsia in the multiparae.

**Conclusion:** In nulliparous women, a history of maternal pre-eclampsia was associated with more than doubling of risk of pre-eclampsia. In multiparae, this association was not observed, although a history of pre-eclampsia in a previous pregnancy was strongly associated with increased risk, suggesting genetic susceptibility.

## O10

### Influences on childhood obesity in two generations of the 1958 British birth cohort

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**Background:** Prevalence of childhood obesity is increasing in Britain and the rest of the world. Obesity in childhood increases the risk of becoming overweight or obese in adulthood and of developing cardiovascular disease and type 2 diabetes. Few studies have investigated the underlying causes for the secular trends in obesity. The reasons for the recent increases in obesity are not well understood.

**Objective:** To investigate whether the prevalence of risk factors for childhood obesity has changed over time and whether these changes are associated with the increasing trend of obesity.

**Materials and methods:** We used the data from two generations of the 1958 British birth cohort, cohort members with a BMI measure at 7 years, and their offspring aged between 4 and 9 years. Potential risk factors such as parental BMI, maternal smoking during pregnancy, birth weight, breastfeeding, social class, housing tenure and maternal employment in the two generations were compared using multi-level models to account for the within family correlations. The associations between BMI standard deviation scores (SDS) and potential risk factors were compared across generations using multilevel analysis.

**Results:** Offspring were, on average, fatter than cohort members: mean BMI SDS for offspring was 0.18 (sd = 1.13) vs. -0.02 (sd = 1.01) for cohort members. Preliminary analysis suggests that higher parental BMI and maternal employment were associated with higher BMI in both generations. Interestingly, whereas markers for social deprivation such as social housing, overcrowding and lower social class were associated with a lower BMI in the older generation, these factors were associated with a higher BMI amongst the younger generation.

**Conclusions:** Mean childhood BMI has increased between the two generations. The increase may be partly explained by changes in the prevalence of obesity risk factors and patterns of associations between the risk factors and childhood obesity.



## O11

### Alcohol consumption behaviours and social mobility in men and women of the Midspan Family Study

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**Objectives:** To investigate relationships between alcohol consumption and lifecourse socioeconomic measures.

**Material and methods:** In 1996, 1040 sons and 1298 daughters aged 30-59, from 1477 families took part in a prospective cohort study in Scotland. Both parents had participated in the Renfrew/Paisley study in the 1970s. The offspring completed a questionnaire which included comprehensive questions on alcohol consumption in the previous week. These were used to ascertain weekly units of alcohol consumed and exceeding recommended limits of: 4 units on a day for men or 3 for women; 21 units per week for men or 14 for women; binge drinking of 8 units for men or 6 for women on a day; and consuming alcohol on 5 or more days per week. The percentage who consumed wine, beer and spirits was calculated. Own and father's social class enabled social mobility to be investigated. Groups were defined as stable non-manual, upwardly mobile, downwardly mobile and stable manual. Analyses were carried out using Stata release 9, adjusting for clustering of offspring within families. Means and proportions of alcohol behaviours by father's social class, own social class and social mobility were standardised by 5 year age groups. Men and women were analysed separately due to their differing alcohol consumption.

**Results:** Own social class was more strongly associated with alcohol behaviours than father's social class. More manual than non-manual social class men exceeded the weekly limit, the daily limit, were binge drinkers (45%[95% confidence interval 40% to 50%] v 31%[27% to 35%]) and manual men consumed more units per week. More non-manual than manual social class men and women consumed alcohol on 5+ days. Non-manual women consumed more units than manual women. More downwardly mobile men exceeded the weekly limit (51%[41% to 61%] versus 29%[23% to 35%] for stable non-manual men), the daily limit, were defined as binge drinkers and downwardly mobile men drank the most units per week of the four social mobility groups. Alcohol consumption patterns of stable manual men were more favourable than those of downwardly mobile, but less favourable than stable non-manual and upwardly mobile men. Stable non-manual women were most likely to consume alcohol on 5+ days but very few were binge drinkers (4%). Stable non-manual and upwardly mobile men and women were more likely to drink wine, and downwardly mobile men to drink beer.

**Conclusions:** Men from manual social classes and downwardly mobile men had the least favourable alcohol behaviours but women from non-manual classes drank more than women from manual classes.

## O12

**Transgenerational effects of the Dutch famine: An epigenetic study**

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**Background:** The Dutch famine birth cohort has provided the first evidence in humans that poor nutrition during fetal development can permanently alter cardiovascular and metabolic function. These alterations are detrimental for cardiovascular disease in later life. Animal studies have recently started to unravel the underlying molecular mechanisms. Intrauterine undernutrition leads to persistent alterations to the epigenetic regulation of specific genes, which give rise to altered expression, thereby raising cardiovascular risk. Moreover, animal studies have demonstrated that epigenetic alterations, including gene methylation, can be transmitted to subsequent generations, even when the female offspring of the F1 generation were not exposed to nutritional constraint during pregnancy. More importantly, these effects are linked to a phenotype with increased cardiovascular risk.

**Objective:** First, we aim to assess whether individuals exposed to famine in utero have a different methylation pattern compared to unexposed individuals. We hope to establish that these epigenetic alterations are responsible for the detrimental effects of maternal undernutrition during gestation on the offspring's (F1) cardiovascular health. Secondly, we aim to provide evidence that these epigenetic alterations are absent in the mothers who were exposed to famine during pregnancy, but are present in the children and persist in the grandchildren. We will investigate whether inherited epigenetic alterations in the grandchildren are associated with an increased cardiovascular disease risk.

**Methods:** To address aim 1, methylation status of specific candidate genes in 793 members of the Dutch famine birth cohort shall be studied. Comprehensive information on adult cardiovascular risk has already been collected for this cohort at ages 50 and 58 years. Aim 2 will be addressed by performing a study in three generations; women who were pregnant around the time of the Dutch famine 1944-1945 (F0), their children (F1) and their grandchildren (F2). DNA methylation patterns will be assessed in 80 grandmother-parent-child sets. Additionally, we will investigate the cardiovascular risk profile in the F1 and F2 generation in order to study the transgenerational effects of intrauterine famine exposure on a functional level. Information on a large range of physical and mental health determinants will be collected through web-based questionnaires. Data collection starts in the fall of 2008.

**Relevance:** If this study shows that the detrimental effects of intrauterine famine exposure are based on epigenetic alterations, and that these are passed down to the next generation, this may have important implications on public health. Moreover, this study will contribute to the further elucidation of the pathophysiology of cardiovascular disease. Improving the health and nutrition of pregnant women may not only be a promising strategy to prevent cardiovascular disease in the next generation, but for future generations as well.

## O13

### Premature deaths cluster in families – A population-wide study

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**Objective:** Infant deaths cluster in families, but beyond infancy, little is known about familial aggregation of premature deaths. We hypothesized that an individual's risk of premature death would be influenced by prior premature deaths of any age in family members.

**Material and methods:** For all Danish residents registered in the Civil Registration System, 1968-2005, information was linked to the Causes of Death Register and the Danish Family Relation Database, yielding a cohort of 4,870,821 persons with  $\geq 1$  relatives (93 million persons-years and 73,278 deaths). Mortality rate ratios (relative risks) for premature death (before age 40 years) in individuals with a family history of premature death, compared to individuals without such a history, were estimated by log-linear Poisson regression.

**Results:** Persons with a family history of premature death were 46 percent more likely themselves to die prematurely than persons without such a family history (relative risk [RR] = 1.46; 95% confidence interval = 1.42-1.50). Relative risks were higher for concordant age at death, a close kinship relation, and similar causes of death. As expected, certain natural causes clustered among first degree relatives (RRs ranged 1.81-618), but unnatural causes of death, such as from non-simultaneous motor vehicle injuries, other injuries, and suicides also clustered (RRs = 1.80, 3.53, and 4.23, respectively). Previous family history of premature death in first degree relative also increased the risk of dying from another cause (overall RR = 2.08 and 1.33).

**Conclusion:** Premature deaths due to similar and dissimilar causes cluster in families.

**O14****Depressive symptoms in nursing students and newly qualified nurses – a population based longitudinal study over education and early professional career**

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**Objective:** Mental health varies over the course of education and early professional career. Newly qualified professionals go through a transition period when they are vulnerable to the demands of the trade and still uncertain of their capabilities. We aim to investigate changes in the level of depressive symptoms over education and the first two years of newly qualified nurses. Based in previous cross-sectional findings on depression in first year nursing students we will associate level and change in depressive symptoms to age, gender and living conditions.

**Material and methods:** We use data from the first five data collections in a nation-wide and population based cohort (LANE-longitudinal analysis of nurse education) of nursing students who began their education in the spring of 2002 (n=1700). All students at any of the 26 colleges and universities in Sweden offering nursing education in the target term were asked to participate. Overall 73% students responded and make up the cohort that has been followed by annual self reported questionnaires. The internal attrition over five years is 33.3 percent which left us with 1134 respondents two years after graduation. The outcome variable is captured by the Major Depression Inventory and has been collected at all time points. The covariates age and gender were calculated from the national personal registration number; living conditions (marital status, parental status, members of the household) was asked for at all five points in time. Data on achieved degree and work status were gathered at time point four and five. All analyses will be adjusted for depression at baseline. The data is balanced with missing due to 1. attrition from a specific data collection and 2. dropout. We plan to use response profiles as means for analysis.

*The following hypotheses will be tested:*

- The overall level of depression change over education and early career.
- The overall level and development of depression depend not only on education and time in the profession but age, gender and living conditions.

**Results:** Analysis has been initiated and will be available for presentation in the fall of 2008.

**O15****The association between birth weight and depression: the mediating effect of age**Ian Colman<sup>1</sup>, Peter B. Jones<sup>2</sup>, Diana Kuh<sup>3</sup> and Tim J. Croudace<sup>2</sup>

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**Objective:** A compelling biological model suggests that maternal prenatal stress may influence brain development and permanently program a maladaptive response to stress. This theory is tested in human populations by studying birth weight, an indicator of prenatal stress, or age of developmental milestones, and indicator of brain development, and mental health in adolescence and adulthood. However this association has not been consistently shown, with many studies reporting an association between low birth weight and later depression, and many others finding no such association. The objective of this study was to investigate whether the conflicting results may be mediated by age of the sample at the time depression was assessed.

**Methods:** Data from the Medical Research Council National Survey of Health and Development (the 1946 British birth cohort) was used. A structural equation model was tested on 4,264 survey members in which adolescent depression/anxiety (age 13 and 15) and adult depression/anxiety (ages 36, 43 and 53) were predicted by birth weight and age of developmental milestones (sitting, standing, walking, speaking). Additionally, age of developmental milestones was predicted by birth weight. Father's social class and sex were also included in the model as predictors of birth weight, developmental milestones, and depression/anxiety.

**Results:** The structural equation model had excellent model fit according to several indices of fit (confirmatory fit index = 0.995, Tucker-Lewis index = 0.993, root mean square of approximation = 0.026). A path of prediction from birth weight to age of developmental milestones to adolescent depression/anxiety to adult depression/anxiety was significant (all direct connections  $p < 0.001$ ). Notably, direct paths from birth weight ( $p = 0.25$ ) and age of developmental milestones ( $p = 0.23$ ) to adult depression/anxiety were not significant.

**Conclusions:** Birth weight and age of developmental milestones are strong predictors of adolescent mental health. Associations of birth weight and age of developmental milestones with adult mental health may be a consequence of an indirect association through adolescent mental health. This research supports the fetal programming theory for depression and anxiety, and suggests that improved mental health of women during pregnancy can have a significant long-term benefit for the offspring.

## O16

## Analysing multiple time scales using Bayesian intensity estimator

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**Objective:** A common problem in epidemiological longitudinal studies is to analyze simultaneously multiple time scales. Besides age and calendar time, time since start of exposure or time since important life events are typically in focus. Including these multiple time scales in analyses is a methodologically demanding exercise. In epidemiology, discrete time Poisson regression models and Cox's proportional hazards regression are commonly used. The disadvantage of the former is the need for discrete time, and of the latter being able to use only one time scale. An alternative approach is to use intensity models (Andersen et al. 1993), which allow multiple time scales and the usage of continuous time. Arjas & Gasbarra (1994) applied Bayesian inference and approximated the hazard rates by piecewise constant functions, and proposed prior distributions for the levels, and both the number and the locations of the jump points of the piecewise constant functions thus allowing flexible approximation of the "true" underlying hazard rate. Piecewise constant functions can be easily combined together using, for example, addition, multiplication or time shifting operations to model the intensity process. Härkänen (2003) implemented this methodology in a software package.

**Material and methods:** We describe shortly Bayesian intensity estimator. An application example of pharmacoepidemiological analysis of association between medication use and attempted suicide or death is presented (Haukka et al. 2008). Applications to other areas of epidemiology such as cancer research are discussed.

**Results:** There were 1611 patients with a mean follow-up time of 4.3 years. Current use of antipsychotics was associated with decreased mortality due to suicide (HR 0.52, 95% CI 0.34–0.81,  $p=0.004$ ), but no significant decrease in mortality was observed during current use of antidepressants (0.66, 0.41–1.08,  $p=0.099$ ), when compared to past use.

**Conclusions:** In a population of suicidal schizophrenic individuals antipsychotic medication treatment was associated with lower mortality from suicide and all-causes. Antidepressive medication was associated with lower all-cause mortality when used in combination with antipsychotics.

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## O17

## Sex ratio at birth – association with maternal eating disorders

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**Objective:** Variation in sex ratio at birth is interesting as biological phenomenon and from an evolutionary point of view. Overall, slightly more boys than girls are born. However, pregnancy complications as well as environmental exposures including maternal nutrition are claimed to be associated with minor alterations in sex ratio at birth. Mechanisms behind such associations are unknown. The aim of the present study was to examine the association between eating disorders and sex ratio at birth.

**Material and method:** Data collection was conducted as part of the Norwegian Mother and Child Cohort Study, a population based study recruiting pregnant women at mid-pregnancy, collecting biological specimen and questionnaire data. 38 340 women participated in the present study. Information on eating disorders was self-reported through questions related to DSM-IV criteria for these disorders. Four broadly defined categories were established: Anorexia nervosa, bulimia nervosa, binge eating disorder, and eating disorders not otherwise specified-purging type (EDNOS-P). Data on maternal weight and height, smoking, education, parity and income were likewise collected from the questionnaires. Information on birth outcome originated from Medical Birth Registry of Norway. Poisson regression was used to estimate unadjusted and adjusted ratios.

**Results:** Sex ratio at birth estimates across eating disorder subtypes is presented in the table below:

Eating disorder	Sex ratio (male/female)	Proportion male (95% CI)	Risk ratio (95% CI)	
			Unadjusted	Adjusted *
Anorexia nervosa	0.84 (16/19)	0.46 (0.32, 0.66)	0.90 (0.63, 1.29)	0.89 (0.62, 1.27)
Bulimia nervosa	0.89 (157/177)	0.47 (0.42, 0.53)	0.92 (0.82, 1.04)	0.93 (0.83, 1.04)
EDNOS-P	1.86 (26/14)	0.65 (0.52, 0.82)	1.28 (1.02, 1.60)	1.28 (1.02, 1.60)
Binge eating disorder	1.12 (1 044/934)	0.53 (0.51, 0.55)	1.04 (0.99, 1.08)	1.04 (0.99, 1.08)
No eating disorder	1.04(18288/17665)	0.51 (0.50, 0.51)	Ref	

\* Adjusted for gestational age, mother's age, pre-pregnancy BMI, smoking, education, income, parity

**Conclusion:** Although the numbers are small, the findings suggest an influence of eating disorders on sex ratio at birth, and that the direction of effect may differ according to eating disorder subtype. Adjusting for factors potentially influencing the sex ratio did not alter the findings.

## O18

### **Born black, brown or white, why do ethnic inequalities in early childhood health and development exist? Findings from the UK Millennium Cohort Study**

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**Background:** Early childhood health and development is important in two ways: first as a set of contemporary markers, and second as predictors of future health and life chances. Early-mid childhood is a crucial time in the lifecourse, with concurrent rapid development and transition into formal education. Markers of early childhood health and development are socially patterned, with children from advantaged backgrounds doing better compared with their disadvantaged peers. The existence of ethnic inequalities in adult health is well established, and our recent work in the UK has revealed stark ethnic inequalities in markers of early childhood health and development. The reasons for ethnic inequalities in health are not fully understood, but the most widely investigated explanations include socioeconomic, behavioural, genetic and cultural pathways, and a growing body of literature suggests a role for the experience of racism and discrimination in forging ethnic health inequalities.

**Objectives:** This paper examines explanations for ethnic inequalities in markers of health and development: obesity, asthma and wheezing illness, cognitive ability and socioemotional behaviour in 3 and 5 year old children. Specifically: 1. we assess the contribution of socioeconomic, psychosocial, behavioural and cultural factors in explaining observed ethnic differences in health and development; 2. we examine whether experience of racism and discrimination are transmitted from the parent to the child generation and whether this translates into poor health and developmental outcomes.

**Methods:** The UK Millennium Cohort Study (MCS) is a large nationally representative longitudinal sample of children born in 2000-2002, and their parents, with over-representation of ethnic minority groups. Data on socioeconomic, psychosocial, behavioural and cultural characteristics, the experience of racism and discrimination, health and development, were collected during home visits and interviews. The ethnic groups considered in this paper were Black Caribbean, Black African, Pakistani, Bangladeshi, Indian and White.

**Results:** Explanations for ethnic differences appeared to vary according to ethnic group, and by specific markers of health and development. For example the Black Caribbean disadvantage for asthma and wheezing illness was explained by socioeconomic factors, whilst the Pakistani and Bangladeshi disadvantage in cognitive test scores were explained by cultural and socioeconomic factors. Preliminary analysis shows that among parents from ethnic minority groups 33% of mothers and 43% of fathers reported experiencing racism or discrimination in the previous 12 months. The experience of racism and discrimination was associated with increased risk of fair/poor general health (for mothers OR 1.4 and fathers 2.0) and a high score on the Kessler-6 psychological morbidity questionnaire (for mothers 1.4 and fathers 2.2). We will examine effects on markers of child health and development.

**Conclusion:** The pathways to poor health and developmental outcomes among children from different ethnic groups appear different. Experience of racism and discrimination is associated with poor health in parents of young children. Further analysis will reveal whether effects are transmitted to the next generation and whether these impact on child health and development.



## O19

### Childhood IQ does not explain adult health inequalities: A 65-year follow-up of children in Malmö, Sweden

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**Objective:** Intelligence, or IQ, has been proposed as “the elusive fundamental cause of social class inequalities in health”. This idea is controversial: If the health effects of socioeconomic position (SEP) are explained by IQ, this could be taken as an argument for not counteracting inequalities. Conversely, it’s possible that the health effects of IQ are essentially confounded or mediated by SEP. Increased understanding of the relationship between IQ, SEP and health is important for efforts to reduce inequalities.

**Material and methods:** All children attending fourth grade in a Swedish city in 1938 took IQ tests around age ten and were followed for all-cause mortality until 2003, when they were around 75 years old. Information on childhood socioeconomic position was collected around age nine. Data on own educational attainment was collected around age 36. Cox proportional hazards models were used to analyse, primarily, the effect of early IQ adjusting for adult SEP – and the effect of adult SEP adjusting for early IQ.

**Results:** Early IQ was strongly associated with men’s, but not women’s, mortality up to the age of 75. A clear effect of IQ on mortality for men remained when controlling for childhood and adult SEP. Mortality differences by educational attainment were large for both sexes and remained so after controlling for childhood SEP and childhood IQ.

**Conclusion:** IQ is unlikely to be the elusive fundamental cause of social class inequalities in health. Nevertheless, IQ is important in its own right, at least for men. Attention should be focused on the possibility to ensure more optimal environments with respect to the development of children’s cognitive abilities. Such efforts should be complementary to broad changes to reduce socioeconomic inequalities.

**O20****Intergenerational social mobility and cardiovascular mortality among siblings**Sanna Tiikkaja<sup>1</sup>, Marita Olsson<sup>2</sup>, Ninoa Malki<sup>1</sup> and Pär Sparén<sup>1</sup>

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**Background:** Cardiovascular (CVD) mortality is a leading cause of death internationally. Family history of CVD is a risk factor for CVD among offspring and is stronger related to siblings than to parents. In the present study, we analyse the impact of intergenerational social mobility between siblings on the risk of cardiovascular mortality.

**Materials and methods:** The data were extracted from the Swedish Social Mobility Database, which is a linkage between several Swedish population based registries. We restricted the number of siblings to those born 1939-1959 and to 5 siblings per family; in all 1,502,909 siblings were included. In the follow-up period from 1990-2003 were 13, 230 CVD deaths observed. Occupational class in childhood (1960) and adulthood (1990) was categorised as high non-manual, low non-manual, self-employed, high manual, low non-manual and unclassifiable. The siblings' risk of CVD mortality was estimated using alternating logistic regression.

**Results:** Overall, upwardly mobile siblings had lower risk for cardiovascular mortality and the risks varied by adulthood class. Siblings from low to high non-manual class had OR=0.69 (95%CI: 0.62-0.77), compared to stable low non-manual class. While mobile from low manual to high non-manual class had OR=0.85(95% CI: 0.77-0.94), compared to stable low manual class. Increased risks after adulthood class were found for downwardly mobile. Siblings mobile from high non-manual class to high manual had OR=1.21 (95%CI: 1.02-1.45), while mobile to low manual had OR=1.49 (1.27-1.75), compared to stable high manual class. Siblings who were mobile to unclassifiable in adulthood (outside the labour market) had the highest risks for cardiovascular mortality, compared to individuals within the labour market.

**Conclusions:** There are large variations in cardiovascular mortality among siblings after social mobility trajectory. Upwardly mobile siblings generally have lower cardiovascular mortality, compared to siblings remaining stable between childhood and adulthood. Downwardly mobile siblings generally have increased risk for cardiovascular mortality, compared to stable siblings. Particularly high risks were seen among those who were mobile outside the labour market.

## O21

**Does maternal education affect diet in 10-year-old children?**Victoria Cribb<sup>1</sup>, Imogen Rogers<sup>2</sup>, Louise Jones<sup>3</sup> and Pauline Emmett<sup>2</sup>

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**Objective:** To establish whether the educational background of the mother affects dietary intake of three key nutrients in 10-year-old children.

**Methods:** Subjects were part of the Avon Longitudinal Study of Parents and Children (ALSPAC), 14,541 pregnant women enrolled in 1991/92, establishing a cohort of 13,971 children (alive at 12 months of age). In the present analysis, 7474 children were involved (61%) at age 10 years. Three-day diet diaries were used, by the child with parental help, to record all food and drink the child consumed and a short questionnaire asked about types of spread used and other details of commonly eaten foods to aid coding. The child and parent were interviewed with the diary to clarify foods/drinks consumed. Nutrient intakes, averaged over 3 days, were calculated and energy adjustment was performed, using the residuals method, to assess the quality of the diet. Information of highest maternal education level was derived from a questionnaire sent out in pregnancy. For the purpose of this analysis, maternal educational status was classified as low (CSE or vocational), medium (O Level) or high (A Level or degree). Appropriate statistical analyses were performed to compare the 3 groups.

**Results:** Energy intakes were 8.18(1.66) MJ for boys and 7.40(1.49) MJ for girls. The low maternal education group contained 20% of subjects, medium 32% and high 39%. This showed a bias towards higher education when compared to the original sample. There was a gradient in diet quality for calcium, folate and vitamin C in both sexes such that as maternal education level increased so did the amount of each nutrient in the diet.

**Table 1.** Energy-adjusted mean intake (95% CI) of Calcium, folate and Vitamin C at 10 years according to maternal educational status.

Boys				
Nutrients	Low (n=753)	Medium (n=1216)	High (n=1427)	p-value for trend
Calcium (mg)	706 (690-723)	750 (738-763)	756 (745-768)	0.000
Folate (µg)	195 (191-200)	204 (200-207)	212 (208-215)	0.000
Vitamin C (mg)	65.0 (61.6-68.3)	71.8 (68.8-74.8)	81.6 (78.7-84.5)	0.000
Girls				
Nutrients	Low (n=748)	Medium (n=1209)	High (n=1477)	p-value for trend
Calcium (mg)	708 (692-724)	721 (709-733)	754 (743-766)	0.000
Folate (µg)	191 (187-195)	195 (192-199)	205 (202-208)	0.000
Vitamin C (mg)	67.6 (64.1-71.3)	75.1 (72.2-78.1)	90.6 (87.7-93.6)	0.000

**Conclusions:** The quality of children's diet at age 10 was related to maternal education. Inequality in family background has an impact on child diet that could have a detrimental affect on later health outcomes.

**O22****Diet throughout childhood and age at menarche in a contemporary cohort of British girls**

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**Objective:** To investigate associations between dietary intakes throughout childhood and age at menarche in a contemporary cohort of British girls.

**Materials and methods:** The Avon Longitudinal Study of Parents and Children (ALSPAC) enrolled pregnant women in 1991-92, resulting in a total cohort of 14,062 live births (48% female). Diet of the children was assessed by parent-completed food frequency questionnaires at 3 and 7y of age, and by a 3-day unweighed food diary (with interview) at ten years. Age at menarche in girls was assessed by interview and was categorised as before or after 12y 8m, the median age in this cohort. Data for all variables were available for 3298 girls.

**Results:** Higher energy intakes at 10y were positively associated with the early occurrence of menarche, but this association was removed on adjusting for body size. Total and animal protein intakes at 3 and 7y were positively associated with the occurrence of menarche (adjusted OR for a 1sd increase in protein at 7y 1.14 (95% CI 1.04, 1.26)). Higher intakes of polyunsaturated fat at 3y and 7y were also positively associated with the occurrence of menarche. Meat intake at 3y and 7y was strongly positively associated with reaching menarche by 12y 8m (OR for menarche in the highest versus lowest category of meat consumption at 7y was 1.75 (95% CI 1.25, 2.44)).

**Conclusions:** These data suggest that higher intakes of protein and meat in early to mid childhood may lead to earlier menarche.

## O23

**Maternal vitamin D intake during pregnancy is inversely associated with asthma and allergic rhinitis in 5-year-old children**

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**Objectives:** Vitamin D is known to have a number of immunological effects and it may play a role in preventing allergic diseases. The aim is to study the effect of maternal intake of vitamin D during pregnancy on the emergence of asthma, allergic rhinitis, and atopic eczema by the age of 5 years in children participating a population-based birth cohort study.

**Material and methods:** Children with HLA-DQB1-conferred susceptibility for type 1 diabetes participating the Type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study were invited to the allergy study. Of the children born between October 1997 and September 2001, 1669 (78% of those 2145 invited) provided complete information about exposures (= food and nutrient intake of the mother during pregnancy) and outcomes (=the child's history of allergic symptoms). The child's history and symptoms of asthma, allergic rhinitis, and atopic eczema was assessed by a validated questionnaire at 5 years. Maternal diet was assessed by a food frequency questionnaire. The association between maternal dietary variables and asthma and allergic rhinitis in the child was analysed using Cox proportional hazards regression. Logistic regression was used to analyse associations between dietary variables and atopic eczema. The models were adjusted for relevant potential confounders.

**Results:** The mean maternal intake of vitamin D was 5.1 (SD 2.6) µg from food and 1.4 (2.6) µg from supplements. Only 32% of the women were taking vitamin D supplements. When adjusted for potential confounders, high maternal intake of vitamin D from food was related to decreased risk of asthma [hazard ratio, (HR) 0.80 (95% confidence interval (CI) 0.64–0.99)] and allergic rhinitis [HR 0.85 (95% CI 0.75–0.97)]. Vitamin D supplements alone were not associated with any outcome. Adjustment for maternal intake of other dietary factors did not change the results.

**Conclusion:** High maternal vitamin D intake from foods during pregnancy may be associated with decreased risk of asthma and allergic rhinitis in childhood.

**O24****Vitamin D supplementation is associated with reduced risk of preeclampsia in nulliparous pregnant women**

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**Objective:** A recent study showed that nulliparous women who develop preeclampsia had low concentrations of vitamin D in serum sampled in mid-pregnancy. The aim of this study was to estimate the association between intake of vitamin D from diet and supplements and preeclampsia development in women participating in MoBa.

**Methods and subjects:** Women participating in MoBa answered questionnaires at gestational weeks 15 (a general health questionnaire), at weeks 17 to 22 (a food frequency questionnaire) and at week 30 (general health questionnaire). The pregnancy outcomes were obtained from the Medical Birth Registry of Norway (MBRN). Nutrient intake was calculated from foods and dietary supplements. Relative risks were estimated as odds ratios, and confounder control was performed with multiple, logistic regression. In this study 23,423 nulliparous pregnant women were included.

**Results:** The odds ratio of preeclampsia for women with a vitamin D intake of 15-20 µg/day compared to less than 5 µg/day was 0.76 (95% confidence interval 0.60,0.95). Looking only at intake of vitamin D from supplements, a 27% reduction in risk of preeclampsia (OR: 0.73, 95% confidence interval 0.58, 0.92) was found for women taking 10-15 µg/day as compared to no supplements.

**Conclusions:** These findings are consistent with other reports of a protective effect of vitamin D on preeclampsia development. However, since vitamin D intake is highly correlated with the intake of long chain n-3 fatty acids in the Norwegian diet, further research is needed to disentangle the separate effects of these nutrients.

## O25

### Lipid profiles in middle-aged men and women after prenatal famine exposure: the 1944-45 Dutch famine

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**Background:** Many studies in humans have related birth weight to lipid profiles in adulthood. Fewer have estimated associations directly attributable to maternal nutrition during pregnancy.

**Objective:** To determine if famine exposure of pregnant women during specific periods of gestation is associated with a more atherogenic profile in their adult offspring examined at age 58 years.

**Design:** In 2003-5, we studied (1) 359 singleton men and women born between January 1945 and March 1946 in three clinics in Amsterdam, Rotterdam, and Leiden whose mothers were exposed to the 1944-1945 famine during pregnancy, (2) a control group of 313 unexposed same-sex siblings of the above individuals, and (3) a control group of 299 singletons born in the same three institutions during 1943 or 1947. A lipid profile was obtained after an overnight fast. We defined four time windows for famine exposure (weeks 1-10 of pregnancy, weeks 11-20, weeks 21-30, and weeks 31 to delivery) based on mother's last menstrual period from medical records and distributed food rations during the famine.

**Results:** Female offspring with prenatal famine exposure at any time in pregnancy had a more dyslipidemic pattern characterized by elevated total cholesterol (0.27 mmol/l; 95% CI 0.07–0.46;  $p=0.007$ ), triglycerides (0.17 mmol/l; 95% CI 0.03–0.31;  $p=0.02$ ), and LDL-cholesterol (0.17 mmol/l; 95% CI 0.01–0.36;  $p=0.06$ ) compared to unexposed same sex controls. This pattern was not seen in men, with tests for heterogeneity by gender being significant at  $p<0.01$  for total cholesterol and LDL cholesterol but not for triglycerides. The increases in total cholesterol and LDL-cholesterol were independent of body mass index (BMI), waist circumference (WC), and mid-thigh circumference (MTC). The increase in triglycerides was independent of MTC but was attenuated with control for either BMI or WC. There was no evidence for associations within specific gestational windows. There was no association between prenatal famine exposure and HDL-cholesterol in either sex.

**Conclusions:** In women but not in men aged ~58 years, we observed an association between prenatal undernutrition and elevated total cholesterol levels and triglycerides. There was also a tendency towards LDL-c elevation. These data suggest sex-specific programming of lipid metabolism by maternal undernutrition in pregnancy.

**O26****Current patterns of diet in community-dwelling older men and women in UK: results from the Hertfordshire Cohort Study**

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**Background:** Much current public health advice to prevent cardiovascular disease and cancer has been based upon evidence of disease-promoting or protective effects of individual nutrients. However the diet is a complex combination of foods, nutrients and non-nutrients and there are interactions between dietary constituents. The relationships between diet and disease may therefore differ from those predicted from nutrient-disease associations. Dietary patterns analysis takes account of the combined effects of foods and nutrients commonly consumed together, and may therefore be a more meaningful measure of dietary exposure, than a consideration of effects of single dietary constituents in isolation. Our knowledge of the dietary patterns of older men and women is limited. There is a need to know more about how dietary patterns vary amongst older men and women in the UK, and to determine how current variations relate to health and disease.

**Material and methods:** From 1911 to 1948, detailed records were kept on all infants born in Hertfordshire, UK. In 1998, 7106 men and women born between 1931 and 1939 were traced. 3217 of these men and women were interviewed between 1998 and 2004; their diets were assessed using an administered version of the EPIC food frequency questionnaire. Dietary patterns were defined using principal component analysis. Fasting blood samples were available for 2781 men and women for determination of triacylglycerol (TAG) and cholesterol concentrations.

**Results:** There were 2 identifiable dietary patterns. The first was characterised by high consumption of fruit, vegetables, oily fish, and wholemeal cereals but by low consumption of white bread, added sugar, full-fat dairy products and chips. This pattern of diet reflects recommendations for a healthy diet, and we called it a 'prudent' pattern in common with other studies. The second pattern was characterised by high consumption of vegetables, processed meat, offal, fish, red meat and puddings but by low consumption of milky drinks, reduced fat spread and breakfast cereals. This pattern was less easy to interpret. It had some elements of a 'western' dietary pattern seen in other studies, but was also characterised by frequent consumption of vegetables. It may represent a more traditional pattern of eating, and we called it a 'traditional' pattern. Degree of compliance with the 'prudent' dietary pattern was related to differences in blood lipids; higher 'prudent' diet scores were associated with lower fasting TAG concentrations, and higher HDL:LDL ratios in both men and women (lipid values adjusted for age, alcohol intake and BMI, all  $P < 0.05$ ). TAG and HDL:LDL ratios were not related to compliance with the 'traditional' dietary pattern.

**Conclusion:** These dietary patterns identify very large differences in food choice and food consumption amongst these older adults, which are related to differences in blood lipid profile. Ongoing follow-up studies will enable us to assess how these patterns relate to subsequent morbidity and mortality, and the extent to which these measures of dietary exposure may be more useful than a consideration of the effects of single nutrients.



## O27

## Life course dairy consumption in relation to arterial stiffness at adult age: The Amsterdam Growth and Health Longitudinal Study

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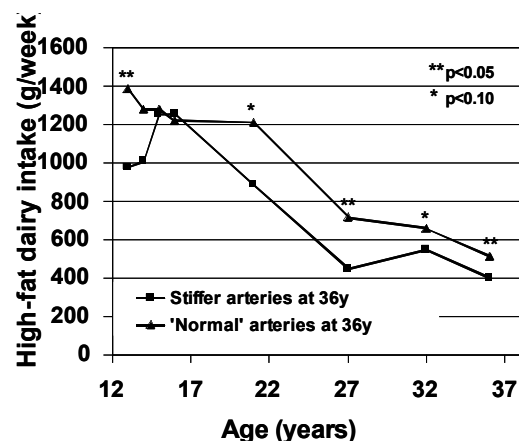
**Objective:** It has been suggested that dairy consumption may reduce the risk of obesity and cardiovascular disease. Previous studies, however, were usually cross-sectional whereas long-term nutritional exposure, particularly during adolescence, may be more important for health later in life. Furthermore, effects of low-fat and high-fat dairy have been suggested to be different. Therefore, the aim of the present study is to investigate life course dairy consumption (from adolescence into adulthood) in relation to arterial stiffness (early marker of cardiovascular disease) at adult age.

**Material and methods:** Dairy intake (g/week) was repeatedly measured between the ages of 13 and 36 years in participants (N=374) of the Amsterdam Growth and Health Longitudinal Study (AGAHLS). Ultrasound was used to measure the distensibility and compliance of the carotid, femoral and brachial arteries, and the carotid Young's elastic modulus, at age of 36 years. A summary variable for stiffness was created by mean z-scores of all stiffness estimates. General Estimated Equations (GEE) were used to assess the time course of total dairy, high-fat dairy, and low-fat dairy intake in subjects with 'stiffer' arteries (upper tertile of mean z-score) versus 'normal' arteries (lowest 2 tertiles of mean z-score). Dairy intake was ln-transformed because distributions were skewed.

**Results:** Overall, high-fat dairy consumption decreased over time, whereas consumption of low-fat dairy increased. The time course of total dairy consumption did not significantly differ between participants with stiffer and normal arteries (based on mean Z-scores), except that subjects with normal arteries consumed significantly more dairy at age 13 (568 g/week, after back-transformation). When distinguishing high-fat and low-fat dairy, results showed that there was no difference in low-fat dairy intake, but subjects having stiffer arteries consumed significantly less high-fat dairy consumption at ages 13, 21, 27, 32, and 36 years (but not at ages 14, 15, and 16 years) as compared with subjects having normal arteries (differences ranging from 112 to 407 g/week), as shown in the Figure.

The results were consistent for individual stiffness estimates in the 3 different types of arteries. Adjustment for smoking, alcohol intake and physical activity did not change the results. Adjustment for total energy-intake only slightly attenuated the differences.

**Conclusion:** Our results suggest that a higher intake of high-fat dairy may contribute to a lower risk of developing arterial stiffness.



## O28

**Opportunities for molecular cancer research in the Tromsø Study**Anne-Sofie Furberg<sup>1,2</sup>, Merethe Kumle<sup>3</sup>, Inger Njølstad<sup>1</sup> and Egil Arnesen<sup>1</sup>

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**Objective:** The Tromsø Study is a prospective study of entire birth cohorts and random samples in the municipality of Tromsø. This large cohort offers unique opportunities for research on cancer epidemiology among men and women in North Norway, including molecular analyses. We aim to summarize information in The Tromsø Study database and biobank that gives prospects for future national and international studies on cancers at different sites.

**The Tromsø Study:** The Tromsø Study includes five repeated health surveys from 1974 till 2002 and a sixth ongoing survey. A total of 38,164 men and women aged 12-97 years have participated in at least one of the completed surveys. The participation rate has been about 80%. The Tromsø Study IV in 1994-95 was the largest survey and included 27,158 people. All data from questionnaires, clinical measurements and blood sample analyses in each survey are available in quality-controlled electronic files presented through NESSTAR (<http://tromsundersokelsen.uit.no/tromso/>). These highly complete data have formed the basis for several significant epidemiological studies on chronic diseases and the detection of major lifestyle and environmental risk factors for cardiovascular disease and diabetes, in particular. The 11-digit personal identification number makes it possible to link The Tromsø Study participants to The Cancer Registry of Norway. The number of incident cases of cancer in The Tromsø Study since date of examination through December 2006 is for the following major sites: female breast cancer n=407, prostate cancer n=339, total lung cancer n=331, total colon cancer n=256, and total malignant melanoma n=115. Tumor blocks for the cancer cases in The Tromsø Study are stored at the Department of Pathology, University Hospital of North Norway. The Tromsø Study IV was the first survey to provide data and blood samples to the Cohort of Norway (CONOR), which per today includes 9 additional surveys, the largest being The North-Trøndelag Study (HUNT), The Hordaland Health Study (HUSK), and The Oslo Health Study (HUBRO). DNA has been extracted from blood coagula of the more than 27,000 participants in Tromsø IV as part of Biohealth Norway.

**Prospects for future cancer studies:** Epidemiological cancer research in The Tromsø Study is timely and highly wanted. Firstly, there are great opportunities for studies of separate and combined effects of genes and environment on the risk of cancer among men and women in North Norway. Nested case-control studies will require genotyping of cases and a set of controls; a multigenic approach with combinations of a panel of common single nucleotide polymorphisms (SNPs) in candidate genes of the same or related pathways may be most useful for the study of genetic susceptibility to cancer in this setting. Secondly, there are great opportunities for studies of etiologic heterogeneity of selected malignancies. Malignant tumors at a certain site generally represent a variety of diseases with different pathology and clinic. It is generally thought that the aetiology of the cancer subtypes varies, and epidemiologic studies comparing risk factors for different subtypes may clarify the biology of the disease. Therefore, it will be most interesting to do tumor analysis including tissue microarray for molecular analysis of cases in The Tromsø Study. The Cancer Research Group of The Tromsø Study was founded this year and consists of a core group of epidemiologists with a longstanding interest in population-based cohort studies of chronic diseases among people of North Norway. A co-ordinated, well functioning local partnership on cancer research in Tromsø, will promote sound and relevant use of screening data and DNA/genetic information, and be a stepping-stone to new national and international collaborative research opportunities and funding, as already initiated within the BioHealth/CONOR collaboration with HUNT and international research groups in breast cancer, lung cancer and kidney cancer, among others.

## O29

### The Swiss Inflammatory Bowel Disease Cohort Study (SIBDCS): founding and first observations

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**Background:** After a pilot population-based cohort, established in the Canton de Vaud between July.03 and Dec.04 with the aim of estimating for the first time the prevalence rate of IBD in Switzerland, the project was expanded in 2006 to become national-wide. Besides studying risk factors associated with the disease, major aims of the study relate to appropriateness of therapy, health resource consumption and influence of new biological therapies and psychosocial aspects linked with exacerbation of the disease. A Biobank has been especially set up for the study in order to study coupling effects of genetics on clinical observations.

**Material and methods:** 6 major IBD centers at Swiss university-based tertiary hospitals recruit patients as well as physicians outside the centers (in regional hospitals and private practices). All adult or pediatric IBD patients, with permanent residence status or being treated regularly in Switzerland are eligible for enrolment, on condition that a radiological-, endoscopic- or surgery-confirmed diagnosis had been established at least 4 months prior to inclusion or after at least one recurrence of the symptoms. Patients are followed up once a year. Socio-demographic, clinical and psychosocial data are collected through physician and patient questionnaires. In 2 IBD centers out of 6, IBD alerts have been created through the hospital computer system in order to track patient's unscheduled events occurring during the year.

**Results:** 81 physicians are participating since 1st. Nov 06 to patient recruitment, 75% from the 6 major centers, 11% from regional hospitals and 14% are private practitioners. 1039 patients were enrolled, 60% suffering from Crohn's disease and 38% from ulcerative colitis. In 29 cases, the diagnosis was an indeterminate colitis. The proportion of females is 50.4%. Mean age of the cohort is 43 yrs (+/- 15), ranging from 16 to 89 years. 74% of the patients have already responded to the first questionnaire and 15% are on hold (time to sending  $\leq$  3 months).

**Conclusion:** The newly-established Swiss IBD cohort study was launched 15 months ago and offers a real challenge in acquiring data about epidemiology of IBD in Europe, as well as evaluating patient health care and costs linked to these chronic diseases.

**O30****Follow-up measurements in a longitudinal study: design of the Amsterdam Born Children and their Development (ABCD) cohort**

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The ABCD – Amsterdam Born Children and their Development – study is a long term, large scale cohort study, examining the relationship between maternal lifestyle and psychosocial conditions during pregnancy and the child's health at birth as well as in later life. The study specifically addresses differences in health and health behavior among ethnic groups. The study started out in 2003, when 12373 pregnant women were invited to participate in the study at their first antenatal visit to their obstetric careprovider (around the 12th week of pregnancy). A total of 8266 women (54% Dutch, 46% non-Dutch origin) filled out a questionnaire (response rate 67%), and among these, 4389 women donated a blood sample for nutrient analysis. Eighty-five percent of the respondents gave permission for follow-up study (n = 7050).

The first follow-up phase took place from June 2003 to December 2004. Pregnancy outcomes were obtained through the Youth Health Care department of the Public Health Service, and a infant questionnaire was sent to the mothers 3 months after birth (response rate 74%). The second follow-up phase of the ABCD children, at age 5, has commenced in June 2008 and will continue until December 2009. Measurements include a questionnaire for the parents (covering sociodemographics, the child's health, behaviour and psychosocial development, lifestyle and nutrition, maternal psychosocial health, and family medical history), a questionnaire for the child's teacher (covering behaviour and psychosocial development), and a consultation at the child's school. During this consultation, risk factors for obesity and metabolic disease as well as cognitive development will be measured. Measurements include a) a fingerprick, allowing for the measurement of cholesterol, lipid profile and glucose; b) anthropometric measures of weight, height, waist and hip circumference, and percentage body fat; c) blood pressure and heart rate variability; and d) cognitive tests (Amsterdam Neuropsychological Tasks). An anticipated 5000 children will be measured over the two-years time period, and first results are expected in 2010.

**O31****Do maternal weight gains during pregnancy link with offspring body mass index and blood pressure at 21 years? Evidence from a birth cohort study**

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**Background:** Maternal weight gain in pregnancy is positively associated with offspring body mass index (BMI) and obesity risk in childhood, but whether this increased risk extends into adulthood or results in increases in other cardiovascular risk factors, such as elevated blood pressure (BP) is unclear.

**Methods and results:** We used a population-based birth cohort of 2432 individuals (50% males) born in Brisbane, Australia, between 1981 and 1983 to prospectively examine the association between maternal gestational weight gain and offspring BMI and BP at 21 years. We have found that greater maternal weight gain during pregnancy was associated with greater BMI. In our study offspring BMI was on average 2.70 (95% CI: 1.30, 4.09) kg/m<sup>2</sup> higher for every kg per week greater maternal weight gain in pregnancy after adjustment for potential confounding factors. A 1 kg/m<sup>2</sup> greater BMI at age 21 was associated with on average greater systolic blood pressure (SBP) of 0.66 (95% CI: 0.55, 0.76) mmHg. Thus, if the effect of maternal weight gain on offspring BMI were expected to directly translate into an effect on SBP we would expect SBP to be on average 1.78 mmHg greater for every kg per week greater maternal weight gain in pregnancy (2.7×0.66). This compares to an observed confounder adjusted association of 2.09 (95% CI: -1.60, 5.79) mmHg. Hence SBP was greater at age 21 by an amount equivalent to that predicted by the effect of maternal weight gain on offspring BMI at age 21, but in this study sample the effect was imprecisely estimated and had with confidence intervals that included the null value.

**Conclusions:** Our findings show that greater weight gain in pregnancy is associated with greater offspring BMI into early adulthood and that this may translate into higher SBP in offspring. Further large studies are required to confirm an effect of maternal weight gain in pregnancy on a range of offspring cardiovascular risk factors.

## O32

**Distinct life course developmental patterns of body fatness as predictors for metabolic syndrome components: A Latent Class Growth Mixture Modelling Analysis**Trynke Hoekstra<sup>1</sup>, Celestina Barbosa-Leiker<sup>2</sup> and Jos W.R. Twisk<sup>1,3</sup>

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**Background:** The Metabolic Syndrome (MS) is characterised by a clustering of multiple cardiovascular disease risk factors. The prevalence is increasing worldwide and the need for prevention is widely recognised, moreover because the MS is in itself an evident risk factor for Diabetes Mellitus type (DM2) and cardiovascular diseases. Many prevention programmes focus on weight loss, as body fatness has been recognised as an evident risk factor for the MS (components). But, for prevention programmes to be successful, comprehensive understanding is needed of developmental patterns of body fatness during childhood, adolescence and adulthood and of the relationships between different patterns and the MS.

**Purpose:** The purpose of the study is to analyse the developmental patterns of body fatness from childhood through adulthood (age 13-42) thus determining the number and characteristics of distinct body fatness trajectories *and* relate the distinct subgroups to MS components later in life, revealing subgroups specifically at risk.

**Methods:** Data were obtained from the Amsterdam Growth and Health Longitudinal Study, AGHLS (N=325), an ongoing observational cohort study of apparently healthy male and female participants with ten rounds of measurement over a period of thirty years. The focus of the AGHLS is mainly on (relationships between) growth, health and lifestyle. Body fatness was measured by sum of four skinfolds (SSF). Four components of the MS were investigated; fasting glucose values, triglycerides, HDL-cholesterol and mean arterial pressure. Advanced statistical analyses (*latent class growth mixture modelling*) were conducted to obtain distinct developmental trajectories of SSF and linear regression analyses were performed to assess associations between MS components and the distinct subgroups.

**Results:** Analyses revealed three distinct life course (age 13-42) trajectories of SSF; a normative group (used as reference for regression analyses) (75.1%), a progressively overweight group (8.6%) and fluctuating group (16.3%). The trajectories were significantly associated with all components but fasting glucose levels, showing some profound differences between the normative and the progressively overweight group especially, even after correction for lifestyle variables (log transformed **fasting glucose levels**  $\beta=1.00$  (95% CI 0.97-1.04) comparing fluctuating group to reference and  $\beta=1.01$  (95% 0.96-1.06) comparing overweight group to reference, log transformed **triglycerides**  $\beta=0.97$  (95% CI 0.84-1.11) comparing fluctuating group to reference and  $\beta=1.19$  (95% CI 0.98-1.44) comparing overweight group to reference, **HDL-cholesterol**  $\beta=0.04$  (95% CI -0.08-0.15) comparing fluctuating group to reference and  $\beta=-0.29$  (95% CI -0.43- -0.14) comparing overweight group to reference and **mean arterial pressure**  $\beta=1.24$  (95% CI -1.60-4.07) comparing fluctuating group to reference and  $\beta=6.49$  (2.78-10.21) comparing overweight group to reference.

**Conclusion:** In an apparently healthy population, life course trajectories of SSF were significantly associated with most MS components at adult age, showing importance of distinct developmental patterns of body fat, providing promising opportunities for improving public health.

## O33

### Intergenerational influences on childhood BMI: the effect of parental BMI trajectories

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**Background:** Parental obesity in adulthood is a strong predictor of offspring obesity. Whether parental BMI at earlier life stages is associated with offspring BMI is unknown.

**Objectives:** To assess whether BMI and BMI gain of parents recently in adulthood are more strongly associated with offspring BMI than BMI or changes in parental BMI in childhood.

**Material and methods:** Two generations in the 1958 British birth cohort were studied, including cohort members (parents generation) with BMI at 7, 11, 16, 23, and 33y (n=16794) and a one-third sample of their offspring selected in 1991 and aged 4-18y with a plausible BMI measure (n=2908). We applied multilevel models to allow for within-family correlations.

**Results:** Childhood BMI increased on average by 0.25-1.10 kg/m<sup>2</sup> between the two generations, depending on gender and age group and overweight/obesity increased from 10% to 16%. Parents' BMI in childhood and adulthood independently influenced offspring BMI: there was no significant difference in their strength of influence. For example, adjusted increase in BMI for offspring aged 4-8y was equivalent 0.37 and 0.23 kg/m<sup>2</sup> for a SD increase in maternal BMI at 7y and at 33y respectively. Similar patterns were observed for risks of overweight/obesity and for paternal BMI at most ages.

**Conclusions:** Excessive BMI gains of parents during childhood and adulthood were both associated with higher BMI and obesity risk in their offspring.

## O34

**Aetiology of overactive bladder: evaluation of a diet and lifestyle model involving diabetes and obesity in women using graphical modelling**C.W. McGrother<sup>1</sup>, M.M.K. Donaldson<sup>1</sup>, J. Thompson<sup>1</sup>, D. Tincello<sup>2</sup> and A. Wagg<sup>3</sup>

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**Objectives:** Urinary incontinence and related storage symptoms constitute a common, distressing and costly disorder. The main storage disorder in older women is overactive bladder (OAB). Previous studies implicate diabetes in the pathogenic process for OAB and obesity as causal for Stress Urinary Incontinence (SUI). The aim of this study was to evaluate the hypothesis that physical activity and related modifiable lifestyle factors, implicated in the development of diabetes and associated obesity, contribute to the onset of OAB, and to identify the most likely pathways through which they exert their effects.

**Material and methods:** a secondary analysis of a prospective cohort of 7046 women aged 40 and above, with diet, lifestyle, comorbid and social factors measured at baseline, and urinary outcomes at one year follow-up. A logical causal chain graph was created within which potential factors were grouped into 4 successive blocks: “immutable” (parity and age) → “modifiable lifestyle” (dietary glycemic index (GI), energy intake and physical activity) → “intermediate morbidity” (diabetes and obesity) → “urinary outcomes” (OAB and SUI). A standardised literature review of epidemiological studies was undertaken to identify those prospective (i.e. longitudinal) and cross-sectional associations that were supported by 3 or more previous epidemiological studies and this formed the basis for an initial evidence-based model. The modifiable and intermediate prospective associations identified by the review were: high GI to diabetes and obesity; low physical activity to diabetes and obesity; high energy intake to obesity; diabetes to obesity; and obesity to OAB and SUI. Similar cross-sectional associations were: high GI with high energy intake; high physical activity with high energy intake; and OAB with SUI. Prospective associations for immutable factors were: age (positively) to OAB, diabetes, obesity, physical activity and (negatively) to energy intake; plus parity (positively) to OAB, SUI and obesity. The directions of associations identified in the review were consistent with the sequence within the logical causal chain model. The evidence-based model was evaluated in 2 stages: stage 1 evaluated the relationships between all the factors identified in the review, with a sensitivity analysis for ADL (model 1). In stage 2, model 1 was adjusted for general confounding – poor diet, smoking and socio-economic group (model 2). Graphical chain modelling (MIM) and STATA were used to estimate the contribution, and likely pathways, of factors related to the onset of OAB.

**Results:** All hypothesized factors identified were retained as potential contributors within the causal network for OAB. Reported low physical activity was a direct risk factor for the onset of OAB, RR 2.47 (95% CI 1.82, 3.36). The hypothesized direct link between obesity and OAB became indirect through stress urinary incontinence. This relationship was maintained following adjustment for ADL in model 1, and other general confounding factors in model 2. Strong associations were confirmed for physical activity in relation to obesity and diabetes. The hypothesized direct links of glycaemic index with both diabetes and obesity became indirect via physical activity.

**Conclusions:** The strength of the current study lies in the extent to which it investigates all potential associations in the model and thereby reveals hidden confounding factors as potential mechanisms within the model. Lifestyle factors implicated in the development of diabetes and obesity also appear to contribute to the onset of OAB. The main pathways implicated involve low physical activity directly and indirectly via obesity and stress urinary incontinence.



## O35

**Changes in trunk fat mass and peripheral lean mass are associated with changes in carotid arterial stiffness in a healthy population – a 6-year follow-up study**

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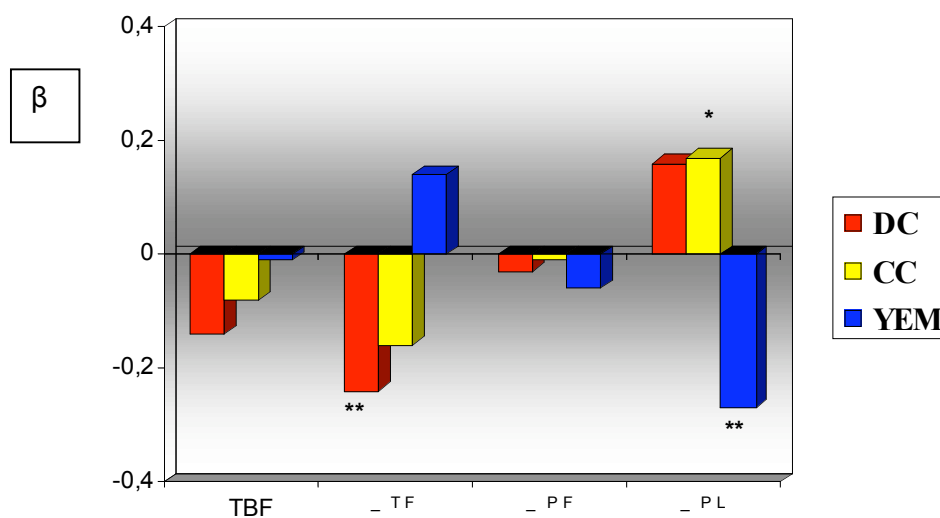
**Introduction:** In cross-sectional studies, total body fat mass and particularly central fat distribution are associated with increased arterial stiffness. How *changes* in body fat and body fat distribution impact on *changes* in large artery stiffness is unknown.

**Methods:** Data were derived from the Amsterdam Growth and Health Longitudinal Study on healthy, middle-aged subjects (n=268,142 women), in whom body composition and arterial stiffness estimates were measured at the age of 36 and again at the age of 42. Total and regional (head, trunk, arms and legs) body fat distribution were determined by dual-energy x-ray absorptiometry. Peripheral fat or lean mass was calculated by adding the fat or lean mass of the legs to that of the arms. Ultrasound imaging was used to measure the distensibility (DC) and compliance coefficients (CC) of the carotid, femoral and brachial arteries, and carotid Young's elastic modulus (YEM) as estimates of peripheral stiffness. The carotid-femoral pulse-wave velocity (PWV) was assessed as an estimate of central stiffness. Multiple linear regression analyses were used to investigate the association between changes total body fatness (TBF) and body fat distribution (determinants) and changes in arterial stiffness (outcomes). Standardized betas ( $\beta$ ) are reported.

**Results:** After adjustment for gender and changes in mean arterial pressure (model 1), increases in TBF were *adversely* associated with increased carotid stiffness, although not significantly (*Figure*). Increases in trunk fat (TF), however, were consistently associated with increases in carotid stiffness (i.e. lower DC, CC and greater YEM) and similarly though not significantly so with increased brachial and femoral stiffness (data not shown). In contrast, increases in peripheral lean (PL) mass were *favourably* associated with decreased carotid stiffness (i.e. greater DC, CC and lower YEM). After additional adjustment for the other body composition variables (model 2) the above mentioned associations for TF and PL became stronger ( $p < 0.05$  or  $p < 0.10$ ). Indeed, increases in PF became *favourably* associated with decreased carotid stiffness, although not significantly. Further adjustment for changes in biological risk factors (i.e. total/HDL cholesterol, triglycerides, HbA1c, resting heart rate (model 3) did not materially change any of the above associations. Regarding central stiffness, associations with carotid-femoral PWV were inverse, especially PL ( $\beta$ : -0.46,  $p < 0.10$ ). However, for TF the association was inconsistent ( $\beta$ : -0.07 in model 1 and 2;  $\beta$ : 0.07 in model 3).

**Conclusions:** Increases in TF during adulthood have adverse effects on carotid stiffness, whereas increases in PL may counteract this. Moreover, an increase in PL has an favourable impact on aortic PWV.

**Figure.** Associations between 6-yr changes in body composition and carotid arterial stiffness (model 1,  $\Delta$ : changes in, \*\* $p < 0.05$ , \* $p < 0.10$ ).



**O36****Ethical Dilemmas: solutions from the Avon Longitudinal Study of Parents And Children (ALSPAC) Ethics and Law Committee**

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**Background:** The Avon Longitudinal Study of Parents and Children (ALSPAC) enrolled over 14000 pregnant mothers during 1991 & 1992. ALSPAC's main goal is to understand the ways in which the physical and social environment interact, over time, with genetic inheritance to affect a child's health, behaviour and development. The cohort mothers with their partners and children continue to give vast amounts of data: physical, psychological, social, educational, environmental, biological and genetic. From the outset of planning for the study it became clear that sound legal and ethical advice would be necessary in order to guarantee appropriate protection for the study participants including those yet to be born.

**ALSPAC Ethics & Law Committee:** The Committee was set up during the initial piloting phase in order to advise on the ethical and legal aspects of the study. Much has changed in the last nineteen years in relation to the laws, ethics and governance of medical research. The Committee, alongside NHS Research Ethics Committees (RECs) have ensured that all ALSPAC research has been comprehensively reviewed. The ALSPAC committee has provided an integrated legal and ethical perspective and thorough scrutiny of detail not possible by the RECs. The RECs have provided a necessary independent perspective. Many other groups and committees have contributed in part to the ethical review.

**Dilemmas:** The ALSPAC Ethics & Law Committee have grappled with issues concerning recruitment, retention, confidentiality & anonymity, consent & assent, divulging results, data linkage & access, as have most longitudinal cohort studies. The Committee has also had to deal with conflicting advice from the RECs. I will describe some of the dilemmas which the Committee has considered and their conclusions so that the study could be continued without obstructing the maximal use of data in line with the study aims while simultaneously not compromising the protection of the study participants.

**Conclusion:** The solutions to each ethical dilemma decided on by the ALSPAC Ethics & Law Committee is unlikely to be identical to other committees, as each has to work in the context of the legal and ethical milieu of their own time and place. Nevertheless such solutions could be of interest and benefit to others faced with similar dilemmas.

## O37

### Input of longitudinal data in the health information system

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**Objective:** In Belgium, political and health decision-makers wish to strengthen their knowledge of the population's health status by adding longitudinal data to the national Health Information System (HIS). Indeed repeated measures of one's health, put together in an organised system would allow to combine the complementary information, to better follow the changes that individuals experience and to further understand the series of events which leads to good or bad health status. This paper provides a breakdown of the elements needed to insert such a longitudinal approach into a HIS.

**Methods:** This on-going study leans on three complementary pillars: the elaboration of a conceptual framework established on the basis of an international comparative review; the definition of variables useful in a long-term perspective; and the study of the operational aspects with regard to their collection and use.

**Results:** Despite specific constraints, several strategies can help to build a dynamic approach: the usual carrying out of longitudinal studies, the coupling of data, the establishment of electronic medical records and the implementation of registers. Several health topics and indicators deserve particular long-term attention such as the self-perceived health, some pathologies (asthma, hypertension, diabetes...), the functional health or certain health behaviours (especially tobacco consumption). However international initiatives indicate that the construction of a longitudinal vision implies also the fulfilment of other complex requirements. First of all, concerning the legal background that should balance, on the one hand, the protection of individual rights and, on the other hand, the need to collect data in order to evaluate the performance of the health system and to establish sound public health policies. Then, decisions concerning the configuration of the longitudinal HIS should be taken, that will for instance allocate the tasks, responsibilities and means of the collection, analyse and diffusion of the data; ensure the physical protection of the data; promote the quality of the data as well as the use of a unique health identification code. Relying on those international examples, the Belgian health authorities, which launched a project of improvement of the national HIS through the addition of a longitudinal component, might take advantage of the current implementation of an electronic platform of health data exchanges to achieve their objective.

**Conclusion:** Applying a longitudinal approach to the health sector would contribute to the development of a nationwide coherent vision of the population's health status, support the sustainability of the health system and would take part in an evidence-based medicine strategy. In addition to the technological investments, this would necessitate some cultural changes in order to facilitate the exchange of data.

## O38

**Estimation the proportion of sub-clinical invasive breast cancers that would go in spontaneous regression if not detected at mammography**Per-Henrik Zahl<sup>1</sup> and Jan Mæhlen<sup>2</sup>

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**Objective:** The introduction of screening mammography is associated with a 50% long-term increase in the breast cancer incidence rates. The decline in the incidence rate after multiple screening rounds does only explain a tenth of the 50% incidence increase. We have recently published that this discrepancy only can be explained by spontaneous regression of many invasive breast cancers in the absence of screening mammography. In addition a large number of ductal carcinoma in-situ (DCIS) is detected at mammography. It is well known that many DCIS will go in spontaneous regression while other many progress to invasive cancer. DCIS detected at mammography are treated as early stage invasive breast cancer. Thus, because i) DCIS may progress to invasive breast cancer and ii) DCIS is treated as invasive breast cancer, one should study the regression rate of both simultaneously.

**Materials and methods:** We compared cumulative breast cancer incidence in age-matched cohorts of women residing in four Norwegian counties before and after the initiation of biennial mammography. The screened group included all women who were invited for all three rounds of screening during the period 1996-2001 (age 50 through 64 in 1996). The control group included all women who would have been invited for screening had there been a screening program during the period 1992-1997 (age 50 through 64 in 1992). All women in the control group were invited to undergo a prevalence screen at the end of their observation period. Counts of incident invasive breast cancers were obtained from the Norwegian Cancer Registry.

**Results:** As expected, before the age-matched controls were invited to screening the cumulative incidence of invasive breast cancer was significantly higher in the screened group (4-year cumulative incidence: 1479 vs. 850 per 100,000; RR = 1.74). After the prevalence screening in controls, the cumulative incidence of invasive breast cancer remained 27% higher in the screened group (6-year cumulative incidence: 2206 vs. 1739 per 100,000; RR = 1.27 (95% CI: 1.22–1.36). Because the cumulative incidence among controls never reached that of the screened group, many DCIS and breast cancers detected by repeated mammographic screening would not persist to be detectable by a single mammogram at the end of six years and must go in spontaneous regression.

Many invasive breast cancers are not detected at mammography screening (so-called interval cancers). In age group 50-69 in Norway, the rate of interval cancers is about 100 per 100,000. The rate of invasive breast cancers before screening started was about 200. Thus, about 50% of all predicted cancers are not detected at mammography screening. Furthermore, the incidence rate for those attending the screening program including DCIS is almost 400 per 100,000. The unaccounted incidence increase for those attending the screening program is 200 per 100,000.

**Conclusion:** About 2 of 3 cases diagnosed at mammography screening are unaccounted and must have gone in spontaneous regression in the absence of mammography screening.

## O39

**Predicting the risk of hospitalisations from a longitudinal perspective.  
The Northern Finland 1966 Birth Cohort**

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**Objective:** To take a new and detailed approach to factors possibly associated with hospitalisations as a process attached to the individual.

**Materials and methods:** Routine data on hospitalisations during the lifecourse linked to The Northern Finland 1966 Birth Cohort were analysed. The cohort consists of information obtained from 12,231 children and their mothers living in the provinces of Oulu and Lapland with expected delivery dates in the year 1966. The occurrence of hospital admissions is analysed considering time to event, type (all diagnoses taken into account) and number. Factors from the lifecourse potentially associated to such information were selected from a set of combined characteristics such as clinical and biological, demographic, socioeconomic, and behavioural, neurobehavioral and developmental. Multivariate statistical methods for the reduction of dimensionality were used in the variable selection process. Poisson regression was applied to study predictors for the number of hospitalisations per period of life. Binary and multinomial logistic regressions were applied to identify factors affecting repeated hospitalisations. Finally, survival analyses, in particular competing risks models, were used to study risk factors influencing the time to admission within specific group of diagnoses.

**Results:** Analyses of individual trajectories of admissions should consider information on sex and previous diagnoses since particular admission histories alter probability of subsequent events. The subject's susceptibility to experience more admissions than others at different periods of life seems to be influenced mainly by demographic and socioeconomic factors. Progression to health conditions requiring hospitalisation seems to be more affected by factors from the clinical and biological, and behavioural, neurobehavioural and developmental group of covariates. As for the repeated admissions due to the same diagnosis groups, social class and some demographic characteristics are the influential factors.

**Conclusion:** Our study provides evidence that early-life factors predict the risk of hospitalisations. The study consists of an analysis of a complex structure of multi-factorial associations between hospitalisations and their possible predictors. The data comes from a large prospective cohort and the time sequence of factors is very well defined. It provides epidemiological evidence at an individual level and very precise information on patterns of hospital admissions.

**O40****Transgenerational effects of prenatal exposure to the Dutch famine on neonatal adiposity and health in later life**

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**Objective:** Maternal undernutrition during gestation is associated with increased metabolic and cardiovascular disease in the offspring. We investigated whether these effects may persist in subsequent generations.

**Methods:** We interviewed 855 men and women born in the Wilhelmina Gasthuis in Amsterdam, the Netherlands, around the time of the 1944-1945 Dutch famine (F1), who were exposed or unexposed to famine in utero, about their offspring (F2).

**Results:** F1 famine exposure in utero did not affect F2 (n=1496) birth weight, but, among the offspring of F1 famine exposed women, F2 birth length was decreased (-0.6 cm, p adjusted for F2 gender and birth order = 0.01) and F2 ponderal index was increased (+1.2 kg/m<sup>3</sup>, p adjusted for F2 gender and birth order = 0.001). The association remained unaltered after adjusting for possible confounders. The offspring of F1 women who were exposed to famine in utero also 1.8 (95% confidence interval 1.1 to 2.7) times more frequently had poor health in later life (due to miscellaneous causes) than that of F1 unexposed women.

**Conclusion:** F1 famine exposure in utero was associated with increased F2 neonatal adiposity and poor health in later life. Our findings may imply that the increase in chronic disease after famine exposure in utero is not limited to the F1 generation, but persists in the F2 generation.

## O41

### Frailty as an index of deficit accumulation in the MRC Cognitive Function and Ageing Study

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**Background:** Frailty is characterised by a decline in physiological reserve leading to health problems, weakness, disability, and increased vulnerability to risk factors for disease. Frailty is strongly linked to ageing and frail individuals are at increased risk of death or institutionalisation, making frailty an important target for ageing research. A recently developed approach to measuring frailty is by an index of deficit accumulation known as the ‘frailty index’. This is defined as the proportion of age-related deficits seen in an individual, where deficits can include health conditions, risk factors for health, disabilities, or other biomarkers. Frailty indices have been calculated using several large longitudinal studies.

**Methods and results:** The MRC Cognitive Function and Ageing Study (MRC CFAS) is a longitudinal study of ageing representative of the older population of England and Wales, including 13000 participants aged 65 years and older at baseline and with multiple follow-up waves completed over ten years. We describe a frailty index calculated using data from MRC CFAS, including deficits in health as well as cognitive and physical function. We describe the distribution of frailty in sub-groups of the population, and show that the frailty index predicts long and short-term mortality at least as well as chronological age. We describe the longitudinal changes in frailty and explore the sensitivity of the frailty index to the selection of the deficits included.

**Conclusions:** Our results further illustrate the validity and potential applications of the frailty index. Frailty indices can be estimated using data from existing longitudinal studies and used as a comprehensive measure of health status and susceptibility to adverse events that can be compared across populations and settings.

## O42

**NeuroEPIC: Principles, study design, and an example of cigarette smoking associated with amyotrophic lateral sclerosis incidence**Valentina Gallo<sup>1</sup>, Paolo Vineis<sup>1</sup>, and Lefkos Middleton<sup>2</sup>

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**Objective:** The world's population is ageing at an increasing pace worldwide. In 2000, it was estimated that there were 4 million Europeans suffering from Alzheimer's disease (AD) and this figure has been projected to almost triple by the year 2050. About 40% of people over 85 years suffer from AD, and another 10% from Parkinson's disease (PD). Amyotrophic lateral sclerosis (ALS) is another devastating neurodegenerative disease whose incidence increases with age. There are currently no effective preventive measures, screening tests or disease modifying therapies for neurodegenerative diseases and available treatments are purely symptomatic. Research on risk factors and predictive markers have yielded mainly inconclusive or contradictory findings, and a clear picture of the unique and combined effects of exposure and genotype to neurodegeneration is yet to emerge. We aim at set up NeuroEPIC study within the European Prospective Investigation into Cancer and nutrition (EPIC) study. Cigarette smoking has been reported as a "probable" risk factor for ALS.

**Materials and methods:** All cases of AD, PD and ALS will be ascertained and we will investigate the role of environmental, behavioural, nutritional, metabolic and genetic risk factors and their interactions in susceptibility to neurodegeneration. Epidemiological analyses exploring the contribution of environmental risk factors in developing the diseases of interest will be carried out on the entire cohort whilst selected hypotheses relating to gene-environment interactions and biomarkers will be tested in case-control studies nested within the cohort. In the analysis of ALS, a total of 517,890 healthy subjects were included, resulting in 4,591,325 person-years. Cases were ascertained through death certificates. Cox hazard models were built to investigate the role of smoking on the risk of ALS, using packs/years and smoking duration to study dose-response.

**Results:** For PD and AD, existing disease registries will permit case-linkage for immediate investigation. In the other countries we will utilize case ascertainment methodologies that have already been validated as reliable and low-cost tools for the identification and validation of non-cancer diseases within EPIC. The following sources of information will be used for case ascertainment: 1) hospital discharge records; 2) outpatient clinical records; 3) drug registries; 4) other potential local sources of information such as telephone follow up. For ascertained cases, we will apply capture-recapture methods to determine positive and negative predictive value. Also, screening tests for detecting Mild Cognitive Impairment (MCI) will be validated in the relevant languages and calibrated on a series of well studied demented and non demented subjects to be used in a second phase of the project for the identification of MCI subjects within EPIC. This will allow studying the determinants of the progression from MCI to dementia.

A total of 118 subjects died from ALS, resulting in a mortality rate of 2.69 per 100,000/year. Current smokers at recruitment had a two-fold increased risk of dying from ALS compared to never smokers (HR=2.01 95% C.I. 1.20-3.36), while former smokers had a 60% increased risk (HR=1.63, 95% C.I. 1.03-2.57). The number of years spent smoking increased the risk of ALS (p for trend<0.001). Those who smoked more than 33 years had almost a two-and-half-fold increased risk of ALS compared with never smokers (HR=2.47, 95% C.I. 1.50-4.07). Conversely, the number of years since quitting smoking was associated with a decreased risk of ALS compared with continuing smoking.

**Conclusion:** These results on smoking in ALS strongly support the hypothesis of a role of cigarette smoking in the aetiology of ALS. We hypothesize that this could occur through lipid peroxidation via formaldehyde exposure.



## O43

### Light drinking in pregnancy, a risk for behavioural problems and cognitive deficits at 3 years of age?

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**Background:** The link between heavy drinking during pregnancy and consequent fetal alcohol syndrome is well established. However, it remains unclear whether consuming relatively low levels of alcohol during pregnancy is related to subsequent developmental problems in children.

**Objective:** To determine whether there was an association between mothers' light drinking during pregnancy and risk of behavioural problems, and cognitive deficits in their children at age 3 years.

**Methods:** Data from the first two sweeps of the nationally representative prospective UK Millennium Cohort study were used. Drinking patterns during pregnancy and behavioural and cognitive outcomes were assessed during interviews and home visits. Behaviour was assessed using the Strengths and Difficulties Questionnaire, and cognitive ability by the British Ability Scale (BAS) and the Bracken School Readiness Assessment (BSRA).

**Results:** Children born to light drinkers were less likely to have behavioural difficulties compared to children of abstinent mothers. Boys born to light drinkers were less likely to have conduct problems (OR 0.59) and hyperactivity (OR 0.71) compared with those born to abstainers. These effects remained in fully adjusted models. Girls were less likely to have emotional symptoms (OR 0.72) and peer problems (OR 0.68) compared with those born to abstainers. These effects were attenuated in fully adjusted models. Boys born to light drinkers had higher cognitive ability test scores (standard deviates) BAS (0.15) BSRA (0.24) compared to boys born to abstainers. These effects remained significant in fully adjusted models.

**Conclusions:** Children born to mothers who drank up to 1-2 drinks per week or per occasion during pregnancy were not at increased risk of clinically relevant behavioural difficulties or cognitive deficits compared with children of abstinent mothers.

## O44

**Who continues to smoke in pregnancy? Great-grandparental and grandparental influences on women's smoking in pregnancy**Ilona Koupil<sup>1</sup> and Bianca De Stavola<sup>2</sup>

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**Background:** Smoking in pregnancy increases the risk of growth retardation and preterm birth, and is also associated with later health problems (sudden infant death, childhood obesity, asthma) in the offspring.

**Methods:** Associations of social characteristics with smoking in early (at enrolment for antenatal care) and late (week 30-32) pregnancy were studied in multivariable logistic regression, adjusted for year of birth, in 8924 Swedish women born 1940-1980, who gave birth to 15,510 third generation descendants of the Uppsala Birth Cohort (UBCoS) in 1982-2002. Archive- and register-based data on grandparental and parental social characteristics were obtained by linkages through personal identification numbers, information on smoking from Medical Birth Register.

**Results:** There were 1942 (22%) mothers who reported smoking in early pregnancy. In addition to expected strong effects of mother's and father's education on prevalence of smoking in early pregnancy (OR 6.8, 95% CI 5.7-8.1 for mother's elementary; 2.7, 95% CI 2.4-3.1 for secondary vs post-secondary education) we noted persisting influences of grandparental and great-grandparental social class and education. The intergenerational influences were only partly mediated by parental education. Women were more likely to smoke in families where grandmothers (paternal or maternal) had lower education (OR 1.9, 95% CI 1.2-2.9 for maternal grandmother's elementary vs higher education, adjusted for mother's and father's education) and in families where father's social background was manual. Of women who smoked in early pregnancy, 74% continued to smoke into late pregnancy. Mother's own education was the main predictor of failing to quit smoking during pregnancy (OR 8.7, 95% CI 3.1-23.8 for elementary, 2.7, 95% CI 1.2-6.2 for secondary vs post-secondary education).

**Conclusions:** Direct grandparental influences on mother's behaviour in pregnancy may produce cross-generational social effects on health and contribute to the persisting social inequalities in health through harmful effects of maternal smoking on health of subsequent generations.

**O45****Reliability and validity of the International Physical Activity Questionnaire in the Nord-Trøndelag Health Study (HUNT) population of men**Nanna Kurtze<sup>1</sup>, Vegar Rangul<sup>2</sup> and Bo-Egil Hustevedt<sup>3</sup>

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**Objectives:** There is no standardized method for the assessment of physical activity (PA). Therefore it is important to investigate the validity and comparability of different measures. The International Physical Activity Questionnaire (IPAQ) has been developed as an instrument for cross-national assessment of PA and has been validated in 12 countries. These instruments have acceptable measurement properties for monitoring population levels of PA among 18-65 year-old adults in diverse settings. However, there are some concerns that IPAQ may over-report PA. The purpose of this study is to evaluate the reliability and validity of IPAQ, short version, last 7-days in the Nord-Trøndelag Health Study (HUNT) population of men.

**Methods:** The questionnaire was administered twice to a random sample of 108 men aged 20-39 and validity by comparing results with  $VO_{2max}$  and ActiReg, an instrument that measures PA and energy expenditure (EE). ActiReg discriminates between the body positions: stand, sit, bend forward and lie and also registers if there is motion or not in each of them or both.

**Results:** Our results for reliability of the IPAQ short version were good for vigorous and fair for moderate activities. Intraclass correlations ranged from a low of 0.30 for moderate activity hours, to a high of 0.80 for sitting hours. Concerning validity, our results suggest that total IPAQ vigorous PA was a moderately good measure of vigorous activity, having moderately strong, significant correlations with  $VO_{2max}$ ,  $r = 0.41$  ( $p \leq 0.01$ ), but correlated not with metabolic equivalent (METs) values of 6 or more measured with ActiReg. Only total IPAQ walking was fair correlated with METs 1-3 and METs 3-6, respectively  $r = -0.27$  and  $0.26$  ( $p \leq 0.05$ ). The index for IPAQ sitting hours per week was moderate correlated with METs values of 1-3 and negatively correlated with METs values of 3-6. Classification of PA in three levels (low, moderate and high) correlated also most strongly with  $VO_{2max}$  ( $0.31$   $p \leq 0.01$ ) and METs 3-6 and METs 1-3 from ActiReg ( $r = 0.32$  and  $-0.31$ ,  $p \leq 0.01$ ). Classification of BMI in three levels (normal, overweight and obese) correlated most strongly negative with  $VO_{2max}$  ( $-0.42$   $p \leq 0.01$ ) and MJ from ActiReg ( $r = 0.31$   $p \leq 0.01$ ).

**Conclusions:** Our results indicate that IPAQ short version for men has acceptable reliability and criterion validity for vigorous activity and sitting. Walking has moderate reliability. Only the IPAQ for walking had a fair correlation with METs 6+. The questions about moderate activity had fair reproducibility and correlated poorly with most comparison measures.

## O46

**The association between maternal exercise and excessive birth weight of the infant – The Norwegian Mother and Child Cohort Study**Katrine M. Owe<sup>1</sup>, Wenche Nystad<sup>2</sup> and Kari Bø<sup>1</sup>

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**Objective:** When birth weight exceed 4500 g, both mother and infant are at greater risk for morbidity compared to mother and infants whose birth weight is within the normal range. Although recreational exercise has been considered an important determinant of birth weight, the literature on the relationship between maternal recreational exercise and the upper extreme of the birth weight distribution is sparse.

**Material and methods:** Using data from the Norwegian Mother and Child Cohort study (MoBa), 36869 singleton pregnancies enrolled between 2001 and 2005 were included. Pregnancies ending before week 37 were omitted from the analysis. Recreational exercise level was defined in terms of frequency. Outcome variable was delivery of a high birth weight infant (>4500g). We used logistic regression analysis to estimate the associations, and the results are presented as adjusted odds ratios (aOR) with 95% confidence intervals (95% CI). The following covariates were included: maternal age, BMI prepregnancy, maternal height, smoking, weight change, hypertension, energy intake, preeclampsia, diabetes/ gestational diabetes.

**Results:** The proportion of infants with a birth weight above 4500g was 5% (n=1854). A low level of recreational exercise (i.e. 1-3 timer per month) in pregnancy week 17 was negatively associated with giving birth to high birth weight infants in nulliparous women only, aOR=0.67 (95% CI 0.49-0.92). The greatest protective effect was observed in nulliparous women exercising at least 3 times a week in week 17, aOR=0.53 (95% CI 0.39-0.72). In week 30, nulliparous women exercising 1-2 t a week were less likely to deliver high birth weight infants compared to non-exercisers, aOR=0.75 (95% CI 0.58-0.96). The odds of giving birth to a high birth weight infant were further decreased with an increased exercise frequency in week 30, aOR=0.61 (95% CI 0.46-0.81). Recreational exercise performed 3 months prepregnancy did neither affect the probability of delivering high birth weight infants in nulliparous nor in multiparous women.

**Conclusion:** A protective effect of exercise frequency in pregnancy weeks 17 and 30 was observed in nulliparous women, only. Recreational exercises performed in late pregnancy did not have a different impact on excessive birth weight compared to pregnancy week 17 in nulliparous women. The probability of delivering high birth weight infants was not affected by exercise performed prepregnancy neither in nulliparous nor in multiparous women.

**O47****Anthropometric outcomes at age 7 years of slow weight gain in infancy**Zia-ud Din<sup>1</sup>, Pauline Emmett<sup>2</sup>, Colin Steer<sup>2</sup> and Alan Emond<sup>2</sup>

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**Objective:** To assess growth outcomes at age 7 in children showing slow weight gain in early and mid infancy.

**Material and methods:** The Avon Longitudinal Study of Parents and Children (ALSPAC) enrolled pregnant women in 1991-92, resulting in a total cohort of 14,062 live births: 11,499 of these had information about weight up to 9 months from routine community-based growth assessments. UK 1991 growth references were used to calculate standard deviation scores. Slow weight gain infants were those in the slowest growing 5% in two time periods; early infancy – birth to 8 weeks (slow; group I, normal; group II); mid infancy – 8 weeks to 9 months (slow; group III, normal; group IV). At age 7 years, 6769 (59%) of the children were measured in a research clinic. SDS were calculated for weight, height and body mass index (BMI) using UK reference data, and for mid arm circumference (MAC) and waist circumference (WC) using internal means (LMS method). Growth outcomes at age 7 in the four groups were compared using appropriate statistical tests.

**Results:** 507 & 480 infants showed slow weight gain in early and mid infancy respectively. At age 7 years, group I children were slightly shorter and lighter than the reference, however their BMI was close to the reference. Group II children were heavier and taller and with a higher BMI than the reference. Group-I were 1.53 Kg lighter and 1.99 cm shorter than group-II children. Group I children had lower mean MAC & WC than Group II children (0.44 cm & 1.18 cm lower respectively). Similarly, Group-III children were much shorter and lighter than the reference and in comparison to group-IV children (3.99 Kg lighter & 3.97 cm shorter than group-IV children); furthermore their BMI was well below the reference and much lower than that of group-IV children (1.37 kg/m<sup>2</sup> lower). Group-III children had a much lower mean MAC & WC than group-IV (1.51 cm & 3.79 cm respectively, lower than group-IV infants).

**Conclusion:** Slow weight gain in both early and mid infancy had an important impact on anthropometric outcomes at age 7. Slow infant weight gain was associated with being shorter and slimmer than normal at age 7 particularly if the slow weight gain occurred in mid infancy.

**O48****Mother's smoking in pregnancy modifies the effects of preterm birth and concurrent body mass index on blood pressure and hypertension in adolescents**

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**Objectives:** To investigate a modifying effect of maternal smoking on associations of size at birth and length of pregnancy with blood pressure in 18-year old men.

**Methods:** We studied associations of length of pregnancy, weight for gestational age (foetal growth rate), and body mass index at age 18 with systolic blood pressure, diastolic blood pressure, heart rate and prevalence of hypertension at age 18 in a register-based cohort of 744 men born 1982-1985. Analyses are stratified by maternal smoking in pregnancy and results are adjusted for age at measurement, place of residence and maternal education.

**Results:** Among sons of smoking mothers, standardised birth weight was negatively associated with systolic blood pressure at age 18, both before and after adjustment for concurrent BMI. Such an association was not present among sons of mothers who did not smoke in pregnancy (p-value interaction 0.037). On the other hand, preterm birth increased the risk of hypertension among sons of non-smoking mothers (p-value interaction 0.027), both before and after adjustment for concurrent BMI. Among sons of non-smoking mothers, standardised birth weight was positively associated with body mass index at age 18, and body mass index was the strongest predictor of high systolic blood pressure (p-value interaction 0.036), pulse rate and hypertension.

**Conclusions:** Mother's smoking in pregnancy is a strong modifier of the associations between foetal growth indicators and later overweight and hypertension. While slow foetal growth appears to increase the risk of hypertension among sons of smoking mothers, preterm birth leads to higher risk of hypertension among those born to non-smoking mothers. Continuity in growth and the effect of body mass index on systolic blood pressure and hypertension is most pronounced in the absence of maternal smoking exposure.

## O49

### Time is on whose side? Time trends in the association between maternal social disadvantage and offspring fetal growth. A study of 1,409,339 births in Denmark 1981-2004

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**Objective:** Fetal growth is highly socially patterned and is related to health across the life course, but how the social patterns of fetal growth change over time remains understudied. We examined the time trends in maternal social disadvantage in relation to fetal growth in the context of a universal welfare state under changing macroeconomic conditions over a 24-year period.

**Materials and methods:** We included all births in Denmark 1981-2004. The main outcome measure was the association between maternal social disadvantage in relation to birth weight for gestational age z-scores over time were analysed using linear regression.

**Results:** All measures of social disadvantage were associated with decreased fetal growth ( $p < 0.001$ ), but with considerable differences in the magnitude of the associations. The association was strongest for non-western ethnicity (-0.28 z-score), low education (-0.19), teenage motherhood (-0.14), single motherhood (-0.13), poverty (-0.12) and weakest unemployment (-0.04). The deficit in fetal growth increased over time for all associations except for unemployment. Also, the measures of social adversity increasingly clustered within individuals over time.

**Conclusion:** Maternal social disadvantage is associated with decreased fetal growth in a welfare state. Social disadvantage is increasingly clustered so that fewer pregnancies are exposed, but those exposed suffer a greater disadvantage in fetal growth. The economic upturn in the last decade did not appear to weaken the association between maternal social disadvantage and decreased fetal growth.

## O50

## Longitudinal changes in weight and fat mass through pregnancy: findings from the Southampton Women's Survey

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**Objective:** Optimal patterns of weight gain in pregnancy are not known. The prevalence of obesity is increasing amongst women of childbearing age, and retention of gestational weight gain is widely recognised. However, there are few longitudinal cohorts with pre-pregnant information, and pre-pregnancy data is usually restricted to recalled measures. The Southampton Women's Survey (SWS) provides a unique opportunity to quantify changes in anthropometry through pregnancy in a large group of contemporary women using measures taken prospectively before the woman became pregnant, as well as during and after pregnancy.

**Material and methods:** The SWS has measured the diet, body composition, physical activity and social circumstances of 12,583 non-pregnant women aged 20 to 34 years living in the city of Southampton, UK<sup>1</sup>. The women who subsequently became pregnant visited the SWS Ultrasound Unit at 11, 19 and 34 weeks' gestation. The women were again interviewed when their child was 6 months old. Anthropometric measurements are available before pregnancy, in early pregnancy (11 weeks), late pregnancy (34 weeks) and at 6-months postpartum from 1987 women who delivered by the end of 2003. A variety of measures were taken including weight and triceps, biceps, subscapular and upper-suprailiac skinfold thicknesses. Using these measures fat mass at each time point was calculated<sup>2</sup>. Pre-pregnancy data were adjusted for age between measurement and conception using linear regression. Change in anthropometric measures was assessed using multi-level models.

**Results:** The median (IQR) weight of women before pregnancy was 65.4 (58.7–74.5) kg. Their median (IQR) fat mass was 20.5 (16.3–26.6) kg. The mean (SD) gains from before to early pregnancy, before to late pregnancy, and before pregnancy to 6 months postpartum are described in the table below.

	Before to early pregnancy	Before to late pregnancy	Before to 6 months postpartum
Weight (kg)	1.4 (4.4)	12.0 (6.2)	2.9 (5.8)
Fat mass (kg)	0.5 (3.5)	5.7 (4.8)	1.2 (4.3)

There were significant gains in weight and fat mass at all three time points compared to before pregnancy (all  $P < 0.001$ ). The gains in weight and fat mass were highest in late pregnancy, as would be expected, although 2.5% of women were lighter in late pregnancy than before pregnancy. 53.8% of women were at least 2kg heavier 6 months after pregnancy than before pregnancy.

**Conclusion:** At 6 months postpartum women tend to retain weight and adipose tissue gained in pregnancy, although there is substantial variability between women. These data will be used to relate patterns of pregnancy weight gain to pregnancy outcomes. We also intend to use information about change in weight along with other sociodemographic information in the SWS to determine which women are at most risk of excessive gestational weight gain; this evidence may motivate future interventions in or around pregnancy, a time when women are vulnerable to weight gain.

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2. Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *Br J Nutr* 1974; **32**: 77-97.



## O51

### Maternal cortisol and birth weight at term

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**Objective:** Prenatal stress may lead to fetal hypothalamic pituitary adrenal (HPA) axis reprogramming through elevated maternal cortisol levels, which in turn may affect fetal growth. This study examined the relation between maternal cortisol and birth weight at term.

**Material and methods:** Data were collected as part of the Amsterdam Born Children and their Development (ABCD) study, a longitudinal population-based cohort study. 8266 pregnant women completed a questionnaire during early pregnancy and 4389 of these women provided an extra blood sample during their first prenatal visit (on average 12<sup>th</sup> week of pregnancy). For this study, we only included native Dutch women who delivered a singleton at term ( $\geq 37.0$  weeks of gestation) and who provided a blood sample. As the diurnal variation in cortisol is high, only those women who gave blood before 10 a.m. were selected. The final sample available for analysis was 288. Linear regression analysis was performed with as outcome measure continuous birth weight (grams) at term.

**Results:** Maternal cortisol, standardized for the time of day and the pregnancy duration at blood collection, ranged from 53.77 – 291.25 microgram/L and was trichotomized around the 50<sup>th</sup> and 90<sup>th</sup> percentile into low (reference group), moderate and high cortisol level. Neonates of women with a moderate or high cortisol level had on average a lower birth weight compared to neonates of women with a low cortisol level. After adjustment for covariates (maternal age, pre-pregnancy maternal height and BMI, education, smoking, parity, gestational age at birth, and fetal gender) maternal cortisol was significantly inversely related to birth weight (regression coefficient [SE]: moderate vs. low: -123.3 [50.1],  $p=.014$ ; high vs. low: -173.0 [80.6],  $p=.033$ ).

**Conclusion:** Compared to neonates of women with low cortisol levels during pregnancy, neonates of women with moderate or high cortisol levels had significantly lower birth weights.

**O52****Hospital readmission in very premature infants: an Italian area based follow-up study**

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**Objective:** An excess of morbidity and increased use of inpatient services, has been reported in very premature infants. To date no Italian data derived from geographically defined cohort are available on hospital readmission of these high risk infants. The aim is to describe re-hospitalization of very preterm infants in the first two years of life after discharge from Neonatal Intensive Care Units (NICUs) in two Italian regions.

**Methods:** The population study included all live births with gestational age 22-31 weeks discharged from Neonatal Intensive Care Units in Lazio and Tuscany Region during 2004. Perinatal clinical data were collected as part of an Italian research project on Very Preterm Pregnancies and Births (ACTION). We used the Regional Hospital Discharge Database to find hospital admissions in the first 2 yrs of life after discharge, using tax code for record linkage with the cohort file. Data were analyzed through descriptive statistics. To estimate the risk for first hospital readmission, adjusting for relevant potential confounders, Hazard Ratio (HR) obtained from Cox proportional hazards model was used.

**Results:** The cohort included 541 infants; among these, 204 (37.7%) were re-hospitalized; overall, 376 readmission were observed with a mean total length of stay of 5.9 days. The two most common reasons for re-hospitalization were respiratory (36.4%) and gastrointestinal (12.8%) disorders. Severe prematurity ( $\leq 27$  wks) (HR 1.58; 95% CIs 1.08-2.31), male sex (HR 1.45; 95% CIs 1.09-1.92) and being discharged from NICUs during the fall period (HR 1.56; 95% CIs 1.06-2.3) predicted re-hospitalization in the multivariate model.

**Conclusions:** Almost one out three very preterm infants was re-hospitalized in the first two years of life. Hospital re-admissions for a very preterm birth could be a sensitive indicator of level of morbidity and quality of follow-up programs in high risk newborns.

## O53

### Outcomes of teacher-rated externalizing behaviour in adolescence: forty year follow-up of a national cohort

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**Objective:** Behavioural and externalizing disorders are very common among adolescents, and cause significant impairment. The objective of this study was to define long-term outcomes associated with symptoms of externalizing behaviour in adolescence in a population-based sample.

**Methods:** Assessments of externalizing symptoms at ages 13 and 15 years were made by teachers on 3,652 members of the Medical Research Council National Survey of Health and Development (the 1946 British birth cohort). Adolescents were assessed by teachers on a scale that included seven externalizing symptoms and those with externalizing behaviour compared to mentally healthy adolescents across numerous outcomes in adulthood, including mental health, family life, social class, unemployment and financial difficulties, and education (at ages 36-53).

**Results:** All negative outcomes measured in adulthood were more common for those with severe or mild externalizing behaviour in adolescence compared to those with no externalizing behaviour. Adolescents with severe externalizing behaviour were more likely to leave school without completing any qualifications (65.2%; adjusted OR=4.0; 95%CI: 2.9 to 5.5), as were those with mild externalizing behaviour (52.2%; adjusted OR=2.3; 95%CI: 1.9 to 2.8), compared to those with no externalizing behaviour (30.8%). On a composite measure of global adversity throughout adulthood that included mental health, family life and relationships, and educational and economic problems, those with severe externalizing behaviour scored significantly higher (40.1% in top quartile), as did those with mild externalizing behaviour (28.3%), compared to those with no externalizing behaviour (17.0%).

**Conclusions:** The results of this prospective, population-based study suggest that adolescents who exhibit externalizing behaviour suffer from multiple social and health impairments that adversely affect them, their families and society throughout adult life. Prevention and treatment of adolescent conduct disorders should be a priority.

**P01****Assessment of the quality of life and its influencing factors in infertile women attending to the Vali-e-Asr Reproductive Health Research Center, Tehran 2006-2007**

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**Background:** Fertility is highly valued in most cultures, and the desire to have a child is one of the most basic of all human motivations. Studies have shown that infertility has negative effects on person's quality of life.

**Objective:** To investigate quality of life and influencing factors in infertile women.

**Design:** With the use of a correlation study, through 3 types of questionnaires, demographic factors, quality of life and irrational parenthood cognitions of the participants were assessed.

**Sample:** Through continuous sampling method 143 infertile women without known physical or psychological disorders filled out questionnaires.

**Results:** Regarding the findings, the quality of life of 48.3% , 36.1% and 15.6% were good, fair and poor respectively. Also, statistically meaningful relations were found between quality of life and history of infertility treatment ( $p=0.011$ ), strength of desire to have child ( $p=0.000$ ), previous. Pregnancy outcome (0.04), and irrational parenthood cognitions ( $p=0.000$ ).

**Conclusions:** As multiple regression analysis showed that the quality of life of infertile women is affected by the irrational parenthood cognitions mostly, identifying this group would result to a better management for allocation of appropriate counseling. We suggest infertile women quality of life to be compared with fertile women.

## P03

### Child abuse and fear of pregnancy in the Mother and Child Cohort Study

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**Background and aim:** Fear of pregnancy can be defined as worries about childbirth and anxiety for the health of the child. Bodily, psychological and social factors may influence the fear. Child abuse might be an element of risk. The quality of reports of pregnant women with a history of physical and sexual child abuse varies, they are few and small. The aim of our study is to look for associations in pregnant women between a history of sexual abuse and / or physical abuse before the age of 18 and fear of giving birth and/or anxiety for the health of the baby.

**Material and method:** This is a sub study in the Norwegian Mother and Child Cohort Study (MoBa). Two self administrated questionnaires answered around the 17<sup>th</sup> and 30<sup>th</sup> week include key data and are merged with data from the Medical Birth Registry of Norway. The main study is ongoing and prospective. Our study is partly retrospective and includes approximately 58 000 pregnant women in the period of 1999-2006. The participation rate is 42.7. Multiple logistic regressions are used.

**Results:** The prevalence of fear of childbirth is 19.3%. 11.3% is anxious for the health of the baby. 2.1% reports physical abuse, 3.2% tells about sexual abuse and 2.2% reports both physical and sexual abuse before the age of 18. Physical, sexual and child abuse in combinations are associated with fear of giving birth and anxiety for the health of the baby. A combination shows the strongest associations. The same results exist for multi parous women who are anxious of the health of the baby. If we add earlier negative birth experiences, there is no association between physical, sexual and both types of child abuse and fear of giving birth. Marital status, adult abuse, pelvic pain, quality of antenatal care and self-efficacy are all associated with fear of giving birth and anxiety for the health of the baby.

**Conclusions:** Our study shows associations between physical, sexual and child abuse in combination and fear of giving birth and anxiety for the health of the baby even if the associations are not strong. Earlier negative birth experiences act stronger in multi pregnant women who fear childbirth. However, results from this huge, Norwegian, selected cohort study shows that fear in pregnancy is complex and associated with many elements of risk. There are few corresponding studies.

**P04****Comparing infant feeding practices among Ugandan infants with a prospective and retrospective study design: weekly one-week infant feeding recalls versus since-birth recalls at 12 weeks of age**

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**Objective:** Exclusive breastfeeding for the first six months of infancy is recommended by WHO as the safest infant feeding alternative. Exclusive breastfeeding is defined as not receiving any other feeds than breast milk and prescribed medicines. In low-resource settings with infant mortality rates more than 4% and/or in settings where formula feeding is not acceptable, feasible, affordable sustainable and safe it is also recommended that mothers with an HIV-positive status breastfeed their infants exclusively for the first six months. Existing WHO recommendations promote frequent interviews of mother-infant pairs in infant feeding promotion or infant feeding and HIV-related studies with one-week recalls: the gold-standard being weekly one-week recalls during the first 3-6 months of infancy. This set-up is often unrealistic in resource-deprived settings, and qualitative studies report it as too time demanding for the participants. We undertook a study among 30 mothers in Eastern Uganda where we compared 12 weekly one-week infant feeding recalls to a less demanding since-birth recall at 12 weeks of age.

**Material and methods:** 30 children from Mbale Municipality in Eastern Uganda were recruited within their first week after birth and followed up weekly for 12 weeks in 2005. A 1-week interview consisting of 24-hour food recall and a proceeding 6-days food recall was performed for 22 locally appropriate food- and liquid items. The prospective information retrieved with the weekly one-week recalls were compared to one retrospective since-birth recall at 12 weeks of age including the same 22 items where the question "when did you receive this for the first time" was added. With these two models we compared first time of introduction of "water-based-feeds, Oral Rehydration Solution and fruit-juices" which re-categorised a breastfed infant from exclusively breastfed to predominantly breastfed. Similarly, we compared the first time for introduction of "milk-based feeds and semi-solid feeds" which re-categorised an exclusively or predominantly breastfed child into a complementary fed child. Kaplan-Meier analysis was used for the prospective and the retrospective approach with SPSS 15.

**Results:** Comparisons between the prospective and retrospective recalls at 12 weeks showed that the mean time for initiation of predominant breastfeeding was 0.5 (0-1.0) weeks in the prospective recalls and 1.6 (0.7-2.6) weeks in the retrospective recalls. The mean time for introducing predominant feeding was 5.2 (3.9-6.6) weeks in the prospective recalls and 6.6 (5.4-7.8) weeks in the retrospective recalls.

**Conclusion:** We conclude that the less costly and less time-consuming infant feeding recalls could be used in resource-poor settings for studies and program evaluation purposes of promotion of exclusive breastfeeding for the first 6 months of infancy. We do not consider the differences found between the two study models of clinical significance. We acknowledge the fact that further studies are needed in order to conclude on cheap and reliable monitoring of safer infant feeding practices with the potential to reduce infant and neonatal mortality globally.

**P05****Associations between maternal pre-pregnancy BMI, exercise during pregnancy and birth weight**

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**Objective:** The results of previous studies investigating the association between maternal exercise during pregnancy and birth weight are inconsistent. In addition, many of these studies have not taken maternal body mass index (BMI) into consideration, despite well-known associations between maternal BMI and birth weight, and between BMI and exercise. We assume that pre-pregnancy BMI determine both the degree of recreational physical activity during pregnancy and has a direct effect on fetal growth. The aim of this study is thus to estimate the direct effects of exercise during pregnancy on birth weight; the direct effect of maternal pre-pregnancy BMI on birth weight; and the indirect effect of maternal BMI on birth weight through exercise during pregnancy.

**Materials and methods:** This study included pregnant women recruited from 1999-2006 in the Norwegian Mother and Child Cohort Study (MoBa) and their offspring. The statistical analyses were based on two self-administered questionnaires during pregnancy, in gestational week 17 and 30, respectively, which were linked to the Medical Birth Registry of Norway (MBRN) with information on birth weight. The effects of maternal BMI and exercise on birth weight were estimated by linear regression models.

**Results:** 43 705 pregnancies were included. The mean pre-pregnancy BMI of the mothers was 24 kg/m<sup>2</sup>, the median exercise frequency in gestational week 17 was 6 times per month, and 4 times per month in week 30. The mean birth weight was 3 677 g. The unadjusted effect of the combined exercise frequency in week 17 and 30 was a 3.9 g decrease in birth weight per unit increase in exercise (1 time/month). Exercise in week 30 tended to have a larger effect than in week 17. The combined effect of exercise after adjustment for other confounders than BMI was a 2.9 g decrease in birth weight per unit increase in exercise frequency. Including BMI in the model as a confounder reduced the effect of exercise to 2.1 g decrease in birth weight per unit increase in exercise. In contrast, the adjusted direct effect of one unit increase in BMI (1 kg/m<sup>2</sup>) was 20.3 g (19.2 to 21.4;  $p < 0.001$ ) increase in birth weight, and the indirect effect through exercise was 0.3 g increase.

**Conclusion:** Our population-based study showed that there is a weak direct association between exercise during pregnancy and birth weight. Taking pre pregnancy BMI into consideration reduced the effect of exercise, whereas pre pregnancy BMI has a strong effect on birth weight.

## P06

### The Tromsø Staph and Skin Study (TSSS)

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**Objective:** *Staphylococcus aureus* is a major cause of bacterial infections, in particular wound infections, but also life-threatening infections. During the last 30 years there has been a rise in the incidence of *S. aureus* infections both in hospitals and in the community. Worldwide, the increasing resistance of this pathogen to various antibiotics complicates treatment of *S. aureus* infections. Importantly, most infections are endogenous, caused by *S. aureus* colonising the patient's nose. Also, *S. aureus* may trigger inflammatory skin disease (i.e. atopic dermatitis and psoriasis), and the majority of patients are colonised with *S. aureus* both in their nose and in the skin lesion. There is an urgent need for effective measures to reduce the *S. aureus* related disease burden and death in the population. On this background, we have established the Tromsø Staph and Skin Study (TSSS), a large population-based cohort and an interdisciplinary research network, for the study of *S. aureus* epidemiology and determinants for persistence and spread of the bacterium in the population. The overall aim of our research is to obtain a better understanding of *S. aureus*' natural population structure and explore host, microbe and environmental factors that may promote *S. aureus* colonisation, subsequent invasion and infection, as well as inflammatory skin disease. Our study will provide novel epidemiological data on *S. aureus* and methicillin-resistant *S. aureus* (MRSA) in Norway. Here we will describe the research methods and design of TSSS.

**Material and methods:** TSSS is part of The Tromsø Study VI. During 2007-2008, entire birth cohorts and random samples in the municipality of Tromsø, a total of 17,455 men and women aged 30-87 years, are invited to a health screening survey. About 12,000 people are expected to participate. We have completed the collection of repeated nasal and throat swab samples (2-6 weeks interval) for the assessment of *S. aureus* colonisation among all attendees aged 30-49 years and random samples of attendees aged 50-87 years during October 2007 till August 2008. All samples have been cultured for the detection of *S. aureus* and MRSA. All *S. aureus* and phenotypic MRSA isolates have been frozen at minus 70°C for further molecular analysis. We have sampled detailed questionnaire data on the presence and severity of skin disease, personal hygiene, and use of antibiotics for our study. The health screening also included a standard clinical examination, blood samples for serum analyses and biobank storage (DNA extraction), and comprehensive questionnaires on health, lifestyle and chronic disease.

**The TSSS Cohort:** A total of 4,307 participants have been tested for *S. aureus* colonisation. We have registered 2,984 individuals with repeated nasal and throat cultures and 1,323 individuals with nasal and throat cultures at one time point only. Among those with repeated cultures, 24% are persistent nasal carriers of *S. aureus* (two positive samples), 9% are intermittent nasal carriers (one positive sample), and 67% are non-carriers (no positive samples). The 11-digit personal identification number makes it possible to link TSSS participants to national health registries (i.e. the Norwegian Cause of Death Register, the National Nosocomial Infections Surveillance NOIS, the Norwegian Prescription Database) and electronic patient records, in prospective studies of risk of *S. aureus* infections and death. Cross-sectional and longitudinal research projects are established along several axes. We work on microbial factors (i.e. successful bacterial clones, determinants for survival on human mucosa), host factors (i.e. inflammatory skin disease, metabolic profile, tonsillectomy, innate immunity, mucosal interaction partners of *S. aureus*) and environmental factors (i.e. ultraviolet-radiation, use of antimicrobials, personal hygiene). Knowledge will be joined to explain the host-microbe-environment triad in *S. aureus* colonisation, infection/disease and death.



## P07

### Coronary care among middle-age inhabitants with acute myocardial infarction in Kaunas in 1996 and 2003-2004

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**The aim** of the present study was to evaluate the peculiarities of the coronary care provided for patients aged 25-64 years with acute myocardial infarction (AMI) depending on sex in Kaunas in 1996 and 2003-2004.

**Material and methods:** Kaunas community-based ischemic heart disease (IHD) register was the source of data. The methods used for the data collection were those applied by the WHO MONICA Project. A special standardized questionnaire designed for a coronary care investigation was used in the present study. All permanent residents of Kaunas City affected by AMI and hospitalized to Kaunas city hospitals from 1<sup>st</sup> January 1996 to 31<sup>st</sup> December 1996 and from 1<sup>st</sup> January 2003 to 31<sup>st</sup> December 2004, were the object of the study.

**Results:** The analysis of coronary care data provided in 1996 and 2003-2004 determined that men with appealed for the first medical aid significantly more rarely in 2003-2004 (respectively, 59.4% and 50.1%,  $p < 0.05$ ). The increasing trend to appeal to the general practitioners for the aid is being observed among men and women (respectively, 24.4% and 29.8% among men and 25.8% and 32.4% among women,  $p > 0.05$ ). Women delayed to consult physicians during the first 4-24 hours in 2003-2004 (respectively, 56.5% and 37.9%,  $p < 0.05$ ). It has been determined that the number of interventional angiographies performed for women has increased more than ten fold during the past decade (respectively, 4.8% and 35.6%,  $p < 0.05$ ), meanwhile it has increased 3.1 fold for men (respectively, 19.8% and 62.3%,  $p < 0.05$ ).

**Conclusion:** Coronary care management during the last decade has changed significantly: patients appealed for medical aid within shorter period of time, more of them approached directly to hospitals by themselves, the number of performed coronary intervention procedures, such as interventional angiographies and percutaneous transluminal coronary angioplasty increased.

## P08

### Identification of life threatening factors associated with pregnancies

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**Objectives:** To see that pregnancies and mother's health are affected by biological, social, cultural, individual behavior, poor life style and provision of health care system. To assess that miscarriage and abortion is highly prevalent among rural area, with imbalance diet, not taking exercise, over weight, obesity and other factors.

**Study design:** Case-control study design was used.

**Sample size:** A total number of 155 including 92 cases and 63 controls were taken.

**Target population:** All cases were collected from pregnant ladies where as the controls were taken from non-pregnant married women/mothers.

**Place of study:** The sample was taken from different hospitals and cases were taken from the community (district Lahore).

**Results:** the over all mean age was  $32.98 \pm 0.532$  years. Weight and height were significantly positively associated (p-value 0.002). There were 134 (86.5%) urban and 21 (31.5%) rural women participated in this research. Among all, 99 (63.9%) women were satisfied from their environment weather rest of the individuals showed their disappointments. The more working hours were led to less resting hours ( $r = -0.303$ , p-value 0.000). 98 (63.2%) subjects were unaware from taking exercise and they never took exercise before or during pregnancy. 74% women reported about their imbalance diet in which 64.8% were pregnant. Personal hygiene was significant among expected women (p-value 0.008). Moreover the threatening statistics of different factors i.e. severe vomiting (p-value = 0.000), severe headache (p-value 0.000), fever (p-value 0.000), diabetes (p-value = 0.008) and constipation (p-value 0.046) were significantly associated with pregnancy. The status of miscarriage was highly associated with rural areas (p-value = 0.000), psychological factors (p-value = 0.033), exercise (0.016), BMI (p-value = 0.008), severe bleeding per vaginum (p-value = 0.000) and history of painful micturation (p-value = 0.011). Abortion was also significantly associated with rural areas (p-values = 0.00000) exercise (p-value = 0.016), BMI (p-value = 0.020) the history of painful micturation (p-value = 0.0000).

**Conclusions:** Women with pregnancies are at high risk to have miscarriage, abortion, complication and other risk factors like Fever, Severe Odema, Painful Micturation, Chronic Cough, Severe Headache, Diabetes and other harmful diseases. Truly speaking our women are cut off from exercise and balance diet which plays a dangerous role to damage their health. They should visit regularly to health consultants for early diagnosis and prevention from risks.

## P09

### The influence of communication in a family on adolescents' risk behaviour

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**Aims:** If parents communicate with their children about risk behaviour and spend high quality time with their children they may empower their children to delay sexual involvement. Little is known about such communication in South Africa. We examined parent-child communication about risk behaviour among parents and their children in the Eastern Cape Province, South Africa.

**Methods:** Parent-child dyads completed confidential questionnaires on sociodemographic factors, parent-child communication, and adolescent's sexual behaviour. Parents and children completed the questionnaires in separate rooms.

**Results:** 178 parent-child dyads participated in the study. The children were 11 to 19 years of age (mean = 13.3), and 62% were daughters. About 85% lived with their mother; but only 56% lived with their father. The parents' mean age was 42, and 54% were mothers. Children reported communicating more ( $P < .0001$ ) and spending more high quality time ( $P = .008$ ) with their mother than with their father. There were gender differences. Girls reported more communication with their mothers than did boys ( $P = .03$ ), and girls spent more high quality time with their mothers as opposed to their fathers than did boys ( $P = .03$ ). There was a significant positive relation between children and parents' reports of communication ( $P = .0005$ ). The results showed that the children who spent more quality time with their mother were less likely to be sexually experienced ( $P = .02$ ). Children reports of communication with their parents were not related to their sexual experience.

**Conclusions:** Inasmuch as there was more communication between mothers and their children, especially daughters, efforts are needed to increase the involvement of fathers with regard to their children, especially sons, and to better equip single mothers to communicate with their sons. The results suggest that it is important for parents to spend high quality time with their children to reduce their children's sexual involvement.

**P10****EPINOR – A ph.d. school for epidemiologic research in the High North**

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**Background:** The Institute of Community Medicine (ISM) at the University of Tromsø (UiT) has long traditions of conducting high quality population-based studies with importance for epidemiological research and health care in the region, as well as for complex epidemiologic challenges world wide. The Tromsø Study, The Finnmark Study, NOWAC (The Norwegian Women and Cancer Study) and SAMINOR are examples of cohort studies with origin at or with large contributions from ISM.

**Organization:** The EPINOR ph.d. school established in 2007 was funded by the UiT and is formally organized as a part of ISM. A board consisting of members from ISM, the research network and ph.d. students has regular meetings to ensure that activities and courses maintain high quality and contribute to build the profile of EPINOR.

**Profile:** The close links to a broad circumpolar research network is an important part of EPINORs profile: The University hospital in Northern-Norway (UNN), Akvaplan-niva, Arctic Monitoring and Assessment Programme (AMAP), Norwegian Institute for Air Research (NILU), Northern State Medical University, Arkhangelsk (NSMU) and The Public Health Research Centre of North West Russia, St.Petersburg (PHRC). The ph.d. school will unify epidemiologic research in the High North and ensure a continued “excellent” quality and diversity in this field.

**Activities:** Established ph.d. courses in epidemiology, statistics, and ethics allow the students at EPINOR to get a deeper understanding of the specific health challenges in the North in a network with students from all over the world. For the time being EPINOR has 25 ph.d. students from Russia, Brazil, Sri Lanka, the Faroe Islands and Norway. The running projects cover a wide range of topics with an epidemiologic focus; cardiovascular disease, diabetes, breast cancer, osteoporosis, rheumatology, occupational medicine, infectious medicine, trauma and health services and environmental pollutants. EPINOR students also work together in seminars for reflection and discussion of topics of common interest. The environment is international with courses and seminars in English.

**How to become an EPINOR associate member:** Ph.d. students may apply to be an associate member of the EPINOR and as such participate in the full package of courses, seminars and workshops. The individual ph.d. courses are open for ph.d.students from other research institutions.

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**P11****HAPIEE study: prevalence of obesity and increased waist-hip ratio and their relation with education level and marital status in Lithuanian urban population**

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**Objective:** Obesity is one of the major risk factors of non-communicable diseases and is responsible for 2-8% of health costs and 10-13% of deaths in Europe. The aim of this work – to estimate the prevalence of obesity and increased waist-hip ratio and their relation with education level and marital status in Lithuanian population aged 45-72 years.

**Material and methods:** Data from the survey performed in the framework of the international HAPIEE (Health, Alcohol, and Psychosocial factors In Eastern Europe) study are presented. Participants were randomly selected from the National Population Register Service. From April 2006 to June 2007, were screened 1923 men and 2374 women (response 55.2%). Body mass index (BMI) was calculated as weight (kg)/height squared ( $m^2$ ). Obesity was defined as  $BMI \geq 30 \text{ kg}/m^2$ . Increased waist-hip ratio (WHR) was defined for men  $>0.9$ , for women  $>0.85$ .

**Results:** Prevalence of obesity was significantly higher in women than in men (45.8% vs. 33.2%); conversely the prevalence of increased WHR was significantly higher in men than in women (77.0% vs. 48.1%). Prevalence of obesity and increased WHR were significantly increased with age. In age groups 45-54, 55-64, 65-72 years the prevalence of obesity was 26.2%, 34.4%, 36.4% for men and 30.1%, 45.2%, 56.3% for women respectively. The prevalence of increased WHR in each age group was significantly higher in men (64.9%, 76.9%, 84.6%, respectively) than in women (32.8%, 47.2%, 58.8%, respectively). Women in the university education group had significantly lower probability of being obese ( $OR=0.61$ ) and having increased WHR ( $OR=0.53$ ) compared to lower than university education group; among men only increased WHR was associated with university degree ( $OR=0.79$ ;  $p=0.05$ ) (data adjusted by age). Marital status was not associated with obesity and increased WHR in men and women aged 45-72 years.

**Conclusion:** The prevalence of obesity and increased waist-hip ratio were associated with sex, age and education level, but not with marital status. Being obese is associated with a higher risk of non-communicable disease, so public health strategies in Kaunas might need to focus on overcoming weight perception.

**P12****Influence of risk factors and their combination on risk of mortality from stroke in Kaunas elderly men**

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**Objective:** The aim of the study was to evaluate an influence of risk factors and their complexes on risk of mortality from stroke in Kaunas elderly men during 10 years follow-up.

**Material and methods:** The random samples of men aged 65-84 years (N=525) were examined during 1995-1996. They were invited from samples of previous epidemiological studies (KRIS and MONICA). Death from stroke was defined according to the International Classification of Diseases (ICD) -9, codes 430-438, and ICD-10, codes I60-I69. For evaluation of influence of risk factors on mortality from stroke data analysis were performed in case-control subdivision – from elderly men who did not had stroke before the study. Case subjects – persons who died from stroke during period of observation (1995-2005 years) (N=17). Control subjects – persons who survived during this period and they were matched for age, and education level (N=34).

**Results:** After logistic regression analysis there were evaluated variables related to risk of mortality from stroke during 10 years period – arterial hypertension (systolic blood pressure/diastolic blood pressure  $\geq 140/90$  mmHg) (OR=11.2; 95%CI 1.27-2.53;  $p=0.022$ ), smoking (current/former) (OR=4.40; 95%CI 1.08-19.0;  $p=0.037$ ), increased level of malondialdehyde as marker of oxidative stress (serum malondialdehyde  $\geq 5.5$  micromol/l) (OR=4.64; 95%CI 1.14-19.9;  $p=0.029$ ); it was obtained a tendency that obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>) also increased a risk of mortality from stroke (OR=5.64; 95%CI 0.99-35.4;  $p=0.051$ ). The rates of complex of two and three risk factors in cases group were significantly higher than in controls group: (a) arterial hypertension and smoking (70.6 vs. 23.5;  $p=0.001$ ), (b) arterial hypertension and increased level of malondialdehyde concentration (52.9 vs. 17.6;  $p=0.009$ ), (c) arterial hypertension, smoking and increased level of malondialdehyde concentration (41.5 vs. 5.9;  $p=0.006$ ).

**Conclusion:** Arterial hypertension, smoking and increased level of malondialdehyde concentration significantly increased a risk of mortality from stroke in Kaunas elderly men during 10 years period.

## P13

### Associations between effects of multi years climate changes and morbidity and mortality rates in the south of Israel

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**Background:** During the last decades climate change has become one of the most central and troublesome issues around the world. Studying the possible effects of climatic changes on health outcomes is very important and complicated because of complexity of involving factors and of the relationships between them. At present, the effects of climatic changes on human health have not yet deeply studied.

**Objectives:** To study the relationships between meteorological changes and changes in general morbidity and mortality (general and specific) rates during a rather long time period in Southern Israel.

**Subjects and methods:** As health outcome, we used daily records of mortality and morbidity rates obtained from a medical center in the Southern Israel during 16 years. As meteorological variables, daily average temperature and humidity were used. We constructed trend functions for all of considered variables by using harmonic analysis based on generalized linear models. In order to study the effect of the changes of the meteorological variables on the changes of morbidity and mortality rates, we constructed the regression models based on trends.

**Results:** We found that the trend of changes in general morbidity was significantly influenced by the trend of daily average temperature (regression coefficient  $B_{temp}=0.673$ ) and daily average humidity (regression coefficient  $B_{hum}=0.085$ ). The similar effects were observed for the trends of general and specific mortality rates.

**Conclusion:** Our findings show that there exist significant associations between climate changes and morbidity and mortality rates changes in the Southern Israel. So, growth of mortality and morbidity rates are significantly associated with heating effect and growth of humidity in considered region.

**P14****Mothers' and fathers' birth characteristics and perinatal mortality in their offspring: a population based cohort study**

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The authors investigated perinatal mortality risk in offspring in relation to maternal and paternal gestational age and birth weight by using generational data from the Medical Birth Registry of Norway, 1967 to 2006. Only singletons in both generations were included, forming 520,794 mother-offspring and 376,924 father-offspring units. Perinatal mortality risk in offspring was inversely associated with the mother's gestational age. A threefold increased risk was found among offspring of mothers born at 28-30 weeks of gestation compared to offspring of mothers born at term (37-43 weeks) (relative risk (RR) = 2.9, 95% confidence interval (CI): 1.9, 4.6). There was also a clear reduction in offspring perinatal mortality risk as maternal birth weight increased. Mothers whose birth weight was < 2,000 grams had a 50% increased risk of experiencing perinatal death compared to mothers whose birth weight was 3,500-3,999 grams. In contrast, perinatal mortality risk in offspring was not significantly influenced by paternal gestational age or birth weight. Weight-specific perinatal mortality risk in offspring was dependent on the birth weight of the mother and the father, that is, offspring who were small relative to their mother's or their father's birth weight were at increased risk of dying in the perinatal period.



**P15****Morbidity of first and recurrent acute myocardial infarction in Kaunas (Lithuania) population during 1983-2004**

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**Objective:** Over the past 20 years an increasing trend of mortality rates of acute myocardial infarction (AMI) was observed in many Eastern European countries. The aim of the study was to evaluate the trends in morbidity of AMI in Kaunas population during 1983-2004.

**Material and methods:** Kaunas population-based ischemic heart disease (IHD) register was the source of data. The methods used for the data collection were those applied by the WHO MONICA project. The object – all permanent residents of Kaunas aged 25-64 years who experienced AMI in 1983-2004. Trends were analyzed using the method of linear regression on logarithms of the age-standardized annual rates.

**Results:** According to the data of IHD register, among Kaunas men aged 25-64 years the average overall morbidity rate of AMI was 417.7/100,000, that among women – 87.7/100,000 in 1983-2004. From 1983 to 2004, the overall morbidity of AMI among Kaunas men aged 25-64 years was without significant changes ( $\beta = -0.3\%/yrs.$ ,  $p = 0.4$ ). Among women, the AMI overall morbidity rates were about 5-fold lower compared to those among men. Among women of the same age the overall morbidity of AMI rates were increasing statistically significantly ( $\beta = +1.5\%/yrs.$ ,  $p = 0.0003$ ). Regression analysis for the data of first and recurrent AMI rates during 1983-2004 revealed that, morbidity of first AMI among Kaunas men aged 25-64 years tended to decrease ( $\beta = -0.7\%/yrs.$ ,  $p = 0.1$ ) and morbidity rates of recurrent AMI during same years period among Kaunas men aged 25-64 years was without significant changes ( $\beta = +0.6\%/yrs.$ ,  $p = 0.3$ ). During 1983-2004, morbidity rates of first and recurrent AMI among Kaunas women aged 25-64 years were increasing statistically significantly, respectively  $\beta = +1.3\%/yrs.$ ,  $p = 0.0003$  and  $\beta = +2.4\%/yrs.$ ,  $p = 0.04$ .

**Conclusions:** During 1983-2004, the morbidity of first and recurrent AMI among Kaunas men was without significant changes, meanwhile among Kaunas women the morbidity of first and recurrent AMI significantly increased.

**P16****Mortality trends of cardiovascular diseases in the middle-aged Kaunas (Lithuania) population during 2001 to 2006**

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**Objective:** Over the past 20 years mortality rates from the main causes of death declined substantially in the most Western European countries, but in many Eastern European countries during the last decades years a rising trend was observed. The mortality rates from the main causes of death in these countries were 2 times higher to compare with the mortality rates in Western European countries. The aim of study was to determine and evaluate mortality rates and trends in the cardiovascular causes of death in the Kaunas population aged 25-64 years during 2001 to 2006.

**Material and methods:** Official mortality statistics data for 2001-2006 were used for the analysis. All mortality rates were age-standardized using World population as the standard. The trends were estimated from the logarithm of the annual age-standardized rates using an ordinary linear regression.

**Results:** During 2001-2006, the overall mortality was without significant changes among Kaunas men and women, respectively +0.05%/yrs.,  $p=0.9$  and -0.5%/yrs.,  $p=0.8$ . During the analyzed period, overall mortality was on the average 923.1/100,000 among Kaunas men aged 25-64 years, meanwhile among women the corresponding rate was 3 times lower (296.6/100,000). During 2001-2006, the mortality of cardiovascular diseases was on the average 301.7/100,000 among Kaunas men aged 25-64 years, meanwhile among Kaunas women the corresponding rate was 4 times lower (71.6/100,000). Analyzed mortality trends from cardiovascular diseases determined, that cardiovascular diseases during 2001-2006 statistically significantly increased by 4.4%/yrs. ( $p=0.02$ ) among Kaunas men and among Kaunas women cardiovascular mortality tended to increase (+5.6%/yrs.,  $p=0.07$ ). Cardiovascular diseases in the structure of overall mortality amounted on the average 32.7% in men and 24.2% in women. During 2001-2006, the cardiovascular diseases in the overall mortality structure increased statistically significantly by 4.4%/yrs. ( $p=0.01$ ) in Kaunas men and by 6.1%/yrs. ( $p=0.04$ ) in Kaunas women.

**Conclusions:** During 2001-2006, in Kaunas population aged 25-64 years mortality trends from cardiovascular diseases statistically significantly increased among Kaunas men, meanwhile between Kaunas women tended to increase.

**P17****Maternal stress during pregnancy and infectious diseases in the offspring: Evidence from the Danish National Birth Cohort**Marion Tegethoff<sup>1,2</sup>, Naomi Greene<sup>3</sup>, Jorn Olsen<sup>3,4</sup> and Gunther Meinlschmidt<sup>1,5</sup>

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**Objective:** Infections are among the most common diseases in infants and children. Even though vaccination programs and medication has helped to substantially decrease their prevalence in most parts of the world, and to improve treatment outcome, factors influencing the susceptibility to infections in humans are largely unknown. Interestingly, psychosocial stress exposure of the mother during pregnancy is associated with alterations of immune parameters in the offspring of animals and humans. Thus, an adverse intrauterine environment may play an important role in predisposing individuals to immune-related diseases. Our objective was to study the association between maternal psychosocial stress during pregnancy and the risk of infectious or parasitic diseases in the offspring during childhood.

**Material and methods:** We followed-up and assessed 66203 mother-child pairs of the Danish National Birth Cohort (DNBC) from early pregnancy into childhood. We conducted cox proportional hazard regression analyses to determine the association between maternal psychosocial stress during pregnancy and offspring risk for the first onset of infectious disease during childhood. As prenatal stress indicators we used two a priori defined forms of maternal stress during pregnancy, which may be associated with different psychobiological patterns, life stress in terms of perceived burdens in major areas of life (e.g. partnership, work), and self-reported emotional stress (e.g. anxiety, nervousness). Stress groups were defined by cutoffs the closest possible to the quartiles of the distribution of the respective stress scores. As outcome measure, we used the first diagnosis of any infectious or parasitic disease of the infant, according to the respective ICD-10 category (codes A00 to B99) obtained from the Danish National Hospital Register.

**Results:** 6674 infants (10.1%) had an infectious or parasitic disease (median age at initial diagnosis: 1.3 years(y) [range: 0-8.3y]; median age at end of follow-up: 6.2y [range: 3.6-8.9y]). After controlling for potential confounders, including postnatal life stress and postnatal emotional stress, low-medium (2<sup>nd</sup> quartile), medium-high (3<sup>rd</sup> quartile) and high (4<sup>th</sup> quartile) (as compared to low) prenatal life stress was linked to an increased risk for the first onset of an infectious or parasitic disease (2<sup>nd</sup> vs. 1<sup>st</sup> quartile: hazard ratio [HR], 1.08; 95% confidence interval [CI], 1.00-1.16; 3<sup>rd</sup> vs. 1<sup>st</sup> quartile: HR, 1.10; 95% CI, 1.03-1.18; 4<sup>th</sup> vs. 1<sup>st</sup> quartile: HR, 1.28; 95% CI, 1.17-1.39). Only high prenatal emotional stress was linked to a slight increased risk for the first onset of an infectious disease (4<sup>th</sup> vs. 1<sup>st</sup> quartile: HR, 1.09; 95% CI, 1.01-1.18).

**Conclusion:** Maternal life stress during pregnancy may be an early risk factor for infectious or parasitic diseases in the offspring during childhood. To the best of our knowledge, this is the first large-scale prospective data based human study of the relationship between prenatal psychosocial stress and infectious diseases. More research is needed to confirm this seminal finding and to examine the potential of stress-reduction during pregnancy to reduce the incidence of infections in the offspring.

**P18****Prenatal stress and respiratory diseases during childhood – Evidence from the Danish National Birth Cohort**Marion Tegethoff<sup>1,2</sup>, Naomi Greene<sup>3</sup>, Jorn Olsen<sup>3,4</sup> and Gunther Meinlschmidt<sup>1,5</sup>

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**Objective:** Prenatal exposure to maternal stress may result in programming of physiological systems in the offspring and, hence, predispose individuals to certain diseases across the life span. For example, in mice, prenatal noise stress enhances vulnerability of the adult offspring to dysfunction of the airway and associated biological pathways. However, to the best of our knowledge, human prospective data on prenatal psychosocial stress and later airway function is still lacking. Our objective was to study the association between maternal psychosocial stress during pregnancy and the risk of respiratory diseases in the offspring during childhood.

**Material and methods:** We followed-up 66203 mother-child pairs of the Danish National Birth Cohort (DNBC) from early pregnancy into childhood. We conducted cox proportional hazard regression analyses to determine the association between maternal psychosocial stress during pregnancy and offspring risk for the first onset of respiratory diseases during childhood. As prenatal stress indicators we used two a priori defined forms of prenatal stress, life stress in terms of perceived burdens in major areas of life (e.g. partnership, work), and self-reported emotional stress (e.g. anxiety, nervousness), which may be associated with different psychobiological patterns. Life stress and emotional stress groups were defined by cutoffs the closest possible to the quartiles of the distribution of the stress scores. As outcome measure, we used the first diagnosis of any respiratory disease of the infant (ICD-10 codes J00 to J99 obtained from the Danish National Hospital Register).

**Results:** Out of 66203 children, 12442 (18.8%) were diagnosed with a respiratory disease. Infants' median age at the end of follow-up was 6.2 years (range: 3.6 to 8.9 years). Infants' median age at initial diagnosis was 1.4 years (range: 0 to 8.4 years). After controlling for potential confounders, including postnatal life stress and postnatal emotional stress, high-medium (3<sup>rd</sup> quartile) and high (4<sup>th</sup> quartile) (as compared to low (1<sup>st</sup> quartile)) prenatal life stress was linked to an increased risk for the first onset of a respiratory disease (3<sup>rd</sup> vs. 1<sup>st</sup> quartile: hazard ratio [HR], 1.14; 95% confidence interval [CI], 1.08-1.20; 4<sup>th</sup> vs. 1<sup>st</sup> quartile: HR, 1.27; 95% CI, 1.19-1.35). Prenatal emotional stress was not linked to an altered risk for the first onset of a respiratory disease.

**Conclusion:** Maternal life stress during pregnancy may be an early risk factor for respiratory diseases during childhood. To the best of our knowledge, this is the first study of the relationship between prenatal stress and childhood respiratory disease. The findings may point to new approaches to reduce respiratory diseases during childhood. Future studies to corroborate the results and to clarify the underlying biological pathways in humans are urgently needed.

**P19****A biobank of primary teeth connected to the Norwegian Mother and Child Cohort Study**

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**Introduction:** Primary teeth can be used as biomarkers of exposure to a number of trace elements, toxic as well as essential. Tooth formation starts at about the 4<sup>th</sup> month of foetal life and continues through the first years of infancy. Trace elements, such as lead and strontium, are incorporated into tooth substance during tooth formation. Prenatally and postnatally formed tooth tissues permanently document early exposures as no other biomarker can, because teeth develop incrementally at a known rate. This allows for the tracking of elemental fluctuations across months, weeks, and even days. A biobank of primary teeth has recently been established within The Norwegian Mother and Child Cohort Study (MoBa) which is a national study comprising 100 000 pregnancies. Mother, father and child are included and there is no limitation for follow-up. Data are collected using questionnaires and biological samples. Specific aetiological hypotheses may be tested by estimating the association between exposure and disease.

**Objectives:** To run a biobank for primary teeth (MoBaTooth) in collaboration with MoBa Study in order to strengthen the collection of biological tissues within MoBa.

**Methods:** The project is a co-operation between the University of Bergen and the Norwegian Institute of Public Health, running the MoBa Study. It is approved by all relevant Authorities. Invitations to donate teeth will be sent to all participating mothers during 2008 – 15, when the child is about seven years (n = 6 171 – 17 336 per year). The invitation contains information about the biobank and an informed consent form to be signed by the parent and returned with the tooth/teeth. The teeth are stored in a dry condition at room temperature in polypropylene tubes having an identification code that can be connected to data in the MoBa database. Relevant projects may apply for analyses of subgroups of teeth together with data from the MoBa database. Tooth substance left after analyses must be returned to the biobank, together with results from the analyses for future investigations.

**Results and perspectives:** The first invitations were mailed in February 2008, and more than 500 teeth had been received by September 15. The extensive panorama of information about the mother, father and child given through MoBa provides a unique opportunity to explore the capability of primary teeth as biomarkers, and may add important knowledge about uptake of elements in the body in the most vulnerable period of life – foetal life and early infancy. Information from MoBaTooth will thus supplement the extensive information within MoBa.

**Conclusion:** Results from MoBaTooth combined with information from the MoBa Study will give valuable information about the association between exposure and disease.

**P20****Ethnic differences in early pregnancy maternal n-3 and n-6 fatty acid concentrations: the ABCD cohort study**

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**Objective:** Maternal nutrition has been proposed as an explanation of the world-wide existing ethnic disparities in birth weight. While n-3 and n-6 fatty acids may be relevant in this context, information on ethnic differences in intake or concentrations of these nutrients is limited. Our study compared early pregnancy maternal n-3 and n-6 plasma phospholipid-associated fatty acid concentrations between Dutch, Antillean, Surinamese, Ghanaian, Turkish and Moroccan women, and subsequently explored the specific role of fish consumption in explaining differences in EPA (20:5n-3) and DHA (22:6n-3), as well as DGLA (20:3n-6) and AA (20:4n-6) concentrations.

**Materials and methods:** In 2003-2004, Amsterdam pregnant women were invited to participate in the Amsterdam Born Children and their Development cohort study. A total of 8266 women completed a questionnaire and 4389 women donated blood around the 13<sup>th</sup> pregnancy week for nutrient analysis. For the present analysis, fatty acid concentrations in plasma phospholipids of 3284 participants (restriction to the main six ethnic groups as based on country of birth) were compared by general linear models, with ethnicity as primary independent variable and maternal age, parity, educational level, pregravid BMI, alcohol consumption and smoking habits as co-variables. For EPA, DHA, DGLA and AA, the potential role of fish consumption was determined by adding this variable to the model.

**Results:** Compared to Dutch women (n=2459), Surinamese (n=292), Antillean (n=64), Turkish (n=168) and Moroccan (n=244) women had lower concentrations of n-3 fatty acids but higher concentrations of n-6 fatty acids except DGLA (p<0.001). Differences were most pronounced in Turkish women, who reported very low fish consumption. Ghanaian women (n=57) had the highest EPA and DHA concentrations but generally lower n-6 fatty acid concentrations (p<0.001). Although they reported the highest fish consumption, adjustment for this variable attenuated differences in EPA, DHA, DGLA and AA concentrations only modestly.

**Conclusion:** In this study, distinct differences in n-3 and n-6 fatty acid patterns were observed between ethnic Dutch women and women from ethnic minority groups. Differences were most pronounced in Turkish and Ghanaian women, who reported the lowest and highest fish consumption respectively. Adjustment for fish intake, however, hardly attenuated the differences in relative EPA, DHA, DGLA, and AA concentrations between the various ethnic groups. Further research into the ethnicity-related differences in maternal n-3 and n-6 fatty acid patterns is warranted, particularly to elucidate the explanatory role of differences in fatty acid intake vs. metabolism.

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