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## DEN 22. NORSKE EPIDEMIOLOGIKONFERANSEN

TRONDHEIM,

29.-30. OKTOBER 2014

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## **The 22<sup>nd</sup> Norwegian Conference on Epidemiology Trondheim, October 29<sup>th</sup> - 30<sup>th</sup> 2014**

Welcome to the 22<sup>nd</sup> conference of the Norwegian Epidemiological Association (NOFE) in Trondheim.

The main topics of this year's conference are causality and register-based research. We want to thank the keynote speakers in particular for their contributions; W. Dana Flanders, Anders Ahlbom, Björn Pasternak, Stein Emil Vollset, Inger Johanne Bakken and Kristine Pape.

Other programme items include the 2014 Publication of the Year award, NOFE's annual meeting and Honorary Membership being awarded to a distinguished member. We are pleased to have a total of 63 abstracts approved for oral presentation this year.

We also wish to thank EPINOR for a productive collaboration and the Department of Public Health and General Practice for financial and practical support.

More than 140 participants are registered for this year's conference and we wish you all a successful conference!

*The organizing committee for the NOFE conference 2014*

*Bjørn Olav Åsvold, Tom Ivar Lund Nilsen, Pål Romundstad and Signe Opdahl*

*Department of Public Health and General Practice, Norwegian University of Science and Technology*

## The 22<sup>nd</sup> Norwegian Conference on Epidemiology Trondheim, October 29<sup>th</sup> - 30<sup>th</sup> 2014

### Programme overview

#### Wednesday, October 29<sup>th</sup>

09:00-10:00	<i>Registration/coffee</i>
10:00-10:05	Welcome
10:05-10:50	<b><i>"Biasing paths"</i></b> Invited speaker: Professor <b>W. Dana Flanders</b> , Emory University, US
10:50-11:00	<i>Short coffee break</i>
11:00-12:15	Oral presentations of submitted abstracts (parallel sessions, <b>A1-5, B1-5, and C1-5</b> )
12:15-13:10	<i>Lunch</i>
13:10-13:55	Oral presentations of submitted abstracts (parallel sessions, <b>A6-8, B6-8, and C6-8</b> )
13:55-14:10	<i>Coffee break</i>
14:10-15:00	<b><i>"From Snow to Doll and onwards: some historical notes"</i></b> Invited speaker: Professor <b>Anders Ahlbom</b> , Karolinska Insitutet, Sweden
15:00-15:10	<i>Short coffee break</i>
15:10-15:55	Oral presentations of submitted abstracts (parallel sessions, <b>A9-11, B9-11, and C9-11</b> )
15:55-16:10	<i>Coffee break</i>
16:10-16:45	Announcement of a new honorary member of NOFE
16:45-17:45	NOFE's annual meeting, with discussion about the future of the Journal
19:00-	<i>Conference dinner</i>

**Thursday, October 30<sup>th</sup>**

09:00-10:15	Oral presentations of submitted abstracts (parallel sessions, <b>A12-16</b> , <b>B12-16</b> , and <b>C12-16</b> )
10:15-10:30	<i>Coffee break</i>
10:30-11:05	Publication of the Year – award and presentation
11:05-11:15	<i>Short coffee break</i>
11:15-12:05	<b>”Registers to address current drug safety concerns – examples from Denmark”</b> Invited speaker: Researcher <b>Björn Pasternak</b> , Statens Serum Institut, Denmark
12:05-13:00	<i>Lunch</i>
13:00-14:15	Oral presentations of submitted abstracts (parallel sessions, <b>A17-21</b> , <b>B17-21</b> , and <b>C17-21</b> )
14:15-14:30	<i>Coffee break</i>
14:30-15:55	<b>“Inspirational relay in registry-based epidemiology”</b> Invited contributors: Researcher <b>Björn Pasternak</b> , Statens Serum Institut, Denmark: <b>“Resources for Register Research in Denmark”</b> Professor <b>Stein Emil Vollset</b> , Department of Global Public Health and Primary Care, University of Bergen and the Norwegian Institute of Public Health: <b>“Health registries, infrastructure and public health research”</b> Senior Advisor <b>Inger Johanne Bakken</b> , the Norwegian Institute of Public Health: <b>“Case-only design in registry-based epidemiological research – When and how can data from cases only be informative?”</b> Postdoctoral fellow <b>Kristine Pape</b> , Department of Public Health and General Practice, NTNU: <b>“Sibling and family study designs”</b>
15:55	Closing

# The 22<sup>nd</sup> Norwegian Conference on Epidemiology Trondheim, October 29<sup>th</sup> - 30<sup>th</sup> 2014

## Detailed programme

### Wednesday, October 29<sup>th</sup>

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09:00-10:00 Registration/coffee

#### Plenary session Haraldssalen

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10:00-10:05	Signe Opdahl	Welcome
10:05-10:50	W. Dana Flanders	Biasing paths

10:50-11:00 Short coffee break

#### Parallel session A1-A5 Haraldssalen

##### Topic: Epidemiological methods

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11:00-11:15	A1	Jon Michael Gran	A multi-state model approach to causal inference and time-dependent confounding
11:15-11:30	A2	Valborg Baste	Propensity score applied on large register data
11:30-11:45	A3	Vidar Hjellvik	Adjusting for unmeasured confounding by applying a correction factor calculated from associations between exposure/outcome and covariates in a validation data set
11:45-12:00	A4	Anja S Lindman	30 days readmission among the elderly – a new quality indicator for hospital performance in Norway
12:00-12:15	A5	Sahar Hassani	Methodological description of the data pre-processing and analyses for the 30-day survival indicator

#### Parallel session B1-B5 Kristiansten

##### Topic: Infectious disease and vaccination

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11:00-11:15	B1	Siri E Håberg	CFS/ME in Norway after infection with pandemic H1N1 influenza virus and H1N1 vaccination
11:15-11:30	B2	Miloje Savic	The Norwegian influenza cohort study (NorFlu): immune responses in H1N1pdm exposed versus non-exposed pregnant women
11:30-11:45	B3	Nina Gunnes	Seasonal and Pandemic Influenza Infection, Vaccination, and Preterm Birth: A Population-Based Registry Study
11:45-12:00	B4	Lill Trogstad	Perinatal outcomes and children's health after prenatal exposure to influenza and influenza vaccination
12:00-12:15	B5	Sara Ghaderi	Pandemrix vaccination or infection with pandemic influenza A(H1N1)pdm09 and risk of Guillain-Barré syndrome

#### Parallel session C1-C5 Munkholmen

##### Topic: Work and employment

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11:00-11:15	C1	Fartein Ask Torvik	Socioeconomic status and sick leave granted for somatic and mental disorders: a prospective study of young adult twins
11:15-11:30	C2	Gunnhild Å Vie	Mortality and work disability in a cohort of Norwegian couples – the Nord-Trøndelag Health Study
11:30-11:45	C3	Ragnhild E Ørstavik	Life satisfaction and work absenteeism – a discordant twin analysis
11:45-12:00	C4	Ingrid S Mehlum	The relationship between socioeconomic position, working conditions and sickness absence in a life-course perspective
12:00-12:15	C5	Silje L Kaspersen	The unemployment effect of health

**12:15-13:10 Lunch**

**Parallel session A6-A8****Haraldssalen****Topic: Lifestyle and cancer**

13:10-13:25	A6	Kristin B Borch	Overall and breast cancer specific survival associated with pre- and post-diagnosis physical activity in Norwegian women
13:25-13:40	A7	Markus D Knudsen	Lifestyle as a predictor of colorectal adenomas in the bowel cancer-screening in Norway – a pilot project
13:40-13:55	A8	Jan Helge S Mortensen	Maternal folic acid supplementation and cancer risk

**Parallel session B6-B8****Kristiansten****Topic: Pain**

13:10-13:25	B6	Ragnhild Lier	Neck and low back pain in parents and their adult offspring: family linkage data from the Norwegian HUNT study
13:25-13:40	B7	Ingunn Mundal	Psychosocial factors and risk of chronic widespread pain: An 11-year follow-up. (The Nord-Trøndelag Health Study)
13:40-13:55	B8	Karin Magnusson	Mental distress is a predictor for disabling multisite pain only in combination with obesity or sleep problems

**Parallel session C6-C8****Munkholmen****Topic: Drugs and toxins in pregnancy and childhood**

13:10-13:25	C6	Ingeborg Hartz	Psychotropic drug use among 0-17 year olds during 2004-2013: a nationwide prescription database study
13:25-13:40	C7	Hilde B Lauritzen	Characteristics of persistent organic pollutants and perfluoroalkyl substances in pregnant Scandinavian women, 1986-1988
13:40-13:55	C8	Kateřina Nezvalová-Henriksen	The effect of prenatal antidepressant exposure on birth weight, gestational age and congenital anomalies – advantages of using a sibling control design
13:55-14:10		Coffee break	

**Plenary session****Haraldssalen**

14:10-15:00		Anders Ahlbom	From Snow to Doll and onwards: some historical notes
15:00-15:10		Short coffee break	

**Parallel session A9-A11****Haraldssalen****Topic: Cardiovascular disease**

15:10-15:25	A9	Geir Aamodt	Investigation of unusual temporal patterns of cardiovascular diseases in Norwegian regions via Bayesian model choice – a CVDNOR study
15:25-15:40	A10	Rupali Akerkar	Atrial fibrillation and risk of mortality among patients with cardiovascular disease in Norway
15:40-15:55	A11	Ragnar Nesvåg	Is the increased risk of cardiovascular disease among patients with schizophrenia and bipolar disorder explained by presence of substance use disorders?

**Parallel session B9-B11****Kristiansten****Topic: Early life exposures**


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15:10-15:25	B9	Ketil Størdal	Infections and the duration of full or partial breastfeeding; results from the MoBa cohort study
15:25-15:40	B10	Lars C Stene	Infant feeding and risk of childhood-onset type 1 diabetes: preliminary data from the PAGE-study
15:40-15:55	B11	Maria Christine Magnus	Grand-maternal smoking when pregnant with the mother and the grand-child's risk of developing asthma: the Norwegian Mother and Child Cohort Study

**Parallel session C9-C11****Munkholmen****Topic: Vitamins**


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15:10-15:25	C9	Tricia L Larose	Cross-Sectional and Prospective Cohort Study of Serum 25-Hydroxyvitamin D Level, Smoking and Lung Function in a General Population of Adults: The HUNT Study
15:25-15:40	C10	Christine L Parr	Vitamin A, D, and E levels in stored plasma samples from pregnant women in the Norwegian Mother and Child Cohort Study: time changes and study implications
15:40-15:55	C11	Marit Waaseth	Characteristics of dietary supplement users
15:55-16:10		Coffee break	

**Plenary session****Haraldssalen**


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16:10-16:45	Announcement of a new honorary member of NOFE
16:45-17:45	NOFE's annual meeting, with discussion about the future of the Journal

**19:00- Conference dinner at Rockheim**


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**Thursday, October 30<sup>th</sup>****Parallel session A12-A16****Haraldssalen****Topic: Cancer epidemiology**

09:00-09:15	A12	Marta Román	Hormone therapy use and the risk of breast cancer in Norway
09:15-09:30	A13	Hege Bøvelstad	Risk factor profiles of women with endometrial and ovarian cancer in the Norwegian Women and Cancer Study (Kvinner og kreft)
09:30-09:45	A14	Tom Grotmol	Genome-wide association study reveals two new susceptibility loci for testicular germ cell tumor
09:45-10:00	A15	Morten Valberg	A Hierarchical Frailty Model for Familial Testicular Germ-Cell Tumors
10:00-10:15	A16	Reza Ghiasvand	Sunscreen use and risk of cutaneous malignant melanoma among women

**Parallel session B12-B16****Kristiansten****Topic: Psychiatry**

09:00-09:15	B12	Jessica Gabin	The Health and Memory Study: Occurrence of Dementia in the Nord-Trøndelag Health Study
09:15-09:30	B13	Magnhild Torske	Anxiety and depression symptoms among farmers. The HUNT Study, Norway
09:30-09:45	B14	Audun Brunnes	The effect of physical activity on mental health problems and well-being among Norwegian adolescents with self-perceived visual impairment – The Young HUNT study
09:45-10:00	B15	Elin Anita Fadum	Acute medication poisoning in adolescents: A national register study of hospital admissions and readmissions
10:00-10:15	B16	Eva Lassemo	The Epidemiology of Post-Traumatic Stress Disorder in Norway

**Parallel session C12-C16****Munkholmen****Topic: Various topics**

09:00-09:15	C12	Edoardo Botteri	Lifestyle and lifestyle changes at the age of fifty as predictors of mortality
09:15-09:30	C13	Berit Feiring	Socioeconomic inequalities in the uptake of vaccine against human papillomavirus in the Norwegian childhood immunization program
09:30-09:45	C14	Mari Vaage Wang	Language development through preschool years: The association with participation in childcare
09:45-10:00	C15	Kari M Aaberg	Validation of epilepsy diagnoses in the Epilepsy in Young Children (EPYC) study – a nationwide population-based study
10:00-10:15	C16	Lisa Aarhus	Adult outcomes for children with hearing loss
10:15-10:30		Coffee break	

**Plenary session****Haraldssalen**

10:30-11:05		Publication of the Year – award and presentation
11:05-11:15		Short coffee break
11:15-12:05	Björn Pasternak	Registers to address current drug safety concerns – examples from Denmark

**12:05-13:00****Lunch**



**Parallel session A17-A21****Haraldssalen****Topic: Health registers**

13:00-13:15	A17	Heidi Jensberg	Norwegian Patient Register as a personally identifiable register: Five years of experience
13:15-13:30	A18	Torunn Varndal	Validity and reliability of the Norwegian Stroke Register and stroke diagnosis in the Norwegian Patient Register
13:30-13:45	A19	Ingunn Björnsdóttir	Quality and transparency of data – a Case from Iceland
13:45-14:00	A20	Lise Lund Håheim	Validation of referral information for elective treatment in hospitals to discharge diagnosis
14:00-14:15	A21	Ragna ES Govatsmark	Was it an Acute Myocardial Infarction?

**Parallel session B17-B21****Kristiansten****Topic: Environmental epidemiology**

13:00-13:15	B17	Anica Simic	Trace elements and type 2 diabetes – two case-control studies in HUNT3
13:15-13:30	B18	Cecilie Dahl	Is copper in drinking water related to risk of hip fracture? And could a possible protective association between calcium and hip fracture be modified by copper?
13:30-13:45	B19	Bo Engdahl	The Nord-Trøndelag Hearing Loss Study – main results
13:45-14:00	B20	Bente Oftedal	Road traffic noise and markers of obesity – a population-based study
14:00-14:15	B21	Gunn Marit Aasvang	Night-time road traffic noise and symptoms of insomnia

**Parallel session C17-C21****Munkholmen****Topic: Obesity**

13:00-13:15	C17	Anne Johanne Søgaard	Body mass index and one single question may predict hip fracture. A NOREPOS study
13:15-13:30	C18	Thomas Sevenius Nilsen	Twinning rates in Norway in relation to Body Mass index and height
13:30-13:45	C19	Kirsti Kvaløy	Genetic effects on longitudinal changes from healthy to adverse weight and metabolic status – The HUNT Study
13:45-14:00	C20	Ragnhild Hovengen	The prevalence of overweight and obesity in The Norwegian Child Growth Study, and the risk for social inequality in child health: a nationally representative study
14:00-14:15	C21	Anna Biehl	Overweight and obesity among children in Norway by family country background
14:15-14:30		Coffee break	

**Plenary session****Haraldssalen**

14:30-15:55		Björn Pasternak	Resources for Register Research in Denmark
		Stein Emil Vollset	Health registries, infrastructure and public health research
		Inger Johanne Bakken	Case-only design in registry-based epidemiological research – When and how can data from cases only be informative?
		Kristine Pape	Sibling and family study designs

**15:55****Closing**

## ABSTRACTS

### A1

#### **A multi-state model approach to causal inference and time-dependent confounding**

**Jon Michael Gran**<sup>1</sup>, Rune Hoff<sup>1</sup>, Odd O. Aalen<sup>1</sup>

1) Oslo Centre for Biostatistics and Epidemiology, Department of Biostatistics, University of Oslo, Norway

**Introduction:** Multi-state models have proven to be a fruitful framework for analyzing event-history data, as the occurrence of an event can be seen as a transition from one state to another. Some of the benefits of this framework are that it is easy to incorporate transient states and multiple events. In this paper we will discuss how interventions can be defined in multi-state models and how they can be used to estimate causal effects.

**Aims:** Our main aim is to estimate the effect of interventions from observational data. We consider two applications; estimating the effect of anti-retroviral treatment for HIV patients, and, the effect of graded sick leave on time to return-to-work from Norwegian registry data. In the HIV example we want to study time-dependent confounding in multi-state models, while we in the sick leave example consider multiple events of interest.

**Methods:** A multi-state model for HIV progression is presented, and a simulation study is performed to illustrate how such a model can be used to generate data with time-dependent confounding between treatment and disease status. For the sickness absence example, transition rates between the various states are estimated from observed data.

**Results:** We show that even simple multi-state models can capture complex dynamics, including feedback such as time-dependent confounding, and be used to estimate causal effects. We also show how multi-state models can be used to simulate full counterfactual datasets. In addition to estimating the causal parameter itself, such simulations prove helpful in defining and understanding the causal contrast in question. In our simulation study we compare these result with more conventional methods for adjusting for time-dependent confounding. Preliminary results using the sickness absence data are also presented.

**Conclusions:** Multi-state models for time-to-event data can be an intuitive framework for defining interventions, and thus be a useful tool in estimating causal effects.

## A2

### Propensity score applied on large register data

Valborg Baste<sup>1</sup>, Anne Marie Fenstad<sup>1</sup>, Leif I. Havelin<sup>1</sup>, Birgitte Espehaug<sup>1,2</sup>

1) The Norwegian Arthroplasty Register, Haukeland University Hospital, Bergen, Norway

2) Centre for Evidence-Based Practice, Bergen University College, Norway

**Introduction:** Propensity score (PS) have been suggested and used as an approach to assess causality in epidemiological studies. Lately, reviewers of studies based on data from the Norwegian Arthroplasty Register (NAR) have demanded analysis with PS.

**Aims:** The objectives of the presentation are to illustrate whether different applications of PS will influence risk estimates in Cox regression analyses based on large register data sets, and to compare these with adjusted relative risk (RR) estimates from standard Cox regression analyses.

**Material and Methods:** NAR was started in 1987 and is a national register for total hip replacements. Revisions of the prosthesis are the most studied endpoint. We included 44720 total hip replacements (2005 until 2013) where there was information on covariates of importance. Fixation of the hip replacements (cemented or uncemented) and risk for later revision due to any cause was studied. Possible confounders in the register were gender, age (in 5 years groups), reason for operation, morbidity, duration of the operation (in groups of 30 minutes) and year of operation. Cox regression analyses were conducted both with adjustment for confounders and for PS and was compared with similar analyses performed on a one-to-one PS matched data set.

**Results and Conclusion:** Among the total hip replacements, 71% were cemented. Number of revised prostheses was 1664 (3.7%). The adjusted RR estimate was 1.3 (95% CI 1.2-1.5) and 1.4 (95% CI 1.2-1.6) for revision after uncemented compared to cemented total hip replacement, adjusted for confounders and PS respectively. With one-to-one PS-matching there were 7165 patients in each group of fixation. The RR for revision among uncemented compared with cemented was 1.5 (95% CI 1.3-1.8). PS matching could be a valuable contribution when large register data are analysed. Further analyses with different use of PS and different outcome will be presented.

## A3

### Adjusting for unmeasured confounding by applying a correction factor calculated from associations between exposure/outcome and covariates in a validation data set

Vidar Hjellvik

Department of Pharmacoepidemiology, Norwegian Institute of Public Health, Oslo, Norway

**Introduction:** Most methods for adjusting for unmeasured confounding implies simplifications and restrictions (e.g. a limited number of uncorrelated dichotomous variables). In the CARING (CAncer Risk and INSulin analogues) project, one work package deals with unmeasured confounding.

**Aims:** To obtain a fully data driven adjustment method that works for various effect estimates (incidence ratio, odds ratio, relative risk) when an arbitrary number of correlated confounders (continuous or categorical) are available in a validation data set, and none or some of these are available in the full data set.

**Methods:** A correction factor is calculated based on measures of the strengths of the following associations in the validation data: i) exposure and  $C_M$  (covariates available in the full data set); ii) exposure and  $C_{ALL}$  (all covariates); iii) outcome and  $C_M$ ; iv) outcome and  $C_{ALL}$ . The associations are quantified in terms of areas under receiver operating characteristic curves (AUCs). To handle 'negative confounding' (at least one covariate is negatively associated with the outcome and positively associated with the exposure, or vice versa), the correlation between each confounder and exposure/outcome is also needed. For a given data set, the correction factor is calculated as a function of the above mentioned AUCs and correlations, and two fixed parameters. The functional form and the parameters were determined by analyzing a wide range of simulated data sets.

**Results:** The method was tested on data from Norwegian health surveys, where 'gold-standard' estimates (adjusted for 7 covariates) of death or cancer risk associated with antidiabetic drug use were compared to 'error-prone' estimates ( $p$  covariates,  $1 \leq p \leq 7$ , were treated as available only in a 10% validation data set). The bias in the error-prone estimates was substantially reduced after application of the correction method.

**Conclusions:** The suggested method may be a useful tool for handling unmeasured confounding.

## A4

### 30 days readmission among the elderly – a new quality indicator for hospital performance in Norway

A. S. Lindman, O. Tomic, D. T. Kristoffersen, S. Hassani, J. Helgeland

Norwegian Knowledge Centre for the Health Services, Oslo, Norway

**Introduction:** Unplanned readmissions are costly and may reflect suboptimal patient care. 30 day readmission is included in the annual reporting of quality indicators on [www.helsenorge.no](http://www.helsenorge.no) in November each year.

**Aim:** Development of the 30 day readmission indicator in Norway.

**Methods:** Patient administrative data from Norwegian health trusts are collected yearly from the Norwegian Patient registry and linked to the National Registry. Readmission is calculated for patients 67 years and older, previously admitted with a diagnosis belonging to eleven diagnosis groups. *Readmission* is defined as an acute admission between 8 hours and 30 days subsequent to a previous hospital discharge (*primary admission*). Logistic regression, followed by a hierarchical Bayes model, is used. The results are stratified by hospital or municipality. Each hospital /municipality is compared with a reference value, defined as the 10% trimmed national average. The readmission probabilities are adjusted for gender and age. Multiple hypothesis testing with a total error rate of 10% is used for outlier detection.

**Results:** The results show that readmissions among elderly patients are common in Norwegian hospitals. The highest readmission rates are observed for asthma/COPD, heart failure and pneumonia, and these three groups cover approximately 2/3 of all readmissions.

**Conclusion:** Significant geographical variations exist, however, for most municipalities and hospitals, the differences are small. Readmission rates do not only reflect hospital quality of care, but also care given by the primary healthcare system in local municipalities. The indicator has led to increased interest in the challenges with readmissions and its role in care coordination in Norway, especially after the publication of the Health sector Coordination reform launched in 2012.

## A5

### Methodological description of the data pre-processing and analyses for the 30-day survival indicator

S. Hassani, A. S. Lindman, D. T. Kristoffersen, O. Tomic, J. Helgeland

Norwegian Knowledge Centre for the Health Services, Oslo, Norway

**Introduction:** The Norwegian Knowledge Centre for the Health Services (NOKC) performs analyses of 30-day survival for patients admitted to Norwegian hospitals at three different levels: hospital level, hospital trust level and regional health authority level. These survival indicators have been published annually since 2011 on [www.helsenorge.no](http://www.helsenorge.no). Since mortality is perceived a negative framing, we use survival rather than mortality as a quality indicator.

**Aim:** To describe the data collection, data pre-processing, and data analyses for the calculation of 30-day survival indicators in depth.

**Method:** Three diagnosis-specific 30-day survival indicators (first time acute myocardial infarction (AMI), stroke and hip fracture) are estimated based on all-cause deaths, occurring in-hospital or out-of-hospital, within 30 days counting from the first day of hospitalization. Furthermore, an all-cause 30-day survival indicator is also calculated. Logistic regression, followed by a hierarchical Bayes model, is used. Each hospital is compared with a reference value, defined as the 10% trimmed national average. Multiple hypothesis testing with a total error rate of 10% is used for outlier detection.

**Results:** Altogether, four 30-day survival indicators are produced annually by NOKC. Since the start of public reporting of the survival indicators in 2011, the methods have been slightly modified. The methods described in this article are the ones that are currently in use.

**Conclusions:** Public reporting of survival/mortality indicators are increasingly being used as quality measures of health care systems. Openness regarding the methods used to calculate the indicators are important, as it provides the opportunity of critically reviewing and discussing the methods in the literature. In this way, the methods employed for establishing the indicators may be improved.

**A6****Overall and breast cancer specific survival associated with pre- and post-diagnosis physical activity in Norwegian women****Kristin Benjaminsen Borch**<sup>1</sup>, **Tonje Braaten**<sup>1</sup>, **Eiliv Lund**<sup>1</sup>, **Elisabete Weiderpass**<sup>1,2,3,4</sup>

1) Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø, Norway

2) Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

3) Department of Research, Cancer Registry of Norway, Oslo, Norway

4) Folkhälsan Research Centre, Samfundet Folkhälsan, Helsinki, Finland

**Introduction:** Previous studies on the impact of physical activity (PA) and breast cancer survival are so far inconclusive.

**Aims:** We aimed to investigate whether PA levels before and after diagnosis of breast cancer, were associated with overall and breast cancer specific survival.

**Methods:** 109.398 healthy women enrolled in the Norwegian Women and Cancer Study 3867 women with breast cancer were identified, whereof 2540 cases were excluded as they did not have complete information on self-reported PA level at enrollment or during follow-up. Hence 1327 women with a breast cancer diagnosis were eligible for inclusion in our present analysis. Follow-up time was defined as the interval between the date of diagnosis of breast cancer and death from breast cancer, date of death from other causes, date of emigration or last complete follow-up of endpoint updated on 31.12.2012. Multivariate cox proportional hazard models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI).

**Results:** *PA before diagnosis:* There were no significant differences in HR of overall or breast cancer specific survival in women with breast cancer whether they had lower or higher PA levels before diagnosis compared to women with moderate PA level. *PA after diagnosis:* we found significant trends ( $P < 0.001$ ) of overall and breast cancer specific survival for PA levels higher than moderate after diagnosis of breast cancer. *PA changes from before diagnosis to after diagnosis:* Overall and breast cancer specific survival increased (HR for mortality = 0.61, 95% CI: 0.46, 0.81 and HR = 0.58, 95% CI: 0.42, 0.80, respectively) among women who had increased their physical activity level after breast cancer diagnosis as compared to those who reduced their PA level from before to after diagnosis.

**Conclusion:** Our study suggests that increasing levels of physical activity after a breast cancer diagnosis increase both overall and breast cancer specific survival.

**A7****Lifestyle as a predictor of colorectal adenomas in the bowel cancer-screening in Norway – a pilot project****Markus Dines Knudsen**<sup>1,2</sup>, Geir Hoff<sup>1,2</sup>, Thomas de Lange<sup>1</sup>, Paula Berstad<sup>1,2</sup>

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**Introduction:** High risk colorectal adenomatous polyps are considered as precursors for colorectal cancer (CRC). Results from previous studies have shown that lifestyle and dietary habits are associated with changed risk for colorectal cancer.

**Aims:** To study the association between lifestyle and colorectal low-risk adenomas and advanced neoplasia detected at screening for CRC.

**Methods:** In the Bowel Cancer Screening in Norway (BCSN) – a pilot project, 140.000 men and women were randomly assigned to Fecal Immunochemical Test for human blood (FIT) or flexible sigmoidoscopy (FS). A subgroup of 14,869 men and women (age 50-74 years) was invited to a lifestyle study and asked to fill in a short questionnaire on lifestyle when invited to screening. The questionnaire included questions on body height and weight, smoking, physical exercise, selected dietary items and alcohol use. The association between lifestyle factors and risk for low-risk adenomas and advanced neoplasia was analyzed. A multiple logistic regression was used to calculate odds ratio (OR) and 95% confidence intervals (95% CI).

**Results:** A total of 4799 screening attendees (2111 in the FS arm and 2688 in the FIT arm) responded in the lifestyle questionnaire. Low-risk adenoma was detected in 291 (6.1%), and advanced neoplasia in 238 (5.0%) of the screening attendees. Total consumption of fruit, vegetables and berries was inversely associated with risk of low risk adenoma (OR 0.90; 95% CI 0.81-0.99). Alcohol consumption above the national recommendations was associated with an increased risk of both low-risk adenomas and advanced neoplasia (advanced neoplasia OR 1.45; 95% CI 1.10–1.93). Smoking was associated with increased risk of advanced neoplasia (OR 2.39; 95% CI 1.66-3.68).

**Conclusions:** Consumption of fruit, vegetables and berries may protect from colorectal low-risk adenomas. Smoking and consumption of alcohol above national recommendations were associated with increased risk of colorectal advanced neoplasia.



## A8

### Maternal folic acid supplementation and cancer risk

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**Introduction:** The World Health Organization recommends women planning pregnancy to consume a daily dose of folic acid to reduce the risk of neural tube defects. However, there are concerns that folic acid supplementation may have a carcinogenic effect.

**Aims:** This study was conducted to examine the risk of maternal cancer after supplemental folic acid use in pregnancy.

**Methods:** A population-based cohort study was conducted comprising 429,004 women with data from the Medical Birth Registry, the Cancer Registry of Norway, and other national demographic registries in Norway from 1999 to 2010. Altogether, 3,781 women were diagnosed with cancer during follow-up. Cox proportional hazards regression models were used to estimate hazard ratios of maternal cancer according to folic acid use prior to and during one or two or more pregnancies as compared to no supplement use.

**Results:** Folic acid supplementation use had no overall effect on cancer risk in women using folic acid supplementation in one (HR 1.08; 95% CI 1.00 – 1.18) or two or more pregnancies (HR 1.06; 95% CI 0.91 – 1.22) ( $p_{\text{trend}}=0.12$ ). Further analyses of 14 cancer types revealed no strong associations between folic acid supplemental use and cancer.

**Conclusions:** Folic acid supplementation before and during pregnancy had no effect on overall cancer risk.

**A9****Investigation of unusual temporal patterns of cardiovascular diseases in Norwegian regions via Bayesian model choice – a CVDNOR study**

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**Introduction:** Statistical methods have been developed to analyze spatio-temporal prevalence rates and spatio-temporal clusters. The methods differ in how to group areas into clusters and depict temporal trends for areas with excess risk of disease risk (cluster). A new model is recently developed that identify areas with unusual temporal trends in small areas (BaySTDetect).

**Aims:** We have two aims. First, use BaySTDetect to identify temporal trends in cardiovascular disease among Norwegian regions. Secondly, validate BaySTDetect to identify spatio-temporal trends in health registries and its public health relevance.

**Methods:** The BaySTDetect model framework is split into two different models: the first will capture a main spatial pattern and main temporal trend for all areas. The second – which is named a specific trend – is designed to capture temporal trends for each area in the study area. Bayesian model choice criteria were used to evaluate which of the two models that best fits to the data. We studied cardiovascular disease (CVD) with ICD-10 codes I00 to I99, including cerebrovascular disease (CER) and coronary heart disease (CHD). We used data from the CVDNOR project. We used the time period 1998 to 2009 and we stratified on gender. We used regions as our geographic areas. Norway is split into 89 regions and they are designed to group municipalities into economic areas.

**Results:** The prevalence rates of cardiovascular disease show relatively steady trends during the time period for both genders. Regions with the largest prevalence rates during the first part of the period showed the largest reduction in prevalence rates. Many regions were identified as unusual and with a temporal trend different from Norway.

**Conclusions:** The BaySTDetect identified successfully unusual temporal trends among Norwegian regions. The method could be helpful in surveillance of disease rates and to improve public health.

## A10

### **Atrial fibrillation and risk of mortality among patients with cardiovascular disease in Norway**

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**Introduction:** The prevalence of atrial fibrillation (AF), now considered a strong determinant of stroke, is anticipated to increase as the population ages. However, little is known regarding the true prevalence of AF and determinants of mortality among patients with AF in Norway today.

**Aim:** To estimate the prevalence of AF and total mortality associated with AF among patients hospitalized with cardiovascular disease (CVD) in Norway over a 5-year period.

**Methods:** Patients with AF (ICD-10 code I48) as main or any secondary diagnosis were identified using data from the “CVD in Norway 2008-2012” which includes data on 393,787 hospitalized patients registered in the Norwegian Patient Registry, with supplemental data from the Cause of Death Registry, and data on level of education from Statistics Norway. Prevalence was calculated using the average Norwegian population for the period 2008-2012. Age and gender-adjusted OR for total mortality and 95% CIs were calculated for selected characteristics.

**Results:** A total of 109,236 patients had AF as main (N=70,456) or secondary (N=38,780) diagnosis during at least one hospitalization. The 5-year prevalence of AF ranged from 0.2%, 1.1%, 7.1%, to 19.3% for ages 20-40, 41-60, 61-80, and 80+ years, respectively. Catheter ablation was performed for 1,762 (1.6%) of AF patients. By the end of 2012, 25.6% of the patients with AF had died. Female gender was associated with lower mortality risk (OR=0.8; 95% CI 0.77-0.82), and high-school and higher education were associated with lower mortality risk compared to a primary education (OR=0.8; 95% CI 0.74-0.79 and OR=0.6; 95% CI 0.55-0.57, respectively). The presence of co-morbidities noted during the hospitalization (heart failure, diabetes mellitus, cerebrovascular stroke and acute myocardial infarction) increased mortality risk.

**Conclusion:** The prevalence of AF is high among those over 60 years of age and is an important consideration in the clinical management of patients with CVD.

## A11

### Is the increased risk of cardiovascular disease among patients with schizophrenia and bipolar disorder explained by presence of substance use disorders?

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**Introduction:** Cardiovascular disease (CVD) is more prevalent in patients with schizophrenia and bipolar disorder compared to the general population. This higher proportion of CVD may be attributed to use of alcohol and other substances of abuse.

**Aims:** To investigate if occurrence of substance use disorders may explain some of the increased risk of CVD among patients with schizophrenia and bipolar disorder.

**Methods:** Diagnoses of any CVD (ICD-10 codes I00-I99) and ischemic CVD (I20-I25) were retrieved for individuals born 1940-1979 and registered at least once with schizophrenia (F20, N=9831) or bipolar disorder (F30-F31, N=19038) in the Norwegian Patient Register in the period 2008-2013. Logistic regression models were fitted to estimate the odds ratio (OR) for CVD among patients with comorbid alcohol use disorder (F10, AUD) or non-alcohol drug use disorder (F11-F19, DUD) when controlling for age and sex.

**Results:** The prevalence of any CVD and ischemic CVD was 19.9% and 4.7%, respectively, among patients with schizophrenia, and 24.0% and 5.3%, respectively, among patients with bipolar disorder. Comorbid AUD was related to higher risk of any CVD in schizophrenia (OR=1.30; 95% CI, 1.09-1.55) and bipolar disorder (OR=1.20; 95% CI, 1.09-1.32), and comorbid DUD was related to increased risk of any CVD in bipolar disorder (OR=1.39; 95% CI, 1.25-1.54). Co-occurrence of DUD was related to higher risk of ischemic CVD in schizophrenia (OR=1.52; 95% CI, 1.14-2.02) and bipolar disorder (OR=1.67; 95% CI, 1.39-2.01).

**Conclusions:** Every fifth patient with schizophrenia and every fourth patient with bipolar disorder were also diagnosed with a CVD. Presence of AUD was related to increased risk of CVD and presence of DUD was related to increased risk of ischemic CVD in both schizophrenia and bipolar disorder.

## A12

### Hormone therapy use and the risk of breast cancer in Norway

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**Introduction:** There is solid evidence that hormone therapy with estrogen plus progestin (EPT) increases risk of breast cancer, and that this risk increase is substantially higher than that associated with estrogens alone (ET). Data are inconclusive on the differential effects of the various preparations available.

**Aim:** To assess the risk of breast cancer in women using different hormone therapies.

**Methods:** Nationwide retrospective cohort study including all women born in Norway 45-79 years in January 1, 2004, with no previous history of cancer, followed until December 31, 2008. The Norwegian Prescription Database provided individual exposure information to ET and EPT. Breast cancer incidence was gathered from the Cancer Registry of Norway. Poisson regression was used to estimate the incidence rate ratios (RR) associated with different hormone exposures.

**Results:** We analyzed data from 686,614 women. During an average of 4.8 years of follow-up (3.3 million women-years), 7,910 invasive breast cancers were detected. Compared with never users, users of ET had a RR of breast cancer of 1.19 (95%CI:1.10-1.29). Users of oral tibolone (Livial), and estradiol (Progynova) had an increased risk (RR:1.91; 95%CI:1.61-2.28, and 1.40; 95%CI:1.16-1.69, respectively). Users of EPT had a RR of 2.58 (95%CI:2.40-2.76). Both, users of fixed combinations and sequential preparations of EPT had an increased risk (RR:2.78; 95%CI:2.57-3.00, and 2.33; 95%CI:1.90-2.84, respectively). Users of the high dose EPT Kliogest (estradiol-norethisterone) had the highest risk of breast cancer (RR:3.26; 95%CI:2.85-3.73). The incidence rates of invasive breast cancer were 2.16 in non-users, 2.68 in ET users, and 5.60 in EPT users, per 1000 women-years. This approximates 1 extra invasive breast cancer for roughly every 1900 women taking ET and for every 290 women taking EPT each year.

**Conclusions:** Hormone therapy was associated with an increased risk of breast cancer, with the highest risk being associated with EPT users, and the high dose estradiol-norethisterone preparation Kliogest.

## A13

### **Risk factor profiles of women with endometrial and ovarian cancer in the Norwegian Women and Cancer Study (Kvinner og kreft)**

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**Introduction:** Endometrial and epithelial ovarian cancer have similar histological subtypes and similar risk factor profiles. We hypothesize that a shared etiology would imply that the hazard ratios of the two cancers with respect to shared risk factors will be similar. Relevant risk factors are mainly related to endogenous and exogenous hormone exposure through reproductive history, use of oral contraceptives and hormone replacement therapy.

**Aims:** The aim of this study was to obtain risk factor profiles of women with endometrial and epithelial ovarian cancer in the Norwegian women and cancer study population, which consists of 172 478 women born between 1943 and 1957.

**Methods:** Information on reproductive status and hormonal risk factor exposure was collected upon enrolment and during follow-up through self-administered questionnaires. During 20 years follow-up time there were 898 cases of invasive endometrial cancer and 555 cases of epithelial ovarian cancer. There were 150456 participants eligible for use as controls. Univariate and multivariate Cox proportional hazards regression was used to obtain hazard ratios for risk factors.

**Results:** Results with risk ratios for parity, breast feeding, oral contraceptive use, hormone replacement therapy, early/late menarche and early/late menopause, BMI and diabetes will be presented at the conference.

**Conclusions:** Will be presented at the conference.

## A14

### Genome-wide association study reveals two new susceptibility loci for testicular germ cell tumour

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**Introduction:** Epidemiological studies support the existence of a genetic component contributing to susceptibility of testicular germ cell tumour (TGCT), and to date 18 risk loci have been reported from genome-wide association (GWA) studies in UK and US populations. The incidence of TGCT is especially high in Western countries, and Norway has one of the highest incidence rates worldwide, twice as high as in the neighbouring country Sweden.

**Aim:** In this GWA study we aimed to identify additional genes important in the aetiology of TGCT, using a large Norwegian-Swedish population.

**Methods:** Saliva-derived DNA from 1326 Swedish and Norwegian TGCT cases was screened for 596,577 tagging SNPs using an Illumina HumanOmniExpressExome chip. After excluding known susceptibility loci, 34 SNPs from 17 regions [ $P < 10^{-4}$ ] were selected for replication in an independent sample set of 806 case-parent triads, 313 cases and 313 controls. Genotyping in the replication stage was performed on a MassARRAY iPLEX system. In addition, 12 of the most recently published regions were included in the replication. A fixed effect meta-analysis of the results from the screening and replication stages was performed. Effect modification by parent-of-origin and effect differences between seminoma and non-seminoma histological subtypes, were also explored.

**Results:** In the initial screening stage, strong enrichment for associated markers was observed, mainly attributable to established variants. Of the 17 novel regions taken forward for replication, two regions, 17q12 and 19q11, were genome-wide significantly associated with TGCT in the meta-analysis. In 17q12 the marker rs7501939 [per allele OR=1.29 (95% CI=1.19-1.40),  $P=1.1 \times 10^{-9}$ ] is situated in an intron of the HNF1B gene, encoding a member of the homeodomain-containing superfamily of transcription factors, and has previously been reported to be associated with prostate cancer. The rs2195987 marker [OR=1.31 (95% CI=1.19-1.45),  $P=3.2 \times 10^{-8}$ ] in 19p12 is intergenic. Of the 12 recently published markers, all but one (HPGDS) were significantly associated with TGCT in this study. No significant effect differences were found between seminoma and non-seminoma tumour types, neither was any parent-of-origin effect observed.

**Conclusion:** This GWA study of TGCT in a Scandinavian population reveals two new susceptibility loci at 17q12 and 19p12, bringing the total number of TGCT risk loci identified so far to 20. These loci should be followed up as promising candidates for functional studies.

## A15

### A Hierarchical Frailty Model for Familial Testicular Germ-Cell Tumors

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**Introduction:** Testicular germ-cell tumors (TGCTs) have been observed to cluster within certain families. This point to a large difference in risk between families, and individuals from different families. One way of quantifying such differences is by estimating *familial relative risks*. It is not given how such measures should be constructed, especially when considering *sibling risks*.

**Aim:** To construct a flexible model that took the family size, and the disease history for each member of the family into account when examining the risk of TGCT in family members of patients. Consequently, an aim was to give estimates of familial risks of TGCT for family constellations that had not previously been reported.

**Methods:** Using a 2-level hierarchical frailty model, we analyzed population-wide data on TGCT status in 1,135,320 two-generational Norwegian families. Follow-up extended from 1954 (cases) or 1960 (unaffected persons) to 2008. The first-level frailty variable was compound Poisson-distributed. The underlying Poisson parameter was randomized to model the frailty variation between families and was decomposed additively to characterize the correlation structure within a family.

**Results:** The frailty relative risk (FRR) for a son, given a diseased father, was 4.03 (95% confidence interval (CI): 3.12, 5.19), with a borderline significantly higher FRR for non seminoma than for seminoma ( $P = 0.06$ ). Given 1 affected brother, the lifetime FRR was 5.88 (95% CI: 4.70, 7.36), with no difference between subtypes. Given 2 affected brothers, the FRR was 21.71 (95% CI: 8.93, 52.76). These estimates decreased with the number of additional healthy brothers.

**Conclusion:** The estimated FRRs support previous findings. However, the present hierarchical frailty approach allows for a very precise definition of familial risk. These FRRs, estimated according to numbers of affected/nonaffected family members, provide new insight into familial TGCT. Furthermore, new light is shed on the different familial risks of seminoma and nonseminoma.



## A16

### Sunscreen use and risk of cutaneous malignant melanoma among women

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**Introduction:** Cutaneous malignant melanoma (CMM) is the most dangerous form of skin cancer and the leading cause of death from skin disease. The incidence of CMM had the highest increase amongst all cancer forms since cancer registration started in Norway in 1954. CMM is now the seventh most frequent incident cancer among Norwegian men and the sixth most frequent among Norwegian women. The current epidemiological evidence of the potential protective effect of sunscreen use to prevent skin melanoma is inconsistent.

**Aims:** To examine the association between sunscreen use and risk of CMM among Norwegian women.

**Methods:** In the Norwegian Women and Cancer (NOWAC) cohort study, we examine the association between sunscreen use and risk of CMM in women aged 40-70 years who completed mailed questionnaires including questions about sunscreen use at Easter holiday and in the summer in Norway or abroad in southern latitudes. The participants were asked about their natural hair and eye colours, skin colour, their history of solar exposure and use artificial tanning beds in different decades of life, skin sensitivity to sun exposure and number of nevi. Poisson regression is used to estimate the association between sunscreen use and risk of CMM.

**Results:** The study sample consists of 147,194 women. The mean age when answering the baseline questionnaire was 53 years (range 41-75 years). The average follow-up until December 2010 was 8.7 years (range, 0.002-13.46). During 1,281,941 person years of observation, 572 incident cases of melanoma were reported to the Cancer Registry of Norway. The mean age at diagnosis was 58.7 years (range, 42-81 years). The analysis is still in progress and we will present our new results in the conference.

## A17

### Norwegian Patient Register as a personally identifiable register: Five years of experience

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Norwegian Patient Register (NPR), the Norwegian Directorate of Health

**Introduction:** The Norwegian Patient Register (NPR) is a key Norwegian health register established in 1997 that covers all publically financed specialized health care. Since 2008, patient unique personal identification numbers have been included in the dataset. In the same period there has been a significant increase in applications for NPR data, from 144 in 2009 to 762 in 2013. In addition, an increasing number of applications link data from several registers. In 2013, 47 out of 61 projects which applied for personally identifiable data were linking data from different sources. In this paper we will review the body of applications for NPR data, and the most challenging aspects that have arisen from the extended use of NPR data.

**Aims:** We aim to identify the common denominators for applicants and projects, and the main challenges NPR is facing, when evaluating applications effectively.

**Methods:** Reviews of NPR's reports to the Norwegian Data Protection Authority between 2009 and 2013, and the experiences of NPR's current advisers at the Section of Data Deliveries (FISL).

**Results:** The results consist of a detailed description of the main challenges NPR is facing:

1. Legal challenges (whether the project and purpose is in accordance with the Norwegian Patient Register Regulation, and other relevant laws and regulations)
2. Relevance of data (whether NPR-data is relevant for the applicant's project)
3. Practical challenges (whether it is possible to find and extract the data)

**Conclusion:** As the number of applications increase, there seem to be a continually change in the profile of applicants and research projects. Notably, while NPR is an increasingly important and evolving source of data for researchers, there are new challenges that need to be addressed. This is important not only for the NPR, but for all the key registries in Norway.

## A18

### Validity and reliability of the Norwegian Stroke Register and stroke diagnosis in the Norwegian Patient Register

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**Introduction:** Medical registers can be a valuable source of data in epidemiological research. However, to be of use in research it is of utmost importance that the registers are valid and reliable.

**Aims:** The main aims of the present research project are to assess the completeness and correctness of stroke diagnoses among hospitalized patients in the Norwegian Patient Register and the Norwegian Stroke Register, and to assess the reliability of the Norwegian Stroke Register.

**Methods:** In order to assess the completeness and correctness of the two registers mentioned, we have studied approximately 5200 hospital stays at St. Olavs Hospital, Levanger hospital, Ålesund hospital and Kristiansund hospital, during the period of April through December 2012. We have extracted data from both the Norwegian Patient Register and the Norwegian Stroke Register, and subsequently two trained research nurses and one of the authors (TV) have reviewed the patients' medical records. Specific criteria were set up to classify the diagnosis as stroke, possible stroke, or no stroke. In cases of uncertainty, an experienced clinician has reviewed the record and determined whether a stroke has occurred. Sensitivity (true positive rate) and specificity (true negative rate) will be calculated per hospital and as sum total.

Furthermore, inter-rater reliability is an important measure in determining how well implementation of a register works. The Norwegian Stroke Register has recently become a national, compulsory register for all hospitalizations with a stroke diagnosis. To investigate the reliability of the register, two experienced nurses have independently of each other entered data on all variables in the Stroke Register for 120 randomly chosen patients. To assess the inter-rater reliability we will use the Cohen's kappa statistics for two raters and a fully crossed design.

**Results:** Data collection is completed and we expect to present the first results from the study by the end of 2014.

## A19

### Quality and transparency of data, – a Case from Iceland

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**Introduction:** Prescription databases with good quality assurance systems are a valuable source of information on use of prescription medicines. The Icelandic Medicines Registry was established by law in 1994, under the auspices of the Icelandic Directorate of Health, and was considered to be fully functioning in 2005.

**Objectives:** To describe coincidental quality issues found in the Icelandic Medicines Registry and consequential actions aiming at mending them.

**Methods:** In August 2011 severe and seemingly random errors in DDD definitions were uncovered in the Icelandic Medicines Registry, leading to a mapping of all DDD definitions used in the database, except DDDs for products that had no registered use in Iceland. Another type of quality concern arose in November 2011, revealing problems in handling of retracted prescriptions, i.e. they stayed in the database. These revelations raised questions about quality in general (assurance and monitoring).

**Results:** The mapping of the DDD definitions revealed discrepancies from the WHO defined DDDs in ~ 10-20 % of the mapped nordic codes (NVnr, unique identifiers for all package sizes and formulations of marketed medications), depending on whether „0“ instead of „“ counted as an error and on what size of difference counted as a discrepancy. The frequency of retractions was ~ 0,1-0,2% of dispensed prescriptions. One single prescription containing 72.712 packages was retracted because it should have contained one package, revealing a dysfunctional alert on high number of items per prescription. Frequency of retractions therefore does not reflect directly to potential magnitude of errors caused by them. Attempts for a couple of years to get the Icelandic Directorate of Health to act on these errors, and/or open the data to analysis for researchers have had limited success.

**Conclusion:** As regards the Icelandic Medicines Registry, there is room for improvement in handling of quality assurance and assessment.

## A20

### Validation of referral information for elective treatment in hospitals to discharge diagnosis

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**Introduction:** Norway introduced priority guidelines for 32 medical fields for elective treatment in the hospitals in the period 2008-2009. Expert groups for each medical field selected a number of conditions for prioritized or non-prioritized treatment influencing waiting time for medical treatment of 399 conditions. The assessment and definition of the conditions were based on clinical signs and symptoms.

**Aims:** The evaluation of the introduction of these guidelines was commissioned by the Directorate for Health to the Knowledge Centre. Data from the Norwegian Patient Registry (NPR) was used. NPR register discharge information of diagnoses by ICD-10 codes. As sufficient information about the referrals was not available in NPR for the study period of 2008-2012, a validation study was undertaken to assess agreement between referral information and hospital discharge diagnoses by a medical record review.

**Methods:** The study took place at four major hospitals, Universitetssykehuset Nord-Norge HF, Akershus universitetssykehus HF, Haukeland universitetssjukehus HF og St.Olavs Hospital, Universitetssykehus I Trondheim. Twenty conditions of ten guidelines were finally selected for review. The agreement between referral information and discharge diagnosis was grouped as 1) Clear agreement between referral and discharge, 2) Poorly formulated referral, 3) Not sufficiently specific but adequate, 4) No agreement. In all, 1854 medical records were reviewed.

**Results:** Overall, the sensitivity was 0.93 (95% confidence interval 0.92 to 0.94). The diagnostic precision measured in the four categories was significantly different between hospitals and overall for 2008, 2009 and combined.

**Conclusions:** Although a limited number of conditions were assessed, we believe the sensitivity of a range of conditions across ten guidelines were sufficiently in agreement allowing the use of NPR data for the main study.

Also presented at ISQua Conference, Rio de Janeiro, Brazil, 6.-8. October 2014.

## A21

### Was it an acute myocardial infarction?

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**Introduction:** Acute Myocardial infarction (AMI) is one of the leading diseases worldwide. Early and correct diagnosis is a key to optimal treatment and prognosis. Cardiac biomarkers together with clinical symptoms and ECG-abnormalities have been important features of the AMI diagnosis. The biomarker troponin is myocardial tissue-specific, and extra sensitive imaging techniques have made it possible to detect very small amounts of myocardial injury or necrosis. As the marker has become more sensitive, its specificity has become poorer and it will arise also in other conditions than AMI. This may threaten the usefulness of registers containing data about patients with myocardial infarction.

**Aim:** Investigate the completeness (true positive rate) and correctness (true negative rate) of the myocardial diagnosis in Norwegian Myocardial Infarction Register (NorMI) and Norwegian Patients Register (NPR). Investigate conditions for troponin elevation and differences in level of troponins.

**Method:** All patients admitted directly to St. Olavs Hospital with measured values of troponin in the period 1.7.2012 -31.12.2012 are included in the study. From the patient journals we made a “gold standard for AMI” based on levels of troponin, clinical symptoms, and ECG/imaging abnormalities. We also included information on other conditions prior to troponin elevation. The gold standard will be compared to NorMI and NPR as soon as we have the data available.

**Preliminary results:** Within the six month period over 14 600 samples of troponin were taken, distributed on 6 655 patients. Among patients with troponin over detected value (>30 ng/L) and with St. Olavs Hospital as primary hospital, only 23% got the diagnosis AMI. Comparing with the gold standard, we found about 75 % completeness and 100 % correctness in the patient journals. We have not yet compared the diagnosis in NorMI and NPR. Further results will be published in early 2015.

## B1

### CFS/ME in Norway after infection with pandemic H1N1 influenza virus and H1N1 vaccination

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**Introduction:** The etiology of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is unknown, and the distribution of CFS/ME in the population has so far not been well described. The condition has been linked to both infections and autoimmunity.

**Aims:** We wanted to estimate sex- and age-specific incidence rates of CFS/ME in Norway using population-based registry data. Another aim was to study associations between H1N1 influenza infection and H1N1 vaccination during the 2009 influenza pandemic and development of CFS/ME in the Norwegian population.

**Methods:** We linked information from several nation-wide registries to estimate incidence rates of CFS/ME. Cox regression models estimated the risk of CFS/ME in the follow-up period from October 2009 through December 2012 according to exposure to pandemic influenza and vaccination with Pandemrix.

**Results:** There were 5,797 patients registered in the Norwegian Patient Register with CFS/ME during 2008-2012, with 3,846 new cases from October 2009 through 2012. The incidence rate varied with age, with a first peak in the age group 10-19 years and a second peak from 30-39 years. Among the new CFS/ME cases, 38.7% had been vaccinated with Pandemrix, compared to 39.2% in the rest of the population, resulting in a hazard ratio (HR) of 0.97 (95% confidence interval [CI]: 0.91-1.04) for CFS/ME after vaccination. A total of 5.9% of new CFS/ME cases were diagnosed with influenza during the pandemic compared to 2.5% of the rest of the population (HR=2.04, 95% CI: 1.78-2.33).

**Conclusion:** CFS/ME has two age peaks in the population. Our results suggest that infection with the pandemic influenza virus increased the risk of CFS/ME. Pandemic vaccination did not appear to influence the risk.

**B2****The Norwegian influenza cohort study (NorFlu): immune responses in H1N1pdm exposed versus non-exposed pregnant women**

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**Introduction:** Consequences of in utero exposure to influenza are largely unknown. In Norway, a cohort of pregnant women and their children, the Norwegian Influenza Pregnancy Cohort (NorFlu), was established during the influenza pandemic in 2009. The cohort comprises about 3200 mother and child pairs of which 2600 paired biological samples were collected. Information on immunization, health and diseases is available from questionnaires and national health registries.

**Aims:** The specific aim of this study was to analyze the correlation between humoral and cellular responses to influenza exposure and the risk of influenza illness symptoms (ILI).

**Methods:** A nested case-control study among women who were not vaccinated against H1N1pdm was initiated. Selection criteria for the cases were: pregnancy in the first trimester corresponding to the main pandemic peak (October to December 2009), and hemagglutination inhibition assay (HAI) titer values equal or above 20. Controls were randomly selected among the women who were pregnant during the same time period with HAI=0, and no reported ILI.

**Results:** Based on the inclusion criteria 82 cases and control pairs were selected. The median value of the HAI titers for the cases was 40 (range from 20 to 320). Among the cases 51% reported ILI: fever and cough and/or sneezing. Antibody level was not associated with risk of experiencing ILI. Exposed women had significantly higher numbers of IFN $\gamma$  producing cells than non-exposed women. Exposed women reporting symptomatic influenza illness had significantly lower levels of CD8 T-cell responses compared to non-exposed women.

**Conclusions:** Preliminary analyses indicate no significant correlation between antibody levels and the risk of experiencing ILI. Specific subset of CD8 T-cells correlated with reduced illness severity among exposed women. The NorFlu cohort provides a unique opportunity to establish correlates of protection against symptomatic pandemic influenza during pregnancy.



**B3****Seasonal and Pandemic Influenza Infection and Preterm Birth:  
A Population-Based Registry Study**

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**Introduction:** Previous studies have shown that exposure to influenza and high fever-related maternal diseases during pregnancy is associated with increased risk of adverse pregnancy outcomes such as preterm birth, fetal death, neural tube defects, and multiple congenital abnormalities. However, findings are not consistent across studies.

**Aims:** The primary aim of our study was to use Norwegian population-based health registry data to assess the association between seasonal and pandemic influenza infection during pregnancy and risk of preterm birth, defined as gestational length less than 37 weeks. Seven different influenza seasons in the period of 2006–2012 (including the 2009 “swine flu” influenza pandemic) were to be explored.

**Methods:** The study sample ( $n = 401,672$ ) comprised singleton births from 2006 through 2012, as registered in the Medical Birth Registry of Norway. Data on influenza infection were obtained from the Directorate of Health (information based on health reimbursements from primary care physicians) and the Norwegian Surveillance System for Communicable Diseases. Cox regression models with time-varying covariates were fitted to estimate crude and adjusted hazard ratios of preterm birth, with associated 95% confidence intervals, for influenza infection during pregnancy. Potential confounders were identified and included in the regression models.

**Results:** Preliminary results indicate no effect of influenza infection during pregnancy on the risk of preterm birth for any of the influenza seasons under study.

**Conclusions:** Seasonal and pandemic influenza infection during pregnancy does not seem to be associated with increased risk of preterm birth.

**B4****Perinatal outcomes and children's health after prenatal exposure to influenza and influenza vaccination**

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**Introduction:** The Norwegian Influenza Pregnancy Cohort (NorFlu) was established in 2009 during the influenza A H1N1 pandemic. Women who were pregnant during the pandemic were recruited. The cohort comprises about 4000 mother and child pairs.

**Aims:** The primary aims are to study

- 1) perinatal outcomes
- 2) children's mental and cognitive development
- 3) maternal immune response and risk factors for severe influenza in pregnancy according to prenatal exposure to influenza infection or immunization.

**Methods:** Questionnaires provide information on numerous covariates, exposures and health outcomes from pregnancy onwards. Follow-up questionnaires at 6, 18 and 36 months have been collected so far. Biological samples from mother and cord blood were drawn at delivery. Clinical assessment in a sample of 4-year old children (N=600) focusing on cognitive and developmental health is ongoing. The possibility of using cellular immune responses as biomarkers for infection and vaccination status is explored.

**Preliminary results:**

- 15 % of the women reported influenza during pregnancy
- 1.5% of the mothers were hospitalized due to influenza
- 40 % of the maternal blood samples had protective HI titers
- 57 % were vaccinated against influenza (Pandemrix)
- 2 % reported use of antiviral medication

**Conclusions:** Short and long-term consequences of exposure to influenza in utero clearly need to be clarified, as do the potential modifying effects of vaccination or anti-viral treatment. The relative importance of antibody-mediated as compared to cell mediated immunity in the protection against influenza, is unclear. Furthermore, the impact of the specific immunological challenges in pregnancy on women's immunological response to influenza infection is largely unknown. Providing unique data including maternal and fetal biological samples, NorFlu has the potential to contribute significantly in increasing our knowledge in these fields.

**B5****Pandemrix vaccination or infection with pandemic influenza A(H1N1)pdm09 and risk of Guillain-Barré syndrome**

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**Introduction:** Guillain-Barré syndrome (GBS) is a rare but serious disease in which the immune system attacks nerve cells causing muscle weakness, paralysis, and in some cases death. The causal mechanisms of GBS are not known, but GBS may be triggered by respiratory infections such as influenza. Concerns regarding development of GBS after influenza vaccination were first raised during the influenza epidemic in 1976-1977 in the United States. However, studies of vaccinations and GBS show contradictory results.

**Aim:** The aim of the current study was to explore the association between exposure to the influenza A(H1N1)pdm09 infection or Pandemrix vaccination and occurrence of GBS.

**Methods:** The total Norwegian population in 2009 was included as our study cohort. Information regarding vaccination, influenza, and GBS diagnosis were obtained from the National registries; the Norwegian Immunisation Register (SYSVAK), Directorate of Health for reimbursement data (KUHR), the Norwegian Surveillance System for Communicable Diseases (MSIS), and the Norwegian Patient Register (NPR). Cox regression analysis with time-varying covariates was used to estimate risk of GBS in a 42-day period following influenza A(H1N1)pdm09 infection or after vaccination with Pandemrix.

**Results:** At the onset of the influenza pandemic in 2009, there were 4,840,084 persons residing in Norway. An influenza diagnosis was recorded for 3% of the population, and vaccination coverage in the total population was 41 %. There were 410 new GBS cases registered between October 1<sup>st</sup> 2009 and December 31<sup>st</sup> 2012. The adjusted hazard ratio (HR) of GBS after an influenza diagnosis was 4.89 (95% confidence interval (CI): 1.17-20.36) and the HR after vaccination was 1.11 (95% CI: 0.51-2.43).

**Conclusion:** Infection with pandemic influenza was associated with a fivefold increased risk of GBS. Vaccination with Pandemrix, on the other hand, was not associated with an increased risk of GBS.

**B6****Neck and low back pain in parents and their adult offspring: family linkage data from the Norwegian HUNT Study****Ragnhild Lier**<sup>1,2</sup>, Tom Ivar Lund Nilsen<sup>1</sup>, Ottar Vasseljen<sup>1</sup>, Paul Jarle Mork<sup>1</sup>

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**Introduction:** Chronic pain in the neck and low back is highly prevalent. Although heritable components have been identified, knowledge about generational transmission of spinal pain between parents and their adult offspring is sparse.

**Aims:** The aim of the current study was to investigate the parent-offspring association of chronic pain localized to the neck, low back, or both (multilevel spinal pain). Further, mother-offspring and father-offspring associations were compared, and possible effect modification by offspring sex and age was assessed.

**Methods:** This study examined the intergenerational association of spinal pain using data from 11 081 parent-offspring trios participating in the population-based HUNT Study in Norway. Logistic regression was used to calculate adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for offspring spinal pain associated with parental spinal pain.

**Results:** In total, 3654 (33%) offspring reported spinal pain at participation. Maternal and paternal spinal pain was consistently associated with higher ORs for offspring spinal pain. The results suggest a slightly stronger association for parental multilevel spinal pain than for pain localized to the neck or low back. Multilevel spinal pain in both parents was associated with ORs of 2.6 (95% CI, 2.1-3.3), 2.4 (95% CI, 1.9-3.1), and 3.1 (95% CI, 2.2-4.4) for offspring neck, low back, and multilevel spinal pain, respectively.

**Conclusions:** Parental chronic spinal pain was consistently associated with increased occurrence of chronic spinal pain in their adult offspring, and this association was particularly strong for multilevel spinal pain. The parent-offspring association of chronic spinal pain was not modified by parental sex, offspring sex, or offspring age.

**B7****Psychosocial factors and risk of chronic widespread pain: An 11-year follow-up study (The Nord-Trøndelag Health Study)**

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**Introduction:** Few studies have used prospective designs in large population surveys to assess the risk of developing chronic widespread pain (CWP).

**Aims:** We wanted to examine (1) how many persons without CWP developed it after 11 years and (2) how anxiety, depression, alcohol use, smoking, sleeping problems, and body mass index (BMI) were associated with this development.

**Methods:** This study was based upon a representative population-based Norwegian cohort attending both the second (1995–1997) and the third (2006–2008) wave of the Nord-Trøndelag Health Study (HUNT2 and HUNT3, respectively). Only those adults attending both surveys (N = 28,367) were included. Approximately 19,000 individuals without CWP in HUNT2 were assessed for later CWP development in HUNT3, where we looked for symptoms of anxiety, depression, monthly frequency of alcohol use, smoking, sleeping problems, and BMI.

**Results:** Data were analysed with logistic regression adjusted for age, sex, education, marital status, physical exercise, and pain symptoms not meeting the CWP criteria at baseline. Twelve per cent of those without CWP developed CWP after 11 years. Anxiety and depression, former and current smoking status, BMI < 18.5 kg/m<sup>2</sup>, BMI ≥ 25 kg/m<sup>2</sup>, and sleeping problems, were all associated with an increased risk of CWP. High and moderate levels of alcohol use were associated with a reduced risk of CWP.

**Conclusions:** In summary, this study indicates that CWP develops over a long-term period for a substantial group of healthy people, and that both psychosocial and lifestyle factors influence the risk of CWP onset.

**B8****Mental distress is a predictor for disabling multisite pain only in combination with obesity or sleep problems****Karin Magnusson<sup>1</sup>, Kåre Birger Hagen<sup>1,2</sup>, Bård Natvig<sup>3</sup>**<sup>1</sup>National Advisory Unit for Rehabilitation in Rheumatology, Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway<sup>2</sup>Department of Health Sciences, Institute of Health and Society, University of Oslo, Norway<sup>3</sup>Department of General Practice, Institute of Health and Society, University of Oslo, Norway

**Introduction:** Multisite pain (MSP) is more disabling than single-site pain. Disabling MSP is an important dimension of chronic widespread pain. Obesity, mental distress and sleep problems predict chronic widespread pain, however these factors' relative and additive predictive effects as well as their contribution to disabling MSP are unknown.

**Aims:** To identify what subgroups have the highest risk of incident MSP.

**Methods:** Persons aged 34-78 years in 2004 with no MSP at baseline participated in surveys in 2004 and 2010 (N=1137). Incident MSP was defined as reporting  $\geq 2$  pain sites on the Standardized Nordic Questionnaire (disabling pain in ten body regions the last year). Obesity was defined as BMI  $\geq 27$  kg/m<sup>2</sup> and mental distress as a General Health Questionnaire-20 sumscore of  $\geq 17$ . Sleep quality was dichotomized into good and poor. We analysed single and combined predictors using multivariate logistic regression adjusted for age, sex and education level. The reference category was no present risk factors (RF) at baseline in all analyses.

**Results:** Baseline mean (SD) age was 51 (12.5) years and 56% were women. 156 (13.7%) participants got incident MSP at follow-up. The presence of more RF at baseline predicted incident MSP (OR<sub>1 RF</sub>, 1.45, 95% CI, 0.84, 2.49, OR<sub>2 RF</sub>, 3.12, 95% CI, 1.84, 5.27, OR<sub>3 RF</sub>, 4.44, 95% CI, 2.31, 8.51). In analyses of specific combinations, only being obese and mentally distressed as well as being mentally distressed and sleeping poorly were significant predictors (OR, 2.78, 95%CI, 1.22, 6.32 and OR, 3.69, 95% CI, 2.11, 6.46, respectively). No single RF predicted incident MSP when adjusted for the other risk factors.

**Conclusions:** Obese, mentally distressed, poorly sleeping people had a 400% higher risk of incident MSP compared to persons with no risk factors. Participants having mental distress had the highest MSP risk, but only in combination with obesity and/or sleep problems.

**B9****Infections and the duration of full or partial breastfeeding; results from the MoBa cohort study**

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**Introduction:** Breastmilk contains factors important for immunity. However, the benefit of full compared to partial breastfeeding the first 6 months and the duration of any breastfeeding as infection prevention in an affluent society is unclear.

**Aims:** To study the association with time of complementary food introduction and risk of hospital admission for infections in infants still breastfed at six months, and whether duration of any breastfeeding was associated with the risk for infections.

**Methods:** In The Norwegian Mother and Child Cohort Study recruiting from 1999-2008, questionnaires were completed at 6 and 18 months of age regarding infant diet and the occurrence and hospitalization for infections. 85 494 participated at six months' age and 70 511 up to 18 months', of whom 25 434 and 22 517 belonged to sibling sets.

**Results:** Hospitalization due to infections during 0-6 months occurred in 3.1% of infants partially breastfed for at least 6 months compared to 3.5% of those fully breastfed for 6 months (adjusted RR 0.94, 95% CI 0.85-1.05). Introduction of solids from 4-5 months was associated with a reduced risk for hospitalization (adjusted RR 0.88, 95% CI 0.80-0.97) compared to full breastfeeding. Higher risk of hospitalization for infections was observed in those breastfed  $\leq$  6 months (10.0%) compared to  $\geq$ 12 months (7.6%, adjusted RR 1.22, 95% CI 1.14-1.31), but with no significant difference for 6-11 months (8.2%, adjusted RR 0.97, 95% CI 0.91-1.03). Within siblings, significantly reduced risk was found only for gastroenteritis and full breastfeeding up to 4 months and partial breastfeeding up to 6 months.

**Conclusions:** Breastfeeding six months or less was associated with a higher risk for infections compared to those breastfed  $\geq$ 12 months. Time for introduction of complementary foods during ongoing breastfeeding seems to be of limited importance in a high-income society to prevent infections.

**B10****Infant feeding and risk of childhood-onset type 1 diabetes: preliminary data from the PAGE-study**

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**Introduction:** Changing incidence and other lines of evidence strongly suggest a role of non-genetic factors in the aetiology of type 1 diabetes, and infant feeding has been hypothesized to influence the risk. The few prospective studies in the field have mostly been small or had limited information on infant feeding.

**Aims:** We aimed to study the association between breastfeeding and age at introduction of solid foods with the risk of type 1 diabetes.

**Methods:** Infant feeding was ascertained using mailed questionnaires when the child in The Norwegian Mother and Child Cohort Study was aged 6 and 18 months. Among 73,385 children born 1999-2009 with data on infant feeding (68% of eligible children), 179 were diagnosed with type 1 diabetes by 2013, according to register linkage to the Norwegian Childhood Diabetes Registry and the Norwegian Patient Register.

**Results:** Using full breastfeeding  $\geq 6$  months as the reference, the odds ratio for those never fully breastfed was 0.90 (95% CI: 0.53-1.54), 0.1-3.9 months 0.97 (95% CI: 0.58-1.60), and 4.0-5.9 months 0.94 (95% CI: 0.60-1.47), when adjusting for gender, birth weight, gestational age, cesarean section, maternal smoking in pregnancy and maternal diabetes. Using any breastfeeding  $\geq 12$  months as the reference, the odds ratio for those never breastfed was 1.97 (95% CI: 0.61-6.36), and there was no significant association for the other categories. Using introduction of solid foods 4.0-5.9 months as the reference, there was no significant association between early ( $< 4$  months of age) or late ( $\geq 6$  months of age) introduction and risk of type 1 diabetes in any of the food groups.

**Conclusions:** In this unique, population-based cohort study, we found no significant association of infant feeding practices and risk of type 1 diabetes in early childhood.



## B11

### **Grand-maternal smoking when pregnant with the mother and the grand-child's risk of developing asthma: the Norwegian Mother and Child Cohort Study**

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**Introduction:** Findings indicate a potential trans-generational influence of prenatal smoke exposure on asthma development but the current evidence remains inconclusive.

**Aim:** To examine the association of grand-maternal smoking when pregnant with the mother and development of asthma in the grand-child.

**Methods:** This study examined the associations of grand-maternal smoking with current asthma at 36 months (N=53,169) and current asthma at 7 years (N=25,394) in the grand-child using the Norwegian Mother and Child Cohort Study. We used log binomial regression to calculate adjusted relative risks (adj. RR) and 95% confidence intervals (CI).

**Results:** A total of 23.5% of mothers reported that their mother smoked when pregnant with them, while 9.6% of mother reported "don't know". Grand-maternal smoking was positively associated with asthma at 36 months, adj. RR 1.15 (95% CI: 1.06, 1.24), and asthma at 7 years, adj. RR 1.21 (95% CI: 1.07, 1.37), in the grand-child. Stratifying by the mother's own smoking during pregnancy, grand-maternal smoking showed the strongest positive association with asthma development among children of mothers who reported smoking before pregnancy, with a weaker association among mothers of children reported never smoking themselves, and no association among children of mothers who smoked during pregnancy. However, the test for multiplicative interaction was not statistically significant (p-value >0.1).

**Conclusions:** Grand-maternal smoking when pregnant with the mother showed a positive association with asthma development in the grand-child. However, we cannot exclude the possibility of residual confounding.

## B12

### The Health and Memory Study: Occurrence of Dementia in the Nord-Trøndelag Health Study

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**Introduction:** Three cross-sectional studies were conducted and known as The Helse Undersøkelse av Nord-Trøndelag (HUNT ) Study, which was initially undertaken in 1984-1986 of all county residents age 22 and over.

**Aims:** The Health and Memory Study (HMS) was initiated in 1995 to observe dementia in this population of Nord-Trøndelag.

**Methods:** In HUNT1, 75,024 individuals were enrolled to establish the prevalence of vascular diseases. HUNT2 was initiated in 1995-1997 with a similar enrollment, 45,000 of whom also participated in HUNT1. Between 2006 and 2008, HUNT3 was conducted, and included 75% of those surveyed in HUNT2. HMS-HUNT (n=1233) links dementia cases from these two studies discovered between 1995 and 2011 from two regional memory clinics and 24 municipal nursing homes. Dementia diagnoses were all adjudicated by a panel of geriatricians using ICD-10 criteria. We estimated the period prevalence using the end-point of the study and present findings stratified by whether cases were ascertained in the community or institutions.

**Results:** 1,233 participants were diagnosed with dementia within the HUNT-HMS study period. Of these, 644 were diagnosed with Alzheimer's Disease (AD), 219 Vascular Dementia (VaD), 124 mixed AD/VaD and 246 other dementias. Of the original participants of HUNT1 and alive in 1995 (n=64,175), there were 29,679 participants included in the present study, whereas 18,611 were excluded due to death prior to the start of the study period and 15,885 were under the age of 60 as of March, 2011.

**Conclusions:** In Norway, the prevalence rates for dementia increased with age and appear higher in women, as in other studies in Europe and North America. However, the rates were lower than expected, likely due to under-ascertainment of residents living at home who may not have been diagnosed. This underscores the importance of community based ascertainment in studies of dementia.

**B13****Anxiety and depression symptoms among farmers. The HUNT Study, Norway**

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**Introduction:** Farming is associated with a number of occupational stressors, and the industry has undergone major changes over the past decades. Previous research suggests that farmers are at risk of mental health problems, but the results remain inconclusive.

**Aim:** Our aim was to study the levels of anxiety and depression among farmers compared to other occupational groups.

**Methods:** Working participants in the HUNT3 Survey (The Nord-Trøndelag Health Study, 2006-2008), aged 20-66.9 years, were included in this cross-sectional study. We compared farmers (women n=317, men n=1,100) with HUNT3 participants working in other occupational groups (women n=13,429, men n=10,026). We classified the general working population according to a simplified version of the Erikson-Goldthorpe-Portocarero social class scheme. We used the Hospital Anxiety and Depression Scale (HADS) to measure anxiety and depression symptoms.

**Results:** Both male and female farmers had higher depression levels than the general working population, but the anxiety levels did not differ. The differences in depression levels between farmers and the general working population increased with age. In an age-adjusted logistic regression analysis, the odds ratio (OR) for depression caseness (HADS-D  $\geq$ 8) when compared to the general working population was 1.49 (95% confidence interval (CI) 1.22-1.83) in men and 1.29 (95% CI 0.85-1.95) in women. Male farmers had a higher risk of depression caseness than any other occupational group (OR 1.94, 95% CI 1.52-2.49, using higher grade professionals as reference). Female farmers had an OR similar to men (2.00, 95% CI 1.26-3.17), but it was lower than other manual occupations.

**Conclusions:** We found that farmers had high depression levels and average anxiety levels compared to other occupational groups. The depression levels of male farmers cannot be explained by a socioeconomic gradient in mental health.

**B14****The effect of physical activity on mental health problems and well-being among Norwegian adolescents with self-perceived visual impairment – The Young HUNT study****Audun Brunnes**<sup>1</sup>, W. Dana Flanders<sup>2</sup>, Liv Berit Augestad<sup>1</sup>

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**Introduction:** Health and health-related behaviours among adolescents should be a prioritized area due to major health challenges emerges in that period of life. Among adolescents with self-perceived visual impairment, however, no studies to date have been carried out to examine the possible promoting and preventive mental health effects of physical activity.

**Aim:** To examine underlying causal effects of physical activity on symptoms of mental health problems and subjective well-being among adolescents with self-perceived normal vision and visual impairment.

**Methods:** The first wave of the study was conducted in Nord-Trøndelag, Norway, during the period 1995–1997, with a follow-up four years later. The sample consisted of 1,417 adolescents aged 12–17 years, whereas 46 of those reported severe visual impairment. General and generalized regression models were used to assess the association of reported vision-specific differences in the baseline levels of physical activity with symptoms of mental health problems and subjective well-being at follow-up.

**Results:** Adolescents with self-perceived visual impairment had on average worse mental health scores and lower physical activity levels at baseline than adolescents with self-perceived normal vision. Those that reported normal vision and less than 1 day per week of physical activity had more mental health problems and lower levels of well-being four years later than those with a higher frequency of activity. However, the differences in mean mental health scores between levels of physical activity were relatively small. Among adolescents that reported visual impairment, these above-mentioned associations were statistically significant among those scoring more towards neuroticism or introversion.

**Conclusions:** Personality could be a possible associative factor in the physical activity-mental health relationship among adolescents that evaluate their impairment in seeing as severe.

**B15****Acute medication poisoning in adolescents: A national register study of hospital admissions and readmissions****Elin Anita Fadum**<sup>1,2</sup>, **Barbara Stanley**<sup>1,3,4</sup>, **Ping Qin**<sup>1</sup>, **Lien My Diep**<sup>1,5</sup>, **Lars Mehlum**<sup>1</sup>

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**Introduction:** Adolescents who ingested a harmful dose of medications are frequently seen in acute hospital settings in Western countries. Usually, these cases represent either accidental overdoses with recreational drugs or intentional self-harm. The risk of repetition is high. Repeated episodes of poisoning constitute severe distress for the patients, a substantial use of health care resources and are associated with an elevated risk of suicide or other premature death. Studies based on national registers may provide updated knowledge of what characterizes those adolescents who are repeatedly re-hospitalized for medication poisoning.

**Aims:** To examine characteristics of hospital admissions and risk-factors associated with re-hospitalization for medication poisoning in adolescents aged 10–19 years.

**Method:** This study used data from the Norwegian Patient Register (NPR) from 2008 to 2011. The main outcome was hospital readmission within this observation period. A complementary log-log regression model was used to fit the data and assess the effect of characteristics at index hospital admission on readmission, estimating hazard ratios (HR) with 95% CIs for covariates having an effect on readmission.

**Results:** Of 1,497 patients, 76.4% were females and 89.8% were aged 15–19 years. At their first hospital admission, one-third received a secondary psychiatric diagnosis and 44.2% received an E-code for intentional self-harm. However, in 51.2% of the females and in 63.5% of the males an E-code for intentionality was not recorded. Nearly one-fifth of the adolescents (18.4%) were re-hospitalized for poisoning by medications. In multivariate analyses, significant predictors for hospital readmission were female sex (HR=2.4, 95% CI 1.7, 3.6), discharge to further treatment (HR=2.3, 95% CI 1.8, 2.9) and psychiatric secondary diagnoses (HR=1.5, 95% CI 1.2, 1.9).

**Conclusion:** In this national study of hospital admissions for medication poisoning in adolescents the majority were females aged 15–19 years. Risk of re-hospitalization was high. Female sex and psychiatric disorders had a strong predictive effect on readmission.

**B16****The Epidemiology of Post-Traumatic Stress Disorder in Norway****Eva Lassemø**<sup>1,2,3</sup>, **Knut Sørgaard**<sup>1,2</sup>, **Inger Sandanger**<sup>2</sup><sup>1</sup>) Nordland Hospital, Bodø, Norway<sup>2</sup>) University of Tromsø, Norway<sup>3</sup>) SINTEF Technology and Society, Health, Trondheim, Norway

**Introduction:** Post-traumatic stress disorder (PTSD) is probably as old as mankind, and has been referred to in literature throughout time. According to international epidemiologic research, 20-90% of the general population is exposed to PTSD level trauma in their life-time. However, only a fraction develops PTSD. Life-time prevalence rate of PTSD is consistently higher in women than in men. This despite the fact that men are consistently more frequently exposed to trauma than women.

**Aims:** Using a Norwegian population sample study, the aim of the present study was to determine lifetime prevalence of exposure to traumatic events as well as PTSD by gender.

**Methods:** Data were from 1,634 men and women, aged 18 and above, participating in the OsLof (Oslo and Lofoten) study. To obtain an accurate diagnosis based on ICD-10 criteria an updated electronic version – CIDI-M 1.1, of the Composite International Diagnostic Interview (CIDI) was used. We included reaction to severe stress, and adjustment disorders (ICD-10 code F43.1).

**Results:** Women and men were exposed to different types of traumatic events. Women were to a greater extent exposed to rape ( $p < 0.001$ ) and sexual abuse ( $p = 0.006$ ). Within the "other" category, women were exposed to more verbal threats/ violence from close relations ( $p < 0.001$ ). Contrary, men were to a greater extent exposed to war events ( $p = 0.007$ ), serious accidents ( $p < 0.001$ ), imprisonment etc. ( $p = 0.001$ ), and witnessed traumatic events happen to others more often ( $p < 0.001$ ). Although men were at a greater risk of exposure to traumatic events, women were four times more likely to meet criteria for PTSD. Of those exposed to traumatic events, 20.4% of women and 4.9% of men developed PTSD ( $p < 0.001$ ).

**Conclusions:** PTSD level trauma and PTSD affects men and women differently. Having this knowledge, it is essential that gender specific coping and treatment strategies are developed.

**B17****Trace elements and type 2 diabetes – two case-control studies in HUNT3**

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**Introduction:** Substantial evidence implies important roles for several trace elements in type 2 diabetes (T2D). One important question is whether the aberrant element level is a result of diabetes, a cause, or homeostatic attempts by the body to rectify a parallel condition associated with the disease. Measuring trace element levels in different stages of the disease could provide some insight into when alterations in these element levels begin.

**Aim:** The objectives of our two studies were to investigate the association of the levels of 26 trace elements in whole blood with the prevalence of T2D in a large, non-selected, geographically defined total population, and to explore if trace element differences in diabetic patients persist with time.

**Methods:** Two matched case-control studies nested within the third Nord-Trøndelag Health Survey (HUNT3) cohort were performed, one in persons who did not have a T2D diagnosis when blood samples were drawn (128 cases, 755 controls), and the other (270 cases, 615 controls) in persons with an established T2D diagnosis. Trace elements were determined in whole blood by HR-ICP-MS after microwave digestion. Multivariable conditional logistic regression was used to test for associations between levels of trace elements and the prevalence of T2D. Odds ratios were adjusted for the potential confounders BMI, waist-to-hip ratio, income, education, smoking and first-degree family history of diabetes. In addition, one-way ANOVA was used to check for association of the trace elements levels (Ca, Fe, and Mg) and disease duration in diagnosed T2D.

**Results:** Iron showed a negative association with T2D in diagnosed patients but positive in undiagnosed patients. Significantly higher levels ( $P_{\text{trend}} < 0.05$ ) of bromine, cadmium, chromium, nickel and zinc were found in undiagnosed T2D, but not in established T2D. Magnesium was negatively associated with diagnosed T2D, and blood magnesium levels were lower ( $P=0.027$ ) in patients with a longer disease duration ( $> 1$  year) than in patients that received their diagnosis less than 1 year before blood samples were drawn. For calcium, boron and lead, significant positive associations were found only in diagnosed T2D, implying that these differences may be a consequence of the disease or its treatment rather than a causal factor. A positive association was found for silver in both undiagnosed and diagnosed T2D. Arsenic, copper, manganese and selenium, previously reported to be implicated in diabetes, were not found to be associated with T2D in our studies. Also, no association was found for cesium, gallium, gold, indium, mercury, molybdenum, rubidium, strontium, tantalum, thallium and tin.

**Conclusions:** Our studies suggest a possible role of boron, bromine, cadmium, chromium, calcium, iron, lead, magnesium, nickel, silver and zinc in type 2 diabetes. In-depth studies of the roles of trace elements in different stages of the disease are warranted.

**B18****Is copper in drinking water related to risk of hip fracture? And could a possible protective association between calcium and hip fracture be modified by copper?**

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**Introduction:** Norway has among the highest rates of hip fracture in the world, even in summer months when the climate is mild. The incidence has been found to vary geographically, with a higher incidence in urban compared to rural areas. The variation in fracture risk may reflect a difference in underlying environmental factors, such as the quality of drinking water. Copper is an essential nutrient that is commonly found in drinking water. Lysyl oxidase, an enzyme that plays a key role in bone formation has been shown to depend on adequate copper intake, and too low copper intakes could lead to reduced bone mineral density. On the other hand, the possible effect on bone by too high copper intake is not known. Calcium in drinking water has been found to increase bone mineral density in randomized clinical trials, and the effect of calcium may be increased with the concurrent intake of trace minerals such as copper. We have previously reported that the incidence of hip fracture in Norway could depend on the concentration of calcium and magnesium in drinking water; however the association between calcium in the water and hip fracture was unclear. Due to a high degree of corrosion of water pipes, it is important to examine whether copper in drinking water is associated with hip fracture in the Norwegian population, and whether the possible protective effect of calcium in the water could be modified across the concentration range of copper.

**Methods:** A trace metals survey in 566 waterworks was linked geographically to hip fractures from hospitals throughout the country (1994-2000). In all those supplied from these waterworks, 5,485 men and 13,642 women aged 50-85 years suffered a hip fracture. Poisson regression models for relative risks of the associations between copper, calcium and hip fracture were fitted. Incidence Rate Ratios (IRRs, 95% CIs) were adjusted for age, region of residence, urbanization degree, type of water source, and pH of the water. Multiplicative interactions between copper and calcium were examined. All analyses were stratified on gender.

**Results:** Men being supplied drinking water with high copper (>56 µg/l, above average) had a 10% greater risk of hip fracture (IRR=1.10, 95% CI: 1.0, 1.18), however this effect was attenuated when adjusting for pH of the water. No significant change in risk with high copper was found in women (IRR=1.05, 95% CI: 1.0, 1.10). Water with low calcium (≤5.39 mg/l, below average) gave a 15% greater risk of hip fracture in men (IRR=1.15, 95% CI: 1.06, 1.23), and a 4% increase in hip fracture risk in women (IRR=1.04, 95% CI: 1.00, 1.09). The association between calcium and hip fracture seemed to vary across levels of copper. In the high copper group, men drinking water with low calcium had a 45% greater risk of hip fracture compared to men drinking water high in calcium (IRR=1.45, 95% CI: 1.07, 1.96). This association was stronger than in the low-copper group (IRR=1.15, 95% CI: 1.06, 1.23).

**Conclusion:** High copper in drinking water may increase the risk of hip fracture; however, high copper may also increase the protective effect of calcium in the water. The relation between these components in drinking water and fracture risk is complex and needs to be studied further.



## B19

### The Nord-Trøndelag Hearing Loss Study – main results

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**Introduction:** The Nord-Trøndelag Hearing Loss Study, which is a part of HUNT2, is the largest population based hearing survey in the world.

**Aims:** To assess the distribution of hearing loss in the population, to investigate the effects of various exposure factors on hearing, to establish its heritability and to evaluate its effect on psychosocial functioning.

**Methods:** 50,799 subjects completed a hearing examination consisting of pure-tone audiometry and two questionnaires. 6,415 subjects were also tested with otoacoustic emissions. The study has been linked to data from HUNT 1-3 and to several registers.

**Results:** Hearing loss was highly related to age with a prevalence of 2% among 20-44 years old and 62% above 65 years. While age explained 30-58% of the variation in hearing loss, all other measured risk factors explained 1-6% depending on sound frequency and age group. Occupational noise had moderate effects only in middle aged and old men. Wood and construction work were among risky occupations. Impulse noise, mainly from hunting, contributed almost equally to hearing deficits as did occupational noise. No increased risk was found for playing in music bands, listening to portable music devices or visiting disco or rock concerts. Minor effects were found for reporting recurrent ear infections and being hospitalized for head trauma. Hearing loss was overly represented among subjects with low socioeconomic status. The heritability of hearing loss was estimated to about 35% and of tinnitus to about 11%. The effect of hearing loss on mental health and subjective well-being was moderate and there was no significant effect on the mental health of the spouse. Otoacoustic emission was a valid test of the functional consequences of hearing loss although not superior to pure-tone audiometry.

**Conclusions:** Hearing loss is very common in the older part of the population. While the genetic contribution to hearing is substantial, a modest part of the variation is explained by known risk factors others than high age.

**B20****Road traffic noise and markers of obesity – a population-based study**

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**Introduction:** Several studies have reported that traffic noise is related to annoyance and sleep disturbances as well as increasing levels of cortisol, indicating physiological stress. Recent epidemiological studies indicate an association between long-term exposure to traffic noise and increased risk of hypertension and cardiovascular diseases (CVDs). Furthermore, poor sleep has been associated with increased risk of diabetes type 2, CVD and obesity.

**Aims:** We investigated the relationship between road traffic noise and obesity markers. Furthermore, we explored the modifying role of noise sensitivity, noise annoyance, and sleep disturbances.

**Methods:** We used data from a population-based study in Oslo, HUBRO (N=15,085). Measurements were used to define body mass index (BMI), waist circumference (WC), waist-hip ratio (WHR), and these binary outcomes: BMI  $\geq 30$  kg/m<sup>2</sup>, WC  $\geq 102$  cm (men) / 88 cm (women), and WHR  $\geq 0.90$  (men) / 0.85 (women). Modelled levels of road traffic noise ( $L_{den}$ ) were assigned to each participant's home address. Linear and logistic regression models were used to examine the associations.

**Results:** Overall, the results indicated no associations between road traffic noise and obesity markers. However, in highly noise sensitive women (n=1,105) a 10 dB increase in noise level was associated with a slope of 1.02 (95% confidence interval (95% CI): 1.01, 1.03) for BMI, 1.01 (95% CI: 1.00, 1.02) for WC, and an odds ratio of 1.27 for WHR  $\geq 0.85$  (95% CI: 1.03, 1.57). The associations appeared weaker in highly noise sensitive men. We found no effect modification of noise annoyance or sleep disturbances.

**Conclusions:** In an adult urban Norwegian population, road traffic noise was positively associated with obesity markers only among highly noise sensitive women.

**B21****Night-time road traffic noise and symptoms of insomnia**

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**Background:** An exposure-response relationship has been demonstrated for the association between road traffic noise and self-reported sleep disturbances attributed to traffic noise. Few population-based studies have focused on the association between road traffic noise and general sleep disturbances, such as symptoms of insomnia.

**Aims:** The aims were to study the associations between night-time road traffic noise and the self-reported symptoms of insomnia; difficulties falling asleep, awakenings during the night, and waking up too early.

**Methods:** The study population is from Health and Environment in Oslo (HELMILO) (2009-10) (N = 13,019). Data on health and sleep was collected by a postal questionnaire. Insomnia symptoms were defined as sleep problems occurring  $\geq 3$ -5 times per week. Modeled noise levels were assigned to each participant's home address. Logistic regression models were used to analyze the associations. In addition to analysis of the total study population, separate analyses were performed among individuals with bedroom facing a road.

**Results:** After adjustment for potential confounders, statistically significant associations were found between noise exposure and all three symptoms of insomnia in the total study population. Among individuals with bedroom facing a road, *difficulties falling asleep* and *waking up too early* were significantly associated with road traffic noise.

**Conclusion:** Night-time road traffic noise was associated with symptoms of insomnia. The effect estimates were higher for the associations between noise exposure and *difficulties falling asleep* among individuals with bedroom facing a road, compared with the total study population.

## C1

### **Socioeconomic status and sick leave granted for somatic and mental disorders: a prospective study of young adult twins**

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**Background:** Low socioeconomic status (SES), indexed by low income and education, has consistently been found to be a strong predictor of sick leave. This relationship is not simply explained by health differences. Several causal and non-causal explanations exist for SES differences in sick leave. This study utilizes a population-based sample of employed young adult twins to estimate (i) the degree to which education and income are prospectively related to the total level of sick leave and sick leave granted for mental and somatic disorders, and (ii) whether these associations are confounded by familial factors or likely to be causal.

**Methods:** Registry data on educational attainment and income at age 30 and subsequent sick leave were available for 6,103 employed young adult twins, among which there were 2,024 complete twin pairs. Population level associations and fixed effects within twin pairs were estimated.

**Results:** Low education and income were associated with sick leave granted for both mental and somatic disorders at the population level, and with the total level of sick leave. Associations were attenuated within dizygotic twin pairs, whereas no statistically significant associations between SES and sick leave were found within monozygotic twin pairs.

**Conclusion:** Low SES indicates a risk for sick leave granted for both mental and somatic disorders among young adults, but these associations are most likely confounded by factors that are common to co-twins. Achieving higher education or income is therefore not likely to strongly affect sick leave in young adulthood.

## C2

### **Mortality and work disability in a cohort of Norwegian couples – the Nord-Trøndelag Health Study**

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**Introduction:** Poor health is clustered in couples, due to pre-existing similarities or influence between partners. Partner's education and major life events like widowhood or hospitalisation of a spouse is associated with increased mortality. Studies on how other health measures might influence the partner's mortality and work ability are scarce.

**Aims:** To study possible consequences of living with a spouse with poor health or unhealthy life style on mortality and work disability.

**Methods:** 18,943 couples from the HUNT2 Study (1995-97) were linked to national registries and followed until December 2007, identifying deaths and disability pension retirements. Couple's mean exposures were included together with the individual's deviation from the couple mean in discrete time multilevel logistic regression.

**Results:** There was weak evidence of associations between partner's health and risk of dying. Associations between couples slightly exceeded associations within couples for smoking (OR within 1.55 (95% CI 1.37-1.76) OR between 1.89 (95% CI 1.71-2.09)) and education (OR within 1.07 (95% CI 0.99-1.15) OR between 1.16 (1.10-1.22)). Indicators of partner's health, such as self-rated health (OR within 3.18 (95% CI 2.82-3.60) OR between 3.99 (95% CI 3.56-4.48)), insomnia (OR within 1.38 (95% CI 1.17-1.63) OR between 2.12 (95% CI 1.79-2.52)) and symptoms of depression (OR within 1.48 (95% CI 1.25-1.75) OR between 2.00 (95% CI 1.70-2.35)) were, however, associated with risk of work disability. Illness associated with problematic psychosocial factors displayed stronger associations with work disability among partners than somatic diseases.

**Conclusions:** This study did not indicate strong consequences of living with a spouse with poor health or unhealthy life style on mortality. It did, however, indicate strong associations of partner's health and life style with work disability. Supporting vulnerable families might improve healthy aging and occupational health.

**C3****Life satisfaction and work absenteeism – a discordant twin analysis**

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**Background and aims:** During the past years, data from population based twin registries have become increasingly important in studies of work absence, which is a major public health and economic challenge in many developed countries. Sick leave (SL) and disability pension (DP) are influenced by a wide range of medical, psychological and psychosocial factors, but little is known about how life satisfaction affects absenteeism. This study employs a discordant twin design to explore to what degree life satisfaction predicts DP and SL in young adults, independently of symptoms of common mental and somatic disorders.

**Methods:** In the Norwegian twin registry, data from questionnaires and interviews from 7,698 young adults have been linked to highly reliable official registries on long term sick leave (LTSL) and disability pensioning (DP) between 1998 and 2008. Data on life satisfaction (a six point scale from very unsatisfied to very satisfied), mental distress (SCL-5), and musculoskeletal pain (lumbar spine, neck/shoulder and muscular pain) were retrieved from a 1998 questionnaire, thus obtaining a prospective design. For SL we constructed a variable reflecting the proportion of days employed (eligible for sick leave) the subject was on LTSL. For the preliminary analyses, we used logistic regression models for both outcomes, with DP and having high levels of LTSL (more than 10%) as dependent variables, first corrected for dependency by GEE and subsequently using the “fixed effects” option in STATA for the discordant twin design.

**Preliminary results:** After excluding subjects who got their DP prior to year 2000 (n=72) the final sample included 7,626 twins, including 3,055 complete pairs and 1,516 singletons. Forty-two percent were male, and mean age at last follow up (2008) was 35.5 years (range 29-41). By 2008, 181 subjects had received DP, and 63.7% of the sample (47.4% of males and 76.0% of females) had at least one period of LTSL. Preliminary results showed that adjusted for age, sex and educational attainment, life satisfaction was significantly negatively associated with both DP and LTSL (OR for each level of increasing LS 0.59, CI 0.51-0.65 and 0.78, CI 0.73-0.82 respectively). The associations remained significant after adjusting for mental distress and musculoskeletal complaints (ORs 0.72, CI 0.61-0.85, and 0.91, CI 0.85-0.98). In the discordant twin analyses, the associations remained significant with similar effect sizes when all zygosity groups were analyzed together (ORs 0.68, CI 0.47-0.98 and 0.85 CI 0.74-0.97). Further analyses will be presented at the conference.

**Preliminary conclusion:** Life satisfaction seems to protect against work absenteeism in young adults, independently of symptoms of common mental and somatic disorders, and independently of common environmental and possibly genetic confounding.

## C4

### **The relationship between socioeconomic position, working conditions and sickness absence in a life-course perspective**

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**Introduction:** Socioeconomic position (SEP) in childhood and in adulthood, and work environment factors are predictors of sickness absence (SA).

**Aims:** Our objective was to examine the relationships between these factors in a life-course perspective, which has hardly been done previously.

**Methods:** Our study sample was all employed individuals who partook in the HUNT study and who were born between 1967 and 1976 (N=4530). Outcome was the risk of at least one SA episode in 2009. Educational attainment (5 categories) served as indicator of adult SEP, whereas highest parental education level and father's average income during early childhood (0–6 years) were indicators of childhood SEP. Work factors were job control, physically demanding work and shift work. Risk ratios (RRs) were estimated using Poisson regression.

**Results:** 29% of the women and 17% of the men had SA during follow-up. There was a strong gradient according to adult SEP for both genders. The age-adjusted RR for having an SA episode, comparing highest and lowest educational levels, was 2.83 for women and 3.85 for men. The RR was marginally weakened in women (-4%) and strengthened in men (+18%), after adjusting for childhood SEP (Model 2). Including all work factors in the model reduced the RRs by 20% compared to Model 2 (RR 2.20 and 3.62, respectively), the largest impact for physically demanding work (15% reduction in RR).

**Conclusions:** There were strong social gradients in SA, partly mediated through work environment factors in a life-course perspective. We found gender differences that are difficult to explain.

**C5****The unemployment effect of health. A prospective (1995-2008) cohort study linking the Norwegian HUNT study to national registers on unemployment, social insurances and socioeconomic status****S. L. Kaspersen<sup>1</sup>, K. Pape<sup>1</sup>, G. Å. Vie<sup>1</sup>, S. O. Ose<sup>2</sup>, S. Krokstad<sup>1</sup>, J. H. Bjørngaard<sup>1</sup>**

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**Introduction:** Most studies on associations between health and unemployment have investigated how unemployment influences health (causation hypothesis). Less attention has been paid to the reverse causal direction; how poor physical and mental health may increase the risk of becoming unemployed (selection hypothesis). In order to provide future labor markets with healthy workers and appropriate job creation- and vocational rehabilitation programs, we need to know who is at risk.

**Aims:** The aim of the study was to investigate mental and physical health selection to unemployment in Norway.

**Methods:** Self-reported health data from 36249 participants in the Norwegian HUNT2 study (1995-97) was linked to national registers on unemployment, pensions and medical benefits from 1992 until 2008. Cox' proportional hazard models estimated the hazard ratios (HR) of unemployment, comparing participants with and without symptoms of common mental disorders measured by the Hospital Anxiety and Depression Scale (HADS). We adjusted for several somatic and lifestyle-related potential confounders. Furthermore, we did separate analyses on the risk of unemployment associated with the somatic and lifestyle related variables. Confidence intervals (CI): 95 % level.

**Results:** Anxiety only (HR 1.13 (CI 0.99-1.27) and comorbidity (anxiety and depression, HR 1.42 (CI 1.21-1.67)) were associated with an increased risk of unemployment in the fully adjusted model. In age stratified analyses, the corresponding HRs for participants <50 years old were 1.17 (CI 1.03-1.33) and 1.35 (CI 1.13 – 1.62), while participants >50 had an estimated HR of comorbidity on 1.72 (CI 1.21-2.43). Physical handicap, chronic somatic conditions, self-rated health, physical activity, body mass index and smoking were significantly associated with the risk of unemployment.

**Conclusion:** We find evidence for health selection to unemployment in Norway. Health, especially mental health, should be a topic of great importance in traditionally non-medical social security services like unemployment benefits and job creation- and vocational rehabilitation programs.



## C6

### **Psychotropic drug use among 0–17 year olds during 2004–2013: a nationwide prescription database study**

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**Introduction:** Treatment of children and adolescents with psychotropic drugs is an area of continuous interest. Information on trends in use in unselected populations is limited.

**Aims:** To examine prevalences of psychotropic drug use in the period 2004–2013 among Norwegians aged <18 years, overall and in subgroups of psychotropic drug.

**Methods:** Prescription data on psychotropic drugs (2004–2013) were drawn from the Norwegian Prescription Database. Relevant psychotropic drugs included were: antipsychotics (ATC-group N05A), anxiolytics (N05B), hypnotics/sedatives (N05C), antidepressants (N06A) and centrally acting sympathomimetics referred to as stimulants (N06BA), and the centrally acting antihistamine alimemazine (R06AD01) (used for childhood insomnia in Norway). One-year prevalences of psychotropic drug use was estimated (per 1000 inhabitants <18 years).

**Results:** During the study period there was a decrease in overall use of psychotropic drugs in the youngest boys and girls, and in particular among 1–2 year olds, attributed to decreasing alimemazine use (from 36.6 to 10.7/1000 in 1-year old boys and from 26.9 to 8.7/1000 in girls). Use of hypnotics/sedatives among 1–2 year olds remained stable in the period in both gender. From the age of 8 years and onwards, an annual increase in use of psychotropic drug use was observed in both genders, attributed to an increasing use of hypnotics/sedatives(melatonin), and antidepressants, among adolescent girls in particular. Stimulants increased among those aged  $\geq 6$  years in the period 2004–10, but remained stable throughout 2013 in both gender.

**Conclusions:** Increasing psychotropic drug use in 2004–2013 is attributed to increasing use of hypnotic/sedatives (melatonin), stimulants among those aged  $\geq 6$  years, and antidepressants in  $\geq 15$  years of age. From 2010 and onwards use of stimulants seems to have leveled out in both genders, whereas use of hypnotic/sedative drugs shows a pattern of a continuous annual increase. Decrease in overall psychotropic drug use in the youngest children is attributed to decreasing use of alimemazine.

## C7

**Characteristics of persistent organic pollutants and perfluoroalkyl substances in pregnant Scandinavian women, 1986-1988**

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**Introduction:** The fetal period is one of the most vulnerable stages of human development, and exposure to persistent organic pollutants (POPs) and perfluoroalkyl substances (PFASs) *in utero* have been associated with adverse effects on fetal development, including growth restriction. The aim of this study was to examine the importance of demographic and dietary factors on these substances in maternal serum.

**Methods:** The study was part of a population based prospective multicenter study of para 1 and 2 women in Trondheim and Bergen, Norway, and Uppsala, Sweden. Serum from 483 women was collected in 1986-1988 at around 17 weeks of gestation. Analyses of several polychlorinated biphenyl (PCB) congeners, pesticides and metabolites, in addition to perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) were conducted. Associations between the POP and PFAS concentrations and demographic and dietary variables were evaluated using multivariable linear regression.

**Results:** All of the different POPs increased with increasing maternal age, and almost all decreased significantly with the year of blood draw. The PFOA and PFOS concentrations, on the other hand, *increased* with the year of blood draw. Total breastfeeding duration was associated with reduced levels of both the POPs and PFASs examined. High POP concentrations were associated with high education level. Of almost all the contaminants, the women from Uppsala had significantly higher concentrations than their peers from Trondheim or Bergen. Levels of PFOA and PFOS increased with time since the most recent pregnancy, and with higher household income. There were significantly lower levels of PFOS among the smokers than non-smokers. Elevated concentrations of most of the POPs and PFASs were found in high consumers of fish spread and oily fish.

**Conclusions:** Maternal age, breastfeeding duration and study site was the most important predictors for the POPs, while breastfeeding duration, study site and time since the most recent pregnancy explained most of variation in the PFAS levels. Higher socioeconomic status seemed to be associated with higher levels of both POPs and PFASs. High intake of fish spread and oily fish were associated with most of the POPs and PFASs.

**C8****The effect of prenatal antidepressant exposure on birth weight, gestational age, and congenital anomalies – advantages of using a sibling control design**

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**Introduction:** Whilst the detrimental effect of depression on pregnancy outcome is well documented, antidepressant safety during pregnancy remains disputed particularly due to confounding by indication. Sibling studies can be used in an attempt to address this issue by using discordance in maternal exposures whilst maintaining socio-demographic and genetic factors constant.

**Aims:** To determine whether low birth weight, prematurity, and congenital anomalies can be attributed to prenatal antidepressant exposure as such or maternal medical, socio-demographic, and/ or genetic factors.

**Methods:** Sibling control analysis via linkage of the Norwegian Mother and Child Cohort Study (MoBa) (information on prenatal antidepressant exposure) and the Medical Birth Registry of Norway (MBRN) (information on birth weight, gestational age, congenital anomalies). We will model low birth weight (birth weight < 2500g), prematurity (gestational age < 37 weeks), and congenital anomaly diagnoses based on prenatal antidepressant exposure using fixed effects modelling whilst adjusting for maternal illness and prenatal co-medication use.

**Preliminary results:** In total 30 603 eligible siblings were identified and 354 (1.1%) were discordantly exposed to antidepressants. Mean difference in birth weight and gestational age between discordant sibling clusters: 456.2 grams (sd 403.4), 1.52 weeks (sd 1.7); for concordant sibling clusters: 440.2 grams (sd 431.1), 1.40 weeks (sd 2.24). Socio-demographic and medical characteristics differed among concordant and discordant siblings. Preliminary adjusted comparisons of average difference between discordant and concordant siblings indicated no association between prenatal antidepressant exposure and low birth weight ( $\beta$  -5.7 grams; 95%CI -96.2 to 84.7), prematurity ( $\beta$  -0.2 weeks; 95%CI -0.6 to 0.2), or major congenital anomalies (adjusted OR 0.4; 95%CI 0.1-1.8).

**Conclusions:** Fixed effect modelling using discordant siblings will enable us to determine whether associations between prenatal antidepressant exposure and low birth weight, prematurity, and congenital anomalies are attributable to the drug exposure itself or maternal medical, socio-demographic, and/ or genetic factors.

## C9

**Cross-Sectional and Prospective Cohort Study of Serum 25-Hydroxyvitamin D Level, Smoking and Lung Function in a General Population of Adults: The HUNT Study**

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**Introduction:** Prospective studies on serum 25-hydroxyvitamin D (25(OH)D) level and lung function (LF) in general adult populations are scarce, and the association remains unclear. Modification of this association by smoking status has been suggested.

**Aims:** To study the inter-relationship of serum (25(OH)D) and smoking with LF in a cross-sectional (n=1293) and prospective (n=922) study, including a random sample of adults from the Nord-Trøndelag Health Study (HUNT2 and HUNT3).

**Methods:** LF was measured at both HUNT2 and HUNT3 by spirometry and included: forced expiratory volume in 1 second percent predicted (FEV<sub>1</sub> % pred.), forced vital capacity (FVC % pred.), and FEV<sub>1</sub>/FVC ratio. We used multiple linear regression models to estimate adjusted regression coefficients ( $\beta$ ), and 95% confidence intervals (CI).

**Results:** In cross-sectional analysis, never smokers irrespective of serum 25(OH)D level, had the most favorable FEV<sub>1</sub>% pred., and FEV<sub>1</sub>/FVC ratio. After follow-up, never smokers showed the least decline in LF (e.g.  $\beta$  for never smokers with 25(OH)D level <50nmol/L for FEV<sub>1</sub> % pred. = -3.07, 95% CI:-5.05 to -1.09;  $\beta$  for FEV<sub>1</sub>/FVC = -1.52, 95% CI:-2.69 to -0.36). Amongst ever smokers, serum 25(OH)D level  $\geq$ 50 nmol/L was significantly associated with higher FEV<sub>1</sub> % pred. ( $\beta$ =2.82%, 95% CI: 0.70% to 4.95%), in the cross-sectional study. After follow-up, ever smokers with serum 25(OH)D level  $\geq$ 50 nmol/L showed significantly less FEV<sub>1</sub>/FVC ratio decline compared to smokers with 25(OH)D levels <50 nmol/L ( $\beta$  = -0.99%, 95% CI: -1.97% to -0.01%). However, the difference in FEV<sub>1</sub>/FVC ratio decline was minor in never smokers with 25(OH)D  $\geq$ 50nmol/L compared to the <50nmol/L group.

**Conclusion:** In a general population of Norwegian adults, never smoker status – irrespective of serum 25(OH)D levels, was strongly associated with favorable LF measures and less LF decline. Amongst ever smokers, higher serum 25(OH)D levels may be protective against LF decline.

## C10

### **Vitamin A, D and E levels in stored plasma samples from pregnant women in the Norwegian Mother and Child Cohort Study: time changes and study implications**

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**Introduction:** When biological samples are stored over time as in biobanks, the measured level of a biomarker at a given time point can be affected by a number of factors such as degradation, freeze-thaw cycles, procedures for sample retrieval and mixing, assay reproducibility, instrument drift or changes in analytical methods. In case-control and case-cohort studies all samples should therefore be handled equally and analyzed together. When this cannot be achieved for practical or economic reasons, statistical corrections may be necessary to prevent biased comparisons.

**Aims:** To investigate the effect of pooling sub-samples of mothers with plasma analyzed for vitamin A, D, and E at two different time point in a case-cohort study of childhood asthma nested within the Norwegian Mother and Child Cohort Study.

**Methods:** Plasma was collected from about 3,400 pregnant women (median 18 weeks gestation) in 2002-2004, mailed to the biobank at the Norwegian Institute of Public Health and stored at  $-80^{\circ}$  C until analysis in 2010-2011 (t1) or 2014 (t2) at the same laboratory. A random sample (n=100) was measured twice to assess time changes (t1-t2) within persons and to have a basis for doing regression calibration, if necessary.

**Results:** The mean change in concentrations within persons was relatively small, but statistically significant for all vitamins ( $p < 0.001$ ). The mean (min, max) difference was 4.9 (-53, 42) % for 25-hydroxy vitamin D3 and 4.4 (-26, 32) % for all-trans retinol, indicating a decrease, but -13 % (-63, 15) for alfa-tocopherol, indicating an increase over time. Further results on potential effects on estimates of disease risk will be presented.

**Conclusions:** Epidemiological studies using biomarker measurements from stored samples should consider the potential for biased group comparisons when samples are not analyzed together, and the need to collect additional data for doing statistical corrections.

## C11

### Characteristics of dietary supplement users

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**Introduction:** Sales figures for dietary supplements in Norway increased steeply from 1986 to 2005 and levelled out between 2006 and 2011 according to The Norwegian Association of Herbal Manufacturers and Retailers. Descriptions of dietary supplement use in Norway are scarce but data from the Norwegian Women and Cancer study (NOWAC) suggest that use of cod-liver oil among Norwegian women is associated with variables that may be markers of a healthy life style.

**Aims:** To describe the pattern of dietary supplement use among middle-aged Norwegian women, with regards to health and life style characteristics.

**Methods:** This is a cross-sectional analysis within NOWAC, which is a national population based cohort study with random selection of participants. Questionnaire data on dietary supplement use was collected from 2003 to 2006 among a subgroup of women born 1943-57 (response rate 72%).

**Results:** Out of 3231 women 2293 (71%) used dietary supplements, and 1528 (47%) used dietary supplements and medication concurrently. Among the dietary supplement users, 1383 (60%) used more than one supplement product and 277 (12%) used more than three. Dietary supplement use was associated with age, education, medication use and markers of a healthy life style (physical activity, lower BMI and non-smoking). The association between medication use and dietary supplements use was mainly due to higher use of supplements among women using medication for less serious disorders.

**Conclusions:** The majority of middle-aged Norwegian women use dietary supplements and one in ten use more than three dietary supplement products. Use is associated with higher age, higher education, markers of a healthy life style and use of medication for less serious disorders.

## C12

### Lifestyle and lifestyle changes at the age of fifty as predictors of mortality

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**Introduction:** The association of lifestyle and lifestyle changes with mortality in middle-aged adults is poorly documented.

**Aims:** To study the effect of lifestyle and lifestyle changes on mortality in individuals aged 50-55 years.

**Methods:** In the Norwegian Colorectal Cancer Screening Prevention trial (NORCCAP), individuals aged 50-55 years, randomized to colorectal cancer screening or no screening, were invited to a lifestyle sub-study. Lifestyle was assessed by questionnaire at inclusion in 2001 (n=8,485) and in 2004 (n=7,135). A lifestyle-score was calculated assigning one point for every favourable lifestyle characteristic independently associated with all-cause mortality. We analysed the impact of baseline lifestyle-score and three-year lifestyle-score changes on mortality, by fitting univariate and multivariable survival analyses.

**Results:** After 10 years of follow-up, 317 individuals (3.7%) died, of whom 155 (49%) from cancer, and 58 (18%) from cardiovascular disease. Current non-smoking, physical activity ( $\geq 1$  time / week) and fruit, berries, and vegetables consumption ( $> 2$  courses / day) were independently inversely associated with all-cause mortality. Individuals reporting none (n=290), one (n=1,911), two (n=3,338) or three (n=2,556) of those behaviours at baseline had a 10-year mortality of 9.7%, 5.9%, 2.9% and 2.4%, respectively ( $P < 0.001$ ). With regard to lifestyle changes, an increase of one point from 2001 to 2004 was associated with 22% mortality reduction (HR 0.78, 95% CI 0.61-0.99 adjusted for age, sex, baseline score, and study arm). Among individuals with a bad lifestyle score (0 or 1) in 2001, those who improved to a good lifestyle score (2 or 3) in 2004 had 39% decreased mortality compared to individuals remaining with a bad lifestyle score (HRs 0.61, 95% CI 0.37-1.00 adjusted for age, sex, baseline score, and randomized study arm).

**Conclusions:** Lifestyle at age 50-55 years strongly influences mortality in the next ten years. Favourable lifestyle changes after age 50 can improve life expectancy.

## C13

### **Socioeconomic inequalities in the uptake of vaccine against human papillomavirus in the Norwegian childhood immunisation programme**

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**Introduction:** Vaccine against human papillomavirus (HPV) was implemented in the Norwegian Childhood Immunisation Programme in 2009. Although the HPV vaccine, like other vaccines in the programme, is given free of charge within the public health service, the uptake of HPV vaccine is lower.

**Aim:** The aim of this nationwide register-based study was to assess the impact of maternal education and income on initiation and completion of HPV vaccination.

**Methods:** The study included all girls eligible for HPV vaccination during the first three programme years. The Norwegian Central Population Registry was linked with socioeconomic data from Statistics Norway and information on HPV vaccination from the Norwegian Immunisation Registry. Risk differences (RD) and confidence intervals (CI) were estimated with Poisson regression.

**Results:** Of the 84 139 girls in the study sample, 78.3% received the first dose of HPV vaccine and 73.6% received all three doses. Initiation of HPV vaccination increased from 71.8% in the first birth cohort offered HPV vaccine (girls born 1997) to 82.6% among girls born in 1999. High maternal education was associated with lower probability of initiating HPV vaccination, while high maternal income increased the likelihood of initiating vaccination. The associations were strengthened in the multivariable analysis, RDs = -5.5% (95% CI: -7.0%, -4.0) and 10.1% (95% CI: 9.0, 11.3) for highest compared to lowest education level and highest compared to lowest income quintile, respectively. The negative effect of maternal education on initiation of HPV vaccination was only seen in daughters of mothers with income below median value.

**Conclusion:** Socioeconomic inequalities in the uptake of HPV vaccine in the publicly funded school-based immunisation programme in Norway were detected. The opposing effects of maternal education and income are puzzling and warrant further studies.



## C14

### Language development through preschool years: The association with participation in childcare

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**Introduction:** Delayed language development is amongst the most common developmental difficulties seen in preschool children. We know that about half of the children experiencing such difficulties grow out of their delays and continue with what seems like a normal language trajectory by the end of the preschool period. One possible arena for identifying factors correlated with a healthy language development is attendance in high quality child care.

**Aim:** Using longitudinal data on child development and participation in high quality child care, we aim at identifying specific quality factors in the day care centers that predict healthy language development. Our hypotheses are that quality factors differentiate children with persistent difficulties from those who grow out of their difficulties from age 3 to 5.

**Method:** Using data from the Norwegian Mother and child cohort study (MoBa), we investigate approximately 7000 five year old Norwegian children enrolled in high quality child care. Day care quality is measured at five. The quality measures include indicators of structural quality, such as child group size, educational level of staff etc., and process quality, such as mapping child development and relationship between child and teacher etc. A variety of language measures are included at 5 years. Longitudinal analyses of language development will be done using the Ages and Stages Questionnaire (ASQ).

**Preliminary analyses:** Preliminary analyses reveal weak but positive associations between good quality child care and language development. The strongest correlation seems to be with language development and the relationship between teachers and children.

**Results/conclusion:** Norwegian day care centers are generally of higher quality than day care centers in most other countries. According to results from the present study there are reasons to believe that attendance in day care is positively correlated with good language development. In particular a good relationship between the teacher and child is positively associated with good language skills.

## C15

### Validation of epilepsy diagnoses in the Epilepsy in Young Children (EPYC) study – a nationwide population-based study

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**Introduction:** Epilepsy is one of the most frequent neurological disorders in children. The diagnosis is based on the occurrence of at least two unprovoked epileptic seizures. Much is still unknown with regards to etiologies, risk factors, and developmental trajectories. Population-based, prospective child cohorts are valuable platforms for expanding existing knowledge.

**Aims:** The aim of the Epilepsy in Young Children (EPYC) study is to use the Norwegian Mother and Child Cohort (MoBa) for research on childhood epilepsy. This first part of the EPYC is a validation study of recorded epilepsy diagnoses.

**Methods:** Potential epilepsy cases in MoBa are identified through: (1) parental report of epilepsy in MoBa questionnaires and/or (2) a diagnosis of epilepsy (ICD-10 G40\*) in the Norwegian Patient Register (NPR). The NPR records diagnoses from Norwegian specialist health services. All potential cases are validated through medical record reviews, clinical telephone interviews, and specialist reviews of EEGs and MRIs. Two pediatric neurologists classify the epilepsy.

**Results:** We have identified 840 children with epilepsy diagnoses recorded in the NPR. Of 770 potential cases reviewed, 536 (70%) met the criteria for epilepsy. There were substantial differences between counties; 38%—91% having epilepsy, median 71,5%. Among the 234 children incorrectly coded as having epilepsy, 24% had a single EEG as part of investigations for disorders such as learning disorder, attention-deficit hyperactivity disorder or autism spectrum disorder, 76% had other paroxysmal events; most frequent condition was febrile seizures (14%); the rest had syncope, sleep disturbances, spells or other medical/behavioral problems.

**Conclusions:** Registry data are a useful source of case identification for studies of childhood epilepsy. However, all potential cases should be validated, because a large proportion does not meet the criteria for the diagnosis, and large regional differences may be missed if only a subset is included.

## C16

### Adult outcomes for children with hearing loss

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**Introduction:** Knowledge about long-term hearing prognosis is important to achieve correct hearing management and patient information.

**Aims:** To examine the effects of different types of hearing loss in childhood on hearing and tinnitus in adulthood.

**Methods:** Population-based cohort study of 32,786 adults (aged 20-56 years) who underwent pure-tone audiometry in the Nord-Trøndelag Hearing Loss Study. As children, the same individuals underwent screening audiometries in a primary school hearing investigation, including Ear, Nose & Throat examination when indicated.

**Results:** Compared to adults with normal hearing at the school screenings (n=29,720), adults with childhood hearing loss (n=3066) had poorer hearing and reported more tinnitus. The effects were adjusted for age, sex and noise exposure. Childhood hearing disorders associated with a clinically relevant hearing loss and tinnitus in adulthood were as follows: hearing loss in combination with chronic suppurative otitis media; hearing loss associated with a history of recurrent acute otitis media and, sensorineural hearing loss (SNHL). The effects of these conditions on adult hearing were significantly moderated by age (20-56 years), but not by noise. Age stratified analyses revealed a larger effect in middle-aged adults (40-56 years) compared to younger adults (20-39 years). No association between childhood hearing loss and adult tinnitus was found after adjustment for adult hearing threshold.

**Conclusions:** Complicated and chronic suppurative otitis media in childhood are associated with hearing loss and tinnitus in adulthood. It appears that these conditions, as well as childhood SNHL, are associated with a slightly faster deterioration of hearing through adulthood. Our study revealed no altered susceptibility to noise associated with childhood hearing disorders. Only permanent childhood hearing loss increases the risk of tinnitus in adulthood.

**C17****Body mass index and one single question may predict hip fracture. A NOREPOS study\***

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**Introduction:** Low body weight is a risk factor for hip fracture, and self-perceived health is a strong predictor of later disease and mortality.

**Aims:** To examine the risk of hip fracture combining self-perceived health and Body Mass Index (BMI) in women and men 65 years and above.

**Methods:** Cohort of Norway comprises ten population-based health surveys in Norway (1994-2003). Information about socio-demographic factors, lifestyle, health and diseases were obtained by questionnaires. Weight and height were measured. Hip fractures treated in Norwegian hospitals (1994-2008) were retrieved from computerised patient registers. The analyses in this paper are limited to participants 65 years and above with valid baseline data on self-perceived health, BMI, important covariates and subsequent hip fractures – i.e. 17,127 women and 20,030 men. A variable was constructed with 9 values combining BMI-tertiles and self-perceived health (poor, not so good, good/very good). Cox's proportional hazards models were used to estimate hazard ratios (HR).

**Results:** During median 8.0 years of follow up, 1,963 women and 1,035 men suffered a hip fracture. Age-adjusted risk of hip fracture increased with decreasing BMI ( $p < 0.001$ ) and decreasing self-perceived health ( $p < 0.001$ ). Women in the lowest BMI-tertile with poor self-perceived health had HR=3.6 (2.7-4.9) for hip fracture after adjustment for age, height and smoking, compared with women in the highest BMI-tertile reporting good/very good health. The corresponding HR in men was 6.3 (4.4-9.2). Additional adjustments for other possible confounders, only slightly attenuated the associations.

**Conclusions:** The risk of hip fracture was more than a 3.5-fold increased in women and more than a 6-fold increased in men with poor self-perceived health and BMI below 25 compared with women and men with good/very good health and high BMI. A combination of one question and measured BMI could be a useful tool in clinical practice among elderly.

\* NOREPOS=The Norwegian Epidemiologic Osteoporosis Studies

## C18

### **Twinning rates in Norway in relation to body mass index and height**

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**Introduction:** It is well known that there has been a significant increase in the twinning rate in Norway and other industrialized countries the last three decades. This trend is mostly attributed to delayed childbearing and the use of various assisted reproductive technologies (ART). For Norway a 50 % increase in the incidence of twinning was reported from 1988-2004, even after excluding ART and adjusted for age, and thus remain unexplained. Several studies have noted the role of Body Mass Index (BMI) and height in twinning, being positively correlated with both. Previous twinning studies based on the Medical Birth Registry of Norway (MBRN) have not been able to investigate this since the mother's weight before pregnancy and height was not available at that time.

**Aims:** To investigate the role of Body Mass Index (BMI) and height in twinning.

**Methods:** MBRN is a mandatory nationwide registry comprising all births in Norway since 1967. At the end of 2012 the registry contains information on 2707 721 births. Data on mothers weight before pregnancy and height was collected from 2007 and is currently being reported from around 40 % of birth clinics. Logistical regression was used to test the effect of BMI and height on the twin incidence.

**Results:** Preliminary results show that BMI is significantly associated those who have a BMI of between 30-35 (OR 1.17 95 % CI 1.003-1.38). For those who are underweight (BMI< 18.5) there is a decreased risk of having a twin pregnancy (OR 0.65 95 % CI 0.48-0.88). Height above an baseline of <168 cm is associated with increased risk of twinning (OR 1.11 95 % CI 1.07-1.16).

**Conclusions:** This shows that BMI and height are drivers of twin incidence.

## C19

### Genetic effects on longitudinal changes from healthy to adverse weight and metabolic status – The HUNT study

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**Introduction:** Obesity has become a major global health burden with comorbidities such as metabolic syndrome (MetS), type 2 diabetes and cardiovascular disease. The complexity of disease timing and susceptibility is still poorly understood.

**Aims:** To study the genetic influence on weight gain and increased metabolic risk during adulthood.

**Methods:** Twenty seven previously identified obesity, eating disorder or metabolic risk susceptibility SNPs were tested for association with weight or metabolically related traits longitudinally in 3999 adults participating both in the HUNT2 (1995-97) and HUNT3 (2006-08) surveys. Regression analyses were performed with changes from normal weight to overweight/obesity or from metabolically healthy to adverse developments with regards to blood pressure, glucose, HDL cholesterol, triglycerides levels or metabolic syndrome (MetS) as outcomes.

**Results:** The most substantial effect on BMI-based weight gain from normal to overweight/obesity was observed for the *DRD2* variant ( $P=3.9 \times 10^{-4}$ , adj.  $P=0.015$ ). Furthermore, nominal significant effects were observed for rs560887 (*G6PC2*), rs2075356 (*GHRL*), rs268 (*LPL*), rs10838738 (*MTCH2*) and rs4074134 (*BDNF*). When testing for association to longitudinal adverse developments with regards to blood pressure, blood lipids and glucose, only rs964184 (*ZNFR259/APOA5*) was significantly associated ( $P=5.7 \times 10^{-7}$ ) to unfavourable triglyceride changes after multiple testing. At nominal significance: rs569356 (*OPRD1*), rs268 (*LPL*), rs6810075 (*ADIPOQ*), rs964184 (*ZNFR259/APOA5*) and rs10838738 (*MTCH2*) were associated to various metabolic risk factors. The rs560887 (*G6PC2*), rs533123 (*OPRD1*), rs1049353 (*CNR1*) and rs10242595 (*IL6*) were nominally significant with overall changes to MetS with sex specific effects identified for *IL6* and nearly for *CNR1*. Pleiotropic effects on metabolic traits were observed for several genetic variants cross-sectionally, *ZNFR259/APOA5*, *LPL* and *GRB14* being the most important.

**Conclusions:** *DRD2* exhibits effects on weight gain from normal weight to overweight/obesity. Other variants known to influence reward/addiction processes or eating disorder susceptibility such as *OPRD1*, *BDNF*, *GHRL* and *CNR1*, showed associations to developments of overweight/obesity or adverse metabolic status.

## C20

### **The prevalence of overweight and obesity in The Norwegian Child Growth Study, and the risk for social inequality in child health: a nationally representative study**

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**Introduction:** Overweight and obesity in childhood can have serious consequences for children's health, and may contribute to maintain social inequalities. The Norwegian Child Growth Study (NGS) is an ongoing nationwide study monitoring height, weight and waist circumference among third graders in the same 127 schools, every second year.

**Aims:** The main objective is to monitor overweight, obesity and waist circumference among a nationally representative sample of third graders over time. Secondly, we want to investigate whether this differs in groups according to social background and urbanity.

**Methods:** Almost nine out of ten pupils attended the study in 2008-10-12. The parents gave their written consent, which also allowed us to link the anthropometric measurements to registries. The prevalence of overweight/obesity was calculated based on International Obesity Task Force (IOTF) cut-off values and abdominal obesity as weight-to-height ratio ( $WtHR \geq 0.5$ ). Anthropometric measures were calculated in the national sample, and according to area of residence, maternal education and parental marital status.

**Results:** In 2008 the prevalence of overweight/obesity in boys was 13.6 percent, while in 2010, 15.9 percent and 14.1 percent in 2012. For girls respectively the prevalences were 16.5, 19.8 and 17.6 percent. The average proportion of overweight/obesity and abdominal obesity did not increase during the period, neither among boys nor girls. However, overweight/obesity and abdominal obesity seems to be distributed unevenly. Our findings suggest the proportion to be almost twice as high among pupils living in small municipalities compared to large municipalities. Maternal education level and parental marital status seems to play an important role regarding overweight among children.

**Conclusions:** There is a need in child health promotion and prevention to be aware of groups to encourage good health and prevent social inequality in early childhood.

## C21

### Overweight and obesity among children in Norway by family country background

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**Introduction:** The last decades an increased proportion of immigrants have characterised the population composition in Norway like in other Western countries, and studies have shown that overweight/obesity is more prevalent in some immigrants groups than in the host population. We aimed to examine whether family's country background was associated with general overweight/obesity and abdominal obesity among children and to identify whether there are gender differences.

**Methods:** Height, weight and waist circumference were measured in a nationally representative sample of 3166 eight-year-olds in the 2010 Norwegian Child Growth study. Measurements of both general overweight (including obesity) using IOTF cut-offs, and abdominal obesity (waist-to-height ratio  $\geq 0.5$ ) were included. Ethnicity was determined on the basis of their parents' country of birth; Norwegian, Non-Western and Western. Adjusted prevalence ratios (PR) were calculated by log-binomial regression. Socio-economic position was not adjusted for due to obvious differences in parental education-level in these groups.

**Results:** Children with Non-Western background had 33% higher prevalence of general overweight (including obesity) and 64% higher prevalence of abdominal obesity compared to children with Norwegian background (p-values for difference for both measurements=0.01). The prevalence of general and abdominal overweight/obesity among children with Western background was lower but did not differ significantly compared to children with Norwegian background. Interaction term gender and country background was non-significant for all the anthropometric measurements (p>0.30) and gender stratified analyses were not performed.

**Conclusion:** In this nationally representative study, children with Non-Western background had significantly higher prevalence of general overweight (including obesity) and abdominal obesity compared to children with Norwegian background. The gender difference on overweight/obesity did not differ across country background.



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