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of The Norwegian Epidemiological  
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## THE 7TH NORDIC CONFERENCE ON EPIDEMIOLOGY AND REGISTRY- BASED HEALTH RESEARCH – NORDICEPI 2015

OSLO,

SEPTEMBER 21<sup>ST</sup> - 23<sup>RD</sup> 2015

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## **The 7<sup>th</sup> Nordic Conference on Epidemiology and Registry-based Health Research – NordicEpi 2015 Oslo, September 21<sup>st</sup> - 23<sup>rd</sup> 2015**

We welcome everyone to the 7<sup>th</sup> Nordic Conference on Epidemiology and Registry-based Health Research being held in Oslo this year. The main themes of this year's conference are cohorts, biobanks and registry-based research. Between the Nordic countries there are a substantial number of registers and research databases that stem from administrative health registers and epidemiologic studies. Epidemiological research in the Nordic countries have given us, and will continue to give us, new information that may have substantial influence both on public health and clinical medicine.

The keynote speeches this year represent the themes of the conference and the keynote speakers have made outstanding contributions to epidemiology and public health. The keynote speakers are Jørn Olsen, Denmark, David Leon, Kay-Tee Khaw, and Cathy Elks, UK, Odd O. Aalen, Norway, and Christopher Murray, USA.

The scientific content of the conference includes 136 abstracts accepted as oral presentations, 3-min oral poster presentations, or poster presentations based upon peer review. The research presented covers a wide range of research methods and topics all aimed towards ultimately improving the health status of Nordic populations. The research includes etiologic studies with implications for clinical management and primary prevention, as well as analytical approaches to research challenges, and research infrastructure development. We thank the presenting authors and the abstract reviewers for their contribution to the program.

NordicEpi 2015 would not be possible without the support and assistance by our Nordic colleagues and we thank them for their contributions to the Scientific Committee. We look forward to showing our beautiful capital to all our Nordic colleagues.

The NordicEpi 2015 conference is designed to facilitate learning about epidemiologic research in the Nordic countries, share experience from the participants' research projects, give a Nordic overview, and meet colleagues across the different research themes. In all, we hope this will be an inspiring venue for all involved and we wish you all a happy and inspiring conference.

### **Special thanks for financial support**

We are most grateful for the financial support by NordForsk ([www.nordforsk.org](http://www.nordforsk.org)) and the Norwegian Research Council ([www.forskningsradet.no](http://www.forskningsradet.no)), and for the support received from the commercial sponsors (Alfasoft, Illumina, FluidX, Bergman Diagnostika and the Norwegian Seafood Council). The commercial sponsors had no role in the planning of the conference program. We would also like to express our sincere gratitude to the City of Oslo for generously hosting the conference reception in the City Hall.

***On behalf of the committees for the NordicEpi 2015 conference and the Norwegian Epidemiological Association (NOFE)***

***Grace Egeland, Norwegian Institute of Public Health & University of Bergen, Leader of NOFE***  
***Lise Lund Håheim, Norwegian Knowledge Centre for the Health Service & University of Oslo,***  
***Chair Scientific Committee, NordicEpi 2015***

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# The 7<sup>th</sup> Nordic Conference on Epidemiology and Registry-based Health Research – NordicEpi 2015

## Oslo, September 21<sup>st</sup> - 23<sup>rd</sup> 2015

### Programme overview

#### Monday, September 29<sup>th</sup>

11:00-13:00	Norwegian Epidemiological Association (NOFE) 25 <sup>th</sup> anniversary and annual meeting
13:00-14:00	Lunch
13:30-14:30	<i>Registration</i>
14:30-14:40	Welcome
14:40-15:05	Opening of the conference <b>Geir Stene Larsen</b> , Ministry of Health and Care Services, Norway
15:05-15:45	<b><i>“Cohorts, biobanks, and registry research, the Nordic situation”</i></b> Lecture by <b>Jørn Olsen</b> , Aarhus University, Denmark
15:45-16:15	<i>Coffee break</i>
16:15-17:00	<b><i>“The widespread decline in cardiovascular mortality: a poorly understood triumph”</i></b> Lecture by <b>David Leon</b> , London School of Hygiene and Tropical Medicine, UK
18:00-20:00	Welcome reception at Oslo City Hall

#### Tuesday, September 22<sup>nd</sup>

08:30-09:00	Registration
09:00-09:45	<b><i>“Is ageing modifiable: What can we learn from cohort studies?”</i></b> Lecture by <b>Kay-Tee Khaw</b> , University of Cambridge, UK
09:45-10:00	<i>Coffee break</i>
10:00-10:45	<b><i>“Big data, big opportunities: Using genetics and epigenetics to understand the aetiology of complex traits and diseases”</i></b> Lecture by <b>Cathy Elks</b> , University of Bristol, UK
10:45-11:15	3-minutes oral presentations of posters
11:15-11:45	<i>Coffee break with poster viewing</i>
11:45-12:30	Parallel session I: Oral presentations of submitted abstracts (A1-3, B1-3, C1-3 and D1-3)
12:30-13:30	<i>Lunch</i>
13:30-15:00	Parallel session II: Oral presentations of submitted abstracts (A4-9, B4-9, C4-9 and D4-9)
15:00-15:15	<i>Coffee break</i>
15:15-17:00	Parallel session III: Oral presentations of submitted abstracts (A10-16, B10-16, C10-16 and D10-16)
19:00-	<b><i>Conference dinner at Tjuvholmen Sjømagasin</i></b>

**Wednesday, September 23<sup>rd</sup>**

08:30-09:00	Registration
09:00-09:45	<b><i>“Causal inference in event history analysis”</i></b> Lecture by <b>Odd O Aalen</b> , University of Oslo, Norway
09:45-10:30	<b><i>“Disease burden and risk factors in the Nordic countries – a global perspective”</i></b> Lecture by <b>Christopher Murray</b> , University of Oslo, Norway
10:30-11:00	<i>Coffee break with poster viewing</i>
11:00-12:30	Parallel session IV: Oral presentations of submitted abstracts (A17-22, B17-21, C17-22 and D17-22)
12:30-13:30	<i>Lunch</i>
13:30-15:10	<b><i>“Cohorts, biobanks, and registry research, the Finnish situation”</i></b> Lecture by <b>Anssi Auvinen</b> , University of Tampere, Finland  <b><i>“Cohorts, biobanks, and registry research, the Swedish situation”</i></b> Lecture by <b>Magnus Stenbeck</b> , Karolinska Institutet, Sweden  <b><i>Cohorts, biobanks, and registry research, the Danish situation</i></b> Lecture by <b>Lau Caspar Thygesen</b> , University of Southern Denmark  <b><i>“Cohorts, biobanks, and registry research, the Icelandic situation”</i></b> Lecture by <b>Thor Aspelund</b> , University of Iceland and the Icelandic Heart Association  <b><i>“Cohorts, biobanks, and registry research, the Norwegian situation”</i></b> Lecture by <b>Camilla Stoltenberg</b> , Norwegian Institute of Public Health, Norway
15:10-15:20	<i>Closing of the conference</i>
16:00-19:15	Post-conference seminar: <b>Validity issues in mortality studies</b>

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# The 7<sup>th</sup> Nordic Conference on Epidemiology and Registry-based Health Research – NordicEpi 2015

## Oslo, September 21<sup>st</sup> - 23<sup>rd</sup> 2015

### Detailed programme

#### Monday, September 29<sup>th</sup>

##### Pre-conference programme

##### Bristol Hall

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11:00-13:00	Norwegian Epidemiological Association (NOFE) 25 <sup>th</sup> anniversary and annual meeting
13:00-14:00	<i>Lunch</i>
13:30-14:30	<i>Registration</i>

##### Plenary session

##### Bristol Hall

Session Chairs: Lise Lund Håheim and Per Magnus

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14:30-14:40	Grace M Egeland	Welcome
14:40-15:05	Lise Lund Håheim Geir Stene Larsen	Opening of the conference
15:05-15:45	Jørn Olsen	Cohorts, biobanks, and registry research, the Nordic situation
15:45-16:15		<i>Coffee break</i>
16:15-17:00	David Leon	The widespread decline in cardiovascular mortality: a poorly understood triumph
18:00-20:00		<i>Welcome reception at Oslo City Hall</i>

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**Tuesday, September 22<sup>nd</sup>**

08:30-09:00		<i>Registration</i>	
<b>Plenary session Bristol Hall</b>		Session Chairs: Grethe Tell and Vidar Hjellvik	
09:00-09:45	Kay-Tee Khaw	Is ageing modifiable: What can we learn from cohort studies?	
09:45-10:00		<i>Coffee break</i>	
10:00-10:45	Cathy Elks	Big data, big opportunities: Using genetics and epigenetics to understand the aetiology of complex traits and diseases	
10:45-11:15		3-minutes oral presentations of posters	
	P1	Rune Kvåle	Prostate cancer incidence and mortality trends in four Nordic countries 1975-2012 in men aged under and over 80 years
	P14	Katrine M Owe	Recurrence risk of pregnancy-related pelvic girdle pain. A population-based cohort study
	P26	Thora M Kjærulff	Finasteride use in the male populations of Denmark, Finland, Norway and Sweden
	P27	Morten Andersen	Use of a concept dictionary to integrate different medical classification systems in a multi-country study
	P29	Gerhard Sulo	Younger women do not experience improvements in acute myocardial infarction hospitalization rates – a nationwide study using data from the ‘Cardiovascular disease in Norway 2008-2012’ project
	P33	Jeanette T Jørgensen	General practice utilization in Danish Diet, Cancer, and Health Cohort
	P41	Fartein A Torvik	Contributions of different common mental disorders to sickness absence
	P48	Hanne K Carlsen	Potential health risks associated with exposure to sulphur dioxide from a volcanic source in Iceland
11:15-11:45	P1-P24		<i>Coffee break with poster viewing</i>
<b>Parallel session I, A1-A3 Bristol Hall 1</b>		Session Chairs: Camilla Stoltenberg and Thor Aspelund	
<b>Topic: Work-related epidemiology</b>			
11:45-12:00	A1	Jose H Alfonso	Self-reported occupational skin exposures and risk of long-term sick leave in Norway: a prospective study of the general working population
12:00-12:15	A2	Solbjørg M Myrtveit	Chronic pain and whiplash; is causal attribution associated with ability to work?
12:15-12:30	A3	Sigurd Mikkelsen	Risk of knee meniscal disease in a cohort of airport baggage handlers
<b>Parallel session I, B1-B3 Bristol Hall 2</b>		Session Chairs: Vidar Hjellvik and Marit Veierød	
<b>Topic: Methods</b>			
11:45-12:00	B1	Susanne Strohmaier	Causal Mediation analysis in life-course epidemiology
12:00-12:15	B2	Karina L Møller	Occupational exposure to ultrafine particles among airport employees – Combining personal monitoring and Global Positioning System
12:15-12:30	B3	Ulf A Strömberg	Geomapping of advanced-stage melanoma incidence – a method for addressing skin screening targets



**Parallel session I, C1-C3****Olavssalen****Topic: Environmental epidemiology**

Session Chairs: Anssi Auvinen and Tom K Grimsrud

11:45-12:00	C1	Nikoline N Knudsen	Lithium in drinking water and suicide: A Danish nationwide register-based cohort study using spatial analysis
12:00-12:15	C2	Kristine Vejrurp	Prenatal Methylmercury Exposure and Language Delay at three years
12:15-12:30	C3	Ida H Caspersen	The influence of pre- and postnatal exposure to dioxins and polychlorinated biphenyls on ADHD symptoms and cognitive functions in Norwegian preschool children

**Parallel session I, D1-D3****Mauriske****Topic: Infections**

Session Chairs: Magnus Stenbeck and Elisabeth Strandhagen

11:45-12:00	D1	Håkon Bøås / German Tapia	Safford virus, a human cardiovirus, and persistent islet autoantibodies in a longitudinal birth cohort study
12:00-12:15	D2	Espen Enerly	A registry-based long-term follow-up study of the quadrivalent HPV vaccine in the Nordic countries
12:15-12:30	D3	Nina Gunnes	Influenza Infection in Pregnancy and Risk of Fetal Death: A Norwegian Registry-Based Cohort Study
12:30-13:30			<i>Lunch</i>

**Parallel session II, A4-A9****Bristol Hall 1****Topic: Cancer**

Session Chairs:

Elisabeth Strandhagen and Tom K Grimsrud

13:30-13:45	A4	Katja Kemp Jacobsen	Cigarette smoking (active and passive) and mammographic density in the Danish Diet, Cancer and Health cohort
13:45-14:00	A5	Marta Román	Risk of different breast cancer subtypes by type of menopausal hormone therapy
14:00-14:15	A6	Mette L Lousdal	Effect of organized mammography screening on stage-specific incidence in Norway: population-based study
14:15-14:30	A7	Marte M Reigstad	Risk of Childhood and Adolescent cancer after Assisted Reproductive Technology in Norway
14:30-14:45	A8	Mette H Møller	Trends in stage-specific incidence of prostate cancer in Norway, 1980-2010: A population-based study
14:45-15:00	A9	Inger K Larsen	Different cancer incidence trends in Norwegian counties

**Parallel session II, B4-B9****Bristol Hall 2****Topic: Methods**

Session Chairs: Henrik Støvring and Miia Artama

13:30-13:45	B4	Sjur Lehmann	Validity of Acute Caesarean Section Registration in the Medical Birth Registry of Norway
13:45-14:00	B5	Jon M Gran	Causal inference in a multi-state model for sickness absence and return to work
14:00-14:15	B6	Per-Henrik Zahl	Bias in observational studies of the association between menopausal hormone therapy and breast cancer
14:15-14:30	B7	Sören Möller / Ulrich Halekoh	The Heritability of Breast Cancer among women in the Nordic Twin Study of Cancer
14:30-14:45	B8	Andrea Bellavia	Evaluating survival percentiles
14:45-15:00	B9	Harald Weedon-Fekjær	Risk time splitting for precise evaluation of screening programs; The importance of exact separation of comparison groups

**Parallel session II, C4-C9****Olavssalen****Topic: Child and maternal health**

Session Chairs: Thor Aspelund and Jørn Olsen

13:30-13:45	C4	Arthur Chortatos	Pregnancy complications and birth outcomes among women experiencing nausea only or nausea and vomiting during pregnancy in the Norwegian Mother and Child Cohort Study
13:45-14:00	C5	Petter Kristensen	Birth weight, perinatal mortality, and the family: a sibling study of singletons born at term in Norway, 1967-2011
14:00-14:15	C6	Védís H Eiríksdóttir	Pregnancy-induced hypertensive disorders before and after a national economic collapse: a population based cohort study
14:15-14:30	C7	Iqbal Al-Zirqi	Risk factors for complete uterine rupture after trial of labor in intact uterus
14:30-14:45	C8	Ketil Størdal	Duration of breastfeeding and risk of coeliac disease in the MoBa cohort
14:45-15:00	C9	Agnes Gísladóttir	Maternal exposure to sexual violence and subsequent neonatal outcomes

**Parallel session II, D4-D9****Mauriske****Topic: Cardiovascular disease**

Session Chairs: Per Magnus and Marta Ebbing

13:30-13:45	D4	Jo S Stenehjem	The combined effect of obesity and physical activity on risk of hypertension: the Nord-Trøndelag Health Study, Norway
13:45-14:00	D5	Laila A Hopstock	Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: The Tromsø Study 1979-2008.
14:00-14:15	D6	Anne E Eggen	The seventh Tromsø Study survey 2015-2016. Anything new? Short preliminary report.
14:15-14:30	D7	Elías F Guðmundsson	Analysis and comparison of death rates from ischemic heart disease in the Nordic- and Baltic countries during the period 1981-2009, in the age group 25-74 years.
14:30-14:45	D8	Kirsti Lund Vik	Transgenerational effects of parental cardiovascular disease and risk factors on offspring mortality: family-linkage data from the HUNT Study, Norway
14:45-15:00	D9	Annette K Ersbøll	Health atlas – mapping the acute myocardial infarction incidence in Denmark
15:00-15:15			<i>Coffee break</i>

**Parallel session III, A10-A16****Bristol Hall 1****Topic: Cancer**

Session chairs: Grethe Tell and Magnus Stenbeck

15:15-15:30	A10	Jo S Stenehjem	Pulmonary function in lymphoma survivors after high-dose chemotherapy with autologous stem cell transplantation: a national cross-sectional study
15:30-15:45	A11	Shadi Azam	Hormone replacement therapy, mammographic density, and breast cancer risk: a cohort study
15:45-16:00	A12	Jan H S Mortensen	Maternal supplemental folic acid and risk of childhood cancer
16:00-16:15	A13	Jo S Stenehjem	Exercise capacity in lymphoma survivors after high-dose chemotherapy with autologous stem cell transplantation: a national cross-sectional study
16:15-16:30	A14	Stefan Lönnberg / Suzanne Cambell	Cervical cancer prevented by screening: long-term incidence trends by morphology in Norway
16:30-16:45	A15	Marta Román	Risk of breast cancer after false positive results in mammographic screening
16:45-17:00	A16	Svetlana Sosnina	Health effects of parental radiation exposure: hemolymphoblastoses

**Parallel session III, B10-B16****Bristol Hall 2****Topic: Miscellaneous topics**

Session chairs: Jørn Olsen and Anssi Auvinen

15:15-15:30	B10	Torkjel M Sandanger	Smoking-induced genome-wide methylation changes with time since smoking cessation, and subsequent changes in gene expression
15:30-15:45	B11	Ann K Knudsen	The Norwegian Burden of Disease Project – aims for the Norway project and results for Norway from the Global Burden of Disease (GBD) Project 2010
15:45-16:00	B12	Marianne B Johnsen	Leisure time physical activity and the risk of hip or knee replacement due to primary osteoarthritis – a population based cohort study The Nord-Trøndelag Health Study (HUNT)
16:00-16:15	B13	Simon Øverland	A work-focused intervention to increase work participation in common mental disorders. Multicenter RCT with registry-based long-term outcomes.
16:15-16:30	B14	Karina S Olsen	Stress related to a suspicious mammogram – potential transcriptomic effects
16:30-16:45	B15	Audun Brunes	Visual impairment, physical activity, and all-cause mortality – The HUNT Study
16:45-17:00	B16	Grete H Bratberg	Gender differences and gender convergence in alcohol use over the past three decades. The HUNT Study, Norway

**Parallel session III, C10-C16****Olavssalen****Topic: Child and maternal health**

Session chairs: Per Magnus and Henrik Støvring

15:15-15:30	C10	Karl Mårild	Infections and Risk of Celiac Disease in Childhood: A Prospective Nationwide Cohort Study
15:30-15:45	C11	Elisabeth K Bjelland	Pelvic pain after childbirth: a longitudinal population study
15:45-16:00	C12	Ingvil K Sørbye	Does migration influence preterm birth rates? A comparison between estimates for source countries and rates after migration to Norway
16:00-16:15	C13	Ragnhild Flingtorp	The use of multiple Norwegian health registries to assess vaccine safety: Congenital anomalies among infants born to mothers exposed to the HPV vaccine during pregnancy
16:15-16:30	C14	Olga A Kharkova	Maternal smoking and predictors of quitting smoking during pregnancy; the Murmansk county birth registry, Northwest Russia
16:30-16:45	C15	Ingvil K Sørbye	Birthweight in Norway by the maternal country of birth
16:45-17:00	C16	Anne L Brantsæter/ Helle M Meltzer	Diet during pregnancy – does it matter in a well-nourished population?

**Parallel session III, D10-D16****Mauriske****Topic: Pharmacoepidemiology**

Session chairs: Marit Veierød and Vidar Hjellvik

15:15-15:30	D10	Andrius Kavaliunas	The influence of immunomodulatory treatment on the clinical course of multiple Sclerosis
15:30-15:45	D11	Marte Handal	Use of Folic acid and antidepressants during pregnancy and child language development
15:45-16:00	D12	Maria C Magnus	Prenatal and infant paracetamol exposure and development of asthma: the Norwegian Mother and Child Cohort Study
16:00-16:15	D13	Angela Lupattelli	Risk of preeclampsia after use of antidepressants in pregnancy: a study from the Norwegian Mother and Child Cohort Study
16:15-16:30	D14	Solveig Sakshaug	Long-term users of z-hypnotics – high level of co-medication with other addictive drugs
16:30-16:45	D15	Ingeborg Hartz	Antidepressant drug use among adolescents during 2004-2013 – a population-based linkage study between the nationwide prescription database and patient register
16:45-17:00	D16	Mari Hoff	Use of anti-osteoporotic drugs among women in central Norway after a forearm fracture

19:00-

*Conference dinner at Tjuvholmen Sjømagasin*

**Wednesday, September 23<sup>rd</sup>**

08:30-09:00			<i>Registration</i>
<b>Plenary session Bristol Hall</b>			Session Chairs: Marit Veierød and Marta Ebbing
09:00-09:45		Odd O. Aalen	Causal inference in event history analysis
09:45-10:30		Christopher Murray	Disease burden and risk factors in the Nordic countries – a global perspective
10:30-11:00	P25-P49		<i>Coffee break with poster viewing</i>
<b>Parallel session IV, A17-A22 Bristol Hall 1</b>			Session Chairs: Marta Ebbing and Thor Aspelund
<b>Topic: Cardiovascular disease</b>			
11:00-11:15	A17	Bjarne M Nes	Cardiorespiratory fitness in cardiovascular risk prevention: the HUNT Study
11:15-11:30	A18	Ekaterina Sharashova	Secular changes in cardiovascular risk factors in the general population; the Tromsø study 1986-2007.
11:30-11:45	A19	Børge Moe / Tom I L Nilsen	Glycaemic control in people with diabetes influences the beneficial role of physical activity on cardiovascular mortality. Prospective data from the HUNT Study, Norway.
11:45-12:00	A20	Rupali Akerkar	Acute myocardial infarction and stroke in Norway 2012-2013: Regional variations in age-adjusted hospitalization rates and survival.
12:00-12:15	A21	Aleksandra Pirnat	Pre-pregnant lipid levels and triglyceride/HDL-cholesterol ratio in one-child mothers
12:15-12:30	A22	Hilde K R Riise	Pregnancy complications and later maternal morbidity and mortality in Norwegian women
<b>Parallel session IV, B17-B21 Bristol Hall 2</b>			Session Chairs: Per Magnus and Anssi Auvinen
<b>Topic: Mental health</b>			
11:00-11:15	B17	Gunnhild Å Vie	Couples' self-reported health before and after disability pension over two decades – the HUNT Study
11:15-11:30	B18	Bjørn H Strand	ApoE Gene and Lifestyle Interactions for Risk of Dementia Mortality
11:30-11:45	B19	Erika Olsson	Vitamin D does not predict dementia or cognitive impairment – a 20 year follow up study in community living old men.
11:45-12:00	B20	Mika Gissler	The impacts of childhood conditions on young adults' secondary level education in the 1987 Finnish Birth Cohort.
12:00-12:15	B21	Mikael Thinggaard	Advances in survival among the very old are seen across the spectrum of health and functioning

**Parallel session IV, C17-C22****Olavssalen****Topic: Obesity**

Session Chairs: Elisabeth Strandhagen and Jørn Olsen

11:00-11:15	C17	Haakon Meyer	Abdominal obesity and the risk of hip fracture in postmenopausal women: Results from the Nurses' Health Study
11:15-11:30	C18	Linn M Sorbye	Pre-pregnant body mass index, gestational weight gain and physical activity: effects on Apgar score in a prospective pregnancy cohort
11:30-11:45	C19	Marit Næss	Intergenerational transmission of overweight and obesity from parents to their adolescent offspring – a HUNT Study.
11:45-12:00	C20	Trine T Eik-Nes	Women's weight and disordered eating in a large community sample: The HUNT study
12:00-12:15	C21	Eleni Papadopoulou	Caffeine intake during pregnancy and early growth and obesity in childhood
12:15-12:30	C22	Anne B Hansen	Night-shift work and risk of diabetes in the Danish Nurse Cohort

**Parallel session IV, D17-D22****Mauriske****Topic: Infrastructure**

Session Chairs: Camilla Stoltenberg and Tom Grimsrud

11:00-11:15	D17	Johanna Ekström	Promoting reuse of research data- The Scania Metadatabase for Epidemiology
11:15-11:30	D18	Hilde Engjom	Obstetric health system structure and perinatal outcomes in Norway
11:30-11:45	D19	Morten Andersen	Implementing a Nordic Common Data Model for register-based pharmacoepidemiological research
11:45-12:00	D20	Bodil Stenvig	Visualizing a Research Infrastructure giving access to Nordic Health Data
12:00-12:15	D21	Sonja Myhre	The eRegistry for maternal and child health: Legal and ethical guidance for low and middle income countries
12:15-12:30	D22	Anne Kouvonen	National Trends in Main Causes of Hospitalisation in Working-Age Population, Finland, 1976 to 2010
12:30-13:30			<i>Lunch</i>

**Plenary session****Bristol Hall**

Session Chairs: Elisabeth Strandhagen, Tom K Grimsrud, Henrik Støvring and Vidar Hjellvik

13:31-13:50	Anssi Auvinen	<i>Cohorts, biobanks, and registry research, the Finnish situation</i>
13:50-14:10	Magnus Stenbeck	<i>Cohorts, biobanks, and registry research, the Swedish situation</i>
14:10-14:30	Lau C Thygesen	<i>Cohorts, biobanks, and registry research, the Danish situation</i>
14:30-14:50	Thor Aspelund	<i>Cohorts, biobanks, and registry research, the Icelandic situation</i>
14:50-15:10	Camilla Stoltenberg	<i>Cohorts, biobanks, and registry research, the Norwegian situation</i>
15:10-15:20	Signe Opdahl	Closing of the conference

## List of posters

### Presentation by authors Tuesday 22<sup>nd</sup> 11:15 – 11:45

#### Cancer

P1	Rune Kvåle	Prostate cancer incidence and mortality trends in four Nordic countries 1975-2012 in men aged under and over 80 years
P2	Lyudmila Lebedeva/ Andrej M Grjibovski	Survival of patients with colon cancer before and after implementation of the National project “Health” in the Arkhangelsk Region, Northwest Russia: a registry-based study.
P3	Merete Ellingjord-Dale	The association between risk factors and breast cancer subtypes in a cohort from the Norwegian Breast Cancer Screening Program
P4	Hilde Langseth/ Randi Gislefoss	Integrating research activities in the Janus Serumbank and Cancer Registry of Norway
P5	Nailya R Kabirova	Cancer incidence among the descendants of the exposed fathers
P6	Katrine D Skyrud	Regional variation in cancer survival and the impact of stage, socioeconomic status, comorbidity and treatment
P7	Bjørn Fjukstad	Interactive omics data exploration in epidemiological studies
P8	Cassie Trewin	Trends in breast cancer incidence and mortality by education level in Norway, 1971-2009
P9	Christian Jonasson	Cancer prevalence and incidence in the Nord-Trøndelag Health Study
P10	Marta Román	Balancing the benefits and harms among women targeted by the Norwegian Breast Cancer Screening Program
P11	Ann K Knudsen	Does it help to worry? The prospective association between health anxiety and cancer detection
P12	Mikhail E Sokolnikov	Radiation epidemiology studies of Mayak workers
P13	Michael Osipov	Epidemiological Registry: Protecting Patients from Medical Exposure

#### Child and maternal health

P14	Katrine M Owe	Recurrence risk of pregnancy-related pelvic girdle pain. A population-based cohort study
P15	Iqbal Al-Zirqi	Risk factors for complete uterine rupture after trial of labor in scarred uterus
P16	Inger J Bakken	Incidence of febrile seizure in young children
P17	Védís H Eiríksdóttir	The effect of the economic collapse on birth outcomes in Iceland: a 4 year follow-up
P18	Andrea Mikkelsen/ Kirsten Mehlig	Associations between blood fatty acids and allergy in a sample of children in Europe

#### Work-related epidemiology

P19	Lau C Thygesen	Subacromial shoulder disorders among baggage handlers: an observational cohort study
P20	Charlotte Brauer	Associations between occupational lifting and low back disorders – registry based data from the Copenhagen Airport Cohort
P21	Ingrid S Mehlum	Do psychosocial working conditions mediate social inequalities in musculoskeletal and psychiatric sickness absence in a life-course perspective?

#### Obesity

P22	Jonas M Kinge	Educational inequalities in obesity and gross domestic product: evidence from 70 countries
P23	Ingeborg Forthun	Maternal body mass index and risk of cerebral palsy
P24	Anne Jølle	Elevated FINDRISC in a general population. The HUNT DE-PLAN Study in Norway

**Presentation by authors Wednesday 23<sup>rd</sup> 11:15 – 11:45****Pharmacoepidemiology**

P25	Ingunn Björnsdóttir	Prescription registry quality responsibilities, – a case from Iceland
P26	Thora M Kjærulff	Finasteride use in the male populations of Denmark, Finland, Norway and Sweden
P27	Morten Andersen	Use of a concept dictionary to integrate different medical classification systems in a multi-country study
P28	Ingunn F Tvete	A five year follow-up prescription registry study: the impact of starting with diazepam versus oxazepam

**Cardiovascular disease**

P29	Gerhard Sulo	Younger women do not experience improvements in acute myocardial infarction hospitalization rates – a nationwide study using data from the ‘Cardiovascular disease in Norway 2008-2012’ project
P30	Lise Lund Håheim	Oral infections predict mortality. A 12 ½-year follow-up of the Oslo II-study
P31	Grace M Egeland	Mediators of the educational gradient predicting post-delivery hypertension in women: A linkage study between Norwegian Mother and Child Cohort and the Norwegian Prescription Database.
P32	Marie S Kristensen	Evaluation of the psychometric properties in a core Heart-disease health-related Quality-of-Life questionnaire (the HeartQoL) in a Danish population with atrial fibrillation

**Miscellaneous topics**

P33	Jeanette T Jørgensen	General practice utilization in Danish Diet, Cancer, and Health Cohort
P34	Magnus Stenbeck	Sharing experiences and programming code for register based research
P35	Jonas M Kinge	Musculoskeletal disorders in Norway: prevalence of chronicity and use of primary and specialist health care services
P36	Ulrika Hahn-Lundström/ Alessandro Gasparini	Association between age, renal function, disease progression, and the probability of renal replacement therapy initiation using nationwide data from the Swedish Renal Registry
P37	Thomas S Nilsen	Historical twinning rates in Norway
P38	Catherine E Bowen/ Vegard Skirbekk	How long do young adults want and expect to live?
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P41	Fartein A Torvik	Contributions of different common mental disorders to sickness absence
P42	Eivind Ystrøm	Common genetic and environmental risk factors for psychosis, mania, and personality disorders
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P44	Annette L Kleppang	The psychometric properties of the Hopkins Symptom Checklist – 10: A Rasch analysis based on Norwegian adolescent data.
P45	Kristin Gärtner	Alcohol and Drug Use among Internationally Adopted Adolescents: Results from a Population-Based Study of Norwegian Adolescents.
P46	Lau C Thygesen	Can municipality-based post-discharge follow-up visits including a general practitioner reduce early readmission among high-risk people 65+ years old? Results from a randomised controlled trial

**Environmental epidemiology**

P47	Bente Oftedal	Noise sensitivity, noise exposure and subjective health complaints
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**Infections**

P49	Sara Ghaderi	Occurrence of encephalitis after an influenza infection: A population-based cohort study in Norway
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## ABSTRACTS

### A1

#### **Self-reported occupational skin exposures and risk of long-term sick leave in Norway: a prospective study of the general working population**

**Jose H. Alfonso**,<sup>1,2</sup> Tore Tynes,<sup>3</sup> Jacob P. Thyssen,<sup>4</sup> Jan-Ø. Holm,<sup>2,5</sup>  
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**Introduction:** The overall evidence for occupational skin exposures as risk factors for physician certified long-term sick leave (LTSL) in the general working population of Norway is limited.

**Aims:** To investigate the impact of occupational skin exposures on physician-certified LTSL, and to estimate the population-attributable risks (PAR) attributable to skin exposures.

**Methods:** Randomly drawn from the general population, the cohort comprised working women and men aged 18-69 years (N=12 255, response at the baseline=61%) (Nationwide Survey of Level of Living – Working Conditions (Statistics Norway)). The study measured 11 occupational chemical, physical and biological exposures in 2009, and medically confirmed LTSL of 16 days or more during 2010 was the outcome of interest (Norwegian Labour and Welfare Administration's sickness benefit register). Adjustment for a wide range of competing explanatory variables such as mechanical, psychosocial work factors, and sociodemographic factors was made.

**Results:** After adjustments in the multivariate analysis, the most important predictors for LTSL for men were skin exposure to cleaning products (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.1 to 2.5), and waste (OR, 2.1; 95% CI, 1.1 to 3.7), while for women it was water (OR = 1.3; 95% CI, 1.0 to 1.6). The population risk that was attributable to these factors was 14.5%.

**Conclusions:** This study underlines the contribution of occupational skin exposures to cleaning products and waste among men; and water among women as important risk factors for LTSL. The PAR of 14.5% suggests a potential for prevention in the general working population of Norway.



## A2

### Chronic pain and whiplash; is causal attribution associated with ability to work?

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**Background:** Though most individuals who experience whiplash recover rapidly, some develop chronic whiplash, a condition characterized by pain and reduced ability to work.

**Aim:** We aimed to investigate whether attributing pain (neck pain or any chronic pain) to whiplash is associated with full time work and receipt of disability pension. Any such association would further be investigated in relation to differences in reported pain and psychological complaints between those attributing pain to whiplash and those not.

**Methods:** Data from the sixth wave of the Tromsø Study (2007-08, n=12,981) were analyzed. Using logistic regression analyses, the odds ratio (OR) of working full time and of receiving disability pension was computed for individuals attributing their chronic neck pain to whiplash compared to individuals reporting chronic neck pain due to other causes (reference category). Analyses were adjusted for socio-demographics, pain characteristics and psychological distress. These same analyses were run, comparing individuals attributing any chronic pain to whiplash compared to individuals reporting any chronic pain due to other causes.

**Results:** In individuals reporting chronic neck pain and in individuals reporting any chronic pain, the odds of working full time was significantly lower (crude OR= 0.73 (95%CI: 0.55-0.97) and OR=0.61 (95%CI: 0.47-0.80) respectively) and the odds of receiving disability pension significantly higher (crude OR= 1.58 (95%CI: 1.18-2.12) and OR= 2.02 (95%CI: 1.53-2.66) respectively) when pain was attributed to whiplash. For both chronic neck pain and any chronic pain the association between pain attribution and work and benefit status remained significant after adjusting for pain and psychological distress.

**Conclusions:** Individuals attributing their chronic pain to whiplash are less likely to work full time and more likely to receive disability pension than individuals with chronic pain due to other causes. This association remains after adjusting for pain characteristics and psychological distress.

## A3

### Risk of knee meniscal disease in a cohort of airport baggage handlers

**Sigurd Mikkelsen**<sup>1</sup>, Lau C. Thygesen<sup>2</sup>, Ellen B. Pedersen<sup>1</sup>, Karina L. Møller<sup>2</sup>, Tine Alkjær<sup>3</sup>, Henrik Koblauch Baldvinsson<sup>3</sup>, Erik Simonsen<sup>3</sup>, Charlotte Brauer<sup>1</sup>

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**Introduction:** Meniscal diseases are common and often related to acute sports injuries. Studies of risks associated with long-lasting loads on the knees are few, and information on exposure and outcome may not be independent.

**Aims:** To study the effect of cumulative years as a baggage handler on the incidence of meniscal disease.

**Methods:** We used electronic company employment and union member registers to establish a historical cohort of unskilled workers who had been gainfully employed some time during the period from 1990 to 2012, either as a baggage handler in Copenhagen Airport or with other employers in the greater Copenhagen area (Copenhagen Airport Cohort). We followed the cohort in national Danish registers to obtain information on diagnoses, surgery, mortality, migration, and pensioning. The primary exposure measure was cumulative years as a baggage handler and the outcome was a hospital discharge diagnosis of a meniscal disease or surgery on the menisci. We adjusted for effects of age, education, calendar year and use of mechanical aids to reduce baggage handling loads.

**Results:** Baggage handlers (N=3,313) had a higher incidence of meniscal disease than the reference group (N=64,060). The adjusted incidence rate ratio (IRR<sub>Adj</sub>) was 1.54 (95% confidence interval(CI): 1.25-1.92). The incidence for baggage handlers increased by increasing cumulative exposure during the first 5 years as a baggage handler (IRR<sub>Adj</sub>=1.79 per 5 years (95%CI: 1.21-2.66) and then decreased to reach unity after 20-25 years as a baggage handler.

**Conclusion:** In this large cohort study we found that the risk of meniscal disease increased during the first five years as a baggage handler and then slowly decreased. A causal effect of baggage handling on meniscal disease may explain the increasing risk during the first five years. The subsequent slow decrease may be explained as a vulnerability effect or a healthy worker effect.

**A4****Cigarette smoking (active and passive) and mammographic density in the Danish Diet, Cancer and Health cohort**

**Katja Kemp Jacobsen**<sup>1</sup>, Elsebeth Lynge<sup>1</sup>, Ilse Vejborg<sup>2</sup>, Anne Tjønneland<sup>3</sup>, My von Euler-Chelpin<sup>1</sup>, Zorana Andersen<sup>1</sup>

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**Introduction:** Smoking is a newly recognized risk factor for breast cancer, but the biological mechanism remains unknown, and may involve mammographic density (MD), one of the strongest biomarkers of breast cancer risk.

**Aims:** We aimed to examine if active and passive smoking were associated to MD in pre- and postmenopausal women.

**Methods:** For the 5,356 women (4,489 postmenopausal) participants in the Danish Diet, Cancer and Health cohort (1993-1997) who attended mammographic screening in Copenhagen (1993-2001), we used MD assessed at the first screening after cohort entry. MD was defined as mixed/dense or fatty. Information on smoking (status, duration, intensity, passive smoking) was assessed at cohort baseline (1993-1997) via questionnaire. Logistic regression was used to estimate associations (odds ratios (ORs) and 95% confidence intervals between smoking and MD, adjusting for confounders, and separately by menopause, hormone therapy (HT) use and body mass index (BMI).

**Results:** Majority of women, 2,026 (56.5%) had mixed/dense MD. 2,214 (41.4%) of women were current and 1,175 (21.9%) past smokers. Current smokers had lower odds (OR: 0.86, 95% confidence interval: 0.75-0.99) of having mixed/dense MD compared to never smokers, while former smoking was not associated with MD. Women who initiated smoking before age 16 years (0.79, 0.64-0.96), smoked  $\geq 15$  cigarettes per day (0.83, 0.71-0.98), smoked  $> 30$  years (0.86, 0.75-0.99) had smallest odds of having mixed/dense breast. The odds of having mixed/dense breasts increased with increasing time since smoking cessation, with ORs in women who quit smoking  $> 20$  years ago as compared to current smokers (1.37, 1.01-1.67). There was no effect modification between active smoking and MD by menopausal status, HT use or BMI.

**Conclusions:** Active smoking decreases MD, indicating that the pathway between smoking and breast cancer risk does not involve MD.

**A5****Risk of different breast cancer subtypes by type of menopausal hormone therapy**

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**Introduction:** There is substantial evidence that menopausal hormone therapy is a risk factor for breast cancer, with combined estrogen and progestin therapy (EPT) presenting a greater risk than estrogen therapy (ET) alone. Data are inconclusive on the effects that different estrogens and progestin therapies have on tumour characteristics.

**Aims:** To assess the associations of oral ET formulations of estradiol, tibolone and EPT preparations of estradiol-norethisterone (NETA), with histological subtypes and hormone receptor status of breast cancer.

**Methods:** Nationwide retrospective cohort study including data from 686,614 Norwegian women, aged 45-79 in January 2004, followed until December 2008. The Norwegian Prescription Database provided information on HT use. Breast cancer incidence was obtained from the Cancer Registry of Norway. Poisson regression was used to estimate incidence rate ratios (RR) and 95% confidence intervals (CI).

**Results:** During an average 4.8 years of follow-up, 8877 breast cancers were diagnosed. Compared with non-users, there was some increased risk of breast cancer overall with oral ET (RR:1.26; 95%CI: 1.04-1.56) and tibolone (RR:1.91; 95%CI: 1.61-2.28), and substantial increased risk associated with combined EPT (RR:2.76; 95%CI: 2.52-2.97). Use of estradiol and tibolone was more strongly associated with lobular cancers (RR:2.00; 95%CI: 1.22-3.29; and RR:2.56; 95%CI: 1.57-4.15, respectively), and ER+/PR+ tumours (RR:1.71; 95%CI: 1.31-2.24; and RR:2.58; 95%CI: 2.04-3.25, respectively). These associations were almost twice as large for the EPT preparations. Users of oral estradiol-NETA preparations of Kliogest®, Activelle®, and Trisekvens® showed a strong association with lobular cancers (RR:4.57; 95%CI: 3.18-6.58; RR:4.50; 95%CI: 3.51-5.76; and RR:3.76; 95%CI: 2.00-7.04, respectively), and ER+/PR+ tumors (RR:3.80; 95%CI: 3.11-4.64; RR:3.79; 95%CI: 3.32-4.32; and RR:3.65; 95%CI: 2.61-5.10, respectively).

**Conclusions:** Users of estradiol-NETA components of Kliogest®, Activelle® and Trisekvens® were strongly associated with breast cancer overall and also with certain tumour characteristics, such as lobular cancer and cancer expressing ER and PR.

## A6

### Effect of organized mammography screening on stage-specific incidence in Norway: population-based study

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**Introduction:** Down-staging of breast cancer is essential for effective mammography screening. In a previous study of breast cancer screening, we reported increased early-stage incidence without subsequent reductions in late-stage. The study did not, however, account for the gradual introduction of screening across counties.

**Aims:** To compare the stage-specific incidence in birth cohorts invited to screening with incidence prior to organized screening relative to younger, concurrent cohorts based on counties.

**Methods:** We designed a population-based, open cohort study covering the introduction of organized screening in Norway, county-by-county during 1995-2004. Data on stage, birth year, and county of residence at date of diagnosis were obtained from the Cancer Registry of Norway for all women born 1917-1980 and diagnosed with first-time in situ or invasive breast cancer 1987-2011 (29.4 million person-years). Trends in stage-specific incidence in cohorts invited for screening were compared to younger cohorts by Poisson regression adjusted for calendar time, age, and their potential interaction. For the younger reference group “pseudo-implementation” of the program was constructed. Lead-time was accounted for by extension of follow-up for birth cohorts to include the compensatory drop. Moreover, tumor size was analyzed as an alternative outcome. Missing information was multiply imputed.

**Results:** When including the compensatory drop, we found a 70% (95% CI: 52%; 90%) increase in localized cancers in birth cohorts invited to screening compared to a younger reference group. At the same time the incidence of advanced stages (III and IV) remained stable with a 7% increase (-14%; 33%). Findings were similar for tumor size.

**Conclusions:** Screening was followed by a considerable increase in early-stage cancers, but no corresponding decrease in late-stage cancers despite longer follow-up of cohorts and a more precise measure of exposure than in the previous study. Whether the findings are compatible with long lead-times, overdiagnosis or other explanations is unclear.

## A7

**Risk of childhood and adolescent cancer after assisted reproductive technology in Norway**

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**Introduction:** An increasing number of children are born after assisted reproductive technology (ART), and their health is therefore of interest. Several studies have found elevated risks of cancer in children conceived by ART, whereas others have not.

**Aims:** The aim of the current study is to compare cancer risk in children born after ART in Norway to that in children born after natural conception.

**Methods:** Information on all children born in Norway between 1984 and 2011 was extracted from the Medical Birth Registry of Norway (MBRN). Cancer data on these children was obtained by linkage to the Cancer Registry of Norway (CRN). Follow up was started at birth, and ended on the first cancer, death, emigration, or 31<sup>st</sup> December 2011. A Cox proportional hazards model was used to calculate hazard ratio (HR) and 95% confidence intervals (CI) for cancer between ART children and non-ART children. The overall cancer risk was assessed, as well as the risk for the most common childhood cancer sites. Adjustments were made for year of birth, sex, birth order, birth weight, gestational length, area of residence and maternal age at birth.

**Results:** A total of 1 628 658 children made up the study cohort, out of whom 25 587 were born as a result of ART. There were 51 cancers in the ART group, and 4503 in the non-ART group. No increased risk of overall cancer was found, HR 1.23 (95% CI 0.91-1.66). The risk of leukemia was increased for ART children compared to controls, HR 1.67 (95% CI 1.02-2.73).

**Conclusions:** This population-based cohort study found elevated risk of leukemia in children born after ART, but no overall risk increase of cancer, compared to children conceived without ART.

**A8****Trends in stage-specific incidence of prostate cancer in Norway, 1980-2010: A population-based study**

**Mette H. Møller**<sup>1</sup>, Ivar S. Kristiansen<sup>2</sup>, Christian Beisland<sup>3</sup>, Jarle Rørvik<sup>4,5</sup>, Henrik Støvring<sup>6</sup>

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**Background:** Opportunistic PSA-testing intends to advance diagnosis thereby shifting the stage distribution towards less advanced stages.

**Aims:** To estimate changes in the stage distribution of prostate cancer (PC) after the introduction of opportunistic PSA-testing.

**Methods:** From the Cancer Registry of Norway we obtained cancer stage, age and year of diagnosis on all men over the age of 50 diagnosed with PC during the period 1980-2010 in Norway. Three calendar-time periods were defined: One before the introduction of PSA-testing (1980-1989) and two after reflecting increasing diagnostic intensity, (1990-2000 and 2001-2010); and three age groups: men eligible for screening (50-65 and 66-74) or older (75+). Birth-cohorts were categorized into four intervals: <1910, 1916-1925, 1926-1940 and >1941. We used Poisson regression to conduct a cross-sectional and a cohort-based analysis of trends in the incidence of localised, regional and distant cancer, respectively.

**Results:** The annual incidence of localised PC among men aged 50-65 and 66-74 rose from 41.4 and 255.2 per 100,000, respectively, before the introduction of PSA-testing to 137.9 and 418.7 in 2001-2010 afterwards, corresponding to 3.3 (CI: 3.1; 3.5) and 1.6 (CI: 1.6; 1.7) fold increases. The incidence of regional cancers increased by a factor seven and four among men aged <75 and 75+, respectively. The incidence of distant cancers among men aged 75+ decreased from 218.8 to 155.1 per 100,000, corresponding to a decrease of 0.7 (CI: 0.7; 0.8). The cohort-based analysis showed that the incidence of localised and regional PC shifted downwards to younger men, with a gradually decreased incidence of distant cancer in more recent cohorts.

**Conclusion:** Opportunistic PSA-testing substantially increased the incidence of localised and regional PC among men aged 50-74 years. The increase was not fully compensated in absolute numbers by the decrease in incidence of distant PC in older men, although it decreased by 30%.

## A9

### Different cancer incidence trends in Norwegian counties

**Inger K. Larsen**, Tor Å. Myklebust, Trude E. Robsahm, Tom K. Grimsrud, Tom B. Johannesen, Gry B. Skare, Solveig Hofvind, Steinar Tretli, Giske Ursin, Bjørn Møller

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**Introduction:** Time trends in cancer incidence are pivotal when evaluating the effect of temporal changes in risk factors. Similarly, descriptive geographical differences in the rates can support the association to known geographical distributions of risk factors and potentially give rise to new hypotheses that may explain why some cancers are more or less frequent.

**Aims:** To present the cancer incidence trends for selected cancer sites, by sex and county.

**Methods:** Age-standardised incidence rates with corresponding 99% confidence intervals were calculated by sex and county for all cancers combined, and for the 14 most common cancer types. Secular trends are presented for five-year periods over the 60 year period 1954–2013 for all 19 counties.

**Results:** Large differences in the rates for all cancers combined were observed, most pronounced for men. In the last five year-period (2009–13), the age-standardised incidence rate per 100 000 was lowest in Finnmark (men 333.4, women 258.9) and highest in Vestfold (men 419.6, women 318.0). Among cancer sites with the largest differences between the counties were malignant melanoma, non-melanoma skin cancer, lung cancer and prostate cancer. For malignant melanoma, a distinct north/south- gradient was observed, with a notable exception in Sør-Trøndelag. The earlier start in declining rates for lung cancer incidence in Oslo and Akershus corresponds with an earlier change in smoking habits in these counties. Some significant, but smaller, variations were seen for other cancer sites.

**Conclusions:** Although the population has been subject to the same national cancer preventive strategies, and a largely uniform health care system, distinct geographical patterns were observed. These variations give useful information both for national and local preventive policies.



**A10****Pulmonary function in lymphoma survivors after high-dose chemotherapy with autologous stem cell transplantation: a national cross-sectional study**

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\*\*Co-senior authors

**Introduction:** High-dose chemotherapy with autologous stem-cell support (HDT-ASCT) has been a treatment option for advanced/high-risk lymphomas for more than two decades. Radiotherapy (RT) and some types of chemotherapy are associated with pulmonary dysfunction among cancer survivors in general, but scarcely investigated among lymphoma survivors (LSs) treated with HDT-ASCT.

**Aims:** To compare pulmonary function between treatment groups, and identify predictors of impaired pulmonary function.

**Methods:** All LSs >18 years and treated with HDT-ASCT in Norway 1987–2008 were eligible for this national cross-sectional study, conducted 2012–2014. A total of 194 LSs, without heart failure, performed tests of pulmonary function and completed a questionnaire including smoking. Treatment data were collected from hospital databases and medical records. Measures of pulmonary function were compared with those predicted from age-, weight-, and gender-adjusted reference values. Treatment groups were compared using t-tests, and binary Poisson regression was used to estimate adjusted risk ratios (RR) of impaired pulmonary function (<80%-predicted) associated with disease relapse (post HDT-ASCT) and smoking. The statistical significance level was 0.05.

**Results:** Among LSs treated with chest RT, mean %-predicted forced expiratory volume in 1s FEV<sub>1</sub> was 86.7±14.7% vs. 92.4±15.5% in LSs without such treatment ( $P = 0.012$ ). Corresponding values for forced vital capacity (FVC) were 92.7±14.5% vs. 98.3±15.1% ( $P = 0.010$ ). Mean gas diffusion capacity (DLCO, mmol/kPa/min) and FEV<sub>1</sub> (L/min) were lower among those treated with doxorubicin  $\geq 300$  mg/m<sup>2</sup> vs.  $< 300$  mg/m<sup>2</sup> ( $P = 0.019$  and  $P = 0.042$ , respectively). Disease relapse was associated with 50% increased risk of impaired DLCO vs. no relapse, and smokers had twice the risk of impaired FEV<sub>1</sub> and DLCO vs. never smokers.

**Conclusions:** Monitoring of pulmonary function in LSs after HDT-ASCT is suggested for those treated with chest RT and high-dose doxorubicin, for those with a disease relapse, and for smokers.

## A11

### Hormone replacement therapy, mammographic density, and breast cancer risk: a cohort study

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**Introduction:** High mammographic density (MD) is a strong predictor of breast cancer (BC) risk. Hormone replacement therapy (HRT) is an established risk factor for BC, and shown to increase MD.

**Aims:** To examine whether MD mediates an association of HRT with the risk of BC.

**Methods:** For 4,501 participants in the Danish Diet, Cancer and Health cohort (1993-1997) who attended mammographic screening in Copenhagen (1993-2001), MD were assessed at the first screening after cohort entry. MD was defined as mixed/dense or fatty. Use, duration, and type of HRT and potential confounders were assessed by questionnaire at the cohort baseline. BC diagnoses were obtained from Danish Cancer registry, until 2012. The association between HRT and MD, and HRT and BC were analyzed by using logistic and Cox's regression models, respectively with adjustment for confounders.

**Results:** 2,444 (54.3%) women had mixed/dense breasts and 229 (5.39%) developed BC during follow-up. Majority of women (51.5%) were HRT users and 35.9% were current users at baseline. HRT users had significantly higher odds of having mixed/dense breasts (Odds Ratio (OR) and 95% confidence interval (CI): 1.59; 1.33-1.91) than never HRT users. Having mixed/dense MD was significantly positively associated with the BC risk (Hazard Ratio (HR) and 95% CI: 1.74; 1.29-2.34). HRT users had significantly higher risk of BC than non-users (HR; 95% CI: 1.56; 1.19-2.04), and after adjustment for MD associations attenuated (1.48; 1.29-2.34). The BC risk related to HRT higher in women with mixed/dense (1.79; 1.19-2.68), than with fatty breasts (1.34; 0.68-2.61), although there was no statistically significant difference (p-value for interaction 0.32).

**Conclusions:** Positive association between HRT and BC was not mediated by MD. The adverse effect of HRT on BC seemed to be limited to women with dense breasts.

## A12

### Maternal supplemental folic acid and risk of childhood cancer

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**Introduction:** Folic acid supplementation prior to and during the first trimester of pregnancy is recommended to prevent neural tube defects. However, concerns have been raised regarding folic acid and cancer risk.

**Aims:** This nation-wide cohort study examined the risk of childhood cancer after supplemental folic acid in pregnancy in a population without mandatory folic acid food fortification.

**Methods:** Data was retrieved from the Medical Birth Registry of Norway, the Cancer Registry of Norway, and other national registries. Cox proportional hazards regression models with time since birth as the time variable were used to estimate hazard ratios (HRs) with 95% confidence intervals (95% CIs) for childhood cancer according to maternal folic acid and multivitamin use prior to and/or during pregnancy as compared to no supplement use. During follow-up (1999-2010), 799 childhood cancer cases were identified.

**Results:** No associations were found between perigestational use of folic acid only (HR 1.13; 95% CI 0.92–1.38), concomitant folic acid and multivitamin supplementation (HR 1.02; 95% CI 0.83–1.25), and childhood cancer risk overall ( $p_{\text{Trend}}$  0.60). Furthermore, no changes in the risk estimates were found for leukemia, lymphoma, central nervous system tumors, neuroblastoma, Wilms tumor and soft-tissue tumors.

**Conclusion:** Folic acid supplementation before and/or during pregnancy showed no overall effect on childhood cancer risk. Furthermore, no significantly increased risk was seen for subgroups of cancers.

**A13****Exercise capacity in lymphoma survivors after high-dose chemotherapy with autologous stem cell transplantation: a national cross-sectional study**

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**Introduction:** High-dose chemotherapy with autologous stem-cell support (HDT-ASCT) has been a treatment option for advanced/high-risk Hodgkin and non-Hodgkin lymphomas for more than two decades. Exercise capacity has been inversely related to adverse late-effects of cancer treatment, such as cardiovascular morbidities, and is of particular interest in this intensively treated group of cancer survivors.

**Aims:** To compare exercise capacity between lymphoma survivors (LSs) treated with HDT-ASCT with reference values from the general population, and to identify predictors of exercise capacity among LSs.

**Methods:** All LSs >18 years treated with HDT-ASCT in Norway 1987–2008 were eligible for this national cross-sectional study, conducted 2012–2014. A total of 194 LSs, without heart failure, performed a bicycle ergometer exercise test measuring peak oxygen uptake (VO<sub>2</sub> peak), and completed a questionnaire including physical activity level. Treatment data were collected from hospital databases and medical records. VO<sub>2</sub> peak among the LSs was compared with that predicted from age-, weight-, and gender-adjusted reference values. Effects of therapeutic exposures and physical activity level on VO<sub>2</sub> peak were estimated using linear regression. The statistical significance level was 0.05.

**Results:** Mean percent predicted VO<sub>2</sub> peak was 107.6±22.2% and 102.0±19.7% in women and men, respectively. Minutes/week and intensity of physical activity were positively related to VO<sub>2</sub> peak (*P*-trends 0.059 and 0.005, respectively). Bleomycin dose was inversely related to VO<sub>2</sub> peak (*P*-trend 0.049), and VO<sub>2</sub> peak decreased with increasing doses of doxorubicin (*P*-trend = 0.113). No association was detected between chest radiation therapy and VO<sub>2</sub> peak.

**Conclusions:** Exercise capacity after HDT-ASCT among LS was close to that predicted from reference values. Although exercise capacity tended to decrease with increasing doses of bleomycin and doxorubicin, it increased with increasing intensity of physical activity, which in turn may play an important role to counteract adverse late-effects in this patient group.

## A14

### Cervical cancer prevented by screening: long-term incidence trends by morphology in Norway

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**Introduction:** Both major types of cervical cancer, squamous cell carcinoma (SCC) and adenocarcinoma (AC), are causally related to persistent infection with high risk human papillomavirus. Screening has primarily been effective at preventing SCC, while having little effect on the incidence of AC.

**Aims:** To describe trends in cervical cancer incidence in Norway from 1956 to 2010, and to estimate the proportion of cervical cancer prevented by screening.

**Methods:** The Cancer Registry was used to identify all 19,530 malignancies in the cervix diagnosed in the period 1956-2010. We analysed incidence trends of cervical cancer, stratified by type, and projected SCC incidence in the absence of screening by assessing changes in the incidence rate of AC. Joinpoint analyses were used to estimate the average annual percentage change for each cancer type.

**Results:** The majority (82.9%) of malignancies were classified as SCCs, 10.5% as ACs, and the remaining 6.6% were of other or undefined morphology. The average annual percentage change of the age-standardised incidence was -1.0 (95% CI: -2.1, 0.1) for cervical SCC, 1.5 (95% CI: 1.1, 1.9) for cervical AC, and -0.9 (95% CI: -1.4, -0.3) for cervical cancers of other or undefined morphology. The projected age-standardised incidence rate of cervical SCC in Norway, assuming no screening, was 28.6 per 100,000 woman-years in 2010. When compared to the observed SCC rate of 7.3, this corresponds to an estimated 74% reduction in SCC, or a 68% reduction in the total cervical cancer burden, due to screening.

**Conclusions:** Cytology screening has impacted cervical cancer burden more than suggested by the overall observed cervical cancer incidence reduction since its peak in the mid-1970s. The simultaneous substantial increase in cervical adenocarcinoma in Norway is presumably indicative of an increase in exposure to HPV over time.

## A15

### Risk of breast cancer after false positive results in mammographic screening

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**Introduction:** Mass screening of breast cancer inevitably leads to some false positive results in disease-free women. Few studies have evaluated how false-positive results influence subsequent breast cancer risk.

**Aims:** To assess the risk of screen detected breast cancer in women with false-positive screening results.

**Methods:** We used data from the long-standing population-based screening programs of Copenhagen Mammography Register in Denmark, the Norwegian Breast Cancer Screening Program, and the Spanish Breast Cancer Screening Program. An overall population of 111,988 screened women in Denmark, (1991-2008), 488,106 in Norway (1996-2010), and 914,490 in Spain (1990-2006) were included in the study. Poisson regression was used to estimate the relative risk (RR) and 95% confidence intervals (CI) of screen detected breast cancer for women with a false-positive result compared with women with negative tests.

**Results:** We analyzed a total of 1,514,448 women aged 50-69 years who underwent 5,673,870 screening exams. During an average 5.8 years of follow-up, 16,933 screen detected breast cancers were identified (DCIS and invasive cancers), and 202,767 women (13.4%) had a false-positive result. The adjusted relative risk of breast cancer after a false-positive test was 2.01 (95%CI: 1.93-2.09). A false positive result at first screen conferred a lower risk than a false positive result at later screens (RR=1.86, 95%CI: 1.77-1.96; and RR=2.42, 95%CI: 2.21-2.64, for first screen, and third screen or more, respectively). The risk decreased with increasing number of screen exams after the false-positive result (RR=3.95, 95%CI: 3.71-4.21; RR=2.51, 95%CI: 2.33-2.72; and RR=1.25, 95%CI: 1.17-1.34, for one screen, two screens, and three or more screens after the false-positive result, respectively).

**Conclusions:** Women with false-positive results had a two-fold risk of screen detected breast cancer. The risk remained significant three or more screens after the false-positive result. Women should be informed of this risk in order to promote regular screening participation.

## A16

### Health effects of parental radiation exposure: hemolymphoblastoses

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**Introduction:** Lympho-hematopoietic malignancies in children are characterized by etiological heterogeneity. The question is, whether parents' occupational exposure represents potential childhood cancer risk factor.

**Aims:** To find the relations between preconceptional exposure to prolonged external  $\gamma$ -radiation of the Mayak Production Association workers and hematological malignancies in their children.

**Methods:** This epidemiological study is based on Children's Registry and includes all children, who were born in the city of Ozyorsk, located near the first Russian nuclear industry complex Mayak, which started operation in 1948. Dosimetry information was obtained from Mayak worker cohort. Data on cancer morbidity was acquired from Cancer Registry. We used nested case-control approach, defining case as person with hemolymphoblastose diagnosed and control as person with no such diagnosis matched to case on sex, birth year and parents age at birth. We calculated odds ratio (OR) with 95% confidence interval (CI).

**Results:** The study group included offspring under 25 years old (81 children, among them 49 boys and 32 girls), diagnosed with hematological malignancy while living in Ozyorsk in 1949-2009. The control group included 324 children with no malignancies diagnosed (boys-196, girls-128). Average total whole-body external  $\gamma$ -ray dose before conception in mothers of study group was 292.5 mSv (20.7-1,272.9), in fathers it was 240.7 mSv (2.7-3,121.8); in mothers of control group – 458.1 mSv (2.8-2,797.8), in fathers – 334.7 mSv (0.3-3,025.6). Acute leukaemia was the main contributor to the structure of hematological malignancies. The odds ratio OR 0.89 (CI 0.54-1.46) indicated no relation between the level of preconceptional radiation exposure in parents and hematological malignancies in their offspring.

**Conclusions:** We did not see any impact of preconceptional prolonged external  $\gamma$ -radiation exposure in parents on risk of hematological malignancies. Apparently, that it testifies both the reproductive system protectability and the presence of various mechanisms, impeding transgenerational carcinogenesis.

**A17****Cardiorespiratory fitness in cardiovascular risk prevention: the HUNT Study****Bjarne M. Nes, Javaid Nauman, Ulrik Wisløff**

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**Introduction:** Cardiorespiratory fitness (CRF) is a key modifiable determinant of cardiovascular disease (CVD) and all-cause mortality risk, but rarely measured in primary prevention and for risk stratification. Developed algorithms that estimate CRF without exercise testing may be a practical approach for use in healthcare settings.

**Aims:** The aim of this study was to assess the predictive value of estimated CRF and evaluate the contribution of traditional clinical risk factors in CVD risk stratification.

**Methods:** This prospective cohort study included 38,480 apparently healthy participants (18,721 men and 19,759 women), 30-74 years, from the second wave of the HUNT Study in Norway. CRF was estimated by non-exercise algorithms and participants divided into tertiles based on sex-specific thirds of each 10-year age group. Cox-proportional hazards models were used to predict risk of CVD deaths. The added predictive value of clinical risk factors (hypertension, high total cholesterol and low HDL cholesterol) were evaluated by Harrell's C-statistic and net reclassification improvement (NRI).

**Results:** After a median follow-up of 16.3 (range, 0.04 to 17.4) years, there were 1133 CVD deaths (734 men and 399 women) out of 3863 deaths in total. CRF was a strong predictor of cardiovascular deaths after adjusting for multiple established risk factors. C-statistic for CRF and CVD deaths was 0.804 and 0.845 for men and women, respectively, increasing to 0.808 and 0.852 when adding clinical variables ( $p=0.04$  and  $p=0.03$  in men and women, respectively). NRI was only 1.4% ( $p=0.40$ ) and 5.2% ( $p=0.03$ ) in men and women, respectively, after adding clinical variables to CRF in reclassification of CVD deaths.

**Conclusions:** Estimated CRF was independently associated with cardiovascular mortality. The inclusion of traditional risk factors added little to risk discrimination and classification of deaths beyond this simple fitness measurement, which may be proposed as a cost-effective first-line approach in primary prevention settings.



## A18

### Secular changes in cardiovascular risk factors in the general population; the Tromsø study 1986-2007

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**Introduction:** Over the last decades cardiovascular disease (CVD) morbidity and mortality have been reduced in many countries including Norway. This reduction was accompanied by substantial development in the levels of CVD risk factors.

**Aims:** To explore secular changes in CVD risk factors by sex in the Tromsø Study from 1986 to 2007.

**Methods:** The present report comprised 30,758 men and women, aged 30-89 years, who participated in at least one of the 1986-1987, 1994-1995, 2001-2002 and 2007-2008 Tromsø Study surveys, Norway. At each survey, subjects completed two questionnaires, underwent a physical examination and blood collection. Sex and survey specific means and percentages were adjusted for age using linear mixed models or generalized estimating equations, respectively.

**Results:** Age-adjusted means of resting heart rate (RHR) declined substantially during the study period: from 73.4 (Standard Deviation: 13.0) to 64.7 (10.9) beats per minute (b.p.m.) in men, and from 78.3 (12.6) to 66.4 (10.3) b.p.m. in women. Systolic and diastolic blood pressure means declined by 2.8 (95% Confidence Interval: 2.2-3.4) and 2.4 (2.0-2.7) mmHg in men, and by 6.6 (6.0-7.2) and 6.2 (5.8-6.5) in women, respectively. Total cholesterol also decreased substantially. BMI increased and blood pressure treatment became much more common in both sexes. The proportion of smokers halved during the study period. Physical activity level remained virtually unchanged.

**Conclusions:** In general, cardiovascular risk profile has been improved in the general population over the last decades. The decline in RHR was especially notable. The relationship between change in RHR and changes in other CVD risk factors, and their effect on CVD needs to be explored.

**A19****Glycaemic control in people with diabetes influences the beneficial role of physical activity on cardiovascular mortality. Prospective data from the HUNT Study, Norway****Børge Moe<sup>1</sup>, Kristian Midthjell<sup>2</sup>, Tom I.L. Nilsen<sup>1</sup>**

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**Introduction:** People with diabetes who are physically active have substantially lower risk of death from cardiovascular disease, compared to inactive people with diabetes. Whether the beneficial effect of physical activity is modified by glycemic control, is not known.

**Aims:** To examine whether glycaemic control in people with diabetes, measured as glycated hemoglobin (HbA<sub>1c</sub>), influences the role of leisure time physical activity on the increased risk of death from cardiovascular disease.

**Methods:** We prospectively examined the joint association of diabetes according to glycemic control, measured as glycated hemoglobin (HbA<sub>1c</sub>), and physical activity with cardiovascular mortality. A total of 53,549 were followed up for 12 years through the Norwegian Cause of Death Registry. Cox proportional adjusted hazard ratios (HRs) with 95% confidence intervals (CI) were estimated.

**Results:** Overall, 1,710 people died from cardiovascular disease during the follow-up. Compared to the reference group of inactive people without diabetes, people with diabetes and HbA<sub>1c</sub> < 8.0%, had a hazard ratio (HR) of 1.46 (95% CI: 0.96, 2.21) if they were physically inactive and a HR of 1.33 (95% CI: 0.81, 2.19) if they were physically active. Among people with diabetes and HbA<sub>1c</sub> ≥ 8.0%, the corresponding comparison gave HRs 2.69 (95% CI: 2.11, 3.42) and 0.93 (95% CI: 0.64, 1.36), respectively.

**Conclusions:** The data suggest that physical activity should be more strongly encouraged as a therapeutic measure additional to medical treatment, especially among those with most severe hyperglycemia.

## A20

### Acute myocardial infarction and stroke in Norway 2012-2013: Regional variations in age-adjusted hospitalization rates and survival

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**Introduction:** The Norwegian Cardiovascular Disease Registry (NCDR) provides an opportunity to evaluate whether there are regional differences in age-adjusted hospitalization rates and survival concerning cardiovascular disease in Norway.

**Aims:** To compare age-adjusted hospitalization rates and survival of acute myocardial infarction (AMI) and stroke across geographical regions in Norway.

**Methods:** The study population comprised hospitalized patients registered in the NCDR with a primary diagnosis of AMI or stroke during the period 2012-2013. Age-adjusted (Nordic standard population 2000) hospitalization rates per 100,000 were assessed for five geographical regions (East, South, West, Central and North). To study the influence of geographical regions on 30-days and six months mortality, hazard ratios (HR) and 95% CIs were calculated adjusting for age, gender and comorbidity, using Cox proportional hazard models with West Norway as reference.

**Results:** In 2012-2013, a total of 22,486 and 12,831 patients were hospitalized in Norway with a primary diagnosis of AMI and stroke, respectively. Age-adjusted hospitalization rates per 100,000 for AMI and stroke was lowest in West Norway (461 and 349), whereas the highest rates were observed in North Norway (601 and 461). For AMI and stroke the observed 30-days survival in Norway was 91.1 and 86.7%, respectively. Correspondingly, six months survival was 86.4 and 81.8%. For AMI, 30-days and six months mortality was lower in South Norway (HR=0.86; CI: 0.74-0.99 and HR=0.86; CI: 0.76-0.96) compared to West Norway. For stroke, the 30-days and six months mortality was lower in Central Norway (HR=0.80; CI: 0.69-0.92 and HR=0.88; CI: 0.79-0.96) compared to West Norway.

**Conclusion:** Minor differences in the age-adjusted hospitalization rates of AMI and stroke were observed. 30-days and six months survival after AMI and stroke was most favorable in the South and Central Norway, respectively.

**A21****Pre-pregnant lipid levels and triglyceride/HDL-cholesterol ratio in one-child mothers**

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**Introduction:** Dyslipidemia is associated with metabolic syndrome, preeclampsia and gestational diabetes mellitus, conditions that adversely affect pregnancy and may lead to selective fertility.

**Aims:** To examine pre-pregnant lipid levels in relation to number of lifetime pregnancies.

**Methods:** We conducted prospective population- based study of 2751 women giving birth to their first child after participating in the Cohort of Norway (CONOR/1994-2002.), gathering blood samples and data on lifestyle and health factors. CONOR were linked to the Norway Medical Birth Registry, identifying subsequent pregnancies. Odds ratio (OR) for 1 lifetime pregnancy by level of lipids and triglyceride/HDL-cholesterol ratio (TG/HDL), when compared to women with 2+ pregnancies was calculated using logistic regression, adjusted for age at examination, educational level, time since last meal and smoking.

**Results:** A total of 622 women (29%) had 1 lifetime pregnancy. The OR of having 1 lifetime pregnancy for women with levels of HDL-cholesterol less than 1.20 mmol/l (lowest quintile) was 1.7 (95% CI: 1.2-2.3;  $p < 0.05$ ) compared to women with HDL-cholesterol levels greater than 1.84 mmol/l (highest quintile). There was 1.4-fold (95% CI: 1.0-1.9;  $p < 0.05$ ) and 1.7-fold (95% CI: 1.3-2.4;  $p < 0.05$ ) increase in risk of having 1 lifetime pregnancy, if triglyceride levels were 1.09-1.45 and  $>1.45$  mmol/l, respectively (two highest quintiles). Concerning TG/HDL ratio, 1.5-fold (95% CI: 1.1-2.0;  $p < 0.05$ ) and 1.8-fold (95% CI: 1.3-2.5;  $p < 0.05$ ) increase in risk of 1 lifetime pregnancy was found for two highest quintiles (0.73-1.04 and  $>1.04$ , respectively). There were statistically significant trends across HDL-cholesterol, triglyceride quintiles and TG/HDL ratio ( $p < 0.05$ ). No significant associations were found for total cholesterol or LDL-cholesterol.

**Conclusion:** Pre-pregnant lipid levels and TG/HDL ratio were associated with the risk of having 1 lifetime pregnancy. Women with high levels of triglycerides and TG/HDL ratio were at increased risk of having 1 lifetime pregnancy, as were women with low levels of HDL-cholesterol.

**A22****Pregnancy complications and later maternal morbidity and mortality in Norwegian women****Hilde Kristin R. Riise<sup>1</sup>**, Anne Kjersti Daltveit<sup>1,2</sup>, Gerhard Sulo<sup>1</sup>, Grethe S. Tell<sup>1</sup>

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**Introduction:** Preeclampsia (PE), a serious complication of pregnancy, is associated with an increased risk of fetal and maternal mortality.

**Aims:** To study the association between PE and severe pregnancy outcomes and maternal morbidity/mortality in a nationwide study using The Medical Birth Registry of Norway, The Cause of Death Registry and the CVDNOR project.

**Methods:** Pregnancies during 1980-2009 with a gestational age beyond 22 weeks were included. Hazard ratios (HR) for cause-specific maternal morbidity/mortality were computed in Cox regression models separately for PE with and without any complication (small for gestational age, preterm birth, or stillbirth) and for women with one lifetime pregnancy.

**Results:** 659,531 women [mean (SD) age at delivery 25.2 (4.6)] with 1,561,308 births were analyzed. Median follow up time was 20.5 years. 43,674 (6.6%) women experienced  $\geq 1$  preeclamptic pregnancy. Women with PE were more likely to experience any complication compared to those without PE (46.3% vs 27.6%). There were 1464 (0.2%), 159 (0.4%), and 110 (0.5%) deaths from cardiovascular disease (CVD) in all women, women with PE, and women with PE and any complication, respectively. Results on maternal CVD morbidity will be presented. Women with PE in the first pregnancy were less likely to have a subsequent pregnancy. Hence, a higher proportion of women with only one lifetime pregnancy had PE; 5.8% compared to 4.3% in the first pregnancy among multiparous women. The association between PE and CVD mortality was stronger among women with one lifetime pregnancy compared to multiparous women; HR 2.43 ( $P < 0.001$ ) vs 1.84 ( $P < 0.001$ ).

**Conclusions:** Women who experience PE in their first pregnancy are less likely to have subsequent pregnancies. PE was associated with a higher risk of other pregnancy complications. HR for CVD mortality associated with PE was highest in women with one lifetime pregnancy.

**B1****Causal mediation analysis in life-course epidemiology****Susanne Strohmaier<sup>1</sup>, Kjetil Røysland<sup>1</sup>, Hanno Ulmer<sup>2</sup>, Odd Aalen<sup>1</sup>**

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**Introduction:** A cornerstone of epidemiological research is the understanding of mechanisms leading to chronic diseases by studying long-term effects of exposures onto, e.g. the time until a certain event of interest occurs. A statistical key tool to approaching such questions is causal mediation analysis, that allows for a decomposition of the total effect of an exposure into a direct effect and an indirect effect. We aim to exemplify how dynamic path analysis could help to gain more insights about involved pathways in the development from body size to coronary heart disease (CHD).

**Aims:** Gain further insights on underlying mechanisms in the development from body size to CHD.

**Methods:** Fosen and co-authors proposed a model for dynamic path analysis extending the concept of directed acyclic graphs (DAGs) to study processes developing over time. The approach makes it feasible to distinguish between direct, indirect and total effects in the presence of a survival outcome and time-dependent covariates. Recent work has focused on providing a thorough mathematical justification to allow for a causal interpretation of the obtained direct and indirect effects. We suggest how this method can be utilized to incorporate a larger amount of routinely collected information, while still drawing causal conclusions.

**Results:** Previously performed analyses assessing direct and indirect effects of high body mass index (BMI) on CHD only included baseline measurements of potential mediators. We apply the method of dynamic path analysis to data collected within the Vorarlberg Health Monitoring and Promotion Programme (VHM&PP) to illustrate how the effects of BMI are mediated over the entire follow-up period of 20 years.

**Conclusions:** When one attempts mediation analysis to investigate mechanisms that are actually working in time, employing techniques that only incorporate single mediator measurements can distort the real picture and one may risk to deduce false conclusions from such analyses.

## B2

### Occupational exposure to ultrafine particles among airport employees – Combining personal monitoring and Global Positioning System

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**Introduction:** Exposure to ultrafine particles (UFP) has been linked to cardiovascular and lung diseases. At airports combustion of jet fuel and diesel from aircraft and handling equipment emits large numbers of UFP and employees working at an airport may be exposed to high levels. In previous studies the exposure classification is based upon job title classifications and knowledge about high levels of air pollution at the airport or around the airplane, but the relationship between individual exposure to air pollution and job title is not known. Without quantitative data on occupational exposure to UFP compared across job functions the identification of health risks for different occupational groups could be inaccurate.

**Aim:** The aim of this study was to assess the environmental exposure to UFP in a cohort study on cardiovascular diseases among employees working in Copenhagen Airport (CPH) using personal exposure monitoring and Global Positioning Systems (GPS).

**Method:** Personal exposure measurements were carried out for 30 employees from five different occupational groups (baggage handlers, catering drivers, cleaning staff and airside and landside security). They were instructed to wear a personal monitor of particle number concentration in real time and a GPS device. The overall differences between the groups were assessed using linear mixed model.

**Results:** Data showed significant differences in exposure levels among the groups when adjusted for variation within individuals and for effect of time and date ( $p < 0.01$ ). Baggage handlers were exposed to 7 times higher average concentrations (geometric mean, GM:  $37 \times 10^3$  UFP/cm<sup>3</sup>, 95% CI:  $25\text{--}55 \times 10^3$  UFP/cm<sup>3</sup>) than employees mainly working indoors (GM:  $5 \times 10^3$  UFP/cm<sup>3</sup>, 95% CI:  $2\text{--}11 \times 10^3$  UFP/cm<sup>3</sup>). Furthermore, catering drivers, cleaning staff and airside security were exposed to intermediate concentrations (GM: 12 to  $20 \times 10^3$  UFP/cm<sup>3</sup>).

**Conclusions:** The study demonstrates a strong gradient of exposure to UFP in ambient air across occupational groups of airport employees.

## B3

### Geomapping of advanced-stage melanoma incidence – a method for addressing skin screening targets

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**Introduction:** Advocators of skin screening by physicians for melanoma have suggested widespread implementation in the primary care. Yet, there are concerns over how to ensure that appropriate patients will receive recommended screening. One option is to prompt targeted screening on a rational basis.

**Aims:** To identify primary screening targets by evaluating existing local geographic differences in advanced-stage melanoma incidence.

**Methods:** For 9743 patients in the southern and western health care regions of Sweden who had their first primary invasive cutaneous malignant melanoma (CMM) diagnosis in 2004-2013, data including residential area, educational level and clinical stage at diagnosis (I-IV) were obtained from solid registers. A geomap showing how the incidence of advanced-stage (II-IV) CMM varied across 119 residential areas was produced by empirical Bayes estimation of the standardized incidence ratios. The local geographic variation in the diagnostic occurrence of advanced-stage CMM among the patients was assessed in an analogous way.

**Results:** Consistent and pronounced local geographic variations appeared and areas with elevated, intermediate and lowered incidences of advanced-stage melanoma were thereby identified.

**Conclusions:** This application on melanoma demonstrated that geomapping of advanced-stage cancer incidence can be a valuable tool for the purpose of secondary prevention targeting.



## B4

### Validity of acute caesarean section registration in the Medical Birth Registry of Norway

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**Introduction:** Since 1989, the Medical Birth Registry of Norway (MBRN) has registered caesarean section (CS) as “elective” or “acute”. This classification is validated as a basis for a study of trial of labour after a previous CS, with emphasis on the positive predictive value (PPV).

**Aims:** To validate the MBRN variable “acute CS”.

**Methods:** For a random sample of 500 deliveries after a previous CS (1989-2011), maternity units were requested to report CS subtypes in both deliveries, based on hospital records. Data were reported on 476 of the first and 472 of the second deliveries. Of the first deliveries, 68 occurred before 1989, leaving 408 for analysis. A CS is “elective” if it was planned more than eight hours prior to the procedure, and performed as planned. Other CSs are “acute”. “Unspecified CS” was included in the non-acute CS group.

**Results:** Among the 472 women, 4 had no CS first delivery. In the first deliveries, the “acute CS” fraction was 80% (n=323) according to hospital records and 79.4% (n=324) in the MBRN. PPV was 94.8% [91.8%, 96.7%], (negative predictive value (NPV) 81.0% [71.3%, 87.9%], sensitivity 95.0% [92.2%, 96.9%], and specificity 80.0% [70.3%, 87.1%]). In the second deliveries, the “acute CS” fraction was 22.9% (n=108) according to hospital records and 21.0% (n=99) in the MBRN. PPV was 87.9% [80.0%, 92.9%], (NPV 94.4% [91.5%, 96.3%], sensitivity 80.6% [72.1%, 86.9%], and specificity 96.7% [94.3%, 98.1%]).

**Conclusions:** The PPVs are minimum estimates due to inclusion of “unspecified CS” in the non-acute group. We consider the validity of “acute CS” registration in the MBRN as satisfactory for an epidemiological register study of trial of labour after a previous CS.

**B5****Causal inference in a multi-state model for sickness absence and return to work**

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**Introduction:** Multi-state models, as an extension of traditional models in event history analysis, have proven to be a flexible framework for analysing the transitions between various states of sickness absence and work over time. In this paper we study a cohort of participants to work rehabilitation programs and analyse their subsequent sickness absence using Norwegian registry data on sick leave benefits.

**Aims:** Our aim is to use detailed individual covariate information to explain differences in sickness absence and return to work, and to use methods from causal inference to assess the effect of hypothetical interventions. Examples of the latter can be to compare the use of partial and full time sick leave or to estimate the effect of including working life agreements.

**Methods:** Covariate adjusted transition intensities are estimated using Cox proportional hazards and Aalen additive hazards models, while the effect of interventions are assessed using proposed methods based on inverse probability weighting and g-computation.

**Results:** Results from covariate adjusted analyses show great differences in predicted sick leave, disability and return to work for patients with assumed high risk and low risk covariate characteristics. Some, but limited, effects are found in assessment of hypothetical interventions.

**Conclusions:** Detailed covariate information is important for doing precise predictions of sickness absence and return to work in multi-state models, also for patient specific cohorts. Methods from causal inference can provide the needed tools for going from individual predictions to overall effects in such analyses, and identify causal parameters with a straight forward interpretation based on interventions.

**B6****Bias in observational studies of the association between menopausal hormone therapy and breast cancer****Per-Henrik Zahl**<sup>1</sup>, Jan Mæhlen<sup>1,2</sup>

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**Introduction:** During the period 1985-2000 the breast cancer incidence rates increased 50% in the age group invited to mammography screening in many countries. Simultaneously use of hormone replacement treatment therapy (HT) increased 5 times. Several influential observational studies showed that HT was associated with 50-100% increased risk of breast cancer and most for those using combined (estrogen plus progestin) hormone replacement therapy (CHT). In contrast the randomized WHI trial reported that CHT increased the risk by 10% for those not having previously used hormones and 24% when including previous users in the analyses, and estrogen use only was not associated with any increased risk at all. After the WHI trial was published in 2003, use of HT dropped 70% within 5 years while breast cancer rates essentially were unchanged. After 2008 HT use has dropped further and breast cancer incidence rates have started increasing again.

**Aim:** To calculate and to explain the bias in the observational study design.

**Methods:** We used data from the randomized WHI trial and analyzed these data as done in the observational cohort studies to calculate the magnitude of the potential biases in the observational study design.

**Results:** Time varying effect of hormones and categorization of the follow-up time may increase the relative risk for long-term users from 1.10 to 1.48. Selective retrospective reporting of hormones may further increase the relative risk to 1.68.

**Conclusions:** We suggest that the mechanism causing higher relative risk of breast cancer compared to the observational studies is the time-varying effect of CHT on the breast cancer risk and selective retrospective reporting of hormone use. Other risk factors for the increase in breast cancer risk should also be considered and studied, for example overdiagnosis.

## B7

**The heritability of breast cancer among women in the Nordic Twin Study of Cancer**

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**Introduction:** Different kinds of cancer are known to be quite heritable, although the extent to which variation in risk by age is explained by genetic factors remains uncertain. Earlier estimates of cancer heritability have experienced bias due to censoring and competing risk of death.

**Aims:** To estimate the heritability of breast cancer in a large cohort of female Nordic twins avoiding bias due to censoring and competing risk.

**Methods:** We study 21,055 monozygotic and 30,940 dizygotic same sex female twin pairs from the Nordic Twin Study of Cancer cohort the largest in the world, consisting of data from the Danish, Finish, Norwegian, and Swedish twin registries. We incorporate time-to-event analyses to estimate the concordance risk and heritability accounting for right-censoring due to individuals still alive or lost to follow-up and competing risks of death, essential sources of bias that have not been accounted for before. We determine the casewise concordance in monozygotic and dizygotic twins and its dependency on the age at diagnosis. Moreover, we estimate the cumulative heritability using a time-varying biometric ACE-model both on the liability and on the risk scale.

**Results:** We find heritability explaining 31% of the variation while common environment explains 16%, both significantly higher than zero and different from the heritability and common environment one would get from the model ignoring censoring and competing risk. We observe that the heritability and common environment component are relatively stable with age.

**Conclusions:** We find significant heritability and common environment effects in the liability for breast cancer in Nordic Twins. Furthermore, we demonstrate that ignoring the censoring and competing risk, gives heavily biased and misleading results, substantiating the need for taking these factors into account.

**B8****Evaluating survival percentiles****Andrea Bellavia**<sup>1,2</sup>, **Matteo Bottai**<sup>2</sup>, **Nicola Orsini**<sup>1,2</sup>

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**Introduction:** In prospective cohort studies, survival percentiles can be defined as the time points by which specific proportions of the study population have experienced the event of interest. For example, the time by which the first 50% of the individuals have experienced the event is defined as 50th survival percentile, or median survival. The most common approach to survival outcomes is to fix a specific time – usually the end of follow-up – and to estimate survival probabilities, or rates, of the event of interest within the observed time-interval, possibly according to levels of specific exposures or risk factors. Evaluating survival percentiles represents a possible alternative, as it fixes the incidence proportion and evaluates the time points by which different strata of the study population reach that specific proportion of cases.

**Aims:** This presentation will introduce the concept and evaluation of survival percentiles and present the advantages that this approach can accrue to epidemiology.

**Methods:** Statistical modeling of survival percentiles can be accomplished with the Kaplan-Meier method, at the univariable level, and with methods for conditional quantiles of possibly censored outcomes, such as Laplace regression, at the multivariable level.

**Results:** Evaluating survival percentiles allows directly focusing on the time variable. Results are presented in terms of time (i.e. months, years) and measures of associations are interpreted as differences in survival. This approach provides many other advantages that make it appealing to the epidemiologists, such as the possibility of focusing on specific percentiles of interest, evaluating how the association of interest is changing over time, deriving adjusted survival curves, and evaluating interaction in the metric of time on both the additive and multiplicative scale.

**Conclusions:** Evaluating survival percentiles might provide considerable advantages in the evaluation of time-to-event outcomes and should be considered as a possible complement to classical approaches.

**B9****Risk time splitting for precise evaluation of screening programs;  
The importance of exact separation of comparison groups****Harald Weedon-Fekjær<sup>1</sup>, Pål Romundstad<sup>2</sup> and Lars Vatten<sup>2,3</sup>**

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**Introduction:** The aim of cancer screening is to detect the disease early, reducing mortality through earlier treatment. Since screening only can impact cases diagnosed at screening, assessment of mortality following screening should precisely split cases diagnosed before (without potential for screening effect) and after (with potential for screening effect) screening. The effect of screening programs have previously been analyzed using careful matching of screened and non-screened groups, but a substantial amount of the available data has not been used in these analyses due to the matching. While being validly designed, limited statistical precision has often prevented reliable inference of the program's possible effect on mortality.

**Aims:** To develop a method for utilizing all available data on public screening programs in one coherent and precise estimation of the program's effect on mortality

**Methods:** A new two-step multiple Poisson regression approach was developed to precisely assess differences in cancer mortality, by splitting cases diagnosed before and after first invitation to screening. When splitting cases incident pre- and post-screening invitation, weights was added using their respective expected proportions in the absence of a screening effect. These expected proportions of new incident cases were calculated based on the observed time from diagnosis until death among prescreening data. Potential cofounders were adjusted for by multiple Poisson regression analysis, and confidence intervals calculated by bootstrap simulations.

**Results:** The risk time splitting approach yielded considerable lower statistical uncertainty compared to earlier applied methods, without adding any further model assumptions. Applied to Norwegian breast cancer data the width of the confidence interval was almost half of that seen in previous studies.

**Conclusions:** Public screening programs should be evaluated using precise analytic design applying all the available data.

## B10

### Smoking-induced genome-wide methylation changes with time since smoking cessation, and subsequent changes in gene expression

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**Introduction:** A growing number of studies have recently identified strong epigenetic signals related to tobacco smoking. The number of papers describing the evolution of epigenetic changes with time since smoking cessation are however limited. In addition, very few studies have the possibilities to assess the link between epigenetic changes and changes in gene expression as we do here.

**Aims:** To describe the epigenetic changes associated to smoking and the dynamics of these changes following smoking cessation. Furthermore, the aim was to identify transcripts potentially associated with our CpG sites of interest.

**Methods:** Our study includes 333 samples from the Norwegian Women and Cancer Study cohort and 451 samples from the Italian component of the European Prospective Investigation into Cancer and Nutrition. Genome-wide DNA methylation analyses were performed. Log2-transformed expression levels of the 8952 transcripts/genes assayed in NOWAC samples were regressed against methylation levels in a subset of CpG sites found to be associated with smoking.

**Results:** Two distinct classes of CpG sites were identified: sites whose methylation reverts to levels typical of never smokers within decades after smoking cessation, and sites remaining differentially methylated, even more than 35 years after smoking cessation. Among genes whose expression was associated with our candidate CpG sites, LRRN3 appeared to be particularly interesting as it was one of the few genes whose methylation and expression were directly associated, and the only gene in which both methylation and gene expression were found associated with smoking. Our study highlights persistent epigenetic markers of smoking, which are detected decades after cessation.

**Conclusions:** A number of CpG sites remain demethylated even decades after smoking cessation. For a number of these sites demethylation resulted in a significant up regulation of genes.

**B11****The Norwegian Burden of Disease Project – aims for the Norway project and results for Norway from the Global Burden of Disease (GBD) Project 2010**

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**Introduction:** The Norwegian Burden of Disease (Norway-BoD) project was established in 2013, and has close collaboration with the Global Burden of Disease (GBD) project. In 2013, GBD published country-wise estimates of disease and risk factor burden. These estimates will be regularly updated. The aims of the Norway-BoD project and examples of the GBD 2010 estimates for Norway will be presented.

**Aims:** The Norway-BoD project shall contribute to evaluation and validation of the Norwegian GBD estimates, expand the Norwegian datasources available in the GBD project, and expand the analyses on Norwegian disease burden.

**Methods:** GBD estimates give an overview over mortality and morbidity due to diseases, injuries and risk factor in both genders, twenty age groups and across time from 1990 to 2010. Four main measures of disease burden are used in GBD; deaths, years of life lost (YLL), years lived with disability (YLD) and a summary estimate of disease burden, DALY (disability adjusted life years), which is the sum of YLL and YLD.

**Results:** Important causes of deaths and YLLs in Norway are cancer diseases and cardiovascular diseases. The five largest causes of YLDs in Norway in 2010 were low back pain, major depression, anxiety disorders, neck pain and falls. Important risk factors for both mortality and morbidity are unhealthy diet, smoking, high blood pressure, high body mass index, high level of cholesterol and glucose, high alcohol use and physical inactivity. The numbers of DALYs are equally driven by causes of morbidity (YLD) as by causes of mortality (YLL).

**Conclusions:** The estimates from the GBD project gives a unique overview over the disease burden in Norway. Non-communicable diseases are the main contributors to disease burden in both Norway and the western world. The GBD estimates should be critically examined and quality controlled by researchers with knowledge of the Norwegian setting.



**B12****Leisure time physical activity and the risk of hip or knee replacement due to primary osteoarthritis – a population based cohort study.  
The Nord-Trøndelag Health Study (HUNT)**

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**Introduction:** The relationship between leisure time physical activity (LPA) and the development of hip and knee osteoarthritis (OA) or future joint replacement has not yet been clearly defined.

**Aim:** To investigate the association between LPA and the risk of total hip (THR) or total knee (TKR) replacement due to primary OA.

**Methods:** Participants (n=66 863) in the Nord-Trøndelag Health Study (HUNT) from 1995-1997 and 2006-2008 were followed prospectively to identify THRs and TKRs using the Norwegian Arthroplasty Register. Self-reported LPA was classified as inactive, low, moderate or high. The Cox proportional hazards model was used to calculate hazard ratios (HR) according to levels of LPA with adjustments for confounding variables. Analyses were performed by age (<45, 45-59 and ≥60 years) and sex.

**Results:** We identified 1636 THRs and 1019 TKRs due to primary OA during 17.1 years (median) of follow-up. There was a dose-response relationship between LPA and THR in those <45 years at baseline. In comparison to low LPA, high LPA showed a two-fold risk of THR for both men (HR 1.94, 95% CI 1.01-3.74) and women (HR 2.09, 95% CI 1.25-3.50). A similar trend was present for TKR, but only significant for women in the youngest age group. In middle-aged women (45-59 years), high (HR 1.39, 95% CI 1.04-1.86) and moderate LPA (HR 1.81, 95% CI, 1.28-1.58) were associated with increased risk of THR and TKR, respectively. No association was found in the oldest age group.

**Conclusion:** Increasing levels of LPA are associated with the risk of THR and TKR. Our findings suggest a similar effect of LPA on the risk of THR and TKR. The findings were most apparent in those younger than 45 years at baseline, and among women.

## B13

### **A work-focused intervention to increase work participation in common mental disorders. Multicenter RCT with registry-based long-term outcomes**

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**Introduction:** Common mental disorders (CMDs) are a major cause of rising disability benefit expenditures. While cognitive behavioural therapy (CBT) is effective and the treatment of choice for mild to moderate episodes of depression and anxiety, reduced symptom load does not directly translate to return-to-work. We urgently need evidence on programs that can increase work participation in CMDs.

**Aims:** The aim of this study was to evaluate the effectiveness of work-focused CBT and individual job support for people struggling with work participation due to CMDs.

**Methods:** A randomized controlled multicenter trial including 1193 participants was conducted. Participants were on sick-leave, at risk of going on sick-leave, or on long-term benefits. The intervention integrated work-focused CBT with individual job support. The control group received usual care. The main outcome was registry data on work participation at 12 to 36 months after follow-up.

**Results:** Compared to usual care, a larger proportion of participants in the intervention group had increased or maintained their work participation at follow-up (44.2% vs 37.2%,  $P=0.015$ ). The difference remained significant after 18 months (diff: 7.8%,  $P=0.018$ ), and was even stronger for those on long-term benefits (diff: 12.2%,  $P=0.007$ ). Results from the long-term follow up at 36 months are pending.

**Conclusions:** A work-focused CBT and individual job support was more effective than usual care in increasing or maintaining work participation for people with CMDs at 12 to 18 months. This is the first large-scale RCT to demonstrate an effect of a behavioral intervention on work participation for the large group of workers with CMDs. The trial is also a clear demonstration of the utility of registries as data source for objective long-term results in the context of work disability.

**B14****Stress related to a suspicious mammogram – potential transcriptomic effects**

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**Introduction:** The mammography screening program was implemented in Norway between 1996-2004, offering biennial screening to women above the age of 50. We hypothesize that a suspicious mammogram result introduces a considerable amount of psychological stress. Recent studies demonstrate that stress influences gene expression profiles in the blood, potentially introducing bias by masking signals related to a disease of interest. Of women who are called back for a second evaluation, many are confirmed cancer-free. However, while in the clinic, women may contribute blood samples for research purposes. Women who have experienced stress that are used as hospital-based controls in any study may therefore differ from the general population, which may contribute to limiting the generalizability of results.

**Aim:** To explore the potential association between health-related psychological stress and blood gene expression profiles.

**Methods:** In the Norwegian Women and Cancer (NOWAC) cohort we defined two groups of women: A) Non-stressed controls from our general population-based biobank, and B) women called in for further examination after potential abnormalities found on the screening mammogram, donating a blood sample after assumed to experience stress, and later confirmed to be cancer-free. Blood was collected using the PAXgene blood RNA system, and gene expression was measured using Illumina bead chips. Gene expression differences between groups were evaluated using single-gene (t-tests) and gene set level analyses (global test).

**Results:** After adjusting for multiple testing, single gene-level analysis revealed no significant differences at our chosen thresholds for statistical significance. Likewise, targeted analysis of 14 relevant Kegg gene sets did not yield any significant results.

**Conclusions:** The psychological stress related to a positive screening mammogram was not associated with gene expression changes in the blood in this study, but more sensitive data analyses or more tailored study designs may still reveal transcriptomic effects of health-related stress. The finding is reassuring for studies using hospital-based controls.

## B15

### Visual impairment, physical activity, and all-cause mortality: The HUNT Study

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**Introduction:** Several studies show that adults with visual impairment have higher mortality risk compared to sighted adults. Regular physical activity (PA) have been suggested to lower the mortality risk in the general population, but there is lack of documentations of an association between PA and all-cause mortality among adults with visual impairment.

**Aims:** To examine the independent and joint association of self-reported visual impairment and PA with all-cause mortality.

**Methods:** This study included 55,492 participants aged  $\geq 20$  years from the second wave of the Nord Trøndelag Health Study (the HUNT 2 Survey, 1995–1997). The participants were linked to the Norwegian Cause of Death Registry and followed through 2012. Visual impairment and moderate-high intensity PA were assessed by a questionnaire. Cox regression analysis was used to calculate hazard ratios (HRs) with 95% confidence intervals (CIs). The impact of missing data was assessed by multiple imputation.

**Results:** Adults reporting no impairment (SRNI) had somewhat higher mean scores of moderate-high PA than adults reporting severe visual impairment (SRVI), even after standardizing for age and gender. Among 54,160 reporting SRNI, 16.0% died during the 17-year follow-up period. Among 1,332 adults reporting SRVI, 54.4% died during the follow-up. The questionnaire-defined vision categories had non-proportional hazards. For those  $\geq 65$  years, the full-adjusted pooled HR was 1.22 (CI: 1.12–1.33) among adults with SRVI compared to adults with SRNI. Significantly lower mortality risk was found in multivariable models for  $\geq 1$  hour/week of PA compared to no PA ( $p < 0.05$ ).

**Conclusions:** Individuals with SRVI had a higher mortality risk, but the association varied with time and was dependent on how missing data were handled. Weekly hours of PA was associated with lower mortality risk for adults with SRNI and SRVI. However, several sensitivity analyses are planned to evaluate the consistency of the main results.

## B16

### Gender differences and gender convergence in alcohol use over the past three decades. The HUNT Study, Norway

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**Introduction:** Recent increases in women's excessive drinking identified in some countries may raise alcohol-related risks to women's health and justify the need for better studies of gender differences in alcohol use.

**Aims:** To examine changes in men's and women's drinking in Norway over a 20-year period, in order to learn whether such changes have led to convergence of drinking patterns, for example, if women's drinking has increased more than men's.

**Methods:** Repeated cross-sectional studies of a large general population living in a geographically defined area (county) in Norway.

**Findings:** Adult alcohol drinking patterns have changed markedly over 2-3 decades. Alcohol abstaining has become rare. Alcohol consumption, recent drinking and problematic drinking has increased, while drinking to intoxication has declined. Women have moved towards men's drinking patterns in rates of abstaining, regular drinking, intoxication and problematic drinking, but only some of the convergence resulted from greater increases in women's drinking than in men's, and the amount of convergence varied among age groups and among different drinking behaviors.

**Conclusions:** There has been a decline in differences between men and women in most drinking behaviours including problematic alcohol drinking during the last 2-3 decades in this Norwegian general population.

**B17****Couples' self-reported health before and after disability pension over two decades – the HUNT Study**

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**Introduction:** Transition to disability pension is associated with a temporary decline in self-rated health and increased mental and somatic symptoms. The high frequency of disability pensions in Norway has caused concern about non-medical causes of work disability. Previous research indicates that spouses influence each other's mental health. Whether the disability process has any impact on the spouse's health has not been studied.

**Aims:** To study the health of disability pensioners and their spouses before and after disability pension during two decades.

**Methods:** We linked data from HUNT2 (1995-97) and HUNT3 (2006-08) to data on disability pensions and cohabitating couples provided by Statistics Norway. We identified participants who received a disability pension within five years before or after participation in each health study (n=5353/4639) and their partners (n=3689/3024). Using logistic regression, we estimated self-rated health, insomnia and mental symptoms depending on time since disability pension and predicted the probability of poor health for each year.

**Results:** Probability of poor self-rated health peaked around time of disability pension. Levels of poor health were slightly lower in HUNT3 than HUNT2 for those 50 years or older, but not for those younger than 50. Symptoms of depression also peaked around time of disability pension, and more pronounced for participants in HUNT2 than HUNT3. Insomnia and symptoms of anxiety increased somewhat before time of disability pension, but with little decline afterwards. Symptoms of anxiety were higher at HUNT2 than HUNT3. There was no association between time since disability pension and spouse's health.

**Conclusion:** We confirmed a deterioration of health around the time of disability pension, with similar levels of poor health among disability pensioners in the '90s and '00s. Mental health around time of disability pension was better in the '00s. We found no indication of the disability process influencing the spouse.

## B18

### ApoE gene and lifestyle interactions for risk of dementia mortality

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**Introduction:** ApoE allele  $\epsilon 4$  carriers have increased risk of dementia, while  $\epsilon 2$  carriers seem to be protected.

**Aims:** We wanted to investigate the interaction between ApoE genotypes, lifestyle risk factors and dementia related mortality, and to examine the validity of using dementia related mortality as a proxy for a clinical dementia diagnosis in epidemiological studies.

**Methods:** We used a stratified nested case control study with 561 cases and 584 controls. Cases were randomly drawn among dementia deaths in Cohort of Norway (CONOR), and living controls were from the same birth cohort. Conditional logistic regression was used.

**Results:** ApoE  $\epsilon 4$  carriers were at increased risk of dementia related mortality compared to non-carriers (OR=2.46, 95% confidence interval (CI) 1.93-3.13), and  $\epsilon 4$  homozygotes were at particularly high risk (OR=7.86, 95% CI 3.80-13.8), while the  $\epsilon 2$ -type was associated with a lower risk (OR=0.57, 95% CI 0.36-0.91 for  $\epsilon 2\epsilon 3$  versus  $\epsilon 3\epsilon 3$ ). The highest risk for dementia related mortality was found among  $\epsilon 4$  carriers with several lifestyle risk factors ( $\epsilon 4$  carriers who were ever smokers, hypertensive, physical inactive, and had diabetes versus  $\epsilon 4$  non-carriers without these life style risk factors: OR=15.4, 95% CI 4.37, 52.4).

**Conclusions:** Ensuring a healthy life-style seems to be important to prevent dementia for all, but especially for  $\epsilon 4$  carriers. Using dementia death as a proxy for clinical dementia diagnosis in aetiology studies seems to be valid.

**B19****Vitamin D does not predict dementia or cognitive impairment – a 20 year follow up study in community living old men**

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**Introduction:** Vitamin D deficiency has been suggested as a possible risk factor for dementia and cognitive impairment. However the results from longitudinal studies are contradictory.

**Aims:** The aim was to investigate vitamin D, assessed by various methods, in relation to risk of cognitive impairments.

**Methods:** We measured Vitamin D in 1182 71-year old Swedish men by plasma 25-hydroxy-vitamin D (25(OH)D) with high-pressure liquid chromatography-mass spectrometry, dietary vitamin D intake by 7-day dietary record and vitamin D synthesis genetic risk score (grs) according to Mendelian randomization. During 20 years of follow-up 116, 64 and 250 men developed Alzheimer's disease, vascular dementia or all-cause dementia, and another 80 men declined in the Mini Mental State Examination (MMSE). Hazard (HR) and odd ratios (OR) were calculated by Cox and logistic regression respectively and adjusted for potential confounders (age, season, body mass index, education and physical activity).

**Results:** There were no associations between 25(OH)D or dietary vitamin D with any of the outcomes (crude and adjusted HR/OR  $\approx$  1.0 for all continuous exposures). When exposures were categorized adjusted HR for all-cause dementia was 0.88 (95% CI, 0.59, 1.31) in men with  $\leq$  50 nmol/L plasma 25(OH)D versus men  $>$  75 nmol/l. Adjusted HR for all-cause dementia was 0.92 (95% CI, 0.63, 1.32) for the lowest tertile of vitamin D intake versus the highest tertile. The grs of vitamin D were not associated with any of the outcomes e.g. adjusted HR for the continuous grs for all-cause dementia was 1.04 (95% CI, 0.91, 1.19).

**Conclusions:** In this sample of old men no association between vitamin D measured by plasma 25(OH)D, dietary vitamin D intake or genetic risk scoring and long-term risk of Alzheimer's disease, all-cause dementia or cognitive impairment was found.



## B20

### The impacts of childhood conditions on young adults' secondary level education in the 1987 Finnish Birth Cohort

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**Introduction:** Well-being in later life is strongly founded in childhood. The long-term aim of the Finnish education policy is to provide equal educational opportunities to all citizens regardless of their social background or home municipality. Education is closely tied to a person's health and well-being, as well as financial circumstances in adulthood. The 1987 Finnish birth cohort study has thus far shown that problems in well-being are closely connected to lack of secondary level education and mental health- and financial problems tend to accumulate particularly to those without secondary level education.

**Aims:** The aim of this study is to find out how early-life conditions affect a child's later school performance and attainment of degrees. This study aims to identify which factors predict success in the attainment of secondary level degrees, and what are the relevant risk factors for discontinued educational pathways.

**Methods:** The 1987 Finnish Birth Cohort –study follows all, approximately 60 000, persons born in Finland in 1987, from the prenatal period through the year 2012. By combining data from different registers on the socioeconomic and health status of the parents of the cohort members to the information on the degrees that the cohort members have received, logistic regressions are used to identify the salient risk factors for attaining degrees.

**Results:** The preliminary results show that adverse childhood conditions cause a significant impact on the cohort member's educational achievements. Particularly parent's lack of education, financial difficulties and mental health problems are risk factors for children's lacking degree education.

**Conclusion:** The prevention of intergenerational transmission of welfare problems needs to consider the impact of early life conditions on the attainment of further education.

**B21****Advances in survival among the very old are seen across the spectrum of health and functioning**

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**Introduction:** For every ten years since 1950, 20-40% more of a birth cohort survive into their tenth decade in most high-income countries, and the mortality rates have been reduced by half over the last 60 years for nonagenarians. There is widespread concern that the basis for the better survival is overtreatment of severely physically and cognitively disabled individuals.

**Aims:** To investigate whether the advances in survival among the very old are seen primarily in the most disabled individuals or across the spectrum of health and functioning.

**Methods:** The study population comprised two whole Danish birth cohorts: the 1905 Cohort and the 1915 Cohort. At the age of 95 years, both cohorts were invited to participate in a health survey that used the same assessment instrument. In total, 2,670 persons participated in the two surveys and survival was assessed through a 4.3-year follow-up period during which 1,972 (73.9%) died.

**Results:** The chance of surviving to age 95 was approximately 30% higher for people born in 1915 than for people born in 1905, and mortality remained lower in the 1915 Cohort in the follow-up period (HR=0.92, *P*-value=0.016) corresponding to 29% survived to age 99 in the 1915 Cohort compared with 26% in the 1905 Cohort. This advance was seen across different levels of activity of daily living, physical performance, cognitive functioning, self-rated health and life satisfaction for both men and women.

**Conclusions:** People are living longer with advancing cohorts, and the improvement in survival for 95-year-olds born in 1915 compared to 95-year-olds born in 1905 was seen regardless of disability level and self-rated health. This suggests that advances in survival among the oldest old are not due to better survival of the most disabled alone.

## C1

### **Lithium in drinking water and suicide: A Danish nationwide register-based cohort study using spatial analysis**

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**Introduction:** Lithium occurs naturally in drinking water and may have a positive effect on mental health and suicide. In clinical practice, lithium in high therapeutic doses is used as a mood-stabilizer in the treatment of affective disorders. Previous studies performed at an ecological level have found an association between lithium in drinking water and risk of suicide.

**Aims:** The present study examined the geographical distribution of lithium in Denmark and investigated whether long-term exposure to naturally occurring low levels of lithium in drinking water was associated with a reduced risk of suicide at an individual level.

**Methods:** The study population consisted of all 3,671,546 Danish adults ( $\geq 20$  years) of which 12,613 committed suicide between 1990-2006. Information on suicides was obtained from the nationwide Danish Register of Causes of Death. Data on lithium concentrations were obtained through a nationwide drinking water campaign from 2013 including 151 measurements from waterworks supplying approximately 42% of all residents in Denmark. The measurements were interpolated using point kriging and an accumulated lithium exposure was computed for each individual based on municipality of residence every year. Spatial statistics were applied to investigate geographical patterns in lithium levels. Poisson regression analyses were used to investigate the association between accumulated lithium exposure and suicide rate.

**Results:** Significant regional clustering in drinking water lithium levels were found with high levels in Eastern and low levels in Western Denmark. The regression analyses showed a significant dose-response trend of decreasing suicide rates with increasing accumulated lithium exposure. The trend remained after adjustment for gender, age, socioeconomic status, civil status, and calendar year.

**Conclusions:** The findings support the growing evidence of long-term exposure to naturally occurring lithium levels being protective against suicide. If these findings can be further supported they may have implications for individuals at high risk of committing suicide.

## C2

### Prenatal methylmercury exposure and language delay at three years

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**Introduction:** There is a worldwide concern about prenatal methylmercury (MeHg) exposure and its possible neurodevelopmental effect in susceptible children.

**Aims:** To examine whether an association is found between prenatal low-level exposure to MeHg and language delay at three years, adjusting for fish intake, long chain n-3 fatty acids and dioxin and dioxin like-polychlorinated biphenyls (dl-PCB) exposure.

**Methods:** Data from the Norwegian Mother and Child Cohort Study (MoBa). The study sample consisted of 46,750 mother-child pairs. MeHg exposure was calculated from reported seafood intake during pregnancy assessed by a FFQ in mid-pregnancy. Children's language was measured by the Dale and Bishop grammar rating and the Ages and Stages communication scale (ASQ). We calculated odds ratios (OR) and 95% confidence intervals (CI) using logistic regressions.

**Results:** Median MeHg exposure was 0.14 µg/kg body weight/week (range 0.0-1.7). Children without language delay were used as the reference category. The adjusted association between MeHg exposure at the 90<sup>th</sup> percentile and risk of a child having unintelligible speech was OR= 1.98 (95%CI: 1.16, 3.39). Additional adjusting for fish intake strengthened the association (OR= 2.50 (95%CI: 1.21, 5.18)), adjusting for concomitant high exposure to dioxin and dl-PCB weakened the association (OR=1.86 (95%CI: 1.07, 3.23)). High MeHg exposure was also associated with low communication skills (ASQ), with adjusted OR=1.39 (95%CI: 1.07, 1.81).

**Conclusions:** In spite of a prenatal MeHg exposure being low and below the tolerable weekly intake set by the European Food Safety Authority, these results suggest an increased risk of language delay at three years in children of mothers with the highest MeHg exposure (above 90<sup>th</sup> percentile) in this population.

## C3

### The influence of pre- and postnatal exposure to dioxins and polychlorinated biphenyls on ADHD symptoms and cognitive functions in Norwegian preschool children

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**Introduction:** Early-life exposure to persistent organic pollutants (POPs), including polychlorinated dibenzo-p-dioxins/dibenzofurans (dioxins) and polychlorinated biphenyls (PCBs) may result in adverse health effects in children, such as impaired neurodevelopment.

**Aims:** To investigate whether low level exposure to dioxins and PCBs, during pregnancy and breastfeeding affect neurodevelopment in children and result in impaired cognitive functions and ADHD symptoms in Norwegian preschoolers.

**Methods:** We used the Norwegian Mother and Child Cohort Study (MoBa), with the ADHD sub-study (n=1195), to examine early-life exposure to dioxins and PCBs and associations with early ADHD symptoms, IQ, working memory, and language skills in children at 3 years. The influence of maternal dietary exposure to dioxins and PCB during pregnancy was investigated using logistic, linear, and negative binomial regression. Data from MoBa also included breastfeeding duration and relevant covariates, such as maternal age, socioeconomic status, parity, dietary supplements, alcohol and smoking during pregnancy, parental mental health, and birth complications.

**Results:** The estimated maternal exposure to dioxins and PCBs in MoBa was generally low and median intake of dioxins and dioxin-like PCB was 3.6 times lower than the tolerable weekly intake of 14 pg TEQ/kg bw/week. An interquartile range increase in PCB-153 exposure was associated with 1.1% (95% CI:-1.5, 3.8) higher ADHD symptom scores and -0.2 IQ points (95% CI:-0.4, 0.04). The associations were not statistically significant.

**Conclusions:** Maternal dietary exposure to dioxins and PCBs in MoBa was generally low, and not significantly associated with early ADHD symptoms and IQ in preschool children.

## C4

**Pregnancy complications and birth outcomes among women experiencing nausea only or nausea and vomiting during pregnancy in the Norwegian Mother and Child Cohort Study**

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**Introduction:** Nausea and vomiting in pregnancy (NVP), or nausea only (NP) have a prevalence of approximately 50-80% for all pregnancies. The aetiology remains unknown, although it is currently believed to be related to early pregnancy hormones. In studies addressing pregnancy complications and birth outcomes for NVP women, results have often been contradictory.

**Aims:** Using the Norwegian Mother and Child Cohort Study (MoBa), we compared pregnancy complications and birth outcomes for women experiencing NVP or NP, with symptom-free (SF) women.

**Methods:** Pregnancies from MoBa (n = 51,675), were examined. Data on nausea and/or vomiting during gestation and birth outcomes were collected from three questionnaires answered between gestation weeks 15 and 30, and linked with data from the Medical Birth Registry of Norway. Chi-squared tests, one way analysis of variance, and multiple regression analyses were used.

**Results:** When compared to the SF group, NVP and NP groups had significantly increased odds for pregnancy complications such as pelvic girdle pain (adjusted odds ratio, aOR, 2.26, 95% CI, 2.09-2.43, and aOR 1.90, 95% CI, 1.76-2.05, respectively) and proteinuria (aOR 1.50, 95% CI 1.38-1.63, and 1.20, 95% CI 1.10-1.31, respectively) reported around week 30 of pregnancy. Women with NVP also had significantly increased odds for high blood pressure (mean 142/88 mmHg) (aOR 1.40, 95% CI 1.17-1.67) and preeclampsia (aOR 1.13, 95% CI 1.01-1.27) reported around week 30 of pregnancy. Conversely, the NVP and NP groups had significantly reduced odds for unfavourable birth outcomes such as low birth weight infants (aOR 0.72, 95% CI 0.60-0.88, and aOR 0.73, 95% CI 0.60-0.88, respectively), whilst the NP group had significantly reduced odds for preterm births (aOR 0.86, 95% CI 0.78-0.96).

**Conclusions:** We found women with NVP and NP more likely to develop pregnancy complications, yet they display mostly favourable delivery and birth outcomes.

## C5

**Birth weight, perinatal mortality, and the family: a sibling study of singletons born at term in Norway, 1967-2011**

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**Introduction:** Perinatal mortality (PNM) according to birth weight (BW) has the shape of a reversed J on a logarithmic scale. This pattern has been studied in several scientific disciplines but its nature is not well understood.

**Aims:** To study the BW-PNM relation in a sibling design with emphasis on macrosomia and the hook of the reversed J.

**Methods:** All 804,798 mothers with more than one singleton delivery at term notified in the Medical Birth Registry of Norway between 1967 and 2011 were considered; 1,675,094 singletons born at term were participants. Associations between zBW (10 categories z-transformed BW standardized for sex, parity, and gestational week) and PNM were analyzed in multivariable generalized estimating equations (GEE) and fixed-effects (conditional) logistic regression with the mother's identity as panel variable.

**Results:** Grand mean PNM was 4.1/1,000 births; grand mean BW was 3,577g (SD 492). PNM according to zBW showed a reversed J-pattern and was lowest (1.9/1,000) at reference zBW (+1 to +2), with increasingly higher PNM for higher zBW. PNM in the highest (>+4) zBW category (33.7/1,000) was 17-fold higher than reference. This pattern changed only moderately in GEE analyses including potential confounders and mediators. Fixed-effects analysis of siblings discordant for PNM showed a pattern similar to the overall crude results. Deviation from sibling zBW did however modify the zBW-PNM relation strongly: PNM for a given zBW increased the more it deviated from sibling zBW. The hook of the reversed J was mainly restricted to babies with zBW >1.5 higher than their siblings.

**Conclusions:** The association between macrosomia and PNM could not be explained by measured risk factors or unmeasured shared family factors. Babies with zBW deviant from that of their siblings, in either direction, were at increased risk of perinatal death. This modifying effect of sibling size had considerable impact on total PNM.

## C6

**Pregnancy-induced hypertensive disorders before and after a national economic collapse: a population based cohort study**

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**Introduction:** Data on the potential influence of macroeconomic recessions on maternal diseases during pregnancy are scarce.

**Aims:** We aimed to assess potential change in prevalence of pregnancy-induced hypertensive disorders (preeclampsia and gestational hypertension) during the first years of the major national economic recession in Iceland, which started abruptly in October 2008.

**Methods:** Women whose pregnancies resulted in live singleton births in Iceland in 2005-2012 constituted the study population (N=35,211). Data on pregnancy-induced hypertensive disorders were obtained from the Icelandic Medical Birth Register and use of antihypertensive drugs during pregnancy, including  $\beta$ -blockers and calcium channel blockers, from the Icelandic Medicines Register. With the pre-collapse period as reference, we used logistic regression analysis to assess change in pregnancy-induced hypertensive disorders and use of antihypertensives during the first four years after the economic collapse, adjusting for demographic and pregnancy characteristics, taking aggregate economic indicators into account.

**Results:** Compared with the pre-collapse period, we observed an increased prevalence of gestational hypertension in the first year following the economic collapse (2.4% vs. 3.9%; adjusted odds ratio [aOR] 1.47; 95 percent confidence interval [95%CI] 1.13-1.91) but not in the subsequent years. The association disappeared completely when we adjusted for aggregate unemployment rate (aOR 1.04; 95% CI 0.74-1.47). Similarly, there was an increase in prescription fills of  $\beta$ -blockers in the first year following the collapse (1.9% vs. 3.1%; aOR 1.43; 95% CI 1.07-1.90), which disappeared after adjusting for aggregate unemployment rate (aOR 1.05; 95% CI 0.72-1.54). No changes were observed for preeclampsia or use of calcium channel blockers between the pre- and post-collapse periods.

**Conclusions:** Our data suggest a transient increased risk of gestational hypertension and use of  $\beta$ -blockers among pregnant women in Iceland in the first and most severe year of the national economic recession.



## C7

### Risk factors for complete uterine rupture after trial of labor in intact uterus

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**Introduction:** Uterine rupture is very rare in intact uterus in developed world. However, we noticed an increasing trend in its incidence in recent years in Norway.

**Aims:** The aim was to identify the risk factors for complete uterine rupture in intact uteri, through studying a validated sample of mothers having trial of labor (TLO) in the period 1967-2008.

**Method:** This was a retrospective population based study, using the Medical Birth Registry of Norway and Patient Administration System. All records with uterine ruptures, were studied, and information validated.

Population: 1 317 967 mothers with intact uteri, having TOL (1967-2008)

Main outcome measure: Complete uterine rupture

Explanatory variables: Demographic, pregnancy and labor risk factors.

A multivariable logistic regression was used to measure the adjusted odds ratios AORs with 95% confidence intervals (CI).

**Results:** There were 51 complete ruptures after TOL (0.04/1000). Adjusted OR with 95% CI for risk factors for ruptures were: maternal age  $\geq 35$  (2.18; 1.2-3.8), Parity  $\geq 3$  (3.16; 1.8-5.4), Mothers from African Horn versus European (5.24; 1.2-21.7), Previous miscarriages (9.52; 5.2-17.2); Birth weight  $\geq 4000$  gm (2.61; 1.4-4.6), Antepartum fetal death (16.15; 6.6-39.2), Gestational age  $\geq 41$  weeks (1.82; 1.1-3.3), Induced labor (4.88; 2.7-8.7); Induction methods versus spontaneous labor (Prostaglandins: 4.31; 1.7-10.4, Oxytocin: 5.97; 2.9-12.2, Combination Prostaglandin/Oxytocin: 41.26; 17.5-97.1), Augmentation of labor with Oxytocin (14.26; 7.1-28.6), and Breech extraction (73.93; 29.2-214.1).

**Conclusion:** Complete uterine rupture is very rare in intact uterus. Most important risk factors increasing rupture risk at TOL are related to our obstetric interventions such as Induction and augmentation of labor and breech extraction. Antepartum death is an important risk factor indicating reduced vigilance due to the absence of fetal heart. Mothers with previous miscarriages, constitute a high risk group indicating disrupted uterine wall integrity after curettage. Guidelines for management of labor should be updated.

## C8

### Duration of breastfeeding and risk of coeliac disease in the MoBa cohort

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**Introduction:** Breastfeeding has been hypothesised to protect against coeliac disease. However, the recommended 6 months' duration of full breastfeeding and the risk of coeliac disease have not been widely studied.

**Aims:** To study the association between duration of full breastfeeding and subsequent coeliac disease.

**Methods:** The Norwegian mother and child cohort study recruited mothers giving birth from 1999-2009, and those with completed questionnaires at child age 6 months were included. Complete data regarding breastfeeding at 6 months was available for 87 722 participants (671 with coeliac disease) and for up to 18 months for 72 375 participants (577 with CD).

**Results:** A total of 13.7% of the infants were fully breastfed at 6 months. Coeliac disease developed in 10.5/1000 of those fully breastfed < 6 months compared to 7.2/1000 in those with shorter duration (relative risk [RR] 1.45, 95% CI 1.20-1.76). After adjustment for maternal coeliac disease, gender, attained age by 2013 and age at gluten introduction, full breastfeeding for 6 months remained associated with higher risk for later coeliac disease (aRR 1.32, 1.08-1.61). Stratification of the analysis by maternal coeliac disease status during pregnancy showed very similar associations. At age 12 months 38% were still breastfed. Of infants breastfed ≥ 12 months 9.5/1000 developed coeliac disease compared to 7.0/1000 in those with shorter duration (RR 1.35, 1.15-1.59). After adjustment for maternal coeliac disease, gender, attained age and age at gluten introduction, breastfeeding duration ≥ 12 months remained associated with an increased risk for coeliac disease (aRR 1.29, 1.10-1.52).

**Conclusion:** We found a higher risk of coeliac disease in infants fully breastfed for 6 months and for those breastfed ≥ 12 months. The observation remained significant after adjustment and exclusion of mothers with coeliac disease.

## C9

**Maternal exposure to sexual violence and subsequent neonatal outcomes**

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**Introduction:** Stress has been reported as a contributor to adverse neonatal outcomes, such as prematurity and low birth weight. Sexual violence is one of the most common stressful events among women, yet, the evidence on the potential influence of sexual violence on women's subsequent neonatal outcomes is scarce.

**Aim:** To investigate the associations between women's sexual violence exposure in adolescence or adulthood and subsequent adverse neonatal outcomes, when compared to neonates of women with no record of such violence.

**Methods:** We linked detailed, prospectively collected, information on women seeking services at a Rape Trauma Service (RTS) to the nationwide Icelandic Medical Birth Registry (IBR). Women who attended the RTS in 1993-2010 and delivered at least one infant in Iceland through 2012 (on average 6 years later) formed our exposed cohort (n=1067). For each exposed woman's delivery, nine deliveries by women who had not attended the RTS were randomly selected from the IBR (n=9105) matched on age, parity and season of delivery. Both cohorts were restricted to women with Icelandic citizenship who delivered a singleton infant. Poisson regression was used to obtain Relative Risks (RR) with 95% confidence intervals (CI).

**Results:** Our preliminary results point to increased risks of preterm delivery (RR 1.48, 95%CI 1.12-1.96) and admission to the neonatal intensive care unit (RR 1.35, 95%CI 1.05-1.73) when comparing neonates of exposed women to neonates of non-exposed women. Somewhat stronger effects were seen for neonates of women who were assaulted as adolescents. More results will be presented at the conference.

**Conclusion:** The preliminary findings from this population based cohort study indicate increased risks of some adversities for neonates of exposed mothers when compared to neonates of non-exposed women. Mechanisms or possible explanations and preventive strategies will be discussed.

## C10

### Infections and risk of celiac disease in childhood: a prospective nationwide cohort study

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**Introduction:** Studies on early life infections and risk of later celiac disease are inconsistent and have mostly been restricted to inpatient data, retrospective designs or limited statistical power.

**Aims:** We aimed to test whether early life infections are associated with increased risk of later celiac disease using prospective population-based data.

**Methods:** This study, based on the Norwegian Mother and Child Cohort Study, includes prospective, repeated assessments of parent-reported infectious disease data up to 18 months of age for 72,921 children born 2000-2009. Celiac disease was identified through parental questionnaires and the Norwegian Patient Registry. Logistic regression was used to estimate odds ratios adjusted for child's age and sex (aOR).

**Results:** During a mean follow-up period of 8.5 years (range, 4.5-14.5), 581 children (0.8%) were diagnosed with celiac disease. Children with  $\geq 10$  infections ( $\geq 4^{\text{th}}$  quartile) up to age 18 months had a significantly higher risk of later celiac disease, as compared with children with  $\leq 4$  infections ( $\leq 1^{\text{st}}$  quartile) (aOR=1.32; 95% confidence interval [CI]=1.06-1.65; per increase in infectious episodes, aOR=1.03; 95%CI=1.02-1.05). The aORs per increase in specific types of infections were: upper respiratory tract infections: 1.03 (95%CI=1.02-1.05); lower respiratory tract infections: 1.12 (95%CI=1.01-1.23); gastroenteritis: 1.05 (95%CI=0.99-1.11). Similar results were seen in subanalyses on high infection frequency ( $\geq 4^{\text{th}}$  quartile vs.  $\leq 1^{\text{st}}$  quartile) before 6 months of age (aOR=1.28; 95%CI=1.02-1.59) and at age 6-18 months (aOR=1.37; 95%CI=1.08-1.74). Additional adjustments for maternal celiac disease, education level, smoking, birth weight, prematurity, infant feeding practices, birth season and antibiotic treatment yielded largely unchanged results.

**Conclusions:** This comprehensive study complements and extends the results from previous epidemiological studies and are in line with immunological data suggesting that early life infections may play a role in celiac disease development.

## C11

### Pelvic pain after childbirth: a longitudinal population study

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**Introduction:** Factors associated with the development and persistence of pelvic pain after childbirth have been insufficiently studied.

**Aims:** Our aim was to study associations of mode of delivery with onset and clinical course of pelvic pain up to 7–18 months after childbirth.

**Methods:** In this longitudinal population study, we included 20,248 participants enrolled in the Norwegian Mother and Child Cohort Study (1999–2008) who did not report pelvic pain during pregnancy. Data were obtained by four self-administered questionnaires and linked to the Medical Birth Registry of Norway. The association between mode of delivery and onset of pelvic pain were estimated as crude and adjusted odds ratios (OR) with 95% confidence intervals (CI) using generalized estimating equations (GEE) with logit link function (exchangeable correlations). We used GEE with identity link function (unstructured correlations) to assess the clinical course of pelvic pain over time.

**Results:** A total of 4.5% of the women reported onset of pelvic pain 0–3 months postpartum. Compared to unassisted vaginal delivery, operative vaginal delivery was associated with increased odds of pelvic pain (adjusted OR 1.30; 95% CI: 1.06–1.59). Planned and emergency cesarean deliveries were associated with reduced odds of pelvic pain (adjusted OR 0.48; 95% CI: 0.31–0.74 and adjusted OR 0.65; 95% CI: 0.49–0.87, respectively). Planned cesarean delivery, young maternal age, and low Symptom Checklist-8 scores were associated with low pelvic pain scores after childbirth. A history of pain was the only factor associated with increased pelvic pain scores over time ( $P=0.047$ ).

**Conclusions:** New onset of pelvic pain after childbirth was not commonly reported, particularly following cesarean delivery. Overall, pelvic pain scores were rather low at all time points and no obstetrical factors were associated with the clinical course. However, women with a history of pain reported increased pelvic pain scores over time.

## C12

### **Does migration influence preterm birth rates? A comparison between estimates for source countries and rates after migration to Norway**

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**Introduction:** Preterm birth (PTB) rates vary by maternal country of origin; however, whether differences are physiological or pathological remains contested.

**Aims:** We aimed to compare PTB rates in Norway by maternal country of birth to estimates for PTB in the corresponding source countries. We furthermore assessed the impact of migrants' length of residence in Norway on rates of PTB.

**Methods:** We linked birth and immigration data for 55 099 liveborns to women born in Somalia, Pakistan, Iraq, Vietnam, Thailand, the Philippines, Sri Lanka and Turkey from 1990-2010. We calculated the PTB rate with 95% confidence intervals by country group and by length of residence. We used the most recent World Health Organization PTB estimates for source countries for the year 2010 as comparison. The relation between the PTB rates was estimated by Pearson's correlation coefficient.

**Results:** A total of 4 092 preterm births occurred. The PTB rates in source countries were higher in all country groups when compared to rates among migrants. Seven out of eight source countries had PTB rates >10%, whilst among migrants, all groups had PTB rates of <9%. There was no correlation between estimates for PTB in source countries and in Norway ( $R^2=0.255$ ,  $p=0.202$ ). We found a positive trend between PTB rates and length of residence in six out of eight migrant groups. The association was limited to medically indicated births and was linked to maternal diabetes, hypertension and fetal growth restriction.

**Conclusions:** The gap in preterm birth rates between migrants and estimates for their source countries is likely to reflect selection to migration, whereas differences across migrants' length of residence in Norway are likely to be due to a mix of physiological and pathological factors. Subgroups with persisting or increased risk of preterm birth after migration should be targeted for early detection and optimal obstetric management.

## C13

### **The use of multiple Norwegian health registries to assess vaccine safety: Congenital anomalies among infants born to mothers exposed to the HPV vaccine during pregnancy**

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**Introduction:** GARDASIL, a vaccine against human papillomavirus, protecting against cervical cancer and genital warts, is recommended for females 13-26 years old; and routinely offered to 12 year old Norwegian girls. Some may have received GARDASIL during pregnancy.

**Aims:** To assess the feasibility of using Norwegian health registries to identify and describe congenital anomalies (CA) in infants exposed to GARDASIL during fetal life.

**Methods:** We identified infants with CA exposed to GARDASIL during fetal life between 2006-2008 by linking the Norwegian National Vaccination Register (SYSVAK), the Medical Birth Registry of Norway (MBRN), Prescription Registry (PR) and the Norwegian Patient Registry (NPR). In addition, medical information from hospitals for the mother and child with CA were collected. Clinical information was abstracted and assessed by an independent panel of teratologists.

**Results:** More than two years was used to obtain relevant approvals. For the period 2006-2008, 928 vaccinees were identified by linking SYSVAK and MBRN, and 1338 vaccinees by linking SYSVAK, MBRN and PR. Among 181,278 infants, we identified 14,249 CA from NPR and 9,342 CA from MBRN. Linkage between NPR, PR, SYSVAK, and MBRN revealed 23 infants exposed to GARDASIL during fetal life, three of which had CA. Standardized incidence ratio suggested no excessive risk or pattern of CA among infants exposed to GARDASIL as compared to the rest of the population. For two of the infants with CA exposed to GARDASIL during fetal life, medical chart reviews were performed.

**Conclusion:** The registry linkages revealed inconsistencies in registration of GARDASIL exposure and CA status, emphasizing the need for multiple registry linkage. Chart review was not possible for subjects identified through PR, reducing the value of the PR data in our study. Results show no association between pregnancy exposure to GARDASIL and subsequent CA in infants.

## C14

**Maternal smoking and predictors of quitting smoking during pregnancy; the Murmansk county birth registry, Northwest Russia**

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**Background:** The prevalence of female smoking has increased from <5% in the 1980s to >20% in the 2000s. We studied smoking prevalence before and during pregnancy and the factors associated with quitting smoking after pregnancy recognition in the Murmansk oblast, Northwest Russia.

**Methods:** In this cross-sectional study, we used data from the Murmansk County Birth Registry (MCBR) collected during 2006-2011. Independent association between quitting smoking during pregnancy and maternal age, education, marital status, ethnicity, residence, and parity was analyzed by multivariable logistic regression.

**Results:** Of 51,131 women registered in the MCBR, 25.2% were smokers before pregnancy, and 18.9% continued smoking during pregnancy. In the regression model, women aged ≤19 years had lower odds of quitting smoking during pregnancy than older women. Women with secondary (OR: 2.33, 95% CI: 1.86-2.92), vocational (OR: 3.71, 95% CI: 2.96-4.65) and university education (OR: 7.42, 95% CI: 5.89-9.36) were more likely to quit smoking after pregnancy recognition than women with incomplete secondary education. Unmarried women and women with cohabiter were twice less likely to quit smoking during pregnancy compared to married ones. We found a positive linear association between number of previous deliveries and the odds of quitting smoking during pregnancy. OR for rural compared to urban residents was 0.76 (95% CI: 0.68-0.86). Ethnicity was not associated with quitting smoking during pregnancy.

**Conclusion:** Only 6.3% of smokers in the Murmansk oblast quit smoking during pregnancy. Quitting smoking after pregnancy recognition is associated with maternal age, education, marital status, residence and parity. Such result is essential to identify target groups for future smoking intervention campaigns.



## C15

### Birthweight in Norway by the maternal country of birth

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**Introduction:** An increasing proportion of newborns in Norway have foreign-born mothers. Birth weight is known to vary between ethnic groups, but it is less clear if disparities persist among migrant groups.

**Aims:** We examined the association between maternal country of birth and offspring mean birth weight among major migrant groups living in Norway, and assessed any effects of the length of residence in Norway and the level of education among mothers.

**Methods:** We linked birth and immigration data for 29 964 singletons born in Norway to foreign-born women that themselves were born in either Pakistan, Somalia, Iraq, Sri Lanka, the Philippines or Vietnam between 1990 and 2009. Infants born to women of Norwegian origin was the reference (n= 475 951). We calculated mean birth weight in grams (g) with standard deviation (SD) in each group. Associations between the maternal country of birth and offspring birth weight was estimated in linear regression models after adjustment for maternal age, parity, level of education, length of residence in Norway, gestational age and infant sex.

**Results:** Infants in all six migrant groups had a lower mean birth weight compared with infants born to women of Norwegian origin. Among migrant groups, mean birth weight was highest among Philippine women (3402g; SD 578) and lowest among Vietnamese women (3235g; SD 499), (reference: 3581g; SD 591). In adjusted models, the mean birth weight difference was greatest among infants born to Pakistani women (-273g) followed by infants born to Vietnamese (-260g), Sri Lankese (-213g), Somali (-175g) and Iraqi women (-124g). A length of residence of  $\geq 5$  years and higher education was associated to increased birth weight of the offspring. Adjusting for maternal diabetes did not change the results.

**Conclusions:** Maternal country of birth is strongly associated to offspring birth weight with differences of up to 300g.

## C16

### Diet during pregnancy – does it matter in a well-nourished population?

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**Introduction:** The scientific interest in maternal nutrition is increasing and monitoring of dietary intake has become an integral part of pregnancy and birth cohort studies. A new food frequency questionnaire (FFQ) was developed and validated specifically for the Norwegian Mother and Child Cohort Study (MoBa). The MoBa FFQ covered the average intake of food, beverages and dietary supplements during the first 4 to 5 months of pregnancy. It included questions about 255 foods and dishes and has been thoroughly validated. Dietary data is available for 87,700 pregnancies.

**Aims:** To summarize key findings from all studies available of maternal diet and pregnancy outcomes in MoBa and to evaluate the role of maternal diet in a well-nourished population.

**Methods:** The pregnancy outcomes include birth size measures, infants being small and large for gestational age, pregnancy duration, preterm delivery, preeclampsia, gestational weight gain and postpartum weight retention. At present (April 2015) 21 studies of maternal diet and pregnancy outcomes have been published.

**Results:** The results from MoBa diet studies provide strong supporting evidence for lower risk of adverse pregnancy outcomes in women who regularly consume vegetables, fruits, berries, whole grain, fish, dairy, and water. A protective effect of probiotic food items and unprocessed plant foods points to the importance of diet composition for a healthy gut flora and the body's immune response. The results showing negative impact of even low levels of environmental contaminants support the precautionary advice to avoid or reduce consumption of foods with moderate to high content. Our results corroborate that the current dietary recommendations to pregnant women are sound.

**Conclusions:** Results from MoBa indicate that maternal diet is an important modifiable lifestyle factor and that healthy eating may reduce the risk of adverse pregnancy outcomes. Medical antenatal care practitioners should be encouraged to pay more attention to dietary counselling.

## C17

**Abdominal obesity and the risk of hip fracture in postmenopausal women: Results from the Nurses' Health Study****Meyer HE<sup>1,2,3</sup>, Willett WC<sup>1,4,5</sup>, Flint AD<sup>1,4</sup>, Feskanich D<sup>5</sup>**

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**Introduction:** Low weight is an established and strong risk factor for osteoporosis and hip fracture. However, the association between fat tissue, muscle and bone is complex, and abdominal obesity might increase fracture risk. An adverse effect of abdominal fat is biological plausible as inflammation has adverse effects on bone tissue.

**Aims:** To study the association between waist circumference, waist-to-hip ratio and incident hip fractures.

**Methods:** We followed postmenopausal women in the Nurses' Health Study (n= 61,677) between 1986-2012. At baseline and through biennial follow-up, information on hip fracture and potential risk factors for hip fracture was collected. Waist and hip circumferences were reported at baseline and updated in 1996 and 2004. Data were analyzed by Cox proportional hazards regression with updated information on waist circumference, waist-to-hip ratio and confounders.

**Results:** During follow-up, 1168 women sustained a hip fracture. After controlling for known risk factors including BMI, there was a statistically significant association between increasing waist circumference and hip fracture (HR per 10 cm increase 1.13 (95% CI 1.04-1.23) and between increasing waist-to-hip ratio and hip fracture (HR per 0.1 unit increase 1.14 (95%CI 1.04-1.23). The interaction terms between waist circumference and physical activity (p=0.03) and between waist-to-hip ratio and physical activity (p=0.001) were significant. In women with little physical activity (less than the median), the HR in those in the highest category of waist circumference ( $\geq 96$  cm) was 1.58 (95% CI 1.06-2.35) compared to those in the lowest category ( $< 72$  cm), whereas there was no significant association between waist circumference and hip fracture in women with physical activity above the median. A similar pattern was found for waist-to-hip ratio.

**Conclusion:** Indicators of abdominal obesity were associated with increased risk of hip fracture after controlling for BMI. The increased risk was restricted to women with low physical activity.

**C18****Pre-pregnant body mass index, gestational weight gain and physical activity: effects on Apgar score in a prospective pregnancy cohort**

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**Introduction:** Pre-pregnant obesity represents an important risk factor for maternal and fetal complications during pregnancy, delivery and in the neonatal period. Physical activity in pregnancy may improve placental growth and function and hence have beneficial effects on pregnancy outcomes. Studies have found an association between pre-pregnant body mass index (BMI) and low Apgar in the new born, but the evidence for a moderating effect of physical activity and maternal gestational weight gain upon this association is scarce.

**Aims:** To examine the effect of pre-pregnant BMI, maternal gestational weight gain and physical activity on low Apgar score in the new born.

**Methods:** This prospective cohort study used data from The Norwegian Mother and Child Cohort study (1999-2008) and linked data from The Medical Birth Registry of Norway. Singleton pregnancies without congenital anomalies and gestation  $\geq 37$  weeks were included ( $n=89\,490$ ). Pre-pregnant BMI was classified as underweight ( $<18.5$ ), normal weight ( $18.5$ - $24.9$ ), overweight ( $25$ - $29.9$ ), obese ( $30$ - $34.9$ ) and morbidly obese ( $BMI \geq 35$ ). An Apgar score  $\leq 5$  after five minutes was defined as low Apgar. Recreational physical activity was categorised according to frequency per week. Risk estimates were obtained by logistic regression and adjusted for confounders.

**Results:** An increased risk of low Apgar was found in newborn of overweight women ((Odds ratio (OR) 1.3, 95% CI 1.1-1.7)), obese (OR 1.8, 95% CI 1.4-2.5) and morbidly obese (OR 3.0, 95% CI 2.1-4.3), as compared with normal weight women. The modifying effect of gestational weight gain and physical activity are assessed in ongoing analyses and final results will be presented at the meeting.

**Conclusions:** Pre-pregnant overweight and obesity was associated with an increased risk of low Apgar in the newborn. The modifying effect of gestational weight gain and physical activity are assessed in ongoing analyses and final results will be presented at the meeting.

**C19****Intergenerational transmission of overweight and obesity from parents to their adolescent offspring: A HUNT Study****M Næss<sup>1</sup>, TL Holmen<sup>1</sup>, M Langaas<sup>2</sup>, JH Bjørngaard<sup>3</sup>, K Kvaløy<sup>1</sup>**

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**Introduction:** There is a global worry concerning the extent of overweight and obesity development among children and adolescents. The observed weight increase is explained primarily by reduced levels of physical activity and change to a more calorie rich diet. However, the influence of genetics and social environment represented by parents and nearby surroundings, are important factors to consider.

**Aim:** To study the effects of parental BMI and waist circumference on equal measures in their offspring, addressed through adolescent sex stratified analyses considering one or both parents being overweight or obese. To investigate potential changes in parent-offspring weight relationships over time.

**Methods:** Study participants includes adolescent (age 13-19 years) from Young-HUNT1 (YH1, 1995-97) and Young-HUNT3 (YH3, 2006-08) with parents participating in the same surveys, HUNT2 and HUNT3 respectively. The study comprises 5266 full trios from YH1 and 3193 from YH3. Regression analyses are performed with adolescent waist circumference (WC) and BMI as outcomes. Exposure variables include: parental BMI and WC. Covariates to be considered: parents' education level, adolescent' physical activity, vegetable consume as proxy for diet, chronic pain and puberty scores. Siblings are to be taken into account both sex-specifically and on basis of numerical sibling order.

**Results:** Preliminary results indicate differences between girls and boys considering maternal and paternal obesity as predictors for offspring's obesity. Initial testing of co-variates effects indicate the following; Chronic pain seems more often to have effect on girls' than boys' weight. Puberty scores and Age seem to be strongly related to obesity. Parents education level is important for children's BMI but not for WC. Physical activity and intake of vegetables seems to be of greater influence in YH3 than in YH1.

**Conclusion:** Preliminary results indicate interesting aspects related to sex differences, diversified parental effects and change in time from HUNT2 to HUNT3 concerning parent-offspring weight relationships.

**C20****Women's weight and disordered eating in a large community sample:  
The HUNT study**

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**Introduction:** Weight problems and disordered eating (DE) may overlap and it is not unlikely that DE and weight status impact each other adversely. To date there is not sufficient evidence to establish such associations. This paper explores DE, weight, and related behaviours/cognitions such as dieting and weight dissatisfaction among women in a large general population sample.

**Aims:** The aims of the study were to: (1) estimate the prevalence of DE; 2) estimate the prevalence of weight dissatisfaction and dieting, and (3) determine the associations between, weight, DE, weight dissatisfaction and dieting behaviours in a large general population sample of adult women.

**Methods:** A cross sectional study from the Nord-Trøndelag Health Study (HUNT) was conducted on 27,252 women aged 19-99 using an 8-item version of the Eating Attitude Test and the Eating Disorder Scale-5. Data on dieting and weight dissatisfaction were collected from self-reported questionnaires and analysed across weight categories. Standardised measurements of height and weight were collected. Crude and adjusted logistic and multinomial logistic regression models were used.

**Results:** High rates of overweight and obesity were found and DE was associated with weight problems. The prevalence of DE was 12%. In younger ages (19-29), lower weight predicted DE, while increasing weight predicted DE in older women (30-82). The majority of women were dissatisfied with their weight and 54.1% of the women reported dieting. Neither BMI status nor age was associated with dieting or weight dissatisfaction.

**Conclusions:** A high prevalence of disordered eating was found in this study. Our findings highlight that dieting may be instigated by women's weight dissatisfaction, rather than by actual weight. Our results suggest that women's feelings about weight and weight acceptance should be incorporated in public health interventions to achieve more suitable policies for prevention and intervention of weight problems and DE

## C21

### Caffeine intake during pregnancy and early growth and obesity in childhood

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**Introduction:** We have earlier reported that maternal caffeine intake during pregnancy was associated with lower birth weight and higher risk for small for gestational age (SGA). Low birth weight and SGA have been associated with catch-up growth and obesity during early childhood.

**Aims:** To investigate the association between prenatal caffeine intake and early growth and obesity in childhood.

**Methods:** Our study includes 48,791 full-term, singleton mother-child pairs in the Norwegian Mother and Child Cohort Study. Total caffeine intake was calculated from a validated food frequency questionnaire answered in mid-pregnancy. Caffeine intake lower than 200mg/day was characterized as “average intake”, between 200-300mg/day as “high intake” and more than 300mg/day as “very high intake”. Mothers reported child’s weight from 6 months to 8 years in questionnaires. Early growth was evaluated by WHO weight-for-age z-scores and an increase of more than 0.67 of the z-score from birth to 6 months was defined as “catch-up growth”. Children with body mass index above the 85<sup>th</sup> percentile at 7-8 years were defined as overweight/obese.

**Results:** By category of caffeine intake, 17%, 18% and 21% of children had catch-up growth. Children born to mothers with high and very high caffeine intake had 18% (OR:1.18, 95%CI: 1.07, 1.30) and 24% higher adjusted risk (OR:1.24, 95%CI: 1.08, 1.44) of catch-up growth. The prevalence of overweight/obesity at 7-8 years increased by 5% from average to very high caffeine intake. Children born to mothers with very high caffeine intake had 23% higher adjusted risk of overweight/obesity (OR:1.23, 95%CI: 1.01, 1.50) compared to mothers with average intake. Restricted analysis to catch-up growers provided similar, though non-significant results.

**Conclusions:** Our results suggest that high prenatal caffeine intake may change the normal growth trajectory of the child and be related with the onset of obesity; outcomes that have been associated with poorer health later in life.

## C22

### Night-shift work and risk of diabetes in the Danish Nurse Cohort

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**Introduction:** Rotating night shift work disrupts circadian rhythms, and has been associated with obesity and metabolic syndrome, and possibly type 2 diabetes. This will be the first Danish study to investigate the association between night shift work and diabetes and if it is mediated through body weight.

**Aim:** To estimate the effect of night shift work on the risk of diabetes, and evaluate whether body mass index (BMI) may mediate this association.

**Methods:** We used the Danish Nurse cohort with 28,731 participating female nurses, recruited in 1993 (19,898) or 1999 (8,833), when self-reported baseline information on diabetes prevalence, lifestyle and night-shift work were collected. We will follow nurses in the Danish National Diabetes Register (NDR) from 1995 and in Central Person registry for date of death or emigration until 2013. We will model the association between night-shift work and diabetes incidence using Cox proportional hazards model with age as underlying time scale, in several steps: crude model (age adjusted), model adjusted for physical activity, smoking, alcohol use, diet, employment and marital status, and model additionally adjusted for BMI, to evaluate whether effect of night-shift work is mediated through BMI.

**Results:** Out of 28,731 nurses, we excluded 619 with prevalent diabetes (self-reported or detected in diabetes register since 1995), 192 that died before 1995 (start of follow-up in NDR), and 2,669 with missing data on covariates. Of 25,251 women in the final analyses, 1,249 developed diabetes (4.9%) during 15.1 years mean follow-up (incidence rate 3.3 per 1,000 person-years). Of 24,493 nurses with information on night work shift, 1,075 (4.4%) reported working night-shirt. Mean age at baseline was 54.6 years (44-95 years).

**Conclusion:** This study will present incidence of diabetes and reveal if night shift work influences the risk of diabetes, mediated by BMI. The results will be presented at NordicEpi.



## D1

### Saffold virus, a human cardiovirus, and persistent islet autoantibodies in a longitudinal birth cohort study

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**Introduction:** Type 1 diabetes is an autoimmune disease, believed to result from interactions between a susceptible genetic background and environmental factors. Several viruses are suspected to be involved in the development of type 1 diabetes, in particular picornaviruses. The epidemiology and associated symptoms of Saffold virus (SAFV), a human cardiovirus in the picornavirus family, are still not well described.

**Aims:** To describe the epidemiology of SAFV in longitudinal stool samples from children, and to test for potential temporal association with the development of persistent autoantibodies predictive of type 1 diabetes.

**Methods:** A cohort of individuals carrying the HLA genotype associated with highest risk of type 1 diabetes was followed with blood samples taken at 3, 6, 9, 12 months of age, and then annually. Stool samples were collected monthly from 3 to 35 months of age. Blood samples were tested for autoantibodies to insulin, glutamic acid decarboxylase<sub>65</sub> and IA-2, as markers of islet autoimmunity preceding type 1 diabetes. We analysed 2077 stool samples from 27 children with  $\geq 2$  repeatedly positive islet autoantibodies (cases), and 53 controls matched for birthdate, follow-up length, and county of residence. SAFV virus RNA was assayed with a semi-quantitative real-time reverse transcriptase PCR.

**Results:** In total, 53 of 2077 (2.6%) samples were positive for SAFV. Viral quantities ranged from less than one copy/ $\mu$ l to approximately  $10^5$  copies/ $\mu$ l, and sequencing demonstrated that SAFV genotype 2 and 3 were dominant. The frequency of SAFV positivity during follow-up prior to islet autoimmunity was not significantly higher in cases than in controls (odds ratio: 2.06, 95% CI: 0.59-7.20,  $p=0.26$ ). There was also no significant association with other common infection symptoms.

**Conclusions:** SAFV in stool samples is relatively rare. The observed frequency was approximately twofold higher in cases of islet autoimmunity and type 1 diabetes but the association was not significant.

## D2

### A registry-based long-term follow-up study of the quadrivalent HPV vaccine in the Nordic countries

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**Introduction:** FUTURE II (Protocol V501-015) was a 4-year, placebo-controlled, double-blind, randomized efficacy trial of the quadrivalent HPV (qHPV) vaccine on preventing low grade cervical, vulvar, and vaginal intraepithelial neoplasias and anogenital warts. 12,167 women between the ages of 16-23 from 13 European countries were in 2002/2003 enrolled in the study. The Long Term Follow-Up (LTFU)-study (Protocol V501-015-20) is an 10-14 years extension of FUTURE II to further investigate the safety, immunogenicity, and effectiveness of qHPV vaccine on the incidence of HPV-16/18/6/11 related cervical cancer and high grade cervical, vulvar, and vaginal intraepithelial neoplasias. 5,281 (96%) of the 5,493 participants from Norway, Sweden Denmark and Iceland consented to long term follow-up.

**Aims:** Presented here is the logistics and coordination of the LTFU-study in the Nordic countries.

**Methods:** Safety has been assessed by registry linkages including data of deaths, cancers and hospitalizations. Effectiveness follow-up have included registry based search for Pap tests, cervical, vaginal/vulvar biopsies or definitive therapy procedures, collecting tissue blocks from public health biobanks, HPV testing and adjudication of diagnoses through a Nordic Pathology Panel. Immunogenicity has been assessed by serological testing at Year 5, awaiting next round at Year 10. Migration patterns have also been captured.

**Results:** With 7-years of LTFU, we have successfully performed three rounds of safety and effectiveness and one round of immunogenicity follow-up. 2004 tissue blocks have been captured, including blocks from participants that have migrated within the Nordic countries.

**Conclusions:** We conclude that Long Term Follow-Up of the FUTURE II clinical trial is feasible by using population-based health registries and biobanks in the Nordic countries.

## D3

### Influenza infection in pregnancy and risk of fetal death: A Norwegian registry-based cohort 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 assess the association between influenza infection in pregnancy and fetal death. A secondary aim was to estimate the effects of influenza infection in the first trimester and the second or third trimester, respectively, on the risk of fetal death. Eight different influenza seasons in the period from 2006 through 2013 were to be considered.

**Methods:** The study sample comprised more than 400,000 singleton births in 2006–2013 with known gestational age, as registered in the Medical Birth Registry of Norway. Data on influenza infection were obtained from the Norwegian Directorate of Health (information based on health reimbursements from primary care physicians) and the Norwegian Surveillance System for Communicable Diseases. We fitted Cox proportional-hazards regression models with time-varying covariates to estimate the hazard ratio of fetal death for influenza infection in pregnancy, with adjustment for potential confounders.

**Results:** Preliminary results indicated a more than twofold increase in the risk of fetal death following influenza infection in the first trimester during the “swine flu” influenza pandemic in 2009/2010. Hazard ratios corresponding to the remaining influenza seasons under study were not statistically significant.

**Conclusions:** Pandemic influenza infection early in pregnancy seems to be associated with increased risk of fetal death, whereas we found little indication of any risk increase related to seasonal influenza infection.

**D4****The combined effect of obesity and physical activity on risk of hypertension: the Nord-Trøndelag Health Study, Norway****Jo S. Stenehjem**<sup>1,2,3</sup>, Kirsti L. Vik<sup>1,3</sup>, Tom I.L. Nilsen<sup>3</sup>

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**Introduction:** Hypertension is a leading risk factor for cardiovascular disease and cardiovascular mortality, and constitutes a major public-health challenge throughout most of the world. Body mass index (BMI) and blood pressure are positively related, whereas physical activity has been inversely related to blood pressure levels. However, the interplay between obesity and physical activity on the risk of hypertension has not been extensively studied.

**Aims:** To assess if BMI and physical activity are associated with the risk of hypertension, and to examine if physical activity may counteract the possibly increased risk of hypertension in obese persons.

**Methods:** We conducted a longitudinal study of 11,247 men and 15,295 women aged  $\geq 20$  years who participated in the Nord-Trøndelag Health Study (HUNT Study), Norway, first in 1984-86 and then in 1995-97. Poisson regression was used to estimate adjusted risk ratios (RRs) of hypertension ( $\geq 140/90$  mmHg) associated with physical exercise and BMI. We also conducted similar analysis on the risk of severe hypertension ( $\geq 160/100$  mmHg).

**Results:** During approximately 11 years, 4007 men (36%) and 4510 women (30%) developed hypertension. BMI was positively associated with risk of hypertension, whereas the independent effect of physical activity was less clear. The RR of hypertension among obese men who reported no exercise was 1.57 (95% confidence interval (CI), 1.21-2.04) compared to normal weight men with a high exercise level, whereas obese men who reported high exercise levels had a RR of 1.19 (95% CI, 0.70-2.01). Correspondingly, obese and inactive women had a RR of 1.39 (95% CI, 1.11-1.74), while obese and highly active women had a RR of 1.23 (95% CI, 0.93-1.67).

**Conclusions:** High levels of physical exercise may to some extent compensate for the unfavorable effect of obesity on risk of hypertension in both genders, although the increased risk was not fully cancelled out.

**D5****Longitudinal and secular trends in blood pressure among women and men in birth cohorts born between 1905 and 1977: The Tromsø Study 1979-2008**

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**Introduction:** High blood pressure is a modifiable risk factor for cardiovascular disease. Although blood pressure levels have decreased in recent decades, most pronounced in Western countries and in high-income groups, it is still the leading risk factor for global disease burden. Previous population studies of secular trends in blood pressure lack data to follow individuals born in different decades from early and middle adulthood to older age.

**Aims:** To investigate changes over three decades in age-specific systolic and diastolic blood pressure in women and men by repeated measurements from participants in a prospective study.

**Methods:** Blood pressure measurements were obtained from 37,974 women and men born 1905-1977 (20-89 years) examined up to five times between 1979 and 2008 in the population-based Tromsø Study. Mixed models were used to estimate time trends, stratified by sex.

**Results:** Mean systolic and diastolic blood pressure decreased from 1979 to 2008 in both genders in the age groups 30-89 years. The decrease in systolic blood pressure in age group 40-49 years was 10.6 mmHg in women and 4.5 mmHg in men. Systolic blood pressure increased with age in women born 1920-1959 and men born 1920-1949, whereas a decrease or flattening of curve was observed in the younger birth cohorts. The decrease was similar in the 80<sup>th</sup> percentile and the 20<sup>th</sup> percentile of the population blood pressure distribution.

**Conclusions:** A secular decrease in blood pressure from 1979 to 2008 was observed in all age groups. Systolic blood pressure increased with age in the older birth cohorts, whereas no change or decrease was observed in women born 1960-1977 and men born 1950-1977. Trends were more pronounced in women than in men. Similar falls in both ends of the blood pressure distribution points to a population effect rather than a treatment effect of high-risk individuals.

## D6

### The seventh Tromsø Study survey 2015-2016. Anything new? Short preliminary report

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**Introduction:** The Tromsø Study, initiated in 1974, is an epidemiologic, prospective study of health conditions and chronic diseases, and a resource for disease risk factor surveillance. Six surveys have been carried out 6-7 years apart, and the seventh survey started in March 2015 and will continue to the end of 2016. All surveys include questionnaires, biological sampling and clinical examinations and measurements.

**Aims:** The purpose of the seventh survey was to collect new and repeated exposure data from previous and new participants in the Tromsø Study, and to assess the levels of disease risk factors in the population for health-care planning and preventive health projects.

**Methods:** Tromsø 7 includes a main study that comprises two screening visits and follow-up studies. First visit: Questionnaires (paper and on-line). Extended pain questionnaire with body map, dietary questionnaire, measurements of height, weight, hip and waist circumference, heart rate, blood pressure, O<sub>2</sub>-saturation, pain sensitivity, and dental examination. Blood and faeces samples and nose and throat swab cultures are taken. Second visit: Sampling of biological specimens (blood, urine, nose/throat swab cultures) and accelerometry measurements of physical activity. Clinical examinations: 12-lead electrocardiography, cognitive tests, physical function test, visual acuity test, retinal photography and optical coherence tomography, carotid artery ultrasound, spirometry, lung auscultation, bone density measurements (DEXA) and echocardiography.

**Results:** Participants: All persons 40 years and older, and Tromsø study Youth cohort 22-25 years (1200 participants) will be invited (approximately 33 000 persons). We expect a 70% response rate (21 000 participants). Preliminary results on risk factors for cardiovascular disease will be presented.

**Conclusions:** The infrastructure of Tromsø 7 can be visualized as an “umbrella” covering more than 54 projects at the interface between clinical medicine and epidemiology. Tromsø 7 leads to regional, national and international scientific collaboration and contributes updated information on disease risk factors and public health.

**D7****Analysis and comparison of death rates from ischemic heart disease in the Nordic and Baltic countries during the period 1981-2009, in the age group 25-74 years****Elías F. Guðmundsson<sup>1</sup>**, Thor Aspelund<sup>1,2</sup>, Vilmundur Guðnason<sup>1,3</sup>

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**Introduction:** Ischemic heart disease remains one of the main causes of death in Western countries although rates have declined substantially during the last decades. This is largely attributed changes in lifestyle factors such as smoking and diet.

**Aim:** To investigate changes in ischemic death rates in the Nordic- and Baltic countries (NC,BC) during the period 1981-2009 in the age group 25-74 years, and to assess whether trends in these countries are comparable.

**Methods:** Numbers on ischemic deaths and populations by sex and age were obtained from the WHO-mortality database. Age standardized rates were calculated using the Joinpoint (JP) regression program and the European Standard Population 2013. JP compares trends and can determine time points (join points) when significant changes in rates may have occurred. JP calculates the Annual Percent Change (APC) within time periods, as defined by the program, along with the Average Annual Percent Change (AAPC) for the overall period.

**Results:** Ischemic death rates declined in every country, albeit at differing rates. All countries except Iceland had significant join points, first of which occur in 1985-1993 in NC but later in BC; or 1991-1995. The NC displayed similar trends both in terms of absolute values and rates of decline. The BC had higher rates during the whole period. In 1981 BC-men and women on average had 29% and 77% higher rates than NC-men and women, respectively. In 2009 the gap had widened and BC-men and women on average had four times the rates of NC. The average total decline during the period was 79% in NC-males and females compared to 29% and 51% in the BC, respectively.

**Conclusions:** Ischemic death rates have declined in the NC and BC. Observed and modelled trends are similar among the NC while the BC have higher absolute rates and slower rates of decline.

**D8****Transgenerational effects of parental cardiovascular disease and risk factors on offspring mortality: family-linkage data from the HUNT Study, Norway****Vik KL**<sup>1,2,3</sup>, Romundstad P<sup>2</sup>, Carslake D<sup>4</sup>, Davey Smith G<sup>4</sup>, Nilsen TI<sup>2</sup>

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**Introduction:** Cardiovascular disease risk factors are associated between parents and offspring. However, whether this association is reflected in increased offspring mortality has not been extensively studied.

**Aims:** To prospectively examine offspring mortality in relation to parental levels of body mass index, height, blood pressure, resting heart rate, blood glucose and blood lipids, as well as parental smoking, diabetes and cardiovascular disease and mortality.

**Methods:** This family study consists of 32,536 father-offspring and 39,614 mother-offspring pairs who participated in the HUNT Study, Norway. We used Cox regression to estimate adjusted hazard ratios for offspring mortality associated with parental levels of cardiovascular disease risk factors.

**Results:** Fathers' and mothers' reporting of cardiovascular disease (HRs: 1.18; 95% CI 1.04-1.32 and 1.20; 1.07-1.35, respectively), diabetes (HRs: 1.22; 95% CI 1.00-1.49 and 1.21; 1.05-1.40, respectively), and current smoking (HRs: 1.21; 95% CI 1.08-1.36 and 1.30; 1.15-1.47, respectively) was associated with mortality in offspring. An inverse association was found with maternal height (HR: 0.95; 95% CI 0.91-0.99).

**Conclusions:** Offspring mortality was positively associated with several parental cardiovascular disease risk factors, whereas an inverse association was found with maternal height. The results suggest that not only parental cardiovascular disease, but also other cardiovascular disease risk factors could be of importance for risk assessment and disease prevention.



**D9****Health atlas – mapping the acute myocardial infarction incidence in Denmark**

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**Introduction:** Coronary heart disease is a major cause of death in the Denmark with acute myocardial infarction (AMI) constituting a considerable proportion. AMI has severe consequences for the individual and society. The aim was to explore the geographical distribution of the incidence rate of AMI in Denmark. Accurate data on the population, disease and death enable the examination of spatial variation in AMI in Denmark using fine geographical resolution independently of administrative boundaries.

**Methods:** The study population consisted of 3,501,621 Danish residents ( $\geq 30$  years) of which 45,403 (2.7%) men and 28,634 (1.6%) women experienced an incident AMI in Denmark 2005-2011. Data on AMI, age, gender, addresses and geographical coordinates were obtained from national individual-level registers. The incidence rate (IR) for each geographical location (address) was estimated using a generalized linear model with a Poisson distribution, risk time as offset and adjusted for differences in age and gender. An interpolated map was derived by smoothing using inverse distance weighting of the estimated IR.

**Results:** The crude IR rate was estimated at 405 and 238 cases per 100,000 person-years for men and women, respectively. The adjusted IR was estimated at 275 cases per 100,000 person-years (95% CI = [267; 284]). The IR map showed geographical differences with the range of estimates [251; 597] for men and [46; 270] for women.

**Conclusion:** Better knowledge of the geographical variation of AMI may lead to more appropriate allocation of treatment resources and improve our understanding of the etiology of AMI. Further studies are suggested for understanding the reason for the different geographical variation.

## D10

### The influence of immunomodulatory treatment on the clinical course of multiple sclerosis

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**Introduction:** Although disease modifying drugs (DMDs) have proven efficacy in randomised controlled trials, it is still not definitively shown that they influence the long term outcome of multiple sclerosis (MS).

**Aims:** To investigate if DMD treatment affects the long term clinical progression of MS, measured as time to scores of 4 or higher of Expanded Disability Status Scale (EDSS).

**Methods:** Longitudinal, prospective data concerning treatment status and EDSS are collected in the Swedish MS Registry. This study cohort comprised newly diagnosed MS patients at the Karolinska University Hospital between 2001 and 2005. Cox regression was performed with the outcome variable time from the baseline EDSS at diagnosis to EDSS  $\geq 4$ .

**Results:** Patients were divided into two groups, those with early (205 patients that received the first treatment within 24 months from MS onset) or delayed treatment (299 patients that received treatment later). Univariate analysis showed a statistically significant difference for time to reach EDSS  $\geq 4$  between early and delayed treatment groups with those treated late doing worse (hazard ratio of 1.77 (95% CI: 1.15–2.73)). The difference remained statistically significant after adjusting for covariates (age at onset, the baseline EDSS and gender). However, further analysis revealed that the early and delayed treatment groups were very different at the mean of age at diagnosis (32.2 and 39.1 years respectively). When we chose to include age at diagnosis in the Cox proportional hazard model, significance was lost (95% CI for hazard ratio were 0.94–2.35). Interestingly, gender was not a significant covariate in either model while the baseline EDSS remained significant in both analyses.

**Conclusions:** Different approaches to analyze the clinical course of MS show the importance of chosen confounders. Thus, we cannot confirm the beneficiary effect of early treatment in spite of a follow-up time of at an average of 10 years.

## D11

### Use of folic acid and antidepressants during pregnancy and child language development

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**Introduction:** Folic acid supplementation has been suggested to improve neurodevelopment, while Selective Serotonin Reuptake Inhibitors (SSRIs) have been associated with delayed language development. The effect of concomitant use of folic acid and SSRI by pregnant women on child neurodevelopment is unknown.

**Aims:** To determine the effect of simultaneous use of folic acid supplements and SSRI medication by pregnant women on language development in their offspring at age three.

**Methods:** We conducted a cohort study of 45 266 women with 51 747 singleton pregnancies in the population-based Norwegian Mother and Child Cohort study (1999-2008). The association between different combinations of folic acid and SSRI use and language competence in the offspring was investigated using multinomial logistic regression (three outcome categories). Validated self-reported use of folic acid supplements and SSRIs was prospectively collected in subsequent four weeks intervals during pregnancy. Children's language competence was measured by a validated language grammar rating scale.

**Results:** Women reported use of folic acid in 44 417 (85.8%) and SSRI in 372 (0.7%) of the pregnancies, 260 used the two simultaneously. The relative risk ratio (RRR) of lower language competence increased with increasing duration of simultaneous use of folic acid and SSRIs, reaching adjusted RRR= 4.5 (95% CI, 2.5-8.0) and 5.7 (2.5-13.0) for the middle and the most delayed category, respectively, after simultaneous use in 4-8 intervals compared to mothers who used folic acid as recommended and no SSRIs and using the best language competence category as the reference. Using SSRIs, but not simultaneously with folic acid, gave no increased risk.

**Conclusions:** We detected a significant association between long term simultaneous use of folic acid and SSRIs during pregnancy and delayed language competence in the offspring. This surprising result may have a biological explanation, but warrants further studies.

## D12

### **Prenatal and infant paracetamol exposure and development of asthma: the Norwegian Mother and Child Cohort Study**

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**Introduction:** Whether the previously observed association between paracetamol exposure and asthma development is due to confounding by indication remains uncertain.

**Aims:** To examine the association of prenatal and infant paracetamol exposure with asthma development.

**Methods:** We used data from the Norwegian Mother and Child Cohort Study. A total of 53,169 children were included for evaluation of current asthma at 3 years, 25,394 for current asthma at 7 years, and 45,607 for dispensed asthma medications at 7 years in the Norwegian Prescription Database. The association of prenatal and infant paracetamol exposure with asthma development was estimated using log-binomial regression. Confounding by indication was assessed by stratifying paracetamol exposure by maternal respiratory tract infections/ influenza, fever and pain during pregnancy. Secondary analyses included maternal paracetamol use outside of pregnancy, maternal use of ibuprofen during pregnancy and paternal paracetamol use.

**Results:** Prenatal paracetamol exposure only was positively associated with asthma at 3 years (adjusted relative risk 1.21, 95% confidence interval 1.09 to 1.33), asthma at 7 years (1.30, 1.12 to 1.51) and dispensed asthma medications at 7 years (1.22, 1.09 to 1.37). Similarly, infant paracetamol exposure only was positively associated with asthma at 3 years (1.31, 1.17 to 1.46), asthma at 7 years (1.24, 1.04 to 1.49) and dispensed asthma medications at 7 years (1.28, 1.12 to 1.47). Prenatal paracetamol exposure for any of the three indications yielded similar associations with asthma development. The results for prenatal ibuprofen exposure were inconsistent. There was no strong evidence of an association with maternal paracetamol use outside of pregnancy or with paternal paracetamol use.

**Conclusions:** Prenatal and infant paracetamol exposure showed independent positive associations with asthma development. Despite addressing indications and timing of use in a large cohort, it remains difficult to rule out confounding by indication.

## D13

### **Risk of preeclampsia after use of antidepressants in pregnancy: a study from the Norwegian Mother and Child Cohort Study**

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**Introduction:** The risk of preeclampsia after gestational exposure to selective serotonin reuptake inhibitors (SSRIs) and other antidepressants is not determined. While two studies found an association between SSRIs and preeclampsia, two others observed an increased risk after use of serotonin-norepinephrine re-uptake inhibitors (SNRIs) and tricyclic (TCAs), but not SSRIs.

**Aims:** To explore whether use of SSRIs, SNRIs or TCAs may increase the risk of preeclampsia by separating the effect attributable to antidepressants from that of the underlying maternal depression.

**Methods:** The Norwegian Mother and Child Cohort Study and the Medical Birth Registry of Norway constituted the data source. Of the 81,911 pregnant women included, 847 (1.0%) reported use of antidepressants during pregnancy, mostly SSRIs. We categorized exposure according to type of antidepressant use in pregnancy (SSRIs=695, SNRIs=84, TCAs=43) with inclusion of a disease comparison group (non-exposed but depressive symptoms, n=1486). Generalized Estimating Equations analysis was used to determine adjusted relative risk (aRR) and 95% confidence interval (CI) for early preeclampsia (between gestational week 20 and 34). Marginal Structure Model accounting for time-varying exposure during pregnancy was also applied.

**Results:** Compared to non-exposed, women exposed to TCAs during the first trimester had a significant 11.6-fold increased risk to experience early preeclampsia, but not women exposed to SSRIs or SNRIs. Similar findings were observed for the second trimester exposure window. No increased risk for early preeclampsia was detected among non-exposed women with history of major depression and depressive symptoms during pregnancy.

**Conclusions:** Among this Norwegian cohort of pregnant women, use of TCA during pregnancy was associated with an increased risk of early preeclampsia, but not use of SSRIs or SNRIs, or not medicated depression, raising the question whether this association is secondary to drug effect or to unmeasured confounders.

## D14

### Long-term users of z-hypnotics – high level of co-medication with other addictive drugs

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**Introduction:** Z-hypnotics (zopiclone/zolpidem) are increasingly used for treatment of insomnia. Duration of treatment in clinical practice is often much longer than the approved 2-4 weeks.

**Aims:** To study long-term use of z-hypnotics in new users, and co-medication with benzodiazepines (BZD) and opioids.

**Methods:** Data on drugs dispensed to all adult outpatients in Norway (aged 18+) in the period 2007-2013 were obtained from the Norwegian Prescription Database.

Patients with no z-hypnotics dispensed during 730 days prior to the first recorded prescription in 2009 were defined as new users. They were followed over four 365 days periods (1<sup>st</sup> - 4<sup>th</sup> year) from the first prescription. The treatment intensity was measured in number of defined daily doses (DDDs). Co-medication was studied in long-term users (repeated prescriptions in all of the four years).

**Results:** In 2009 there were 92 911 new users of z-hypnotics. The incidence was 2.2% in men and 3.4% in women. 85% started with zopiclone and 15% with zolpidem. 55% of the new users had no refills during the 1<sup>st</sup> year. 13 996 (17%) of the new users became long-term users (15% for men, 18% for women). The proportion of long-term users was similar in new users of zopiclone and zolpidem and increased with age in both genders. Annual amount prescribed to long-term users increased from a median of 120 DDDs the 2<sup>nd</sup> year to 160 DDDs the 4<sup>th</sup> year of follow up. In each year of follow-up one third of the long-term users of z-hypnotics also used BZD and/or opioids.

**Conclusions:** Among new users of z-hypnotics, nearly 20% became long-term users, and the amount dispensed indicates regular use. BZD and opioids were also commonly prescribed to the long-term users. This indicates a not recommended use of z-hypnotics, both with regard to co-medication and duration of use.

## D15

### **Antidepressant drug use among adolescents during 2004-2013: A population-based linkage study between the nationwide prescription database and patient register**

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**Introduction:** Increasing antidepressant use in adolescents in USA, Canada, and some European countries is observed in the period following the black-box warning in younger people in 2004-2005.

**Aims:** To study trends in antidepressant use among 13-17 year old Norwegians; and incidence of use, and characterize incident users in 2012 according to antidepressant drug of choice, co-medication with other psychotropic drugs, and psychiatric morbidity.

**Methods:** Prescription data on antidepressants and psychotropic co-medication were obtained from the Norwegian Prescription Database (2004-2013, and linked to data from the Norwegian Patient Register (NPR) (2008-2012). Psychiatric morbidity was evaluated in incident users of antidepressants in 2012, according to recorded registrations in the NPR of either ICD-10 codes of mental or behavioral disorders (F00-99) or a recorded visit to the child- and adolescent psychiatry sector.

**Results:** Antidepressant use increased in the period; from 4.4 to 5.9 per 1000 in boys and 8.5 to 12.4 per 1000 in girls. Prevalence of antidepressant use increased with age and over time in both genders, most pronounced in 16-17 year old girls from 2009 and onwards. In 2013 10.4 and 27.5 per 1000 of all 17-year old boys and girls had an antidepressants dispensed. Parallel trends of incidence of use were observed. For the incident users in 2012: 78.4% started on an SSRI; most commonly fluoxetine (33.1%), sertraline (27.5%) or escitalopram (16.0%). Co-medication: the most common hypnotic dispensed was melatonin (24.6%). Antipsychotics, stimulants and anxiolytics were dispensed in 13.2, 8.8 and 6%. Overall, 78.7% of the incident users in 2012 had registrations for psychiatric morbidity in the NPR.

**Conclusions:** Antidepressant use has increased, in 16-17 year old girls in particular, from 2009 and onwards. Antidepressants licensed for use in young people (fluoxetine, sertraline) were most commonly used. Four out of five new antidepressants users had registrations for psychiatric morbidity.

**D16****Use of anti-osteoporotic drugs among women in central Norway after a forearm fracture**

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**Introduction:** Forearm fractures are associated with low bone mineral density and increased risk for subsequent fractures. A forearm fracture should thus lead to evaluation for osteoporosis and treatment with anti-osteoporotic drugs (AOD).

**Aims:** Examine time-trends in the prevalence and incidence of treatment with AOD among women the first year after a forearm fracture from 2005-2012.

**Methods:** Data were retrieved from the fracture registry in Nord-Trøndelag and the Norwegian Prescription database (NorPD). Women  $\geq 40$  years with their first forearm fracture between 01.01.2005-31.12.2012 were included. Fracture data were collected from medical records and the X-ray registry. The diagnostic codes (ICD10) included were S52.X and the surgical procedure codes (NCSP) were: NCJ00-99; NCU39+49; TNC31-33 and 39. Data regarding AOD were from the NorPD. AOD were defined as: Bisphosphonates, teriparatide, denosumab and raloxifene. Prevalence and incidence for AOD were stratified for fracture year. The prevalence of AOD use among patients was compared with the prevalence in the population in Nord-Trøndelag. Age-adjusted Poisson regression analyses were performed for time trends 2005-2012.

**Results:** 1434 women (mean age 63.7 years) were included. The first year after the fracture, only 160 (11.2%) fracture patients used AOD and 68 (5.1%) were incident users. Bisphosphonates comprised 98.8% of the AOD use. AOD use among women with forearm fractures were significantly higher compared to the general population in Nord-Trøndelag only in 2006 (17.0%, CI: 11.9-23.5 vs 4.9%, CI: 4.9-4.9), 2007 (10.4% CI: 6.6-15.9 vs 4.9% CI: 4.9-4.9) and 2011 (8.6% CI: 5.2-13.4 vs 4.9% CI: 4.9-4.9). There was a trend towards a decline in AOD use among women with fracture from 2005-2012, but not significant (-0.05,  $p=0.15$ ).

**Conclusions:** The use of AOD after a forearm fracture was low. An increased focus on osteoporosis in doctors and the society are needed.



## D17

### Promoting reuse of research data – The Scania Metadatabase for Epidemiology

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**Introduction:** Extensive and successful research has during the last decades been conducted in Scania. Several of these projects have generated data sets based on surveys or clinical information. Parts of this valuable resource could be used by external researchers to create new studies based on the research materials.

**Aim:** To invent and produce a catalog with epidemiological studies that have been collected within Lund University and Region Skåne.

**Methods:** The study inventory has been conducted in close cooperation with the Swedish National Data Service (SND). Initially, the studies on SND's webpage was checked for studies that were eligible to be included in the metadatabase. By labelling with searchable keywords (EpiHealth, EpiHealth\_Skåne) existing studies were coupled to the Scania Metadatabase for Epidemiology (SME). The next step identified further studies in collaboration with scientists in the region. If the primary researcher gave their approval metadata was registered in SND's web form. Information that is documented include e.g. title, purpose and a general description of the study. The names of the primary researchers are listed, with e-mail information for the contact person.

**Results:** SME was initiated in the fall of 2012 and it currently comprises information about 50 studies, including a total of just over 680,000 study participants as well as biological samples from more than 217,000 individuals. The majority of the studies are population-based studies (n=28) that cover several different areas, e.g. the older generation's health, the relationship between diet and subsequent cancer risk or cardiometabolic diseases. Fifteen of the studies are patient-based and they focus on including patients with among other diseases diabetes or various forms of cancer.

**Conclusion:** We expect that the metadatabase will be used as a source of inspiration for new research and open up new research partnerships by visualizing the research groups and their publications.

## D18

### Obstetric health system structure and perinatal outcomes in Norway

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**Introduction:** How the health systems architecture relates to performance remains a key issue in health systems research. In Norway centralization of obstetric care, particularly emergency obstetric and newborn care, has taken place during the last decades.

**Aims:** To assess the influence of centralization on institution accessibility and neonatal outcomes.

**Methods:** The Medical Birth Registry of Norway and census data from Statistics Norway were linked to obtain a population-based, retrospective cohort of singleton births at gestational age  $\geq 22$  weeks or birth weight  $\geq 500$ g (n=624 074) 1999-2009. Primary outcomes were unplanned delivery outside institution, perinatal death during delivery and up to 28 days, and 5 minute Apgar-score  $< 7$ . Main exposures were annual volume of the obstetric institution and estimated travel time from the mother's census address to the nearest institution. GIS software was used for travel time estimates and the statistical analyses were logistic regression and multilevel analyses adjusting for clustering.

**Results:** Longer travel time was associated with higher risk of unplanned delivery outside institution and these births had 0.5% risk of perinatal death (21/4327). The perinatal death rate was 2.3 per 1000 births (1413/620 074) with a range from 0.1 to 0.3% for delivery in obstetric institutions. Rural basic obstetric care institutions  $< 50$  annual deliveries had a higher risk of perinatal mortality at 37 to 40 weeks gestation (7/1574, adjusted OR 3.6, 95%CI 1.6 to 8.2), there were no differences between the other volume categories when compared to the largest institutions ( $> 3000$  deliveries annually).

**Conclusions:** The perinatal mortality was highest for unplanned delivery outside institution. A higher risk at term in the small rural institutions reflected the lack of emergency interventions and transport delay for acute fetal distress. Our study indicated that further centralization needs careful consideration to avoid an increasing inequality in access to obstetric institutions.

## D19

### Implementing a Nordic Common Data Model for register-based pharmacoepidemiological research

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**Introduction:** Pharmacoepidemiological studies are increasingly performed using a multi-database approach to provide sufficient power to investigate rare adverse events and infrequent exposures. Studying drug effects in populations with different exposure and morbidity patterns also add to the validity of results. Multi-database studies are resource demanding and logistically challenging.

**Aims:** To implement a Nordic Common Data Model (NDM) for use in the CARING (CAncer Risk and INsulin analogues) project.

**Methods:** We used national health registers of drug dispensing, hospital admissions, outpatient clinic contacts, cancer, causes of death and available information on migration and socio-economic factors (education and income) from Denmark (DK), Finland (FI), Norway (NO) and Sweden (SE). Essential variables were mapped to a common relational database structure. Databases for DK, NO and SE were placed on a server at Statistics Denmark (DST) providing secure access, while data from FI were kept separately but could potentially be added. Modular programs for import, validation, creation of analysis datasets and statistical analyses were created in SAS version 9.4.

**Results:** The common database at DST includes 1 million individuals exposed to antidiabetic drugs (DK 310887, NO 197724, SE 513734) and additional unexposed control populations. The database structure is presented. New user cohorts were established for analyses relating anti-diabetic exposure to pre-specified cancer outcomes. We describe the cohorts and present two main approaches for analysis: ‘mega-analysis’ of a common individual-based dataset and separate country-specific analyses followed by aggregate meta-analysis. It is possible to include data from FI in a distributed analysis. Pros and cons of different approaches are described.

**Conclusions:** It was shown to be feasible to map the Nordic health registers to a common data model. The NDM is flexible and extendable, providing the possibility to add other types of events, clinical data and laboratory measurements.

## D20

### Visualizing a research infrastructure giving access to Nordic health data

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**Introduction:** The Nordic data archives are engaged in a project supported by NordForsk to create a prototype of a portal giving access to Nordic health data. The actors are all important parts of the national research infrastructure for health and social sciences in their respective countries and are national Service Providers in the pan-European research infrastructure CESSDA.

**Aim:** To support CESSDA's goal of providing access to data across repositories, nations, languages and research purposes with special emphasis on metadata by development of a common, searchable web portal for all Nordic health research data.

**Method:** The Nordic countries have a tradition of collecting personal data about health and illnesses of their populations in a systematic way using a personal ID number as a key. The data are collected to ensure the best prevention and treatment of illnesses. This way of collecting and organizing data gives new and unforeseen opportunities but also difficulties for the societies. For future benefits it requires an access policy that will result in scientific advantages and provide greater returns from public investments in research activities. Effective access to scientific databases is also a crucial part of the infrastructures brought forward in the European Strategy Forum on Research Infrastructures (ESFRI) Roadmap Reports.

**Results:** Data portal was developed and will be presented. The project will demonstrate the possibility to access data in a trustworthy and efficient manner. This requires taking full advantage of the data and the possibilities offered by new digital technologies and networks. The starting point is the 1.300 scientific studies and databases from health science documented by the four Service Providers in DDI (Data Documentation Initiative).

**Conclusions:** At NordicEpi2015 the project will present a vision of a data portal to get access to Nordic health metadata and data and hope to receive feedback of the vision and engage in dialog with the participants of the conference.

## D21

### The eRegistry for maternal and child health: Legal and ethical guidance for low and middle income countries

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**Introduction:** The Nordic registry tradition and information technology have been described as a goldmine for research opportunities and the new ‘oil.’ Adapting this Nordic approach, the *eRegistry for maternal and child health* is designed to facilitate data collection and use with the intention of improving maternal and child health data, increasing data utilization, and reducing mortality in low and middle income countries.

**Aim:** The aim of this study is to assess the ethical and legal challenges for maternal and child health registries in low and middle income countries in order to identify appropriate governance guidance to facilitate a robust legal framework. Given the highly sensitive nature of reproductive health information, attention to ethical and legal considerations is essential, particularly in countries lacking adequate privacy and security safeguards.

**Methods:** This research investigates the current legal environment in Countdown 2015 countries (i.e., 75 countries with the highest maternal mortality) by utilizing several methodological approaches. An overview of data privacy laws is summarized and supplemented by findings from an internet-based, multi-country survey and a systematic literature review of legal and security measures for health registry data. *The eRegistry Governance Guidance Toolkit*, a document developed to describe best practices for governance, is discussed with respect to these findings.

**Results:** An overview of the literature indicates that the majority of Countdown countries currently lack data privacy legislation. The survey results suggest that many Countdown countries do not have basic privacy protection and data security measures in place. The systematic review reveals that although ethical review clearance has been institutionalized for research endeavors, security and privacy measures are not routinely reported in the literature.

**Conclusions:** To ensure women and children’s privacy in low and middle income countries, maternal and child health registries must provide governance that protects privacy and ensures data security for personal health information.

**D22****National trends in main causes of hospitalisation in working-age population, Finland, 1976 to 2010**

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**Introduction:** The health transition theory argues that societal changes produce proportional changes in causes of disability and death. However, research on long-term national trends in hospitalisation for main diagnostic categories is rare.

**Aims:** The aim of this study was to identify long-term changes in main causes of hospitalisation in working-age adults in Finland, a nation that has experienced considerable and rapid societal change over the last four decades.

**Methods:** National trends in hospital discharges for the five main diagnostic categories were investigated in the data obtained from the Finnish Hospital Discharge Register. Socio-demographic data were obtained from a population database maintained by Statistics Finland. The dates of death, where applicable, were extracted from the National Death Register kept by Statistics Finland. The seven-cohort sample covered the period from 1976 to 2010 and consisted of 3,769,356 randomly selected Finnish residents, each cohort representing a 25% sample of population aged 18 to 64 years. Age-standardised incidence rates for the five main diagnostic categories of hospitalisation were calculated separately for women and men and for different occupational classes. Time-trends were investigated using Cox regression models.

**Results:** Over the period of 35 years, the risk of hospitalisation for cardiovascular diseases and respiratory diseases decreased. Hospitalisation for musculoskeletal diseases increased whereas hospitalisations for mental and behavioural disorders slightly decreased. The risk of cancer hospitalisation decreased marginally in men, whereas in women there was a constant upward trend. Hospitalisations for cardiovascular disease decreased in all occupational classes. The largest increase in hospitalisation for musculoskeletal disorders was observed in manual workers, especially in women.

**Conclusions:** Health transition related to hospitalisations of the Finnish working-age population and a shift in the utilisation of inpatient services took place between 1976 and 2010.

**P1****Prostate cancer incidence and mortality trends in four Nordic countries 1975-2012 in men aged under and over 80 years****Kvåle R<sup>1,2,3</sup>**, Johansen TB<sup>1</sup>, Ellingsen CL<sup>2</sup>, Møller B<sup>1</sup>

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**Introduction:** Early detection efforts and treatment interventions for prostate cancer are most frequent in men aged below 80 years. Thus, analyzing prostate cancer incidence and mortality trends by age may provide results for enhanced interpretation of the trends.

**Aims:** To compare prostate cancer incidence and mortality trends between four Nordic countries in patients aged under and over 80 years.

**Methods:** Prostate cancer incidence and mortality data for the period 1975–2012 in Norway, Sweden, Denmark and Finland were obtained from the NORDCAN database comprising data from the national population-based cancer registries. Age-adjusted incidence and mortality rates were assessed for patients aged 40-79 and 80 or older. Joinpoint regression models were fitted to the age-adjusted incidence- and mortality rates to identify linear changes in the trends.

**Results:** The incidence rates in men aged under 80 increased significantly in all four countries from the early (Norway, Sweden and Finland) to mid-1990s (Denmark). In contrast, decreases in mortality have been observed from the mid-1990s. The total reduction in mortality in men aged below 80 ranged from approximately 40% in Norway to 20% in Denmark. Rapid increases in incidence were observed in the oldest age group from around 1990 in Finland and Norway, and from 1995 in Denmark. Similar increases followed by stabilizations were observed in mortality from the early and mid-1990s in Norway and Sweden, respectively. In Finland, a decrease in mortality in the oldest age-group has been observed from the mid-1990s, whereas mortality was still increasing in Denmark.

**Conclusions:** The notable decrease in mortality in the youngest age group is consistent with improved treatment of prostate cancer patients. Compared to the other countries, a later increase in incidence and a less prominent mortality reduction was observed in Denmark, suggesting a potential contributory effect of PSA-testing followed by early treatment.

## P2

### **Survival of patients with colon cancer before and after implementation of the National project “Health” in the Arkhangelsk Region, Northwest Russia: a registry-based study**

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**Introduction:** Colon cancer is one of the most common cancers worldwide. The incidence of colon cancer in the North of Russia is above the national average and is steadily increasing. The national project “Health” was initiated in 2007 to improve primary health care directed at both earlier detection and better treatment of various medical conditions including cancers and could therefore increase the proportion of detection of colon cancer at early stages in Russia and thus decrease mortality.

**Aims:** To study whether survival of colon cancer patients improved in Russia after initiation of the National project “Health”.

**Methods:** Data on all cases of colon cancer (ICD 10 code: C18) were obtained from the Arkhangelsk Regional Cancer Registry for the period 2000-2011. One- and five-year observed survival was calculated using life-tables. The difference in survival before and after initiation of the National project “Health” was studied using Cox regression with adjustment for stage at diagnosis, patient’s age, gender and place of residence.

**Results:** Altogether, there were 3049 cases of and 1944 deaths from on cancer in 2000-2011. One- and five-year survival increased from 51.3% and 28.1% in 2000-2006 to 52.5% and 30.6% in 2007-2011, respectively. Unadjusted analysis showed a significant increase in the overall survival after initiation of the project (Crude HR=0.89, 95% CI: 0.81-0.97). After adjustment for sex, age, and stage the estimates changed only marginally (Adjusted HR=0.88, 95% CI: 0.80-0.96). In the multivariable Cox model, time period remained the only parameter associated with survival.

**Conclusions:** Better survival of patients with colon cancer after the start of the National project “Health” in the Arkhangelsk region was observed. This improvement is however small and unlikely to be attributed to detection of colon cancer at earlier stages.



## P3

### The association between risk factors and breast cancer subtypes in a cohort from the Norwegian Breast Cancer Screening Program

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**Introduction:** Significant advances have been made in characterizing distinct subtypes of breast cancer based on gene expression profiles. These biomarkers have both a prognostic and predictive significance in breast cancer and are important for tumor growth and metastatic patterns.

**Aims:** The purpose of the present study was to estimate the relative risk for subtypes of breast cancer according to estrogen receptor (ER) and progesterone receptor (PR) status associated with known breast cancer risk factors.

**Methods:** We followed women from 2006 to 2012 who participated in the Norwegian Breast Cancer Screening Program. After exclusions, 302 025 women were left for analyses, of these 3276 had invasive breast cancer. Information on risk factors was collected from standardized risk factor questionnaires that women had answered when they attended the screening. We used Cox proportional hazard regression to measure the hazard ratios (HR) with 95% confidence intervals (CI) for breast cancer cases overall, adjusted for age, body mass index (BMI), education and parity. Logistic regression was used in the breast cancer subtypes analyses, adjusting for age.

**Results:** Women with the highest BMI (>28) had an increased risk of ER+PR+ breast cancer (HR=1.76, 95% CI 1.09-2.82) compared to women with BMI ≤22 (p for trend=0.009). Current estrogen and progesterone therapy (EPT) users had an increased risk of ER+PR+ breast cancer (HR=3.44, 95% CI 1.54-7.72) compared to estrogen therapy only users. Women with a duration of hormone therapy use for more than 10 years, had an elevated risk for ER+PR+ breast cancer (HR=2.91, 95% CI 1.29-6.58) compared to those women with a duration of ≤2 years (p for trend=0.01).

**Conclusions:** Compared with breast cancer overall, the associations between BMI, EPT and duration of postmenopausal therapy were stronger for ER+/PR+ breast cancer.

**P4****Integrating research activities in the Janus Serum Bank and Cancer Registry of Norway****Hilde Langseth and Randi Gislefoss**

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**Introduction:** In recent years there has been an increased interest in utilizing biorepositories in cancer research. The Janus Serum Bank was established in 1973 as a prospective cancer biobank and has since 2004 been fully integrated within the Cancer Registry of Norway. The Janus cohort consist of serum samples from 318 628 individuals. The collection is ideal for studies of biomarkers relevant for aetiology, early diagnosis and prognosis, since samples were collected pre-diagnostically with different span in time before the cancer disease was diagnosed.

**Aims:** The aim of the present communication is to describe the research potential in combining information from a high quality cancer registry with analytical information from a population-based biobank.

**Methods:** All research projects are based on a linkage between the Janus cohort and the Cancer Registry, to identify the most optimal study subjects. The majority of the studies are using a nested case-control design. The cohort is annually linked to the Cancer Registry for update with new cancer cases.

**Results:** The total number of incident cancer cases in the Janus cohort is 69745. In male donors prostate cancer is the most common cancer (n=11139), followed by cancer of the lung (n=4298), colon (n=3030), bladder (n=2595) and malignant melanoma (n=2161). Breast cancer is the most common cancer in female donors (n=8360) followed by genital organs (cervix uteri, corpus uteri and ovaries combined (n=5018), colon (n=2423), lung (n=2412) and malignant melanoma (n=1791). Common aims in Janus studies have been to investigate the association between cancer and infections, environmental and lifestyle exposures as well as biomarkers for early detection of cancer. More recently the samples are used in omics-based research.

**Conclusions:** The Janus Serum Bank has a large research potential given its size, long follow-up time with a large number of subsequent cancer cases.

## P5

### Cancer incidence among the descendants of the exposed fathers

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**Introduction:** The problem of genetic effects of chronic radiation exposure remains insufficiently studied, especially among the descendants of nuclear workers.

**Aims:** Conduction of epidemiological analysis of the effects of preconceptive exposure of fathers by cancer incidence rate among first generation descendants.

**Methods:** A group of individuals from Ozyorsk “Children’s Register” was formed for the cohort study. It comprised 15305 individuals born from 1949 to 1988 whose fathers had measured doses of occupational radiation exposure at Mayak PA by the time of conception. Mean preconceptive external gamma dose was 29.2 cSv. The control group comprised 28415 individuals whose parents had no occupational contact with ionizing radiation sources before conception. Cancer cases were selected from Cancer Register.

**Results:** 186 cancers were diagnosed in the studied cohort in the period 1949-2013. 358 – were diagnosed in the control. The incidence rate in the studied cohort was 38.1 cases per  $10^5$  person-years of follow-up, and in the control – 47.6. Solid tumors prevailed in the incidence structure in both groups. Leukemia incidence in the studied cohort did not exceed incidence among population. No difference between the studied cohort and control in hemolymphoblastosis incidence was found, but the increase in the incidence rate was shown in men (12.1 cases per  $10^5$  person-years) in the studied cohort compared to women (4.8). The significant increase of cancer incidence rate was found in the group of descendants whose fathers had total preconceptive dose over 100.0 cSv or the dose received for 1 year before conception over 10.0 cSv.

**Conclusions:** The present study does not give ground yet to speak about the role of radiation factor in the increase of cancer in the cohort of the descendants of the exposed fathers. In the future the effect of non-radiation factors is planned to be studied.

**P6****Regional variation in cancer survival and the impact of stage, socioeconomic status, comorbidity and treatment**

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**Introduction:** Universal health systems aim to provide equal health care to all citizens, irrespective of socioeconomic status and place of residence.

**Aims:** It is known that cancer survival varies dependent on patient's place of residence, but if it can be caused by the patient case-mix with respect to the prognostic factors stage, socioeconomic status (SES), comorbidity or treatment, is yet to investigate.

**Methods:** National population-based data from the Cancer Registry of Norway were used to identify 258 675 patients diagnosed with cancer from 2002-2011. The six most common cancer sites as well as all sites combined were investigated. The effect of adjusting for prognostic factors on regional variation was investigated, by calculating the mean absolute deviation of the relative excess risks (RER) for all health services regions.

**Results:** All the prognostic factors were highly associated with both survival and region. Statistically significant regional variations of RER of death were found for three out of six cancer sites and for all sites combined in a model controlling for age and sex. For prostate cancer the mean absolute deviation of RER for the regions was 3.3 when adjusting for age and sex, it was 1.3 when adjusting for stage in addition and remained almost unchanged when adjusting for the other factors.

**Conclusions:** Stage, SES, comorbidity and proportion who received treatment differed across the health service regions. Adjustment for stage explained most of the regional differences observed in survival for prostate cancer, and minor for the other sites. The effect of adjustment for SES, comorbidity and treatment was small. Thus, there still exist unexplained variations between the regions which may be due to inequality of care delivered by the health services.

**P7****Interactive omics data exploration in epidemiological studies**

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**Introduction:** Interactive data exploration is the process of exploring datasets looking for relationships and patterns in the data. In scientific disciplines such as epidemiology, data exploration enables an agnostic analysis approach that may be used to find hypotheses and insights not envisioned when the study was designed. Such exploratory analyses require systems that provide ad-hoc interactive visualizations and statistical analyses of large-scale omics datasets.

**Aims:** To investigate the need for an interactive omics data exploration system within systems epidemiology and conduct a requirement analysis for said systems.

**Methods:** We used the Norwegian Women and Cancer (NOWAC) cohort to investigate and develop a requirement analysis for omics data exploration systems for epidemiological cohorts. We used the requirement analysis to develop Kvik, a framework for developing omics data exploration applications.

**Results:** Interactive data exploration is useful in epidemiological studies, and is required for an agnostic omics approach. In the NOWAC study we found that a system for interactive exploration of epidemiological cohorts requires i) familiar interfaces and visual representations ii) lightweight applications making it possible to explore omics data on commodity computers iii) powerful statistics support for advanced analyses iv) interfaces to online knowledgebases. With Kvik we developed multiple applications for exploring omics data from both cross-sectional and nested case-control study designs. Our experiences using interactive applications for exploring epidemiological data proved superior to traditional workflows.

**Conclusions:** Exploring omics data from epidemiological studies requires inter- active visual exploration systems that incorporate statistical analyses, interactive visualizations and interfaces to online knowledge bases. Using Kvik our collaborators have successfully explored omics data from different study designs. Although we have used the NOWAC cohort, the requirement analysis and Kvik is generalizable to data exploration systems for data from other epidemiological cohorts. Kvik is open-sourced at [github.com/fjukstad/kvik](https://github.com/fjukstad/kvik).

**P8****Trends in breast cancer incidence and mortality by education level in Norway, 1971-2009****Cassie Trewin**<sup>1,2</sup>, Giske Ursin<sup>3</sup>, Harald Weedon-Fekjær<sup>4</sup>, Bjørn Heine Strand<sup>5</sup>

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**Introduction:** Higher educated women traditionally have higher breast cancer incidence and mortality rates. However, several countries have reported a narrowing or reversing education gradient in recent decades.

**Aims:** To describe trends in educational inequalities in breast cancer incidence and mortality over four decades in Norway.

**Methods:** Using population and health registry data, we followed all female inhabitants of Norway aged 35 years and over during 1971-2009. Education level was categorised as low (compulsory), middle (basic upper secondary) and high (final upper secondary and tertiary). Using Poisson models, we quantified absolute and relative risk of breast cancer incidence and mortality by education level over eight time periods in the age groups 35-49 years, 50-69 years and 70 years and over.

**Results:** Throughout 1971-2009, we observed significantly higher breast cancer incidence and a tendency for higher breast cancer mortality in middle and high education groups compared to low education group. Absolute and relative educational inequalities in breast cancer incidence narrowed over time among women under 70 years, but widened in the final decade in older women. We found no clear changes over time for educational inequalities in breast cancer mortality. In the final period (2005-09), relative risk of breast cancer incidence among high versus low educated women aged 35-49, 50-69 and 70 years and over was 1.13 (95% confidence interval: 1.02-1.24), 1.21 (1.14-1.29) and 1.44 (1.30-1.58), respectively. The respective relative risks for breast cancer mortality were 0.92 (0.67-1.16), 1.06 (0.90-1.22) and 1.15 (0.99-1.31).

**Conclusions:** Incidence inequalities have narrowed over time in women under 70 years, although differences between education groups remain significant. Mortality inequalities have not changed much over time.

**P9****Cancer prevalence and incidence in the Nord-Trøndelag Health Study**

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**Introduction:** The Nord-Trøndelag Health Study (HUNT) is a large longitudinal population based health study repeated in three cross-sectional surveys; HUNT1 in 1984-1986, n= 77,205, HUNT2 in 1995-1997, n=65,232 and HUNT3 in 2006-2008, n=50,805. Total cancer cases in the HUNT cohorts are currently not known.

**Aims:** To examine the prevalence and incidence of cancer in the HUNT Study.

**Methods:** The entire HUNT1-3 adult cohort (n=106,435) was linked to the Cancer Registry of Norway for the twenty most common cancer diagnoses for the time period 1 January 1984 to 31 December 2012.

**Results:** Overall 13,173 (7,066 men and 6,107 women) HUNT subjects (12.4%) reported in total 14,394 cancer diagnoses. 1,115 subjects reported two primary cancer diagnoses, 93 three, 11 four and 2 subjects had five cancers. The ten most common cancer types were; colorectal (n=2,373), prostate (n=2,368), breast (n=1,760), lung (n=1,298) ureter/bladder (n=757), melanoma (n=679), lymphoma (n=518), pancreas (n=458), leukemia (n=458) and uterus (n=400). The cumulative incidence measured as first cancer diagnosis after HUNT cross-sectional visit were for HUNT1 cohort 15.4% (95%CI; 15.2-15.7%) and 11,861 new cases, HUNT2 cohort 10.3% (95%CI; 10.1-10.6%) and 6,590 new cases, and HUNT3 cohort 3.8% (95%CI; 3.6-4.0%) and 1,837 new cases. In HUNT2 6,590 subjects reported 7,387 cancers during the average 16.5 years follow-up period after HUNT2. The four most frequent cancers were; colorectal (n=1,404), prostate (n=1,389), breast (n=980) and lung (n=772). In HUNT3 1,837 subjects reported 2,098 diagnoses in the average 5.3 years follow-up period after HUNT3 visit. The four most frequent cancers were; prostate (n=413), colorectal (n=376), breast (n=284) and lung (n=209). The cancer prevalence in HUNT2 was 2.4% (n=1,588) and in HUNT3 4.5% (n=2,278).

**Conclusions:** The HUNT cohort and the associated phenotypic information and biobanked samples represent a unique tool for the study of cancer etiology, risk factors and outcomes.

**P10****Balancing the benefits and harms among women targeted by the Norwegian Breast Cancer Screening Program****Marta Román<sup>1,2</sup>**, Sofie Sebuødegård<sup>1</sup>, Ragnhild S. Falk<sup>3</sup>, Solveig Hofvind<sup>1,4</sup>

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**Introduction:** The balance between benefits and harms of mammographic screening is debated. There is considerable evidence that organized screening programs reduce breast cancer mortality, but the extent of mortality reduction and over-diagnosis is inconclusive. Although there are published results on mortality and over-diagnosis, there is no balance sheet weighting the benefits and harms of the Norwegian Breast Cancer Screening Program (NBCSP) of today.

**Aims:** To estimate a balance sheet of benefits and harms for the NBCSP.

**Methods:** Data from published studies using individual level data from the NBCSP were used to assess the reduction in breast cancer mortality versus over-diagnosis. The program invites all Norwegian women aged 50-69 years to biennial mammographic screening. The mortality reduction in the studies varied from 36.8% to 43.0% among screened women, with an average estimate of 39.9%. Estimates of over-diagnosis ranged from 1.8% to 19.6%, with an estimated average of 10.7%. The cumulative risk of a false positive result was 15.9% for additional imaging and 4.1% for an invasive assessment. The benefit-detriment ratio was computed for different scenarios of mortality reduction and over-diagnosis.

**Results:** For every 10,000 women screened according to the invitations and followed until age 79 we estimated that 54-63 women are saved from breast cancer death, 11-126 are over-diagnosed, 1590 have a false positive result with non-invasive assessment and 410 have a false positive result with invasive procedures. The benefit-harm ratio between mortality reduction and over-diagnosis was 0.4, 0.8, and 5.7 under the less favorable, average and most favorable estimates, respectively.

**Conclusions:** Using average estimates showed that about one woman is saved from breast cancer death for each woman over-diagnosed. The ratio estimates varied substantially and should be interpreted with care before it is communicated to women targeted by the screening program.



## P11

### Does it help to worry? The prospective association between health anxiety and cancer detection

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**Introduction:** Health anxiety characterized by a persistent preoccupation of having or being in the process of developing a serious medical condition or disease, usually followed by intense worries, high attention to bodily signs and symptoms, and excessive health care use. Cancer is frequently a specific object in health anxiety. Individuals who have experienced cancer have increased risk for developing health anxiety, but it is not known whether individuals with health anxiety have increased risk for experiencing cancer. It is further not known whether health anxiety may contribute to cancer being detected earlier.

**Aims:** The aim of this study was to examine a potential prospective association between high levels of health anxiety and cancer detection and metastasis among men and women from the general population.

**Methods:** Data on health anxiety levels among male and female participants in the Hordaland Health Study (HUSK) was linked with data on cancer diagnosis and metastasis from the Norwegian Cancer Registry, giving a follow-up ranging from 6 months to 13 years. The analyses were stratified by gender and adjusted for relevant potential confounders.

**Results:** We found no association between baseline health anxiety and cancer detection among women (adjusted HR: 1.21, 95% CI 0.42-3.50), but a positive association was identified among men (adjusted HR: 1.76, 95% CI 1.06-2.91). No statistically significant association was demonstrated between health anxiety and cancer metastasis for either gender, but low numbers may have precluded this analysis.

**Conclusions:** The association between health anxiety and cancer diagnosis identified among men is probably unlikely to be the result of true causal association. Rather, a certain level of health anxiety among men may be advantageous, as it may motivate to self-examination of symptoms, and health care seeking if concerning symptoms are discovered. However, health anxiety may also contribute to over-diagnosis and over-treatment of less malignant cancers.

## P12

### Radiation epidemiology studies of Mayak workers

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**Introduction:** Mayak is the first Soviet industrial complex to provide plutonium-239 for defense purpose. The complex started in 1948. During the period of technology development (1948-1958) number of workers were exposed to substantial doses of exposure to ionizing radiation including external gamma-rays and internally deposited alpha-emitter plutonium-239 (primarily by inhalation intake).

**Aims:** Estimation of risk of the stochastic (carcinogenic) effects of protracted occupational exposure to ionizing radiation.

**Methods:** During 1980s the registry of Mayak workers had been created, which includes today about 26,000 workers, (25% females), 12,000 deaths and 950,000 person-years. Each worker had data of individual monitoring of external exposure level but only about 40% of workers with potential to exposure to plutonium had been monitored for levels of internal alpha-exposure. Average dose of external gamma-exposure in the cohort is 0.26 Gy whereas maximum dose reaches 6.3 Gy (colon dose). Average dose of alpha exposure (liver dose) is 0.25 Gy whilst maximum liver dose of alpha-exposure is about 16 Gy.

**Results:** Stochastic effects demonstrated in this cohort include leukemia (ERR/Gy of 0.57, 95% CI 0.05–2.04), solid cancers other than lung, liver and bone (ERR/Gy 0.16, 95% CI 0.07–0.26). Neither of cancers described above have shown any association with exposure to plutonium.

Cancers in organs of primary plutonium deposition (lung, liver and bone) showed significant alpha-particles dose-response with most deaths attributed to exposure to plutonium. ERR/Gy for lung cancer is 7.1 (95% CI 5.0–11), for liver cancer 2.6 (0.7–6.9) and for bone cancer 0.76 (<0–5.2). Among these sites only lung cancer responded (although insignificantly) to gamma-exposure with ERR/Gy of 0.13 (95% CI -0.04–0.38).

**Conclusions:** Protracted radiation exposure leads to significant increase of carcinogenic risk although an indication exists of lower effects than that of acute exposure.

## P13

### Epidemiological registry: Protecting patients from medical exposure

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**Introduction:** Increasing number of computed tomography (CT) which is characterized comparatively high radiation dose necessitate valuation of medical exposure levels in terms of negative effects of ionizing radiation impact, particularly cancer. It can be performed based on radiation risk analyses using data from register of persons exposed to CT.

**Aims:** To create the registry of persons exposed to X-ray by CT; verify and prepare the data for epidemiological analyses of risk of medical radiation exposure.

**Methods:** The archive protocols of CT examinations of patients for the period from 2007 to 2014 were collected routinely. Based on the protocols the database was created. Information on clinical diagnosis, character of CT-study, individual radiation dose and additional information has been categorized. Verification procedure has been performed that allowed us to exclude false, lost and duplicated data.

**Results:** More than 10.000 records have been merged in database, which forms the Register of CT-exposed persons. Register includes both male and female between 0 and 80+ years with neurological, cardiovascular pathology, neoplasms and other diseases diagnosed. The dose per person per 1 CT-study varied from less than 1 mSv to more than 25 mSv. The peculiarity of the Register is that 15% of population works at the nuclear-industrial complex having professional radiation dose.

**Conclusions:** Using the Register could help in radiation risk assessment to evaluate the permissible levels of medical exposure.

**P14****Recurrence risk of pregnancy-related pelvic girdle pain. A population-based cohort study**

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**Introduction:** Parity is a risk factor for developing pelvic girdle pain (PGP) in pregnancy. Hence, for women with PGP in their first pregnancy, the recurrence rate of PGP is expected to be higher than in women with no PGP. There is a lack of longitudinal analysis of the association between parity and PGP. How the time between pregnancies influence the risk in subsequent pregnancies is not known.

**Aims:** To compare the risk of pelvic girdle pain in the second pregnancy in women with and without PGP in their first pregnancy, and to determine if the risk changes with the time interval between the two pregnancies.

**Methods:** In this population-based cohort study, data from 12532 women with two consecutive singleton pregnancies enrolled in the Norwegian Mother & Child Cohort study were used. Pelvic girdle pain, defined as having severe or mild pain in the anterior pelvis and in the posterior pelvis bilaterally, was obtained by questionnaire in pregnancy week 30. The impact of PGP in first pregnancy on recurrent PGP was estimated as crude and adjusted relative risks (RR) with 95% confidence intervals (CI).

**Results:** Overall, 17.3% (n=2174) of the women developed PGP in the second pregnancy. After excluding women who developed PGP in their first pregnancy (n=1393, 11.1%), PGP occurred in 13.2% of the second pregnancies. PGP during the first pregnancy increased the risk of PGP in the second pregnancy (adjusted RR=3.6, 95% CI 3.3-3.8). The mean time interval between pregnancies did not seem to influence the recurrence risk of PGP.

**Conclusions:** Previous PGP increased the risk of recurrence in a subsequent pregnancy independent of the time interval between the two pregnancies. However, most women who developed PGP in a second pregnancy did not report PGP in the first pregnancy.

## P15

**Risk factors for complete uterine rupture after trial of labor in scarred uterus**

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**Introduction:** Uterine rupture is rare, but known to increase in scarred uteri. Complete rupture is the rarest type, defined as tearing of all layers of uterine wall and is associated with catastrophic maternal and neonatal outcome. As cesarean section (CS) is increasing worldwide, uterine rupture is expected to increase.

**Aims:** The aim of this study was to identify the risk factors for complete uterine rupture in scarred uteri, through studying a validated sample of mothers after trial of labor (TOL) in the period 1967-2008 in Norway.

**Methods:** This was a retrospective population based study, using the Medical Birth Registry of Norway and Patient Administration System. All records with uterine ruptures were studied, and information validated.

Population: 57859 mothers with scarred uteri having TOL.

Main outcome measure: Complete uterine rupture

Explanatory variables: Demographic, pregnancy and labor risk factors.

A multivariable logistic regression was used to measure the adjusted odds ratios AORs with 95% confidence intervals (CI).

**Results:** There were 122 complete ruptures after TOL (2.1/1000). Adjusted OR with 95% CI for risk factors for ruptures were: maternal age  $\geq 35$  (1.54; 1.1-2.3), Mothers from Horn of Africa versus European (5.11; 2.2-11.8), Previous miscarriages (4.94; 3.4-7.4), Birth weight  $\geq 4000$  gm (2.00; 1.3-2.9), Gestational age  $\geq 41$  weeks versus 37-40 weeks (1.54; 1.1-2.2), Induced labor (2.22; 1.5-3.2); Induction methods versus spontaneous labor: prostaglandins (2.77; 1.6-4.6), oxytocin (2.68; 1.4-4.9), combination prostaglandins/oxytocin (18.45 (9.9-34.2), mechanical induction (0.30; 0.07-1.2), and augmentation of labor with oxytocin (4.49; 3.0-6.6).

**Conclusion:** The rate of complete uterine rupture after TOL in scarred uteri is low in Norway. Most important risk factors are related to our obstetric interventions as induction and augmentation of labor. Mothers with previous miscarriages and women from African horn are high risk groups that need extra vigilance. Guidelines for management of labor should be updated.

## P16

### Incidence of febrile seizure in young children

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**Introduction:** Febrile seizures are defined as seizures in children up to 60 months of age, accompanied by fever ( $\geq 38^{\circ}\text{C}$ ) without central nervous system infection. The few studies describing febrile seizure incidence are typically small in terms of the number of subjects.

**Aims:** Our objective was to investigate the occurrence of febrile seizures by sex, age and season among young children in Norway by using data from national health registries.

**Methods:** The study population comprised all Norwegian children younger than 5 years of age registered in the National Registry as residents in Norway during 2008-2013 ( $N > 700\,000$ ). We retrieved information on all encounters for febrile seizures in primary health care from the KUHR database and in specialist health care from the Norwegian Patient Register (NPR). Data were analyzed with Poisson regression and Kaplan-Meier analysis.

**Results:** More boys than girls had febrile seizures and we observed a clear seasonal pattern, with a higher number of febrile seizure episodes during winter months. Cumulative incidence curves showed that few children experienced febrile seizures before 12 months of age, and that the major proportion of first episodes occurred between 12 months and 24 months. From 24 months of age onwards, cumulative incidence was higher among boys. At 60 months of age, approximately 4% of the study population had experienced at least one febrile seizure.

**Conclusions:** By using data from national health registries, we have been able to investigate the incidence of febrile seizures in young children and how the condition varies with age, sex and season.

**P17****The effect of the economic collapse on birth outcomes in Iceland:  
a 4 year follow-up**

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**Introduction:** Studies have indicated an association between economic contraction and adverse neonatal- and infant health.

**Aims:** The aim was to examine the potential effect of the 2008 Icelandic economic collapse on neonatal health, as measured by low birth weight (LBW), preterm birth (PB) and small-for-gestational age (SGA), during the first four years following the major economic recession.

**Methods:** The study leveraged on individual level data from the Icelandic Medical Birth Register. Included in the study were all pregnancies resulting in singleton births in Iceland between September 27<sup>th</sup> 2004 and September 30<sup>th</sup> 2012 (N=35,838). With the pre-collapse period as reference, we used logistic regression analysis to assess changes in LBW, PB and SGA during the first four years after the economic collapse, adjusting for maternal demographic and pregnancy characteristics.

**Results:** Compared with the pre-collapse period, we observed an increased prevalence of LBW and SGA only in the first year following the economic collapse (2.7% vs. 3.4%; adjusted odds ratio [aOR<sub>LBW</sub>] 1.27; 95 percent confidence interval [95%CI] 1.06-1.52 and 1.4% vs. 1.8%; aOR<sub>SGA</sub> 1.29; 95% CI 1.01-1.66). No such increase was observed in the subsequent three post-collapse years. The increase in LBW and SGA was particularly observed among mothers younger than 25 years (aOR<sub>L</sub> 1.60; 95% CI 1.14-2.26 and aOR<sub>SGA</sub> 1.67; 95% CI 1.03-2.70) and mothers not on the labor market (aOR<sub>LBW</sub> 1.51; 95% CI 1.08-2.09 and aOR<sub>SGA</sub> 1.64; 95% CI 1.01-2.67). No changes were observed for PB during the study period.

**Conclusions:** Our preliminary results suggest an increased risk of LBW and SGA in Iceland in the first and most severe year of the national economic recession, which disappeared in the subsequent years. Further, the transient increase was most apparent among socioeconomically disadvantaged mothers.

**P18****Associations between blood fatty acids and allergy in a sample of children in Europe**

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**Introduction:** There is evidence that blood polyunsaturated fatty acids (PUFAs) are increased in subjects with allergy, in particular in young children, and during the allergic reaction.

**Aims:** To compare the level of blood fatty acids (FAs) by allergy status in 2600 children that are a subsample of the European IDEFICS study.

**Methods:** Blood FAs were measured at age 2-9 (baseline) and at the follow-up two years later. Cross-sectional associations between FAs and self-reported allergy at baseline ( $n = 2566$ ) and at 2-year follow-up ( $n = 601$ ) were investigated using linear regression, adjusted for age, sex, country, weight, parental education, number of siblings, and breast feeding. For the subset of children measured at both time points ( $n = 534$ ) we compared the longitudinal change of PUFA in children with persistent, incident, and outgrown allergy with those, who never had allergy.

**Results:** At baseline, children with prevalent allergy had higher PUFA than children without allergy,  $+0.44\%$ , 95% confidence interval =  $(0.12, 0.75)\%$ . This difference was largest in the youngest age group of 2-3.9 year old children,  $+1.20$  ( $0.24, 2.17$ )% and also seen for n-3 PUFA,  $+0.29$  ( $0.07, 0.50$ )%. In the oldest age group (8-9.9 years), lower monounsaturated fatty acid rather than higher PUFA appeared to be associated with allergy. At follow-up, the difference in PUFA by allergy was given by  $+0.68$  ( $-0.15, 1.51$ ) %, independent of age. The longitudinal analysis revealed stable PUFA levels among children without allergy and, at a higher level, among children with persistent allergy. Children that outgrew their allergy showed a decrease in PUFA levels by  $-0.13$  ( $-2.73, 0.06$ )%. Children with incident allergy showed but a weak increase in PUFA.

**Conclusions:** Prevalent allergy is associated with higher levels of PUFA, in particular n-3 PUFA, but the latter is observed in the youngest age group only.



## P19

### **Subacromial shoulder disorders among baggage handlers: An observational cohort study**

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**Introduction:** Musculoskeletal disorders in shoulders are important health problems in the working population with considerable impact on sickness absence, contacts to the health care system and withdrawal from the labour market. Baggage handling is characterized by repetitive work primarily consisting of heavy lifting in awkward positions and time pressure.

**Aims:** To assess the influence of cumulative employment as baggage handler on the risk of incident subacromial shoulder disorders.

**Methods:** This cohort study is based on the Copenhagen Airport Cohort consisting of unskilled men with employment at Copenhagen Airport (CPH) and unskilled men with employment in other firms in the Greater Copenhagen area during the period 1990-2012. Only men were included as there were no women working as baggage handlers at CPH. We followed the cohort in the National Patient Register and Civil Registration System. The primary exposure was cumulative years of employment as a baggage handler and the primary outcome was diagnoses and surgical treatment of subacromial shoulder disorders.

**Results:** The cohort contained 3,396 baggage handlers and 63,909 workers in the reference group. Baggage handlers with longer cumulative years of employment had higher incidence compared to baggage handlers with shorter employment, e.g. baggage handlers with 10-19 years of employment had incidence rate ratio of 2.07 (95% confidence interval, 1.27-3.38) compared to baggage handlers with less than three years of employment. Spline regression showed an increase in incidence within the first few years after employment where after the increased risk remained increased for longer employment.

**Conclusion:** In this large cohort study we found increased incidence of subacromial shoulder disorders for workers with longer cumulative years of employment. These results support that long-term lifting in awkward positions and time pressure influence the risk of clinical relevant subacromial shoulder disorders.

**P20****Associations between occupational lifting and low back disorders – registry based data from the Copenhagen Airport Cohort**

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**Introduction:** Most studies examining physical work-related factors and low back pain are cross-sectional studies with self-reported physical work load and self-reported outcome. However, such studies have methodological weaknesses and are often too inaccurate for studying quantitative exposure-effect relationships.

**Aims:** To study associations between occupational lifting and the incidence of low back disorders with registry based data where exposure and outcome were assessed objectively and independently.

**Methods:** The work of baggage handlers is characterised by daily heavy lifting. We established a historical cohort of airport baggage handlers and a reference cohort of unskilled workers – The Copenhagen Airport Cohort. The employment periods of the participants were registered in electronic company employment registers and union member registers. We followed the cohort in the National Patient Register, the Civil Registration System and registers at Statistics Denmark to obtain information on diagnoses, surgery, mortality, migration, and pensioning. The primary exposure measure was cumulative years of employment as a baggage handler and outcomes were 1) lumbar disc herniation and 2) other low back diagnoses (LBD) defined as diagnoses and surgical treatment for these outcomes.

**Results:** Non baggage handlers (N=65 702) had a lower incidence of LBD, but not of lumbar disc herniation compared to baggage handlers (N= 3473). Baggage handlers with longer employment had a higher incidence of LBD compared to baggage handlers with shorter employment. The linear association of cumulative years of employment on LBD was significantly increased with an incidence rate ratio of 1.14 (95% CI 1.06-1.22) for a five year increase of employment as baggage handler. Length of employment did not affect the incidence of lumbar disc herniation.

**Conclusions:** This large cohort study showed an increased incidence of LBD among baggage handlers. Furthermore an exposure-effect relationship between years of employment and LBD was shown.

## P21

### Do psychosocial working conditions mediate social inequalities in musculoskeletal and psychiatric sickness absence in a life-course perspective?

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**Introduction:** Psychosocial working conditions are predictors of musculoskeletal and psychiatric sickness absence (SA) but do they also mediate socioeconomic inequalities in SA in a life-course perspective?

**Aims:** Our objective was to examine the relationships between these factors in a life-course perspective, including indicators of both childhood and adult socioeconomic position (SEP).

**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 with musculoskeletal and psychiatric diagnoses, respectively. Educational attainment (4 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, job strain, social support and bullying. Risk ratios (RRs) were estimated using Poisson regression.

**Results:** 10.3% of the women and 9.5% of the men had musculoskeletal SA during follow-up, whereas 7.1% and 2.7%, respectively, had psychiatric SA. There were strong social gradients according to adult SEP for both genders and both diagnoses, but strongest for musculoskeletal disorders. The age-adjusted RR for having an SA episode, comparing highest and lowest educational levels, was 5.8 for women and 7.0 for men, for musculoskeletal diagnoses, and 3.4 and 3.7, respectively, for psychiatric diagnoses. The RRs were somewhat weakened in women and strengthened in men, after adjusting for childhood SEP (Model 2). Including all work factors in the model reduced the RRs by 6%-28% compared to Model 2; the largest impact was for musculoskeletal SA among women (14%) and psychiatric SA among men (28%).

**Conclusions:** There were strong social gradients in SA, which were somewhat attenuated when adjusting for psychosocial work factors, indicating that these factors may partly mediate the social gradients in a life-course perspective.

**P22****Educational inequalities in obesity and gross domestic product: evidence from 70 countries**

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**Introduction/aim:** We test the reversal hypothesis, which suggests that the relationship between obesity and education depends on the economic development in the country; in poor countries obesity is more prevalent in the higher educated groups, while rich countries the association is reversed – higher prevalence in the lower educated.

**Methods:** We assembled a dataset on obesity and education including 412 921 individuals from 70 countries in the period 2002-2013. Gross Domestic Product (GDP) per capita was used as a measure of economic development. We assessed the association between obesity and GDP by education using a two-stage mixed effects model. Country specific educational inequalities in obesity were investigated using regression-based inequality indices.

**Results:** The reversal hypothesis was supported by our results, in both men and women. Obesity was positively associated with country GDP only among individuals with lower levels of education, while this association was absent or reduced in those with higher levels of education. This pattern was more pronounced in women than in men. Furthermore, educational inequalities in obesity were reversed with GDP; in low-income countries obesity was more prevalent in individuals with higher education, in medium- and high-income countries obesity shifts to be more prevalent among those with lower levels of education.

**Conclusions:** Obesity and economic development were positively associated. Our findings suggest that education might mitigate this effect. Global and national action aimed at the obesity epidemic should take this into account.

**P23****Maternal body mass index and risk of cerebral palsy**

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**Introduction:** Cerebral palsy (CP) is the most common cause of physical disability in children, affecting about 2 per 1000 live-born. While a few prenatal risk factors have been identified, little is known about causal pathways.

**Aims:** To investigate the association between maternal pre-pregnancy body mass index (BMI) and risk of CP in offspring, both overall and for major CP subtypes.

**Methods:** The study population consisted of 189 410 children in the Mother and Babies in Norway and Denmark (MOBAND) study. MOBAND comprises data from two population-based, prospective birth cohorts: the Norwegian Mother and Child Cohort Study (MoBa) and the Danish National Birth Cohort (DNBC). Information on pre-pregnancy BMI was self-reported in early pregnancy while CP diagnoses were obtained from the respective national cerebral palsy registries. Associations were investigated using log-binominal regression.

**Results:** The two cohorts produced 392 eligible cases of CP (2.1 per 1000 live born). The risk of CP increased continuously with BMI (relative risk [RR] 1.04, 95% confidence interval 1.02-1.06). Compared with mothers in the lower normal weight group (BMI 18.5-22.9), mothers in the upper normal group (BMI 23.0-24.9) had a 40% excess risk of a child with CP (RR 1.4, 1.06-1.8). Excess risk was 60% (RR 1.6, 1.2-2.0) for overweight mothers (BMI 25.0-29.9), and 70% (RR 1.7, 1.2-2.3) for obese mothers (BMI ≥ 30). In the analysis of CP subtypes, we compared mothers above and below the median BMI (22.9). Two subtypes had particularly strong associations with BMI: dyskinetic CP (RR 2.6, 1.2-5.6) and ataxic CP (RR 9.8, 1.3-77). Estimates changed little with adjustment for mother's occupational status, age and smoking.

**Conclusions:** Higher pre-pregnancy maternal BMI is associated with increased risk of CP in offspring. Increased inflammatory processes or other conditions associated with higher BMI may contribute to risk of CP.

**P24****Elevated FINDRISC in a general population. The HUNT DE-PLAN Study in Norway**

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**Introduction:** Cost-effective risk screening tools for diabetes are needed to recognize people at high risk who can be targeted in sustainable prevention strategies for type 2 diabetes. One such tool is the Finnish Diabetes Risk Score (FINDRISC).

**Aims:** To estimate the prevalence of elevated FINDRISC, and the prevalence of abnormal glucose tolerance among people with elevated FINDRISC, in a general population in Norway.

**Methods:** Among 47 694 adult participants without previously known diabetes in the HUNT3 survey (2006-08), we estimated the prevalence of elevated FINDRISC (defined as a score of  $\geq 15$ ) overall and by sex and age. Among 2559 participants with elevated FINDRISC and no previously known diabetes who participated in oral glucose tolerance testing, we estimated the prevalence of diabetes, impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and any of these forms of abnormal glucose tolerance (AGT).

**Results:** The overall prevalence of elevated FINDRISC was 11.0% (95% CI 10.7-11.3). The prevalence was higher in women (12.1%) than in men (9.6%) and increased strongly by age, from 1.5% at age 20-39 to 25.1% at age 70-79 years. Among people with elevated FINDRISC, 34.9% (95% CI 33.1-36.8%) had one form of AGT. Specifically, 9.8% had diabetes, 16.9% had IGT and 8.2% had IFG. In general, these proportions were higher in men than in women, and higher at older age. Thus, among people with elevated FINDRISC aged 80 years or older, 17.6% had diabetes, and 55.5% had one form of AGT.

**Conclusion:** Approximately one tenth of this general adult population in Norway, and one quarter of people aged 70 years or older, was identified as being at high risk of diabetes by using FINDRISC. Among people with elevated FINDRISC, one tenth had already developed diabetes, and one in three had some form of abnormal glucose tolerance.

## P25

### Prescription registry quality responsibilities – a case from Iceland

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**Introduction:** Prescription registries are a valuable source of information on use of prescription medicines. All the Nordic countries have prescription registries that are used for research purposes and to some extent as guidance in decision making. Iceland's Prescription Registry has the added purpose of surveillance of physician prescribing and of patient consumption of narcotic drugs. Such tools must be reliable.

**Aim:** To describe how the Icelandic Directorate of Health handled the reliability responsibility for the Prescription Registry from its establishment until 2015, illustrated with the case of opioids.

**Methods:** Uncovering severe and seemingly random errors in DDD definitions led to mapping of all DDD definitions in use in the registry. After finding in addition another source of errors, a more in-depth examination of quality issues was undertaken. Existing data on quality mapping was requested from the Directorate of Health in January 2013, followed up by reminders and complaints on an as-needed basis. Media coverage of deaths from overdoses of prescription opioids illustrates how the surveillance tool was used.

**Results:** The Directorate of Health has not delivered requested data (22.4.2015) in spite of three rulings confirming delivery obligations. Media covered deaths indicated that neither a death from:

- mixed ketobemidone products (use underestimated, halved),
- injected fentanyl scraped off plaster without even leaving the building where the prescribing physician worked (use overestimated, almost tripled) nor
- fatal overdose of a.o. approximately accurately estimated morphine tablets

seemed to have consequences like narrowing of prescribing permissions for involved physicians.

**Conclusions:** The Registry has not functioned properly as surveillance tool, research basis or decision making aid. Authorities and institutions setting up similar registries should plan carefully before setup. Prospective benefits of monitoring should be balanced against disadvantages and if deciding to monitor, sufficient resources should be ensured for establishing the tool and taking care of quality issues.

**P26****Finasteride use in the male populations of Denmark, Finland, Norway and Sweden**

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**Introduction:** Finasteride 5 mg was marketed in 1992 and 1993 in the Nordic countries for treatment of benign prostate hyperplasia. Even though there is a unique opportunity to study register-based prescription data in the Nordic countries and finasteride has been marketed for more than two decades, patterns of finasteride drug usage are unknown.

**Aim:** The aim of the present study was to perform a drug utilization analysis and describe cross-national differences and similarities in finasteride use between Denmark, Finland, Norway and Sweden.

**Methods:** Cross-national drug utilization patterns of finasteride were analysed using individual-level data from prescription registers in Denmark (1995–2009), Finland (1997–2010), Norway (2004–2009) and Sweden (July 2005–2011). The descriptive analyses included a graphical illustration of the Lorenz curve as well as calculations of the period prevalences, incidence rates and waiting time distributions.

**Results:** Altogether, 266,199 Nordic men had approximately 3 million dispensings of finasteride 5 mg in the study period. Finland had the highest period prevalence and incidence rate (18.2/1000 men and 3.6/1000 person years, respectively) and Denmark the lowest (4.9/1000 men and 1.4/1000 person years, respectively). The therapeutic index ranged from 3.7 defined daily dose (DDD) per 1000 men/day in Denmark to 14.0 DDD/1000 men/day in Finland. The incidence rate of finasteride use increased with age in all four countries. The persistence of finasteride use was relatively high with only 11.6% having a gap of 365 days or more between at least two prescription redemptions. The drug volume was almost equally distributed across finasteride users and we found no evidence for drug abuse, seasonality or relapse tendency in the use of finasteride.

**Conclusions:** Differences in finasteride utilization were observed across Denmark, Finland, Norway and Sweden despite similarities across Nordic countries regarding political systems and health care services. We found no evidence of irrational use.



**P27****Use of a concept dictionary to integrate different medical classification systems in a multi-country study**

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**Introduction:** Studies using register data from multiple countries face the challenges of bringing together data with different structures and integrating different drug and diagnosis classification systems. In the CARING (CAncer Risk and INSulin analoGues) project, data from national health care databases in Denmark, Finland, Norway and Sweden were combined with data from the United Kingdom Clinical Practice Research Datalink (CPRD).

**Aims:** To develop a data model allowing the integration of information from differently structured databases that use different medical classification systems.

**Methods:** In the Nordic health care registers drugs were classified using the Anatomical Therapeutic Chemical (ATC) system and diagnoses using the International Classification of Diseases (ICD) versions 7 to 10. The CPRD uses product codes based on the British National Formulary for drugs and READ codes for diagnoses. Intervention and procedure code systems also differ. We developed a concept dictionary, i.e. a database mapping the concepts of exposures, outcomes and confounders used in the study to terms and codes in different systems.

**Results:** The protocol and analysis plan included 21 exposure concepts, 12 outcome concepts and 31 confounder concepts referring to either drugs or diagnoses. The concept dictionary included 283 ATC codes, 1802 CPRD product codes, 1083 ICD codes and 2979 READ codes. Two datasets were created from the CPRD and Nordic databases, one with drug exposure events and one with clinical events, the latter including both hospital encounters, cancer register diagnoses and causes of death. Translation of codes into concepts could be achieved by SQL queries with the possibility of avoiding to hardcode these into the statistical analysis programs.

**Conclusions:** The concept dictionary was able to serve a dual purpose: as a means of documentation and as an integrated part of the database with the ability to include concepts directly in queries.

**P28****A five year follow-up prescription registry study: the impact of starting with diazepam versus oxazepam****Ingunn Fride Tvete<sup>1</sup>, Trine Bjørner<sup>2</sup>, Tor Skomedal<sup>3</sup>**

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**Introduction:** New benzodiazepines users could develop drug dependency, possibly indicated by dose escalation. Starting on different benzodiazepines might give different risks for dose escalation.

**Aims:** To follow new diazepam and oxazepam users over five years for examining the differences between the two groups.

**Methods:** This was a prescription database study. In a background analysis of individuals starting on diazepam versus oxazepam we conducted logistic regression analyses with gender, age, previous relevant drug dispensations, prescriber's specialty, household income, education level, type of work and vocational rehabilitation support as background variables. Time to reach a daily average of one or more DDD over a three month period was analyzed through a Cox proportional hazard regression model.

**Results:** Altogether 15927 and 3820 individuals started on diazepam and oxazepam respectively. New oxazepam users had more frequently used antidepressants and lithium, antipsychotics, opioids, anti-alcohol and smoke cessation drugs than new diazepam users had. They also had somewhat lower education, lower income, previously received vocational rehabilitation support and to a greater extent not registered work. Even when accounting for differences in sociodemographic status and previously drug use new oxazepam users had a higher risk for dose escalation compared to new diazepam users (HR=1.33(1.17,1.51)).

**Conclusions:** Many doctors prescribed, according to guidelines, oxazepam to individuals that possibly were at risk for developing drug dependency. Still, these individuals were at higher risk for dose escalation, even when accounting for differences in sociodemographic status and previously drug use. Possibly seeking a stronger initial drug effect, possibly a DDD for oxazepam set too low and differences in illness not accounted for might contribute to explain differences in behavior.

**P29****Younger women do not experience improvements in acute myocardial infarction hospitalization rates – a nationwide study using data from the ‘Cardiovascular disease in Norway 2008-2012’ project**

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**Introduction:** Previous studies from Norway have indicated that despite overall declines in acute myocardial infarction (AMI) rates during 1994-2009, younger adults, especially women, experienced less favorable trends compared to their older counterparts.

**Aim:** To explore more recent national trends in AMI hospitalization rates during 2008-2012.

**Methods:** All hospitalizations with an AMI (primary discharge diagnosis coded as I21, I22) among individuals  $\geq 25$  years during 2008-2012 were retrieved from the ‘Cardiovascular disease in Norway 2008-2012’ project. Overall age-standardized and age-specific AMI hospitalization rates were calculated and Poisson regression was used to estimate average annual changes in hospitalization rates by computing incidence rate ratios (IRR).

**Results:** In total, 59 618 individuals (63.7% men) were included in the analyses. Mean age (SD) was 67.5 (13.7) among men and 76.7 (13.0) among women. The total number of AMI hospitalizations was 67 007 (63.1% among men), yielding an average of 1.11 hospitalizations/male and 1.14 hospitalizations/female patients.

During 2008-2012, men experienced an average annual decline in rates of 3% (IRR=0.97; 95% CI 0.96-0.98). All age groups contributed to this decline [25-44 years (IRR=0.95, 95% CI 0.92-0.98); 45-64 years (IRR=0.98, 95% CI 0.97-0.99); 65-84 years (IRR=0.97, 95% CI 0.96-0.98) and 85+ years (IRR=0.96, 95% CI 0.94-0.97)].

The average annual decline in rates among women was 4% (IRR=0.96; 95% CI 0.95-0.97). Age-group specific analyses revealed reductions in rates only among women 65+ years [65-84 years (IRR=0.96, 95% CI 0.95-0.98) and 85+ years (IRR=0.96, 95% CI 0.94-0.97)] while among younger women, rates did not change significantly [25-44 years (IRR=0.96, 95% CI 0.90-1.03) and 45-64 years (IRR=0.99, 95% CI 0.97-1.02)].

**Conclusions:** Despite overall declines in AMI hospitalization rates, less favorable trends (observed earlier in several indicators of AMI occurrence) persist among younger women in Norway.

**P30****Oral infections predict mortality. A 12 ½-year follow-up of the Oslo II-study****Lund Håheim L**<sup>1,3</sup>, Rønningen KS<sup>2</sup>, Olsen I<sup>1</sup>

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**Introduction:** Current research shows that the strength of the association of oral infections to mortality is unclear. In the Oslo II-study performed in year 2000, 5,900 men were studied for tooth extractions and current oral health status.

**Aims:** To study 12 ½-years follow-up of the predictivity of tooth extractions and other oral infections and risk for mortality from cardiovascular disease (CVD) specific diagnoses, all CVD, other causes and total mortality.

**Methods:** The screening data included questionnaire information on oral health status as cause of tooth extractions and current oral infections in addition to several known risk factors for CVD diseases in the men who were 48-77 years old in 2000. Main analyses were by Cox proportional hazard regression analyses as age-adjusted and adjusted for major known risk factors for CVD (total cholesterol, BMI, daily smoking, systolic blood pressure, and education). In addition, analyses were Log rank tests of Kaplan Meier plots.

**Results:** Oral infections (OI) including past infections which had led to tooth extractions and current oral infection predicted total mortality (HR = 1.102, 95% confidence interval (CI) 1.001-1.212) and mortality for other causes than CVD mortality (HR = 1.130, 95% CI 1.006-1.269). Log rank test showed that OI were significant for myocardial infarction, stroke, ischaemic heart disease, angina and hypertension combined, all CVD, other causes of mortality, and total mortality except for aneurysms and heart valve disease. Similar results were observed for tooth extractions on indication of infection alone.

**Conclusions:** This prospective cohort study provides indication for oral infections predicting mortality for specific CVD diagnoses, all CVD, other causes of mortality, and total mortality over a period of 12 1/2- years.

**P31****Mediators of the educational gradient predicting post-delivery hypertension in women: A linkage study between Norwegian Mother and Child Cohort and the Norwegian Prescription Database**

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**Introduction:** Hypertension is an identifiable and modifiable risk factor for cardiovascular disease (CVD).

**Aims:** To evaluate risk factors and population attributable fractions (PAFs) associated with hypertension and to evaluate the primary mediators of the educational gradient in risk among reproductive aged women.

**Methods:** The Norwegian Mother and Child Cohort (MoBa, 1999-2009) was linked to the Norwegian Prescription Database (2004-2013) for information on use of antihypertensives in women after delivery. Women with chronic hypertension prior to pregnancy and deliveries prior to 2004 were excluded, leaving 69,660 pregnancies to 61,971 mothers for analyses. Cox proportional hazards analyses were conducted; mother's pseudo id was entered as a cluster variable; analyses adjusted for important covariates.

**Results:** The mean (SD) maternal age at delivery was 30 years (4.6). A total of 4,417 pregnancies were to women who used antihypertensives after delivery. Women were followed for median of 4 years. Known risk factors for hypertension (i.e., prepregnancy BMI  $\geq 25$ , smoking, diabetes mellitus before/during pregnancy, and advanced maternal age  $\geq 40$ ) were significant predictors of post-delivery use of antihypertensives ( $P < 0.05$ ). Educational level  $\leq 12$  years was associated with an 80% increased risk (HR 1.8; 95% CI 1.6-1.3) relative to educational level  $> 16$  years. A significant interaction term between preterm delivery ( $< 37$  weeks) and preeclampsia was identified ( $P < 0.05$ ), with HRs ranging from 1.4 (95% CI 1.3-1.6) for preterm normotensive pregnancies to 7.5 (95% CI 6.2-8.9) for preterm preeclamptic pregnancies relative to normotensive term pregnancies. The PAF associated with having a pregnancy-related complication (preterm delivery, gestational hypertension, preeclampsia) and with educational level was evaluated and the persistence in the educational gradient in risk was evaluated by considering the percent explained by mediators including pregnancy-related complications and modifiable lifestyle risk factors.

**Conclusions:** The study will aid in the designing of interventions to reduce the educational disparities in CVD risk in women.

**P32****Evaluation of the psychometric properties in a core Heart-disease health-related Quality-of-Life questionnaire (the HeartQoL) in a Danish population with atrial fibrillation**

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**Introduction:** Around 2% in the Western world is affected by atrial fibrillation [AF] and the majority experience an impaired health-related quality-of-life compared to the general population. Currently, investigators commonly use generic and disease-specific HRQL instruments in parallel in order to ensure that most aspects considered of importance for patient's well-being are measured. However, the use of diverse instruments may hinder comparisons across studies and there is a need for a single approach in the HRQL assessment. A newly developed core heart-specific questionnaire (the HeartQoL) is designed to both address disease-specific issues and meet the need for outcome comparisons across the spectrum of cardiac diseases.

**Aim:** To evaluate psychometric properties of the HeartQoL among Danish AF patients treated with radiofrequency ablation [RFA].

**Methods:** Data was collected in two phases: [1] CopenHeart nationwide survey including self-administered questionnaires: the HeartQoL, Short-Form 36 Health Survey and the Hospital Anxiety and Depression Scale. [2] Test-retest of the HeartQoL. The following psychometric analyses were assessed: internal consistency, reproducibility (test-retest) and construct-related validity including convergent and discriminant validity and "known-group comparisons".

**Results:** 462 patients were enrolled [response rate 73%]. The internal consistency was high [Cronbach's  $\alpha \geq 0.90$ ] and the test-retest reproducibility good [intra-class correlation  $\geq 0.90$ ]. The convergent-correlations were strong ( $r \geq 0.78$ ) and the discriminant-correlations [ $r \leq 0.47$ ] were all lower than the convergent-correlations, however not as weak as expected. The HeartQoL showed its ability to distinguish between "known-groups" with different clinical characteristics by demonstrating statistical significant different mean HeartQoL score.

**Conclusion:** The HeartQoL showed satisfactory psychometric properties in terms of internal consistency, reproducibility and construct validity in Danish patients with AF treated with RFA. These findings underpins that the HeartQoL may be a valuable suggestion for a common HRQL instrument aiming to strengthen the benchmark across the spectrum of cardiac diseases including AF.

**P33****General practice utilization in the Danish Diet, Cancer, and Health Cohort**

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**Introduction:** Women consult their general practitioner (GP) more often than men, but little is known what determines gender difference in health seeking behavior.

**Aims:** To describe the utilization of GP in Danish adult population and identify determinants of GP utilization.

**Methods:** We linked 57,053 participants of the Diet, Cancer, and Health (DCH) cohort to the Danish National Health Service Register to obtain data on the GP visits (face-to-face contacts) at the cohort baseline (1993-97), when information on lifestyle (smoking, BMI, alcohol use, physical activity), pre-existing medical conditions, marital, occupational, and educational status, and female reproductive variables, were collected by questionnaire. We used negative binomial regression model to examine association between GP contacts with gender and above-mentioned variables, in crude and fully adjusted model.

**Results:** Of 54,849 DCH participants with complete data on all variables 52% were women. Women contacted GP on average 4.1 (standard deviation 4.5) and men 2.8 (4.0) times per year. In a crude model, women had 48% higher rate of GP visits than men (IRR: 1.48; 95% confidence interval 1.45-1.51), which, attenuated, but persisted in fully adjusted model (1.17; 1.12-1.23). The IRR attenuated the most after adjustment for number of children and hormone therapy (HT) use. In a fully adjusted model, the strongest determinates of GP contacts were pre-existing diseases: hypertension (1.63; 1.59-1.67), diabetes (1.56; 1.47-1.65), angina pectoris (1.27; 1.21-1.34), and stroke (1.25; 1.17-1.35); unemployment (1.20; 1.18-1.21). GP visits were inversely associated with education. Smoking was weakly positively associated with GP visits (1.10; 1.07-1.12), while there was weak or no effect of BMI, alcohol use, physical activity, or marital status.

**Conclusions:** Pre-existing medical conditions, use of HT, and unemployment was identified as leading determinants of GP utilization. However, when adjusting for these factors, results still reveal a remarkable gender difference in the number of GP contacts.

**P34****Sharing experiences and programming code for register based research****Magnus Stenbeck**<sup>1</sup>, **Johan Fihn**<sup>2</sup>, **Elisabeth Strandhagen**<sup>2</sup>

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**Introduction:** SIMSAM (*Swedish Initiative for Research on Microdata in the Social and Medical Sciences*) is an initiative supported by the Swedish Research Council. Within this network, there is an initiative to create a functioning tool for code and code/experience sharing on the net for everyone doing in registered based research, nationally as well as internationally.

**Aims:** to create a function which will serve as a nation-wide tool for exchange of experiences and programming code between researchers using register based information.

**Method:** A workshop entitled "Sharing data and sharing knowledge" organized by SIMSAM INFRA and Swedish National Data Service (SND) in Gothenburg in March 2015 was the starting point for the project. The workshop discussed why, and how to proceed in the future. An example from data sharing via GitHub was shown, and workshop participants discussed technical and practical obstacles and possibilities for an effective sharing system. It was decided to set up a Github organization called #registerresearch. The organization contains groups that are organized around

- 1) Registers (starting with some often used registers)
- 2) Software (program code for the above in SAS, SPSS, R, Excel, etc.) and
- 3) Research topics (programming code for survival analysis, labor market trend analysis etc.)

The service will be provided via the website "registerforskning.se" and the SND portal. It should be open, widely advertised, and easy to reach. Code and other contributions are subject to open access according to the GNU license agreement. Data with legal restrictions (such as personal data), or direct links to them, cannot be uploaded. The site is intended for those who have own access to the data discussed for research and analysis purposes.

**Conclusions:** At NordicEpi2015 the GitHub organization will be presented for the participants of the conference.



## P35

### **Musculoskeletal disorders in Norway: prevalence of chronicity and use of primary and specialist health care services**

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**Aim:** The aim of this study was to estimate the prevalence of chronic musculoskeletal disorders and to estimate the prevalence of persons receiving primary and specialist health services for these disorders.

**Methods:** We used three data-sources. First, four discrete years of the nationally representative cross-sectional Survey of Health and Living Conditions (SHLC) conducted in 2002, 2005, 2008 and 2012 by Statistics Norway. Second, we used the Norwegian Patient Registry (NPR) to estimate the proportion of the population who used specialist health services in 2012. Third, we used the national register dataset for reimbursement of primary care physicians, chiropractors and physiotherapists (KUHR) to estimate the proportion of the population attending primary care physicians, chiropractors or physiotherapists in 2012. Age- and sex-specific prevalence/utilization estimates for musculoskeletal disorders were calculated.

**Results:** In 2012, 18% of men and 27% of women reported musculoskeletal disorders lasting for six months or more in the SHLC. Primary health care services reimbursed for musculoskeletal disorders were used by 37% of women and 30% of men. Of these 32% (women) and 26% (men) were physician contacts and between 5 and 9% physiotherapist or chiropractor or combined contact types. Corresponding numbers for specialist services were 5% in men and 7% in women, where the majority was out-patient consultations. We found that musculoskeletal disorders increased with age, however our results showed no variation in prevalence of chronic disorders between 2002 and 2012.

**Conclusion:** Chronic musculoskeletal disorders were common in the general population, with higher prevalence among women compared to men, and increasing prevalence with age. The use of register data on health service utilization may be a useful source for monitoring population trends, and for estimating the burden in terms of health and health service use.

**P36****Association between age, renal function, disease progression, and the probability of renal replacement therapy initiation using nationwide data from the Swedish Renal Registry**

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**Introduction:** Aging, renal function, and disease progression are known to consistently affect the risk of end-stage renal disease and mortality in patients with chronic kidney disease [CKD].

**Aims:** To investigate the role of age, CKD stage, disease progression, and their interactions on the probability of renal replacement therapy initiation [RRT] in a nationwide referred cohort of CKD stage III-V patients.

**Methods:** Study population consisted in all the patients in Sweden with 18+ years of age and CKD stage III+ included in the Swedish Renal Registry – CKD section from 2005 to 2012, with at least two creatinine measurements. Disease progression rate was estimated as the percentage change in estimated glomerular filtration rate [eGFR] during the first year of follow-up. Multiple imputation was used for covariates with up to 30% missing values. Finally, a fully adjusted Fine & Gray model was estimated.

**Results:** 9215 patients, 64.3% males, with median age 72 years (Interquartile Range [IQR]: 62.3–79.7), median eGFR 20.8 ml/min/1.73m<sup>2</sup> (14.1–28.3), and median progression rate -8.0% (-22.7–6.8). Median follow-up was 3.8 years (2.6–5). 2505 patients started RRT during follow-up. After adjustments, increasing age showed a decreasing risk (sub-hazard) of RRT. Higher CKD stages showed up to a 16 fold increase in risk (stage V vs IIIa). Patients in the lowest tertile of progression rate showed a 2.1 fold increase in risk. No significant interaction was found. Finally, Gray tests for disease progression on subgroups defined by CKD stage showed a significant association with the probability of RRT only for patients with CKD stage IV and V.

**Conclusions:** The risk of RRT is strongly and directly associated with CKD stage, and inversely with age; disease progression strongly influences the risk of RRT, specifically for CKD stage IV-V patients.

**P37****Historical twinning rates in Norway****Thomas Nilsen<sup>1</sup>, Per Magnus<sup>1</sup>, Ragnhild Ørstavik<sup>2</sup>**

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**Introduction:** It is well known that the twinning rate has increased considerably in the developed countries since the 1980's., but it has also been suggested that historically, the twinning rate in the 1960's and 70's was exceptionally low. In Norway, the twinning rate increased from 1.10% in the period 1967-1987 to a maximum of 1.95% in 2002, and then later decreased to 1.60% in 2012. In large part these changes can be explained by first the introduction of, and then the improvement in, assisted reproductive technologies (ART) and changes in maternal age. In order to assess these temporal changes in the twinning rate, one could ask the question: What is the "natural" or "historical" twinning rate?

**Aims:** The aim of the current study is to perform detailed analyses of Norwegian twinning rates for the period 1826 to 2012.

**Methods:** Historical twinning rates have been collected from population statistics, made available online by Statistics Norway, while rates from 1967 onwards are from the Medical Birth Registry of Norway. We will adjust for ART and standardize on maternal age for periods where this information is available/relevant. We will also apply Weinbergs differential Rule in order to assess and discuss the rate of monozygotic to dizygotic twinning, and dizygotic twinning to total fertility.

**Results:** For the whole observation time (1826-2012), the crude mean twinning rate, excluding ART, was 1.25%. From 1871-2012 the mean twin rate, excluding ART and indirectly age-standardized according to the maternal age distribution in 1967, was 1.19%, but with large fluctuations (0.10 to 1.62%). The 2012 adjusted twinning rate is 1.19%, which is the historical mean.

**Conclusions:** When taking historical data into account, and applying indirect standardization techniques, present twinning rates in Norway seem to be close to the historical mean rate.

**P38****How long do young adults want and expect to live?**

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**Introduction:** Several longitudinal studies have demonstrated that people who have more positive attitudes about aging enjoy better health and longer life spans. To date, however, most of research on the association between attitudes towards aging and health/longevity is based on data from middle-aged and/or older adults. Little is known about what young people think about their own aging and whether such attitudes likewise have implications for their health and health behaviors.

**Aims:** To explore young people's subjective life expectancy (how long one expects to live) and preferred life expectancy (how long one wants to live) along with potential antecedents and health consequences.

**Methods:** Data from three samples of university students were collected in Russia ( $N=208$ ), Poland ( $N=335$ ), and Austria ( $N=108$ ). We used multivariate regression analyses to assess whether preferred and expected life expectancy were each related to gender, old age stereotypes, and intergenerational relationships within and outside of the family as well as self-rated health and health behaviors.

**Results:** On average, participants wanted to live longer than they expected to. How long participants wanted to live was related to their stereotypes of old age but not their intergenerational relationships. Wanting and expecting to live longer were both negatively associated with tobacco use and positively associated with physical exercise, self-rated health as well as a higher will-to-live.

**Conclusions:** The results of the study provide first evidence that preferred and subjective life expectancy tap into different constructs. The results indicate that even in young adulthood, stereotypes about old age are related to how young adults' attitudes towards their own aging and further, that how young adults think about their lifespan is associated with their health and health behaviors.

## P39

### Multimodal training intervention: An approach to successful aging

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**Introduction:** Multimodal training interventions (6-MTI) are of special interest for older individuals, because of their high rate of disability, functional dependence and use of healthcare resources.

**Aims:** The purpose of this study was to assess the immediate and long-term effects of a 6-MTI on functional fitness (FF), body composition (BC) and cardio metabolic risk factors (CMRF).

**Methods:** The 6-MTI consisted of daily walking and twice-a-week strength training. The design was a randomized-controlled crossover with four 6-month phases: Baseline assessment, intervention compared with controls, crossover-phase with intervention by control group and an additional 6-month follow-up.

**Results:** After 6-MTI, positive improvement was seen in FF, BC and CMRF. Males and females retained achieved changes or even improved further at 6- and 12-month follow-up measurements.

**Conclusions:** 6-MTI is feasible and beneficial in older populations as an integral part of prevention and management chronic age related disorders.

**P40****Data management: An investment for the future****Elisabeth Strandhagen**

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**Introduction:** Data management is a method used to handle, organise, structure and store research data throughout the research process. A good data management strategy takes into account technical, organisational, structural, legislative and sustainability aspects. It thus helps researchers to keep the data collected and/or used within their project tidy, useable and safe, while at the same time ensuring their longevity.

**Aims:** To support researchers in data management with a web guide on the website at Swedish national data service (SND).

**Methods:** SND works with various support activities to researchers when it comes to organising, maintaining, preserving data and also making them available. One contribution to help researchers with better data management is a web guide divided into six steps related to the research process.

**Results:** Two of the steps are about project planning and writing a data management plan, the other four about data collection, data documentation and short and long-term data storing. One part of the support is a brochure for downloading. SND's data management pages are in Swedish mostly. English-speaking researchers have already access to a wealth of high-quality data management literature, both published and online which there are links to facilitate access. The web guide is based on this literature. The support also includes information about ethical and legislative aspects, and information about the Swedish and European work with open access to data information.

**Conclusions:** The SND web guide on data management is a contribution to ensure the usability and longevity of research data and better meet the demand for open access to data.

**P41****Contributions of different common mental disorders to sickness absence**

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**Introduction:** Mental disorders impair work capacity and are one of the leading causes of sick leave. Few studies have investigated associations between specific mental disorders and sick leave in the population, and previous studies are limited either by being cross-sectional or by using symptom measures rather than clinical diagnoses. In addition, most studies did not distinguish between diagnoses on the sick leave certificates. It is thus not known to what degree different mood, anxiety and alcohol use disorders differentially predict sick leave granted for different diagnostic categories.

**Aims:** We aim to examine the prospective associations between eight common DSM axis 1 mood, anxiety and alcohol use disorders, and later sick leave granted for psychological, musculoskeletal, and other diagnoses, as well as all-cause sick leave.

**Methods:** The sample for the current study consisted of 2,770 twins who participated in psychiatric diagnostic interviews and were followed for eight years with registry data on employment and sick leave. Associations between mental disorders and sick leave were estimated in logistic regression models.

**Results:** All the included mood, anxiety and alcohol use disorders were prospectively associated with sick leave; mood (OR=2.16) and anxiety disorders (OR=2.30) approximately equally strongly, with smaller contributions from alcohol use disorders (OR=1.55). Major depressive disorder had the strongest fully adjusted association with sick leave granted for psychological disorders (OR=2.48). Social anxiety disorder (OR=1.79) and specific phobias (OR=1.99) had the strongest associations with sick leave granted for musculoskeletal disorders.

**Conclusions:** Mood disorders and anxiety disorders have independent contributions to sick leave, whereas the association with alcohol use disorder is lower. Mood disorders seem to influence sick leave granted for psychological disorders most strongly, whereas anxiety disorders are more predictive musculoskeletal sick leave. Due to high prevalences, anxiety disorders often considered relatively mild were associated with most sick leave at the population level.

**P42****Common genetic and environmental risk factors for psychosis, mania, and personality disorders**

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**Introduction:** Personality disorders (i.e. an enduring pattern of inner experiences and behavior that leads to distress or impairment) is phenotypically associated with psychosis. Family studies indicate that the phenotypic associations could be due to common genetic factors.

**Aims:** To estimate the genetic and environmental correlations between symptoms of psychosis, mania, and personality disorders.

**Methods:** We used clinical interview data from young adult Norwegian twins derived from 1408 twin pairs. To model psychiatric phenotypes and minimize measurement error, we used an 'item response theory'-based biometric measurement model.

**Results:** All 10 personality disorders defined in DSM-IV was associated with psychosis. There was a particularly large overlap in genetic factors between psychosis symptoms and borderline, schizotypal and antisocial personality disorder, respectively.

**Conclusions:** There is a considerable overlap in genetic factors, or pleiotropy, between symptoms of psychosis and personality disorders. In the last decade there has been a search for causal variants of specific genes for psychotic disorders. There is a considerable chance that genetic variants causing risk for psychosis are the same genetic variants causing risk for a range of personality disorders.



## P43

### **Self-poisoning with medications: a nationwide investigation on the incidence, comorbidity and repetition in Norway**

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**Background:** Medication poisoning is the most common method for deliberate self-harm in the adult population. A better understanding of this problem is essential in suicide prevention and in management of the patients and relevant medications.

**Aims:** To gain firm insights on the incidence, comorbidity and repetition of poisonings with medication in the population of Norway.

**Methods:** We obtained all records on acute incidence contacts to public hospitals and emergency centers because of medication poisoning from the year 2008 through 2011, and profiled the incidences of medication poisoning according to sex, age and comorbid diagnoses in the first-recorded (index) contacts and in repetitions of the poisoning.

**Results:** We identified an average of 4114 persons who were treated for poisoning with medications each year, corresponding to a rate of 97.3 (95%CI: 94.2-100.4) per 100 000 population in Norway. Of all 19685 incident contacts from 14542 individuals, 62.4% were from women and 35.8% from young adults of 20-34 years old. 16.5% of the patients repeated poisoning with medications during the study period, with the highest rate in young people <20 years old (19.0%) and the lowest in the elderly (3.7%). At the same time, a comorbid diagnosis of psychiatric illness was present in 45.9% of the incident contacts with affective disorders (17.2%) and substance misuses (14.3%) being common diagnoses. A supplemental diagnosis of suicide attempt was given in 33.3% of the contacts. Moreover, psychiatric comorbidity and a diagnosis of suicide attempt at the index contact were strong predictors for repetition of medication poisoning regardless of sex and age.

**Conclusion:** Medication poisoning is an important health problem, especially in female and young populations. Assessment of psychiatric illness and suicidal intention is crucial in treatment of patients with medication poisoning and in efforts to prevent the repetitions.

**P44****The psychometric properties of the Hopkins Symptom Checklist – 10:  
A Rasch analysis based on Norwegian adolescent data****Annette Løvheim Kleppang<sup>1</sup>, Curt Hagquist<sup>2</sup>**

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**Introduction:** Mental health has become an important public health issue. The Hopkins Symptom Checklist is widely used for both clinical and epidemiological purposes to measure mental distress among adolescents and adults.

**Aims:** The purpose of this study was to investigate the psychometric properties of the Hopkins Symptom Checklist (HSCL-10) among adolescents in Norway using Rasch analysis.

**Methods:** The study is based on cross-sectional data from the Norwegian Youth Health Surveys, conducted by the Norwegian Institute of Public Health in 2001 and 2009. The target group comprised 15-16 year olds (10<sup>th</sup> grade students) in Hedmark County, Norway. Ten items with four response categories intended to measure anxiety and depression were analyzed with a focus on invariance, including Differential Item Functioning (DIF) across sample groups such as gender and year of investigation. Also, the categorization of the items, targeting possible multidimensionality and response dependency were analyzed.

**Preliminary results:** The HSCL-10 shows good reliability. As a whole the items work well, but one item, sleeping difficulties, clearly misfit. At a finer level of analysis some items didn't work invariantly across genders and years of investigation.

**Preliminary conclusions:** The HSCL-10 has the potential to measure mental distress among adolescents but there is room for improvements. Whether the misfitting item on sleeping difficulties should be removed needs to be further judged, also considering the content validity of the measure.

## P45

### **Alcohol and drug use among internationally adopted adolescents: Results from a population-based study of Norwegian adolescents**

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**Introduction:** Internationally adopted adolescents are considered to be at increased risk for developing mental health problems. However, little is known about problematic alcohol and drug use in this group. Such use, which is an important indicator of maladjustment, can greatly impact health behaviors later in life.

**Aims:** To examine levels of problematic alcohol and drug use in internationally adopted adolescents compared to their non-adopted peers.

**Methods:** The study is based on information from the youth@hordaland-survey which was conducted in the county of Hordaland, Western Norway, spring 2012. All adolescents born from 1993 to 1995 residing in Hordaland at the time of the study were invited to participate. Among 10 200 participants, 45 were identified as internationally adopted by use of the Central Adoption Registry in Norway.

**Results:** No differences were found between international adoptees and their peers regarding whether or not they had ever tried alcohol or illicit drugs. This is not surprising considering the low number of adoptees in the study. However, the adopted adolescents had a higher mean score on a measure of problematic alcohol and drug use (CRAFFT) compared to their non-adopted peers ( $p < 0.001$ ). More specifically, a higher proportion of adoptees responded affirmatively to the CRAFFT items concerning drinking alone ( $p < 0.001$ ), using alcohol or drugs to relax ( $p = 0.027$ ) and being told by friends or family that they should cut down on their alcohol or drug use ( $p < 0.001$ ). Adjusting the mean scores on the CRAFFT for mental health problems measured by symptoms of depression and ADHD did not alter the associations.

**Conclusions:** Our findings indicate that internationally adopted adolescents experience more problematic alcohol or drug use than their non-adopted peers, also after controlling for mental health problems.

**P46****Can municipality-based post-discharge follow-up visits including a general practitioner reduce early readmission among high-risk people 65+ years old? Results from a randomised controlled trial**

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**Introduction:** Older people admitted to hospital often have complex treatment, rehabilitation and nursing needs. Poor care coordination at the time of hospital discharge can jeopardize patient safety and result in substandard health care, and patients and their caregivers are often ill prepared for the transition from hospital to home.

**Aims:** To evaluate how municipality-based post-discharge follow-up visits including a general practitioner and municipal nurse affect early readmission among high-risk older people discharged from a hospital department of internal medicine.

**Methods:** Centrally randomised single-centre pragmatic controlled trial comparing intervention and usual care with investigator-blinded outcome assessment. The intervention was home visits with general practitioner and municipal nurse within seven days of discharge focusing on medication, rehabilitation plan, functional level and need for further health care initiatives. The visit was concluded by planning one or two further visits. Controls received standard health care services. Patients were people aged 65+ years discharged from Holbæk University Hospital, Denmark, in 2012 considered at high risk of readmission. The primary outcome was readmission within 30 days. Secondary outcomes at 30 and 180 days included readmission, primary health care and municipal services. Outcomes were register-based and analysis used intention-to-treat principle.

**Results:** 270 and 261 patients were randomised to intervention and control groups, respectively. The groups were similar in baseline characteristics. 149 planned discharge follow-up visits were carried out (55%). Within 30 days, 24% of the intervention group and 23% of the control group were readmitted ( $P=0.93$ ). No significant differences were found for any other secondary outcomes except the intervention group received more nursing municipal services.

**Conclusions:** This municipality-based follow-up intervention was only feasible in half the planned visits. The intervention as delivered had no effect on readmission or subsequent use of primary or secondary health care services.

**P47****Noise sensitivity, noise exposure and subjective health complaints**

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**Introduction:** Traffic noise is an important environmental stressor. In addition to the noise levels themselves, individual perception of noise may be essential for adverse health effects. Noise sensitivity is considered a personality trait affecting an individual's reaction to noise, expressing neuroticism. So far, noise sensitivity has been related to noise annoyance, sleep disturbances and use of psychotropic medications.

**Aims:** To investigate the association between noise sensitivity and subjective health complaints (SHC) and to assess whether gender and road traffic noise may modify the relationship.

**Methods:** Data on noise sensitivity and SHC were reported in a survey of 3262 adults. SHC included musculoskeletal, pseudo neurological, gastrointestinal, allergy and flu complaints, totally 29 items with the scale from none (0) to severe (4) according to Eriksen et al. (1999). Modelled road traffic noise ( $L_{den}$ ) at the most exposed façade was assigned to each participant's home address. Associations between noise sensitivity and SHC were analyzed in linear models.

**Results:** After adjusting for potential confounders, preliminary results showed that sum score of SHC increased by 1.29 (95% Confidence Interval (95% CI): 0.65, 1.92) for somewhat sensitive, and by 2.76 (95% CI: 2.05, 3.46) for highly sensitive individuals, both versus the non-sensitive subjects. Adjusting for road traffic noise did not change the associations. We found no effect modification by gender or by road traffic noise. A 10 dB increase in noise levels was associated with an increase of 0.36 (95% CI: -0.03, 0.75) in sum score SHC.

**Conclusions:** Our preliminary results suggest a relationship between noise sensitivity and SHC, which seems independent of the levels of road traffic noise. The relationship was not modified by gender or road traffic noise. The association with SHC was stronger for noise sensitivity than for road traffic noise.

**P48****Potential health risks associated with exposure to sulphur dioxide from a volcanic source in Iceland**

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**Introduction:** The Holuhraun volcanic eruption 2014- 2015 was the largest Icelandic eruption in 200 years. During the 6-month eruption period, it was the largest source of sulphur dioxide (SO<sub>2</sub>) in Europe. SO<sub>2</sub> has been associated with increased symptoms in individuals with respiratory disease and other sensitive individuals.

**Aims:** To determine if SO<sub>2</sub> exposure from the eruption in Holuhraun was a) a risk to the general population and b) professionals who worked near the eruption site.

**Methods:** During the eruption period, the Icelandic Environmental Agency monitored SO<sub>2</sub> levels at measuring stations placed country-wide, and brought online measuring stations already monitoring industries. The legal air quality guidelines for SO<sub>2</sub> are 350 µg/m<sup>3</sup> for one-hour and 125 µg/m<sup>3</sup> for 24-hour time intervals. From nationwide Medicines Registry we will obtain information on dispensed drugs for respiratory disease (including asthma) and Patient Registries (primary care and in-hospitalizations) we will obtain ICD-10 diagnoses made during the study period. Furthermore, a study of lung function in professionals before and after they visited the eruption site was designed.

**Results:** During the study period August 31 2014 – February 27 2015, preliminary analyses suggest that the highest measured 1-hour, and highest 24-hour concentration exceeded air quality guideline more than 10-fold in North Iceland. In the capital area, the highest concentrations were up to 5-fold the air quality guideline limit. In all regions of Iceland, both one-hour and 24-hour air quality guidelines were exceeded x-x times during the study period. Time series analyses revealing potential population health effects are underway/pending and will be presented at the conference.

**Conclusions:** Based on the exposure data, it is possible that SO<sub>2</sub> exposure posed a significant health risk to the general population and professionals who worked near the eruption site during the Holuhraun eruption.

## P49

### Occurrence of encephalitis after an influenza infection: A population-based cohort study in Norway

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**Introduction:** Encephalitis is caused by various infectious agents which may give acute encephalitis or trigger an immunological response causing encephalitis after a lag period. Influenza infection is known to be associated with various neurological complications.

**Aims:** Our aim was to determine the risk of encephalitis after influenza infection.

**Methods:** We used information from national health data-bases with information on the total Norwegian population, approximately 4.8 million individuals. All the influenza cases diagnosed in primary care during 2008-2013 were included in our analysis. The risk of being hospitalized with encephalitis after an influenza infection was estimated by applying Cox regression analyses with time-varying covariates. Various risk windows, from an influenza diagnosis until an encephalitis hospitalization (5 days, one week, two weeks, 4 weeks, 6 weeks, 8 weeks, 3 months and 6 months) were used. The analyses were adjusted for sex and year of birth ( $\leq 1980$  and  $> 1980$ ).

**Results:** There were 2316 patients hospitalized with encephalitis in the period 2008-2013. During this period 609,638 people received at least one a clinical influenza diagnosis in primary care. The risk of encephalitis after an influenza infection was significantly elevated. The risk of encephalitis decreased as the length of the risk window increased. The hazard ratio (HR) within 5 days after an influenza infection was 50.83 (95% confidence interval (CI) 35.09-73.63) while the HR after 6 months after an influenza infection was 3.33 (95% CI 2.63-4.22).

**Conclusions:** Our results indicated that there is an increased risk of encephalitis after influenza infection. The risk of encephalitis was highest a short time after an influenza infection.

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