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konferanse.

DEN 24. NORSKE EPIDEMIOLOGIKONFERANSEN

TROMSØ,
7.-8. NOVEMBER 2017

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The 24th Norwegian Conference on Epidemiology Tromsø, November 7-8, 2017

We would like to welcome you to Tromsø and the 24th conference of the Norwegian Epidemiological Association (NOFE). The NOFE conference is an important meeting point for epidemiologists to exchange high quality research methods and findings, and together advance the broad research field of epidemiology. As in previous years, there are a diversity of topics; epidemiological methods, cardiovascular disease, diabetes, cancer, nutrition, female health, musculo-skeletal diseases, infection and behavioral epidemiology, all within the framework of this years' conference theme; *New frontiers in epidemiology*.

The conference theme reflects the mandate to pursue methodological and scientific progress and to be in the forefront of the epidemiological research field. Our four distinguished keynote speakers are, in view of their expertise and innovative research profiles, invited to feature recent developments and future potentials in epidemiology. Director at The Norwegian Institute of Public Health and professor Camilla Stoltenberg will talk about a knowledge system for public health, and professor Kristian Hveem, NTNU, will talk about studying genetic variations in populations to improve the understanding of reasons for illness and health. Professor Anne Tjønneland will present some perspectives on methodology of data collection in the Danish "Diet, Cancer and Health – Next Generations" study. Finally, professor Magne Thoresen, UiO, will address some statistical challenges in modern epidemiology.

We are pleased that the EPINOR Annual Meeting is held in connection with the NOFE Annual Conference and that so many EPINOR students will join the NOFE conference.

The 2017 NOFE Annual Meeting will be held on Tuesday at 16.15 at the conference hotel, Clarion Hotel The Edge. Following the annual meeting, the Publication of the Year Award and Honorary Membership Award will be presented.

We would also like to welcome you to the Welcome Reception on Tuesday at 19.00. The Welcome Reception will be followed by dinner at the conference hotel, Clarion Hotel The Edge.

Welcome to Tromsø and NOFE 2017!

**The NOFE Steering Committee
and
The organizing committee for the NOFE 2017 Conference**

Kristin Benjaminsen Borch

Bente Morseth

Karina Standahl Olsen

Bjørn Straume

Eiliv Lund

Bente Evjen Schøning/Marie W. Lundblad (EPINOR)

Marko Lukic (EPINOR)

UiT The Arctic University of Norway

The 24th Norwegian Conference on Epidemiology

Tromsø, November 7-8, 2017

Program Overview

Tuesday, November 7th

10:15	Registration (Coffee and refreshments), Clarion Hotel The Edge
11:00	Welcome and opening: NOFE Leader Lise Lund Håheim
11:15	Keynote, invited speaker: Anne Tjønneland, Center for Kræftforskning, Kræftens Bekæmpelse <i>"Diet, Cancer and Health – Next Generations, A population based family study. Methodology of data collection and perspectives"</i>
11:45	Parallel session 1. Oral presentations: <i>Cardiovascular disease/diabetes, A1-A5</i> <i>Cancer, B1-B5</i> <i>Behavioural epidemiology, C1-C5</i>
13:00	Lunch
14:00	Keynote, invited speaker: Camilla Stoltenberg, Folkehelseinstituttet <i>"A knowledge system for public health"</i>
	Keynote, invited speaker: Siri E. Håberg, Folkehelseinstituttet <i>"Centre for Fertility and Health, a new Centre of Excellence"</i>
15:00	Parallel session 2. Oral presentations: <i>Cardiovascular disease/diabetes/obesity, A6-A9</i> <i>Various topics, B6-B9</i> <i>Nutrition, C6-C9</i>
16:00	Coffee break with refreshments
	NOFE's annual meeting
16:15-17:30	Announcement of Publication of the Year Award and Honorary Membership Award
19:00	Welcome reception
20:00	Conference dinner and entertainment, Clarion Hotel The Edge

Wednesday, November 8th

	Parallel session 3. Oral presentations:
09:30	<i>Cardiovascular disease/diabetes, A10-A14</i> <i>Cancer, B10-B14</i> <i>Behavioral epidemiology, C10-C14</i>
10:45	Coffee break with refreshments
	Keynote, invited speaker: Kristian Hveem, NTNU
11:00	<i>"Fra populasjonsbiobanker til storskala genetiske studier – presisjonsmedisinsk satsing utenfor helsevesenet"</i>
11:30	Poster viewing and coffee break
12:30	Lunch
	Keynote, invited speaker: Magne Thoresen, UiO
13:30	<i>"Some statistical challenges in modern epidemiology"</i>
14:00	EPINOR continues v/Bente Evjen Schønning
14:15	Coffee break with refreshments
	Parallel session 4. Oral presentations:
14:30	<i>Cancer, A15-A18</i> <i>Various topics, B15-B18</i> <i>Nutrition, C15-C18</i>
15:45-16:00	Closing the NOFE conference

The 24th Norwegian Conference on Epidemiology Tromsø, November 7-8, 2017

Scientific Program for Parallel Sessions

Parallel session 1

Parallel session A1-A5: Cardiovascular disease/diabetes Margarinfabrikken 1

11:45	A1	Determinants for change in cardiovascular disease risk profile after incident myocardial infarction: The Tromsø Study 1994-2016	Nilsen
12:00	A2	Prevalence of Type 2 Diabetes Mellitus among Sami and non-Sami inhabitants of Northern Norway – The SAMINOR 2 Clinical Survey	Naseribafrouei
12:15	A3	Temporal changes in systolic blood pressure and risk of atrial fibrillation in men and women; the Tromsø Study	Løchen
12:30	A4	Can traditional risk factors explain the higher risk of cardiovascular disease in South Asians compared to Europeans in Norway and New Zealand? Two cohort studies	Rabanal
12:45	A5	Asthma, asthma control and risk of atrial fibrillation: The HUNT study	Cepelis

Parallel session B1-B5: Cancer Prostneset 1

11:45	B1	Coffee consumption and risk of rare cancers in Scandinavian countries	Lukic
12:00	B2	Breast cancer women lack normal lifelong immune response after full-term pregnancies	Snapkov
12:15	B3	Does physical activity reduce the risk of colorectal cancer in women? The Norwegian Women and Cancer (NOWAC) Study	Oyeyemi
12:30	B4	Use of skin care products and risk of cancer of the breast and endometrium	Rylander
12:45	B5	Subtle alterations in gene expression detected in blood prior to metastatic lung cancer diagnosis – the NOWAC study	Nøst

Parallel session C1-C5: Behavioural epidemiology Prostneset 2

11:45	C1	Childhood socioeconomic position and behavioral pathways to adult health	Braaten
12:00	C2	What are good priorities for local health promotion in the elderly population? Choices based on a county survey in southern Norway	Johansen
12:15	C3	Major health-related behaviors and subjective wellbeing in the chronically ill individuals	Lamu
12:30	C4	Disordered eating in Sami and non-Sami Norwegian populations: The SAMINOR 2 Clinical Survey	Kvaløy
12:45	C5	Burden of disease in Norway in 2015 – results from GBD 2015	Knudsen

Parallel session 2

Parallel session A6-A9: Cardiovascular disease/diabetes/obesity Margarinfabrikken 1

15:00	A6	Short-term prognosis of chest pain in Norway	Egeland
15:15	A7	Association of occasional smoking with total mortality in the population-based Tromsø Study, 2001-2015	Løchen
15:30	A8	Pandemic Influenza Diagnosis and Subsequent Risk of Type 1 Diabetes	Ruiz
15:45	A9	Epi-genomewide methylation differences in a group of lean and obese women – A HUNT Study	Kvaløy

Parallel session B6-B9: Various topics Prostneset 1

15:00	B6	Associations between attention-deficit/hyperactivity disorder and autoimmune diseases are modified by sex	Hegvik
15:15	B7	Opportunities and barriers to current use of sensor technologies for exposure assessment	Bartonova
15:30	B8	Gender Differences in Psychiatric Comorbidity: A Population-based Study of 40,000 Adults with Attention-Deficit/Hyperactivity Disorder	Solberg
15:45	B9	Tooth extractions and mortality. A 12 ½-year follow-up of the Oslo II-study	Lund Håheim

Parallel session C1-C5: Nutrition Prostneset 2

15:00	C6	Intake of sugar-sweetened beverages in adolescents from Troms, Norway	Skeie
15:15	C7	Nutrient intake in the 7th survey of the Tromsø Study 2015-16, and comparison with Norwegian national dietary recommendations	Lundblad
15:30	C8	The typical Norwegian fishmeal – a study of the specific way of preparing and eating fish and its potential health risks or benefits	Engeset
15:45	C9	Effects of krill oil and lean and fatty fish on lipoprotein subclasses, plasma metabolites and gene expression in peripheral blood mononuclear cells	Rundblad

Parallel session 3

Parallel session A10-A14: Epidemiological methods Margarinfabrikken 1

09:30	A10	Can chance cause cancer? The surprising implications of familial association in disease risk	Valberg
09:45	A11	Adjusting for unmeasured confounding using validation data. 2-stage calibration simplified	Hjellvik
10:00	A12	Using network analysis as a tool to tease out drug utilization patterns	Svendsen
10:15	A13	Systems epidemiology and the beauty of complex designs – high risk or high gain	Lund
10:30	A14	Dynamic detection of unexpressed genes in microarray mRNA	Møllersen

Parallel session B10-B14: Female health Prostneset 1

09:30	B10	The relation of age at menarche with age at menopause: A population study of 336,778 women in Norway	Bjelland
09:45	B11	Childbirth in the years close to natural menopause – is it possible? The HUNT2 Survey	Gottschalk
10:00	B12	Pregnancy fatty acid status and newborn DNA methylation: the MoBa pregnancy cohort	Parr
10:15	B13	May oxytocin augmentation modify the risk of epidural analgesia for cesarean delivery among nulliparous women in spontaneous labor at term?	Skjeldestad
10:30	B14	Maternal chronic diseases and risk of cerebral palsy in offspring	Strøm

Parallel session C10-C14: Cancer Prostneset 2

09:30	C10	Host characteristics, sun exposure, and site-specific risk of melanoma: a large prospective cohort study in Norway	Ghiasvand
09:45	C11	Epigenetic changes predate melanoma diagnosis	Page
10:00	C12	Lifestyle predictors for non-participation and outcome in the second round of faecal immunochemical test in colorectal cancer screening	Knudsen
10:15	C13	Significantly increased penile squamous cell cancer incidence in Norway from 1956 to 2015	Oruuma
10:30	C14	Lifetime sunburns and melanoma risk	Rueegg

Parallel session 4

Parallel session A10-A14: Cancer

Margarinfabrikken 1

14:30	A15	DNA methylation in blood – challenges and possibilities using data from the Norwegian Women and Cancer cohort	Sandanger
14:45	A16	Terminal digit preference in tumour thickness measurements of melanoma: data from the national melanoma registry	Veierød
15:00	A17	Natural History of Breast Cancers Detected in the Danish Mammography Screening Programme: a Cohort Study	Zahl
15:15	A18	Predicting concentrations of persistent organic pollutants using dietary and demographic variables. The Norwegian Women and Cancer study	Berg

Parallel session B10-B14: Physical activity/nutrition

Prostneset 1

14:30	B15	Using smart devices to measure physical activity in research projects: A review of consumer wrist worn wearables	Henriksen
14:45	B16	Physical Activity and Body Composition among Adolescents; Cross Sectional Results from the Tromsø Study – Fit Futures Cohort 2010-11	Aars
15:00	B17	Associations of leisure-time physical activity and psychological distress with dementia-related mortality: The Cohort of Norway (CONOR)	Zotcheva
15:15	B18	Using metabolic profiling to explore mechanisms that cause LDL cholesterol to decrease following replacement of saturated fat with polyunsaturated fat – a randomized controlled dietary intervention study	Ulven

Parallel session C10-C14: Various topics

Prostneset 2

14:30	C15	Hormonal contraceptive use and <i>Staphylococcus aureus</i> nasal and throat carriage in a Norwegian youth population. The Tromsø Study Fit Futures 2	Stensen
14:45	C16	To which extent can variations in spine surgery rates be explained by variations in needs?	Rudolfsen
15:00	C17	Do new generations of older adults have stronger grip than previous generations? Results for three cohorts of 66-84 year olds in the Tromsø Study: 1994-2016	Strand
15:15	C18	General practice consultations and use of prescription drugs after changes to school absence policy	Bakken

A1

Determinants for change in cardiovascular disease risk profile after incident myocardial infarction: The Tromsø Study 1994-2016

Amalie Nilsen¹, Tove Aminda Hanssen^{2,3}, Knut Tore Lappegård^{1,4}, Maja-Lisa Løchen^{2,5}, Ellisiv Mathisen^{4,7}, Inger Njølstad⁵, Tom Wilsgaard⁵, Laila Hopstock³

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Introduction: Secondary prevention after myocardial infarction (MI) is suboptimal. In Norway, one of four acute-MI hospitalizations are recurrent events. Lifestyle changes with risk factor modification are associated with improved prognosis and reduced mortality.

Aims: To study change, and predictors for change, in cardiovascular risk profile after incident MI using the NORRISK-2 score.

Methods: Participants attending the Tromsø-4 Study in 1994-95 (cohort I, n=10.135) and the Tromsø-6 Study in 2007-08 (cohort II, n=8906) were followed for incident MI up to participation in 2007-08 and 2015-16, respectively. We used linear regression models to investigate changes in NORRISK-2 and predictors for risk factor modification.

Results: A total of 402 (cohort I) and 133 (cohort II) had a first-ever MI during follow-up. In cohort I the proportion of high, medium and low risk changed from 60.4%, 12.0% and 27.6%, to 33.1%, 19.4% and 47.5%. In cohort II, the proportion of high, medium and low risk changed from 45.0%, 13.0% and 42.0% to, 24.0%, 18.0% and 58.0%, respectively from baseline to second screening. The mean NORRISK-2 score increased over time in both cohorts. However, when omitting the main effects of age from the equation the mean score decreased by 1.74 points in cohort I and by 0.94 points in cohort II. Self-perceived good health, enough close friends and being physically active were statistically significant predictors for change in risk score, but only in cohort I. Education, BMI, and mental health symptoms were not significantly related to risk score change.

Conclusions: Age was the main contributor to increased NORRISK-2 score over time. With age excluded, the risk score decreased for both genders in both cohorts. Self-perceived health, friends and physical activity level were predictors for change in risk score in the first but not in the second study period.

A2

Prevalence of Type 2 Diabetes Mellitus among Sami and non-Sami inhabitants of Northern Norway – The SAMINOR 2 Clinical Survey

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4. Department of Medicine, University Hospital of Northern Norway, Harstad, Norway.

Objective. The aim of this study was to determine and compare the prevalence of type 2 diabetes mellitus (T2DM) among Sami and non-Sami inhabitants of rural districts in Northern Norway.

Methods. The SAMINOR 2 Clinical Survey was a cross-sectional population-based study performed in 2012–2014. Recruited participants were inhabitants aged 40–79 years from 10 municipalities in Northern Norway with both Sami and non-Sami populations. A total of 12 455 inhabitants were invited and 6004 responded. Participants completed self-administered questionnaires and underwent clinical examination and blood sampling. In addition to self-report, two cut-offs for HbA1c were applied to categorize diabetics; HbA1c \geq 6.2% and \geq 6.5%.

Results. Total age-standardized prevalence of T2DM (self-report and/or HbA1c \geq 6.2%) in Sami and non-Sami men was 14.5% (95% CI: 12.5–16.4) and 12.0% (95% CI: 10.4–13.5) respectively. Increasing HbA1c cut-off to 6.5% gave total age-standardized prevalence of T2DM at respectively 10.8% (95% CI: 9.1–12.6) and 9.5 (95% CI: 8.1–10.8) in Sami and non-Sami men. Total age-standardized prevalence of T2DM (HbA1c \geq 6.2%) in Sami and non-Sami women was 12.6% (95% CI: 10.8–14.3) and 9.5% (95% CI: 8.2–10.8) respectively. Corresponding prevalence with HbA1c cut-off \geq 6.5% was 8.8% (95% CI: 7.1–10.1) and 7.0% (95% CI: 5.9–8.1) in Sami and non-Sami women, respectively. Regardless of ethnicity, the prevalence of T2DM was lower in women compared to men.

Conclusion. The estimated prevalence of T2DM among inhabitants of the included municipalities was much higher compared to previous estimates, and was significantly higher among Sami women as compared to non-Sami women. There was observed no statistically significant difference in the prevalence of T2DM between Sami and non-Sami men.

A3

Temporal changes in systolic blood pressure and risk of atrial fibrillation in men and women; the Tromsø Study

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Introduction: Although cardiovascular mortality rates have declined dramatically over recent decades, age-standardized mortality rates from atrial fibrillation (AF) increased by 100%. Elevated systolic blood pressure (SBP) is one of the key risk factors for AF; however the association between long-term changes in SBP and the risk of AF in the general population has not been elucidated.

Aims: To assess the association between long-term individual changes in SBP and the risk of incident AF in a large sample of men and women from the general population.

Methods: The Tromsø Study is a large population-based longitudinal study. We included men and women who attended two surveys conducted in 1986-87 and 1994-95, were aged 20 years or older, were not pregnant during examinations, and were free of AF by 1994-95 (n=14,784). Long-term changes in SBP were calculated as a difference between the two surveys' measurements and divided into quintiles. Participants were followed up for incident AF throughout 2013. We used Cox regression to estimate hazard ratios of AF in relation to long-term changes in SBP adjusted for mean values of SBP and other cardiovascular risk factors.

Results: During 20 years of follow-up 720 (9.6%) men and 307 (4.2%) women developed AF. We found an independent association between long-term change in SBP and the risk of AF in men, but not in women. In men, the association was U-shaped: decrease in SBP by more than 4 mmHg increased risk of AF by 41%, increase in SBP by more than 15 mmHg increased the risk by 37%. Additional adjustment for change in hypertension status and in blood pressure treatment had virtually no effect on the associations.

Conclusions: Both long-term increase and decrease in SBP were associated with increased future risk of AF in men, but not in women.

A4

Can traditional risk factors explain the higher risk of cardiovascular disease in South Asians compared to Europeans in Norway and New Zealand? Two cohort studies

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Introduction: Immigrants from South Asia have increased risk of cardiovascular disease (CVD) compared to Europeans. The reasons for this excess risk are unclear, and the role of traditional risk factors is unsettled.

Aims: Our aim was to prospectively examine potential differences in the risk of first cardiovascular disease (CVD) events between South Asians and Europeans living in Norway and New Zealand, and to investigate whether traditional risk factors could explain any differences.

Methods: Participants aged 30-74 years without prior CVD were included in a Norwegian (n=16 606) and a New Zealand (n=129 449) cohort. Ethnicity and cardiovascular risk factor information was linked with hospital registry data and cause of death registries to identify subsequent CVD events. Cox proportional hazards regression was used to investigate the relationship between risk factors and subsequent CVD for South Asians and Europeans, and to calculate age-adjusted hazard ratios (HRs) for CVD in South Asians versus Europeans in the two cohorts separately. We sequentially added the major CVD risk factors (blood pressure, lipids, diabetes and smoking) to study their explanatory role in observed ethnic CVD risk differences.

Results: South Asians had higher total cholesterol (TC)/high density lipoprotein (HDL) ratio and more diabetes at baseline than Europeans, but lower blood pressure and smoking levels. The age-adjusted risk of CVD was higher in South Asians compared to Europeans being 87-92% higher in the Norwegian cohort and 42-75% higher in the New Zealand cohort. South Asians remained with significantly increased risk after adjusting for all major CVD risk factors.

Conclusions: We found that differences in TC/HDL ratio and diabetes appeared to explain some of the excess risk of CVD in South Asians compared to Europeans. Preventing dyslipidaemia and diabetes in South Asians may therefore help reduce their excess risk of CVD.

A5

Asthma, asthma control and risk of atrial fibrillation: The HUNT study

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Introduction: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is associated with adverse cardiovascular outcomes. Asthma affects as many as 30 million individuals worldwide and has negative effects on quality of life and overall health. Shared inflammatory characteristic of these diseases underpins a need of novel investigations of asthma and AF. In addition, asthma control, the primary goal of disease management, could influence the degree of inflammation and thus the potential association between asthma and AF.

Aims: To investigate the associations between asthma, asthma control and AF.

Methods: We utilized 54 567 adults from a large well-defined population cohort “The Nord-Trøndelag Health Study” (HUNT2 and HUNT3) free from AF at baseline. Asthma was self-reported and the participants were categorized into three groups: ever asthma, physician diagnosed asthma and active asthma. The latter group reported asthma medication use at baseline. Asthma control was defined according to the Global Initiative for Asthma guidelines and was categorized into three groups: controlled, partly controlled and uncontrolled. AF was ascertained by linking HUNT data with cardiologist reviewed hospital records from the two hospitals in Nord-Trøndelag.

Results: During a mean follow-up of 15.4 ± 5.8 years, 2 071 (3.8%) participants developed AF. Participants with ever asthma had an estimated 25% higher risk of developing AF (HR 1.25, 95% CI 1.10 – 1.44) compared to participants not having asthma. For diagnosed asthma and active asthma, the estimated risk of AF increased by 43% (HR 1.43, 95% CI 1.22 - 1.67) and 96% (HR 1.96, 95% CI 1.64 - 2.35), respectively. Similarly, the risk of AF was higher in participants with uncontrolled asthma (HR 1.77, 95% CI 1.28 – 2.45) than in those with controlled (HR 1.15, 95% CI 0.95 – 1.40) or partly controlled asthma (HR 1.40, 95% CI 1.15 – 1.72) when compared to those without asthma.

Conclusions: Active and uncontrolled asthma were associated with 2-fold and 1.8-fold increased risk of atrial fibrillation.

A6

Short-term prognosis of chest pain in Norway

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Introduction: There is limited oversight regarding prognosis of patients discharged from hospital or polyclinic with chest pain diagnosis.

Aims: To evaluate risk of ischaemic heart disease (IHD) diagnosis during follow-up after hospitalisation or polyclinic visit with chest pain as the main discharge diagnosis.

Methods: Patients with a main diagnosis of chest pain (ICD-10 diagnoses R072–R074) were identified in the «Cardiovascular Disease in Norway 2008-2012» project that included National Patient Register and Cause of Death Register data. Patients <18 years, patients registered with chest pain or IHD (ICD-10 diagnoses I20–I25) during a two-year look-back period (2008-2009), or patients registered with concomitant IHD diagnosis at discharge with chest pain diagnosis were excluded. The risk of having IHD (diagnosis or cause of death) during follow-up in different patient groups was evaluated using Cox proportional hazard ratios (HR).

Results: The mean (SD) age of the 68,406 chest-pain patients included in analyses was 51.6 (14.9) for men and 56.7 (15.6) for women. During follow-up, IHD was registered in 6,305 patients (9.2%) of whom 156 (2.5%) died due to IHD. In age-adjusted analyses, men were twice as likely as women to have an IHD death after discharge with chest pain-diagnosis (HR 2.0; 95% confidence interval, CI, 1.53–2.9). IHD was recognized in 2.4% of those in the lowest age quartile (18–44 years) increasing to 16.1% in the highest age quartile (≥ 66 years). Within the first 180 days of discharge, cardiovascular diagnostic procedures were reported for 71% of patients. Men were more likely to receive cardiovascular diagnostic procedures within 180 days of discharge (age-adjusted HR 1.15, 95% CI 1.13–1.17), and were more likely to receive an IHD diagnosis than women (age-adjusted HR 1.80; 95% 1.71–1.89).

Conclusions: Long-term evaluation of chest pain patients and assessments of new and existing diagnostic strategies are needed.

A7

Association of occasional smoking with total mortality in the population-based Tromsø Study, 2001-2015

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Introduction: There is a shift in the smoking population from daily smokers to light or occasional smokers. The knowledge about possible adverse health effects of this new smoking pattern is limited.

Aim: We investigated smoking habits with focus on occasional smoking in relation to total mortality in a follow up study of a Norwegian general population.

Methods: We collected smoking habits and relevant risk factors in 4020 women and 3033 men aged 30-89 years in the Tromsø Study in 2001. The subjects were followed up regarding total mortality through June 2015.

Results: Among the participants, there were 7% occasional smokers. Occasional smokers were younger, more educated and used alcohol more frequently than other participants. A total of 766 women and 882 men died during follow-up. After adjustment for confounders we found that occasional smoking significantly increased mortality by 38% (95% CI: 8-76%) compared to never smokers. We report a dose response relationship in the hazards of smoking (daily, occasional, former and never smoking).

Conclusions: Occasional smoking is not a safe smoking alternative. There is a need for information to the general population and health workers about the health hazards of occasional smoking. More work should be done to motivate this often well-educated group to quit smoking completely.

A8

Pandemic Influenza Diagnosis and Subsequent Risk of Type 1 Diabetes

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Introduction: The 2009 pandemic influenza A H1N1 (swine flu) has been associated with the development of autoimmune diseases.

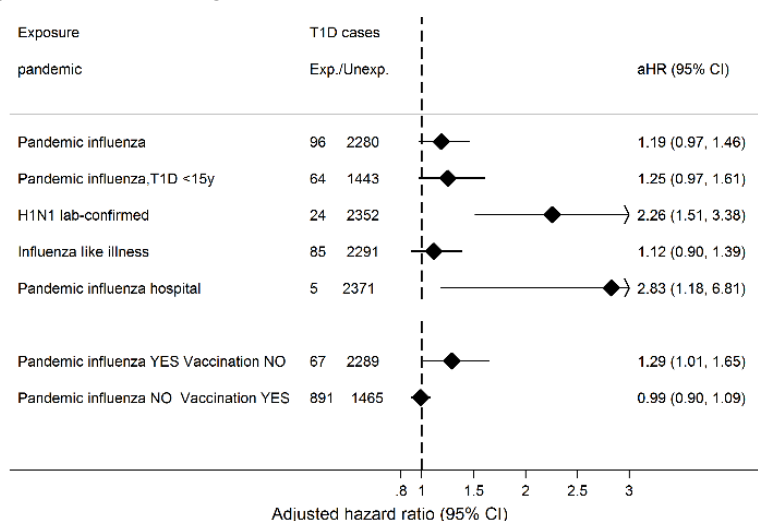
Aims: In this register-based study, we aimed to test whether pandemic influenza diagnosis was associated with increased risk for type 1 diabetes (T1D).

Methods: In this nationwide study, the Norwegian population under age 30 years was followed from June 2009 through June 2014 by linking prospectively collected data from national health registries with patient level information. We analysed data from the Norwegian Patient Register, the Primary Care Database, diabetes medication from the Norwegian Prescription Database, laboratory confirmed influenza A (H1N1) infection from the Surveillance System for Communicable Diseases and pandemic influenza vaccination date from the Norwegian immunisation registry. We defined pandemic influenza as a clinical influenza or influenza like illness diagnosis during the pandemic in Norway, or a laboratory-confirmed influenza A (H1N1). Incident cases of T1D defined as the first registration of at least one T1D in primary or specialist health care and initial insulin treatment continued for at least 6 months. We used Cox regression to estimate hazard ratio for association between pandemic influenza and subsequent risk of type 1 diabetes.

Results: Individuals registered with influenza during the 2009-2010 pandemic had an adjusted hazard ratio (aHR) for type 1 diabetes of 1.19 (95%CI: 0.97-1.46). Laboratory-confirmed influenza A (H1N1), was associated with a two-fold higher risk of T1D before age 30 years (aHR=2.26, 95%CI: 1.51-3.38). We analysed the association between pandemic influenza infection and pandemic influenza vaccination; infection alone is associated with significantly increased risk of T1D (aHR=1.29, 95%CI: 1.01-1.65), Figure 1.

Conclusions: In this large scale, population based cohort, we found evidence that pandemic influenza A (H1N1) may contribute to the risk of T1D.

Figure 1. Association between pandemic influenza diagnosis in primary or specialist care, and risk of type 1 diabetes in up to 2.26 million Norwegians.



A9

Epi-genomewide methylation differences in a group of lean and obese women – A HUNT Study

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Introduction: Differential methylation patterns in obese compared to lean individuals may reflect a bodily state heading towards adverse health outcomes. Gaining knowledge of molecular factors and pathways involved may provide potential targets for treatment and ability of risk factor assessment.

Aims: The aim was to identify genes and molecular pathways related to obesity by comparing epigenome-wide methylation in 60 obese and 60 lean young women.

Methods: Epigenome-wide association was performed with Illumina Infinium HumanMethylation450 BeadChip. Individual CpGs were used as exposure and weight groups as outcome in robust linear estimations: Model 1, no adjustments; Model 2, adjustments for smoking and batch effects; Model 3, adding estimated cell type composition. CpGs p-values were subjected to multiple testing using false discovery rate cut-offs.

Results: The two weight groups differed significantly in several obesity and metabolic related risk factors also at adolescence eleven years earlier. Differential methylation with p-values ≤ 0.05 was observed for 26982 CpG-sites, with overrepresentation of hypomethylation (78%) in obese. The study revealed 10 genome wide significant differentially methylated CpG sites linked to eight genes; *COX6A1P2/FGD2*, *SBNO2*, *TEX41*, *RPS6KA2*, *IGHE/IGHG1/IGHD*, *DMAP1*, *SOCS3* and *SETBP1* and also to an enhancer at chromosome 2. The sites linked to *TEX41*, *IGHE/IGHG1/IGHD*, *DMAP1* and *SETBP1* were novel findings, whilst *COX6A1P/FGD2*, *SBNO2*, *RPS6KA2* and *SOCS3* had been robustly identified previously. Numerous differential CpGs were linked to obesity susceptibility genes; 26 CpG sites within *KCNQ1*, 24 CpG sites within *RPTOR* and five or more within: *KCNMA1*, *MACROD1*, *NAV1*, *CADM1*, *GALNT10* and *SMAD6*.

Conclusions: Five novel CpG sites identified; four linked to *TEX41*, *IGHE/IGHG1/IGHD*, *DMAP1* and *SETBP1* and one being non-gene specific. Hypomethylation was overrepresented in obese and numerous obesity susceptibility genes contained several differentially methylated sites. This study provides potential targets associated with obesity.

A10

Can chance cause cancer? The surprising implications of familial association in disease risk

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Introduction: A wide range of diseases show some degree of clustering in families. A familial aggregation is often quantified in terms of a familial relative risk (FRR). Even if this measure may seem simple and intuitive at first glance -as an average risk prediction- its implications are not straightforward. Furthermore, there is an ongoing debate about the role of chance in cancer development, which was sparked by a Science paper by Tomasetti and Vogelstein. They claimed that two thirds of cancers are due to 'bad luck'. Cancer of the small intestine was deemed the second 'most random' of the cancers studied by Tomasetti and Vogelstein.

Aim: To estimate how the risks for a range of cancers are distributed in the population.

Methods: We use two statistical models for the distribution of risk of disease in a population: A dichotomous risk model that gives an intuitive understanding of the implications of a given FRR, and a continuous risk model that facilitates a more detailed computation of the inequalities in disease risk. Published estimates of FRRs are used to produce Lorenz curves and Gini indices that quantifies the inequalities in risk for a range of cancers.

Results: We demonstrate that even a very moderate familial association in disease risk implies a very large difference in risk between individuals in the population, and we further demonstrate the relation between point estimates of FRRs and the distributions of risks in the population. We show that e.g. small intestine cancer is likely to have a risk distribution that is as skewed as the distribution of wealth in the world.

Conclusions: The risks of the cancers studied are very unevenly distributed in the population. Determinants other than randomness is likely to be much more important for the development of e.g. small intestine cancer.

A11

Adjusting for unmeasured confounding using validation data. 2-stage calibration simplified

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Introduction: In epidemiology, one typically wants to estimate the risk of an outcome associated with an exposure after adjusting for confounders. Sometimes outcome and exposure, and maybe some confounders, are available in a large data set (full data), whereas some important confounders are only available in a validation data set, typically a subset of the full data. A generally applicable method in this situation is the 2-stage calibration (TSC) method. However, the TSC method requires two parameter estimates (λ and μ) that are difficult to compute in commonly used statistical software packages, like R.

Aims: To present, and test the performance of, a simplified, easy-to-implement version of the TSC, where estimates of λ and μ are not needed, for the case where the validation data is a subset of the main data.

Methods: Let C_{all} denote the confounders available in the validation data, and C_{some} the subset available in the full data. The standard TSC estimator is $\tilde{\beta}' = \hat{\beta} - \lambda v^{-1}(\hat{\gamma} - \bar{\gamma})$ where $\hat{\gamma}$ and $\bar{\gamma}$ are effect estimates (e.g. incidence rate ratios) from the validation data, adjusted for C_{some} and C_{all} , respectively, and $\hat{\beta}$ is the effect estimate from the full data, adjusted for C_{some} . Further, $\lambda = \text{cov}(\hat{\beta}, \hat{\gamma} - \bar{\gamma})$, and $v = \text{var}(\hat{\gamma} - \bar{\gamma})$. Assuming that $\lambda = v$, the simplified TSC estimate is $\tilde{\beta} = \hat{\beta} - \hat{\gamma} + \bar{\gamma}$, and $\text{var}(\tilde{\beta}) = \text{var}(\hat{\beta}) - \text{var}(\hat{\gamma}) + \text{var}(\bar{\gamma})$. The performance of $\tilde{\beta}'$ and $\tilde{\beta}$ was compared in an incidence rate ratio setting using both simulated and real data, and for odds-ratio and relative risk estimates using real data.

Results: The simplified version performed generally better than the standard version.

Conclusions: The simplified 2-stage calibration method is easy to implement and performed well. It could be applied e.g. in studies with exposure and outcome from national registries and additional confounders available from health surveys.

A12

Using network analysis as a tool to tease out drug utilization patterns

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Introduction: Understanding the drug utilization patterns at population level is often of interest. However network analyses have rarely been used to explore and visualize these patterns. Our aim was to implement and test the feasibility of this approach in a large dataset from the Norwegian prescription registry (NorPD).

Methods: The dataset contains all pharmacy-dispensed medicines to elderly in Norway during 2013-2014. It consists of more than 40 million dispensed prescriptions from more than 500'000 persons aged 65 and older. We have used Stata 14.2 with the package nwcommands to manage and analyze the data. We have analysed and visualised gender differences, differences between Sogn and Fjordane and Østfold (lowest and highest consumption of medicines in Norway) and finally we have used the method to explore how the use of medicines changed before and after admission to a geriatric ward by linking NorPD data with the Patient Registry. To form the network medicines had to be dispensed within 100 days of each other.

Results: Although the analysis is computationally demanding, it can be used to explore differences between age stratified, gender stratified and specific medicine using sub-populations. The approach is much more suitable for sub-population analyses or analyses using a sample of the full population. The method can show the full pattern of use including unexpected co-use. We will show the results visually at NOFE and describe the process of preparing and running these analyses.

Conclusion: Network analyses is a promising approach to use in studies drug utilization patterns, and it can be applied to a wide variety of research questions.

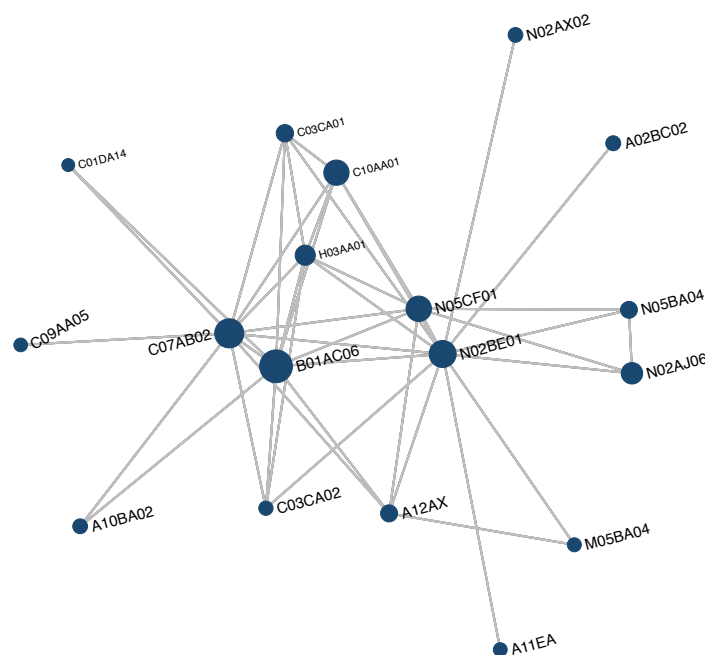


Figure 1. Network of all nodes (substances) where at least 10000 elderly have used the drug within 100 days of each other. Size of node represents the number of users.

A13

Systems epidemiology and the beauty of complex designs – high risk or high gain

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Introduction: Systems epidemiology is a new scientific discipline combining cancer epidemiology with basic biology and clinical research by introducing functional genomics (methylation, transcriptomics). This challenges both standard designs and statistical methods.

Aim: To uncover the rich potential for new and complex designs in systems epidemiology.

Methods: Traditionally epidemiologists has used prospective studies for calculation of individual risk as RR (relative risk). However, RR is an estimator without a time dimension, a nuisance parameter. With new technologies the dynamics of functional genomics can be followed over time before, at and after diagnosis within a prospective design. This includes conceptually different measurements; exposures measured once or more including biomarkers, DNA (SNPs) constant throughout life and functional genomics changing dynamically over time.

Results: Several new design options under the concept of processual research with results taken from the Norwegian Women and Cancer postgenome biobank study will be presented. Functional genomics can be measured in blood or tissues. Typically, one example will be from breast cancer research looking at the differences in gene expression over time from 8 years before diagnosis, at diagnosis and 8 years after demonstrating the opportunities for mechanistic research. The systems epidemiology approach of exploring data and building mathematical models in the large questionnaire study and then testing the hypothesis in gene expression analyses will use as an example breast cancer, gene expression and fertility. Important methodological issues related to the interpretations of single genes or gene sets with information from reductionist experiments to be discussed.

Conclusion: Cancer epidemiology needs to move from static risk estimation towards the dynamics of the carcinogenic process. This complexity demands a complex interaction with biologists, clinicians and statisticians.

A14

Dynamic detection of unexpressed genes in microarray mRNA

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Introduction: In a cell nucleus, the DNA strings with all their genes is stored. Any cell activity – good or bad – is dependent on the transcription of DNA to a multiple of shorter RNA strings. This is referred to as gene expression, measured as the quantity of mRNA strings corresponding to a specific DNA sequence. A major obstacle for statistical analysis on gene expression data is the presence of noise, which makes it difficult to draw valid conclusions. In microarrays, so called *negative control probes* measure the noise, whereas *regular probes* measure the actual gene expression. If the distribution of a regular probe is sufficiently different from the noise distribution, its corresponding gene is considered expressed. The standard method for estimating the noise distribution relies on normality assumption and a cut-off dependent on user-set parameters. The normality assumption does not reflect the actual noise distribution, and the result is sensitive to the parameters.

Aims: A new method, quantifying the *dissimilarity* between a gene and the noise, not relying on normality assumption, is presented.

Method: Let $p_{noise}(x)$ and $p_{probe,j}(x)$ be the probability density functions (pdfs) of the noise and probe number j , respectively. Then the Kullback-Leibler information D is defined as

$$D(j, noise) = \int p_{probe,j}(x) \log \frac{p_{probe,j}(x)}{p_{noise}(x)} dx.$$

Results: Each probe is no longer classified as expressed or not expressed, but its dissimilarity to the noise distribution is measured. The method is demonstrated on a data set from the NOWAC study with 256 samples, analysed on microarrays with about 47, 000 probes. A random sample of negative controls is set aside for validation. The dissimilarity between regular probes and noise will be presented as a distribution, and compared with the standard method using the validation set.

Conclusions: The strength of the new method is its dynamic approach to noise estimation, and possibility of a data-driven threshold instead of user-set parameters.

A15

DNA methylation in blood – challenges and possibilities using data from the Norwegian Women and Cancer cohort

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Introduction: Epigenome wide association studies (EWAS) using blood have successfully identified markers related to diseases, e.g. cancer risks. Furthermore, DNA methylation is a highly informative marker of exposures, e.g. duration and intensity of smoking, with some alterations remaining even 35 years after cessation. It has however, been argued that these alterations are confounded by changes in the blood cell composition. Despite the large increase in number of studies, a number of challenges remain.

Aims: To describe methodological and technological challenges as well as opportunities using DNA methylation data from blood in prospective cohorts, exemplified with data from the Norwegian Women and Cancer cohort using a case-control design for three different cancers.

Methods: DNA methylation data from the Illumina 450k platform is available for prospective breast and lung cancer cases and their age matched controls. For prospective melanoma cases and their age matched controls DNA methylation data is from the new Illumina 850k (EPIC) platform. The consequences of this change will be explored as well as the blood cell composition estimates using DNA methylation and gene expression.

Results: A large part of the variation in DNA methylation data is explained by technological variables like position on the chip and plate as well as batch effects. The different layout of the phased-out, current and future technologies, e.g. design of the 850k chip compared to the 450k chip or to sequenced data introduces new challenges. Further, blood cell composition can be estimated based on profiles of the data, but differ when using gene expression and DNA methylation data. Further, there are challenges when linking DNA methylation data to gene expression data.

Conclusions: DNA methylation data in blood from prospective cancer cases holds great promise, but there are a number of methodological and technological pitfalls that needs careful consideration in prospective studies of cancer.

A16

Terminal digit preference in tumour thickness measurements of melanoma: data from the national melanoma registry

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Introduction: Vertical tumour (Breslow) thickness is recorded in the Norwegian Malignant Melanoma Registry (NMMR) since 2008. T-stage (T1:≤1.0 mm, T2:1.01–2.0 mm, T3:2.01–4.0 mm and T4:>4.0 mm) is the cornerstone of disease classification, forming basis for patient management and prognosis estimation.

Aims: To investigate precision (number of digits recorded) and terminal digit bias (over-representation of certain digits) in Breslow thickness, and consequences for melanoma staging.

Methods: We included all new melanomas in NMMR, 2008–2015. Vital status and date/cause of death from Cause of Death Registry. A smoothing model is fitted to estimate the underlying distribution of Breslow thickness without digit preference.

Results: In 2008–2015, 13 386 patients were diagnosed with a first primary invasive melanoma. Breslow thickness was recorded for 13 057 (97.5%). Mean age at diagnosis was 62.8 years (range 2–98) and median thickness 1.0 mm (range 0.09–85). Thickness was recorded to one decimal place for 78.2%, but also as whole numbers (15.6%) and with two digits after the decimal point (6.2%). Thin tumours were recorded with more precision than thicker tumours. Five was the dominating terminal digit, and the terminal digit 1 was reported in lower frequencies than other terminal digits (among those with one/two digits after the decimal place). Use of the terminal digits 0 and 5 increased with increasing thickness. Preliminary results after fitting a smoothing model indicate that terminal digit preference increased the proportion of patients with T1 tumours and decreased the proportion with T2.

Conclusions: According to guidelines, thickness should be measured to the nearest 0.1 mm but rounding off and a marked preference of terminal digits 0 and 5 were found. Pathologists, clinicians and epidemiologists should be aware that clustering of thickness data around T-stage cut-points may impact melanoma staging with consequent effect on patient management and prognosis.

A17

Natural History of Breast Cancers Detected in the Danish Mammography Screening Programme: a Cohort Study

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Introduction: Analyses of incidence changes during the introduction of organized mammography screening in Sweden and Norway 20-30 years ago suggested that the natural history of many screen-detected invasive breast cancers is spontaneous regression. In Denmark 20% of the population were invited to mammography screening for 1991-94, while the remaining 80% were invited to a first time screening in 2007-10. In Midt-Jylland women aged 50-69 years were invited to a prevalence screening in 2008-9 and then followed-up with biennial screening.

Aim: Here we study the potential of regression of invasive breast cancer in a population where organized screening has recently been introduced.

Method: We compared cumulative breast cancer incidence in age-matched cohorts of women residing in Midt-Jylland before and after the initiation of public screening. A screened group including 120,500 women aged 50-64 years was followed for 6 years after the first invitation to the program. A staggered control group including 114,000 women in the same age range 50-64 years was also followed for 6 years; 4 years without screening and 2 years when they entered the screening program. Screening attendance was 77% in both groups. Data were obtained from the Danish Cancer Registry.

Results: Cumulative risks of breast cancer were 1897 (screened group) and 1175 per 100,000 (control group) after 4 years of follow-up (62% more cancers in the screened group). After 6 years follow-up and a prevalence screening of the control group, the cumulative cancer incidences were 2760 vs. 2417 per 100,000 women, respectively; RR=1.14; (95% CI, 1.08-1.20). The differences in cumulative rates were 722 and 343 per 100,000 women after 4 and 6 years.

Conclusions: Most of the incidence during screening are detection of lesions which natural fate is to regress and not early diagnosis.

A18

Predicting concentrations of persistent organic pollutants using dietary and demographic variables. The Norwegian Women and Cancer study

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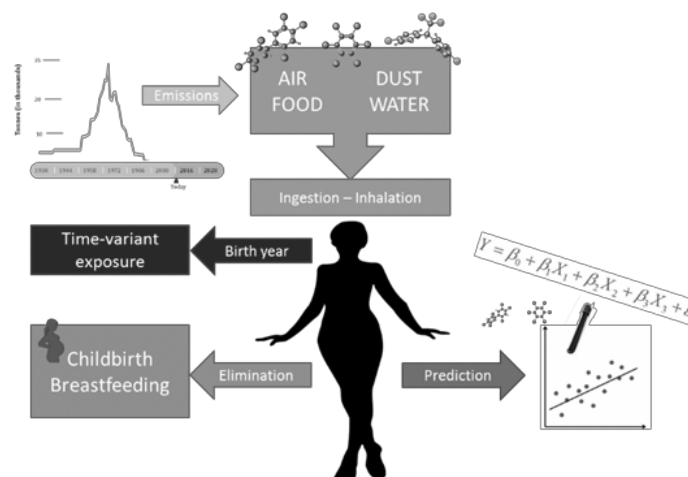
Background: Health effects of persistent organic pollutants (POPs) are difficult to study in humans as the sample number and funding is often limited. Still, dietary and lifestyle variables may predict blood concentrations of POPs. If there is acceptable agreement with measured concentrations, prediction of concentrations in many subjects could be feasible in studies of health effects in large epidemiological studies like the Norwegian Women and Cancer Study (NOWAC).

Aims: To develop statistical models for predicting concentrations of POPs in NOWAC women, using comprehensive food frequency questionnaires (FFQs) and blood concentrations.

Materials and methods: Personal information, FFQs and blood concentrations of POPs were obtained from two subsets from the NOWAC cohort. The most important variables for predicting selected POP concentrations in one subpopulation (N=311) were identified and a corresponding regression model was constructed. The models were validated by predicting concentrations in another subpopulation (N=108). Measured and predicted values were compared by correlation coefficients and weighted Cohen's κ was calculated as a measure of inter-method agreement for quartile categorization of women according to their POP concentrations.

Results: The models explained 22, 33, 34, 44, 43, 43 and 44 % of the variance in p,p'-DDE, PCB -118, -138, -153, -180 and Sum PCBs, respectively. The most important predictors were birth year, breastfeeding and weight change, whereas dietary variables were of varying importance. The predicted blood concentrations were moderately correlated with the measured values with $r_s = 0.24, 0.33, 0.41, 0.50, 0.56,$ and 0.54 for p,p'-DDE, PCB -118, -138, -153, -180 and sum PCBs, respectively. Similar, weighted Cohen's κ was 0.15, 0.24, 0.36, 0.39, 0.40, and 0.42, respectively.

Conclusion: PCB exposure estimated from FFQs show acceptable validity in relation to PCB concentrations in serum, and for quartile categorization of women according to their POP concentrations. The results justify the prediction of selected PCB concentrations in the whole NOWAC cohort.



B1

Coffee consumption and risk of rare cancers in Scandinavian countries

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Introduction: Studies conducted to explore the association between heavy coffee drinking and the risk of less frequently diagnosed cancer sites are scarce.

Aim: To quantify the association between filtered, boiled, and total coffee consumption and the risk of bladder, esophageal, kidney, pancreatic and stomach cancers.

Method: We used data from the Norwegian Women and Cancer Study and the Northern Sweden Health and Disease study. The information on coffee consumption was available from 193,439 participants, out of which 25% were men. We used multivariable Cox proportional hazards models to calculate hazard ratios (HR) with 95% confidence intervals (CI) for five cancer sites by consumption category of total coffee intake.

Results: Compared to light coffee consumers of filtered coffee (≤ 1 cup/day), heavy filtered coffee consumers (≥ 4 cups/day) had a multivariable adjusted HR of 0.74 of being diagnosed with pancreatic cancer (95% CI 0.57-0.95, p for trend across categories = 0.01). We did not observe significant associations between overall and boiled coffee intake and any of the study outcomes in the analyses of the entire study sample and in the analyses stratified according to gender and smoking status. We found an increased risk of bladder cancer among never smokers who were heavy drinkers of filtered and coffee overall (HR_{heavy vs. low} = 1.86, 95% CI 1.12-3.10, p for trend across categories = 0.03; HR_{heavy vs. low} = 1.87, 95% CI 1.01-3.45, p for trend across categories = 0.08 respectively).

Conclusion: Our data suggest that an increased consumption of filtered coffee might reduce risk of pancreatic cancer. We did not find evidence of an association between coffee consumption and the risk of esophageal, kidney, or stomach cancer sites. An increased risk of bladder cancer was confined to never smokers only.

B2

Breast cancer women lack normal lifelong immune response after full-term pregnancies

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Introduction: There is a large body of evidence demonstrating long-lasting protective effect of full-term pregnancies (FTPs) against breast cancer. Despite extensive research, processes underlying this protection remain obscure. Notably, the main theories attempting to explain this phenomenon focus on the local changes in the mammary gland rather than on the systemic processes.

Aims: In this work, we aimed to study the pregnancy-associated differences in peripheral blood gene expression profiles between healthy women and women diagnosed with breast cancer, and thus attempted to provide novel insights into the influence of FTPs on breast carcinogenesis.

Methods: We used a systems epidemiology approach by modelling breast cancer incidence as a function of parity in the Norwegian Women and Cancer (NOWAC) cohort, and then testing the resulting mathematical model using gene expression profiles from blood in a subcohort of these women: the NOWAC post-genome cohort. Lastly, we undertook a gene set enrichment analysis for immunological gene sets.

Results: A linear trend fitted the dataset showing an 8% decrease in risk for each FTP, independent of stratification on other risk factors and lasting for decades after a woman's last FTP. However, when we looked at gene expression, we found that 756 genes showed linear trends in cancer-free controls (FDR 5%), but this was not the case for *any* of the genes in breast cancer cases. Gene set enrichment analyses revealed 588 significantly enriched gene sets (FDR 5%), most of which were of immunologic origin.

Conclusions: We suggest that, after resolution at birth, the immunological tolerance induced by pregnancy promotes lifelong changes in the immune system that hamper breast cancer development. The role of the immune system in FTP protection against cancer should be studied profoundly utilizing both basic research and epidemiology study designs.

B3

Does physical activity reduce the risk of colorectal cancer in women? The Norwegian Women and Cancer (NOWAC) Study

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Introduction: Colorectal cancer (CRC) remains the second most common cancer in women worldwide. It is the second most occurring cancer in women in Norway, and the most common among women above the age of 70. Norway had the highest rate of colorectal cancer in women worldwide in 2012, with a rate of 53.8 per 100,000.

Physical activity (PA) has consistently been associated with reduced risk of CRC. However, this has only been demonstrated more consistently in men, while results of studies in women have been largely equivocal.

Aim: To prospectively examine the relationship between PA and the risk of CRC among women.

Method: We used the NOWAC study – a nationally representative cohort linked with the Norwegian Cancer Registry. We followed 79,184 participants who were free of cancers at enrolment. The participants were aged 30-70 (median age of 51 years) at enrolment in 1991. During an average of 14.6 years of follow-up and 1.16 million person-years, 885 cases of colon and 426 cases of rectal cancers were diagnosed. The median age of diagnosis was 65 years. We used Cox proportional hazards regression to compute the hazard ratios.

Results: We found no association between PA and the risk of colon cancer, at baseline and using repeated measurements, when women with PA level 9-10 were compared to those with PA level 5-6 (at baseline: HR = 0.80, 95% CI 0.56-1.12; *p*-trend = 0.76; using repeated measurements: HR = 0.79, 95% CI 0.51-1.21, *p*-trend = 0.15).

Likewise, we found no association between PA and the risk of rectal cancer (at baseline: HR = 1.40, 95% CI 0.94-2.10; *p*-trend = 0.87; using repeated measurements: HR = 1.31, 95% CI 0.78-2.19, *p*-trend = 0.33).

Conclusions: The women population may need to look beyond PA in order to reduce their risk of colorectal cancer.

B4

Use of skin care products and risk of cancer of the breast and endometrium

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Introduction: Use of skin care products such as body lotion, facial cream and hand cream is common among Norwegian women. Several components in these consumer products (e.g. parabens, phthalates, bisphenols and UV-filters) are classified as known or suspected endocrine disruptors, i.e., compounds that are able to interfere with the endocrine function in humans and wildlife. Concerns have therefore been raised whether extensive use of cosmetics and skin care products could increase the risk of hormone related diseases, e.g. breast cancer and endometrial cancer.

Aims: To investigate the effect of skin care product use on the risk of pre- and postmenopausal breast cancer and cancer of the endometrium among Norwegian women.

Methods: We used data from the Norwegian Women and Cancer study merged with information from the Cancer Registry of Norway. 114 794 participants who returned a questionnaire that included questions on use of skin care products were considered eligible for inclusion. Analyses of pre- and post-menopausal breast cancer and endometrial cancer were carried out in sub-cohorts of the initial sample. Heavy users of skin care products were defined as those creaming their body two times per day or more. Cox proportional hazard models were used to investigate the effect of skin care product use on the risk of breast and endometrial cancer.

Results: Heavy users of skin care products experienced no increased risk of pre-menopausal breast cancer (Hazard ratio (HR, 95% confidence interval): 1.09 (0.89, 1.33)), postmenopausal breast cancer (HR: 1.04 (0.76, 1.41)) or endometrial cancer (HR: 0.79 (0.35, 1.79)) as compared to the light users. We found no evidence of different effects of use of skin care products across the various breast cancer subtypes.

Conclusions: Our preliminary results display no evidence of an increased risk of breast cancer or endometrial cancer among heavy users of skin care products.

B5

Subtle alterations in gene expression detected in blood prior to metastatic lung cancer diagnosis – the NOWAC study

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Introduction: In 2015, there were about 3000 new cases of lung cancer in Norway and around half were diagnosed in women. Cancerogenesis and tumor progression are processes that have systemic responses and recent studies have indicated that there are molecular functional genomic signals, possibly related to immune system alterations, that can be detected in blood before cancer diagnosis.

Aims: This study aimed to assess signals in blood gene expression prior to lung cancer diagnosis in a nested case-control study (N=132 cases of lung cancer, 132 age- and storage-matched controls) using prospective blood samples from the population based Norwegian Women and Cancer cohort.

Methods: We assessed differentially expressed genes among cases and controls by employing linear models for microarray data ('limma') analyses. We further conducted analyses focusing on signals related to time to diagnosis by using our recently developed statistical methods. These methods explore genes as groups according to common changes with time to diagnosis, so called 'curve groups', and calculate local in time statistics across time to diagnosis to reveal subtle differences in gene expression that may not be evident when evaluating genes individually across time to diagnosis.

Results: Preliminary results indicate differentially expressed genes in the metastatic cases as compared to their controls and among those cases that were sampled closest to time of diagnosis. No genes were significantly different across all cases and controls. Further, significant curve groups were identified for the time period closest to diagnosis. Explorations of gene ontology categories and possible biological processes of interesting genes will be presented at the conference.

Conclusions: Focusing analyses of gene expression data on time to diagnosis and metastatic cancers revealed subtle alterations in gene expression in blood collected prior to cancer diagnosis.

B6

Associations between attention-deficit/hyperactivity disorder and autoimmune diseases are modified by sex

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Introduction: Several studies have demonstrated associations between neuropsychiatric disorders, such as attention-deficit/hyperactivity disorder (ADHD), and the immune system, including autoimmune diseases. Since ADHD and many autoimmune diseases show sex-specific properties, such associations may also differ by sex.

Aims: Explore possible associations between autoimmunity and ADHD, and to evaluate whether these associations vary by sex.

Methods: Using Norwegian national registries, we performed a cross-sectional study based on a cohort of 2 500 118 individuals to investigate whether ADHD is associated with common autoimmune diseases. Associations between ADHD and autoimmune diseases in females and males were investigated with logistic regression and effect modification by sex was evaluated. Several subanalyses were performed.

Results: The strongest association was found between ADHD and psoriasis in females, adjusted odds ratio (adjOR) = 1.57 (95% confidence interval: 1.46-1.68) and males, adjOR = 1.31 (1.23-1.40); p-value for interaction < 0.0001. Furthermore, among females, ADHD was associated with Crohn's disease, adjOR = 1.44 (1.16-1.79) and ulcerative colitis, adjOR = 1.28 (1.06-1.54). In contrast, males with ADHD had lower odds of Crohn's disease, adjOR = 0.71 (0.54-0.92), in addition to a trend for lower odds of ulcerative colitis, adjOR = 0.86 (0.71-1.03); p-values for interaction < 0.0001 and 0.0023, respectively. In a group of females where information on smoking and body mass index was available, adjustment for these potential mediators did not substantially alter the associations.

Conclusions: Our findings support previously reported associations between ADHD and diseases of the immune system. The associations differ by sex, suggesting that sex-specific immune-mediated neurodevelopmental processes may be involved in the etiology of ADHD.

B7

Opportunities and barriers to current use of sensor technologies for exposure assessment

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Introduction: New sensor technologies are available for air quality measurements. They could increase the coverage of air quality measurements, and provide individualized information. This could establish exposure profiles with high temporal and spatial resolution, giving information on specific important microenvironments such as traffic. However, questions arise to what extent the technologies are mature for this kind of use.

Aims: The CITI-SENSE project (<http://co.citi-sense.eu>) aimed among other, to investigate sensor technologies to provide individually specific information on air quality.

Methods: From September 2015 to August 2016, we have used at any time a subset of over 60 static and 8 portable platforms using metal oxide sensors, providing information about nitrogen oxides, ozone and particulate matter. The units underwent laboratory and field calibration. The static platforms were placed outside selected public kindergartens in Oslo. Forty volunteers were carrying the portable sensor packs for five days each.

Results: The expectations that the units will provide measurements directly comparable to reference air quality monitors were not met. The platforms require field calibration which is complicated by the fact that the signal is sensitive to local chemical and meteorological conditions. In addition, the portable units operating in conjunction with a mobile phone were difficult for the volunteers to manage. The frequent recordings of position and the Bluetooth communication was a significant drain on the phone battery, rendering continuous monitoring impossible. However, using statistical properties of the signal to construct a high-resolution map has the potential to fulfill the requirements for accurate and precise exposure estimates.

Conclusions: The sensor technologies show significant potential, but a monitoring system based on a network of low-cost sensors is not necessarily cheaper to establish and operate than traditional technologies, and its nature requires rethinking how measurements are used.

B8**Gender Differences in Psychiatric Comorbidity: A Population-based Study of 40,000 Adults with Attention-Deficit/Hyperactivity Disorder**

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Introduction: Previous studies on gender differences in psychiatric comorbidity among ADHD patients have been small and shown conflicting results. Knowledge of gender-specific comorbidity is important to provide tailored treatment and prevention strategies.

Aims: To assess the potential for gender specific interventions, we examined gender specific psychiatric comorbidities among adults with and without ADHD.

Methods: By linking several Norwegian national registries, 40,103 adults with ADHD (44% females), were compared with the remaining population 1,661,103 (49% females), born 1967-1997 and followed until 2015. The prevalence differences (PDs) and ratios (PRs) of anxiety, bipolar, major depressive, personality, schizophrenia spectrum and substance use disorders (SUD) in both genders were evaluated using Poisson regression. Interaction by gender was analyzed on additive (PDs) and multiplicative (PRs) scales. The proportion of psychiatric disorders attributable to ADHD was calculated.

Results: PDs among females with and without ADHD were significantly larger than corresponding PDs among males for anxiety, depression, bipolar and personality disorders, e.g. depression: 24.4 (95% CI, 23.8-24.9) in females versus 13.1 (12.8-13.4) in males. PDs were significantly larger in males for schizophrenia and SUD, e.g. SUD: 23.0 (22.5-23.5) in males versus 13.7 (13.3-14.0) in females. The proportions of psychiatric disorders in the population attributable to ADHD ranged from 5.6 to 16.5%.

Conclusions: PDs associated with ADHD were larger in females than males for four of six psychiatric disorders. To tailor appropriate intervention strategies, clinicians treating adults with ADHD should acknowledge these frequent and gender specific psychiatric comorbidities. The possibility of underlying ADHD when adults present with severe psychiatric symptoms is emphasized by the high population attributable proportions.

B9

Tooth extractions and mortality. A 12 ½-year follow-up of the Oslo II-study

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Introduction: Attention on the associations between oral infections to systemic diseases is increasing. Any association between tooth extractions and mortality has not been fully explored.

Aims: To study the predictivity of number of tooth extractions on mortality over a 12 ½ -year follow-up in elderly men.

Methods: We have performed a 12 ½ -year follow-up of the prospective cohort Oslo II from 2000. The study was the second screening of the Oslo-study of 1972/73. Screening data from 6530 men were eligible for analyses. Oral health information on infections and tooth extractions were self reported. Tooth extractions were grouped as 0, 1-4, 5-9, 10-28, and 29-32, the latter considered to be edentulous. Cox proportional hazards regression analyses were adjusted by age, age and established oral infection confounders, and age and established cardiovascular diseases (CVD confounders. Statistics Norway supplied the mortality data.

Results: In all, 2358 men had died in the period from 2000 to 2012 of whom 742 died from CVD and 1616 men from other causes. There were 4157 men who reported the number of tooth extractions, 673 had no extractions, and 1687 men reported extraction but not the number of these. The trend by tooth extraction category adjusted for CVD confounders were significant ($p < 0.05$) for total mortality and non-CVD causes, but also for CVD when age-adjusted. The hazard rate (HR) for category of 29-32 extractions versus no extractions for non-CVD mortality was 1.50 (95% confidence interval (CI) 1.12-2.00), and for total mortality HR=1.46 (95% CI 1.11-1.92), CVD confounder adjusted. For CVD mortality was age-adjusted HR=1.81 (95% CI 1.18-2.77).

Conclusions: A high number of tooth extraction is associated with increased risk of total mortality and non-CVD mortality, but the association with CVD mortality was weaker. Multiple tooth extractions reflect long term exposure to oral infections.

B10

The relation of age at menarche with age at menopause: A population study of 336,778 women in Norway

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Introduction: A woman's age at menopause influences her life course fertility, aging and risk of early death. Also age at menarche has been associated with future health, but it remains uncertain whether age at menarche is related to age at menopause.

Aims: To estimate the association of age at menarche with age at menopause. We also estimated the interval from menarche to menopause (reproductive period) according to age at menarche.

Methods: In this retrospective cohort study, we included 336 778 women, aged 48-71 years, from the Norwegian Breast Cancer Screening Program (2006-2014). Data was obtained by self-administered questionnaires. We used the Kaplan-Meier method and Cox proportional hazard models to estimate the associations of age at menarche with age at menopause.

Results: Overall, median age at menopause was 51 years [interquartile range (IQR) 49-54 years]. Women with menarche at age 16 or age ≥ 17 had menopause one year later (median 52 years, IQR 49-54 years) than women with menarche at age 13 (median 51 years, IQR 49-54 years, reference group) (crude hazard ratios 0.95; 95% CI: 0.93-0.97 and 0.95; 95% CI: 0.92-0.99). Among women with menarche at age 15 or younger, the hazard ratios of menopause were non-different from the reference group ($P_{\text{non-linearity}} < 0.001$). Median duration of the reproductive period was 38 years (IQR 35-41 years). Since age at menopause was similar for most menarche groups, the reproductive period decreased with increasing age at menarche ($P_{\text{non-linearity}} < 0.001$). Women with menarche at age ≤ 9 had at least 9 years longer reproductive period than women with menarche at age ≥ 17 (median 43 years versus 34 years).

Conclusions: We found that age at menopause was almost independent of age at menarche. Accordingly, women with early menarche had several years longer reproductive period than women with late menarche.

B11

Childbirth in the years close to natural menopause – is it possible? The HUNT2 Survey

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Introduction: Women's mean age at first childbirth has increased. It has been suggested that women are unable to give birth within a 10-year interval prior to menopause, and that such 10-year interval is independent of age at menopause.

Aims: To study the proportions of women who gave birth ≤ 5 years and ≤ 10 years prior to menopause, and whether childbirth in these intervals were dependent of age at menopause and number of childbirths.

Methods: In this cross-sectional study, we included 4157 women, born 1925-1940, from the HUNT2 Survey (1995-1997). We calculated the proportions of women who gave birth ≤ 5 and ≤ 10 years prior to menopause in the study sample as a whole, and according to age at menopause and number of childbirths.

Results: Overall, 2.7% of the women gave birth ≤ 5 years, and 11.7% gave birth ≤ 10 years prior to menopause. Among women with menopause before age 45 ($n=344$), the proportions of women with childbirth ≤ 5 years and ≤ 10 years prior to menopause were 23.5% and 55.5%, respectively. Among women with menopause at age 50 or older ($n=2670$), only 0.1% and 3.4% gave birth ≤ 5 years and ≤ 10 years prior to menopause. The higher number of childbirths, the higher was the proportion of women who gave birth ≤ 5 years and ≤ 10 years prior to menopause. Among women with menopause before age 45, 31.4% of women with 1-2 childbirths gave birth ≤ 10 years prior to menopause compared to 82.1% of women with ≥ 5 childbirths.

Conclusions: More than 10% of all women gave birth within 10 years prior to menopause. Childbirth close to menopause was associated with early menopause and many childbirths. Our findings suggest that absolute age is a better determinant for women's fecundity than age at menopause.

B12

Pregnancy fatty acid status and newborn DNA methylation: the MoBa pregnancy cohort

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Introduction: Maternal fatty acid status in pregnancy may influence early life programming of the immune system and susceptibility to atopy in children through epigenetic modification.

Aims: To investigate if omega-3 status in pregnancy is associated with DNA methylation of candidate genes relevant to immune function or fatty acid biosynthesis in newborns, and if methylation correlates with candidate gene expression. Genome-wide methylation of individual CpGs was examined secondarily.

Methods: We measured fatty acids in maternal whole-blood phospholipids and newborn DNA methylation (Illumina HumanMethylation450 BeadChip), in 934 mother-child pairs from the Norwegian Mother and Child Cohort. We regressed fatty acid concentrations (%) on methylation, adjusting for covariates and cell-type, and calculated direction of effects and gene-based p-values with the “A-clustering” method. Methylation and gene expression (Illumina HumanWG-6 V3 or HT-12 platform) correlations were examined in 276 women from the NOWAC postgenome cohort.

Results: Differential cord blood DNA methylation ($p < 0.05$) was observed for 7 of 20 candidate genes relevant to immune function (*SATB1*, *BCL6*, *TNF- α* , *STAT3*, *GATA3*) or fatty acid elongation (*ELOVL2*, *ELOVL6*). The individual omega-3 fatty acids EPA, DPA, and DHA showed distinct associations. P-values were smallest for EPA and DPA with *SATB1* methylation: $p = 4.46 \times 10^{-6}$ (negative direction) and $p = 2.20 \times 10^{-4}$ (positive direction), respectively. *SATB1* encodes a transcription factor and chromatin organizer essential for controlling genes participating in T-cell development and activation. Methylation at CpG sites within candidate genes correlated with available gene transcripts. Genome-wide associations at the CpG level were not statistically significant.

Conclusion: This population based study suggests that genes relevant to immune function and fatty acid status are under epigenetic regulation by DNA methylation, and that methylation patterns in newborns could be influenced by maternal omega-3 fatty acid status during pregnancy.

B13

May oxytocin augmentation modify the risk of epidural analgesia for cesarean delivery among nulliparous women in spontaneous labor at term?

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Introduction: Maternal age is an established risk factor for Cesarean delivery (CD), whereas epidural analgesia and oxytocin augmentation may modify this relation.

Aims: To investigate the effects and interactions of epidural analgesia, oxytocin augmentation and maternal age on the risk of CD.

Methods: In all, 416 386 nulliparous women with spontaneous onset of labor, ≥ 37 weeks of gestation, singleton infants in cephalic presentation during 2000–2011 from Norway and Denmark were included. In this case-control study main exposure was maternal age, whereas epidural analgesia, oxytocin augmentation, birth weight and time-period were explanatory variables. Chi-square test and logistic regression were used to estimate associations and interactions.

Results: The CD rate increased consistently with maternal age, both overall and in strata of epidural analgesia and oxytocin augmentation. We observed strong interactions between maternal age, oxytocin augmentation and epidural analgesia on the risk of CD. Women with epidural analgesia generally had a reduced risk of CD when oxytocin was used compared to when not used. In Norway, this applied to all maternal age groups, but in Denmark only for women ≥ 30 years. Among women without epidural, oxytocin augmentation was associated with an increased risk of CD in Denmark, while no difference was observed in Norway.

Conclusions: Our results suggest that oxytocin augmentation in nulliparous women with epidural analgesia might be associated with a reduced risk of CD in labors with spontaneous onset, but not in nulliparous women without epidural analgesia. This needs further investigation.

B14

Maternal chronic diseases and risk of cerebral palsy in offspring

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Introduction: Cerebral palsy (CP) is the most common developmental motor disability of childhood affecting approximately 2 pr. 1000 live born. For most cases, antenatal origin is likely, but causal pathways are still unexplored. Genetic aspects, as well as risk factors around conception and pregnancy are important areas for investigation.

Aims: To investigate the impact of maternal chronic disease status on risk of CP in offspring.

Methods: Information on maternal chronic diseases diagnosed before or during pregnancy were extracted from more than 2.7 million births during 1967-2013 using the Medical Birth Registry of Norway. By record linkage to other national registries, we identified 6781 children with CP. Log binominal regression models were used to estimate risk of CP by maternal disease status. To explore the role of genetics, analysis were repeated by paternal disease status.

Results: Several maternal diseases implied a more than 2-fold increased risk of CP in offspring. Maternal diabetes type 1 and type 2 were associated with a 2.4-fold excess risk (relative risk (RR) 2.4, 95% confidence interval (CI) 1.6-3.6) and a 2.8-fold excess risk (RR 2.8, 95% CI 1.6-5.0), respectively. Lupus erythematosus had a 2.6-fold (RR 2.6, 95% CI 0.8-8.0), Chron's disease a 2.5-fold (RR 2.5, 95% CI 1.3-4.8) and multiple sclerosis a 2.2-fold (RR 2.2, 95% CI 1.1-4.9) increased risk. Paternal diseases did not imply the same excess risk as maternal diseases. No paternal disease implied a statistically significant increased risk of CP in offspring and the majority of RR ranging from 0.9-1.2.

Conclusions: We found associations between several maternal chronic diseases and CP in offspring. As no similar associations were found for paternal disease, it is possible that changes in intrauterine environment mediated by chronic inflammation or medication, may be part of the causal pathways.

B15

Using smart devices to measure physical activity in research projects: A review of consumer wrist worn wearables

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Introduction: Regularly conducted population-based studies contribute important new knowledge to medical research. Participation rates are declining worldwide, and researchers are challenged to develop new data collection strategies. With recent advances in mobile sensor technology, privately collect physical activity data can potentially be used as an addition to existing data collection methods. With an increasing number of diverse brands, there is a need for an overview of device sensor support and applicability in research projects.

Aims: The purpose of this review was to get an overview of the status of wrist-worn fitness wearables, analyze the availability of relevant fitness sensors the last seven years, and understand how these trends have affected brand interest. We also aimed to review brand usage in research projects and compare common brands in terms of developer access to collected data for future research.

Methods: We conducted a thorough search in online and offline wearable device databases. For each identified brand, we found additional devices from official brand web sites. We searched for existing wrist-worn fitness wearables with accelerometers, and mapped brand, release year and supported sensors relevant for fitness tracking. For the 11 most relevant brands, we conducted a Medline and ClinicalTrial.gov search to determine brand usage in research projects.

Results: We identified 423 unique devices from 132 different brands. The highest number of new brands were introduced in 2014, with a steady decline in following years. Sensor support increased every year and, excluding accelerometers, photoplethysmography (pulse) is the most common sensor. The five brands most often used in research projects are Fitbit, Garmin, Withings, Misfit and Apple.

Conclusions: There is a large number of devices available with various capabilities. New devices are released every year, promising better measurements and user experience. However, only a few, well established brands, are frequently used in research projects.

B16

Physical Activity and Body Composition among Adolescents; Cross Sectional Results from the Tromsø Study – Fit Futures Cohort 2010-11

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Introduction: The prevalence of overweight and obesity (OWOB) among Norwegian children and pre-adolescents is high, but few studies have investigated body composition among adolescents. There is a lack of Norwegian studies of the association between physical activity and OWOB among adolescents.

Aims: To study the associations between levels of physical activity and Body Mass Index (BMI) and waist circumference in Norwegian adolescents.

Methods: The Fit Futures Cohort Study was conducted in the Tromsø and Balsfjord municipalities in 2010-11. Out of 1,117 invited there were 1,038 participants (participation rate of 93%). We included 959 boys and girls under the age of 18 with a valid measurement of BMI and waist circumference. The associations between self-reported hours of physical activity in leisure time and BMI and waist circumference were explored using linear regression, and adjusted for potential confounders identified by univariable analyses.

Results: There were no statistically significant relationships between self-reported physical activity and BMI for either gender in crude- or adjusted models. Physical activity was associated with waist circumference in univariable analysis for girls, with the least physically active having higher waist circumference ($p < 0.01$). The association remained significant after adjustments for high school specialization and parental body shape ($p < 0.01$). For boys, a borderline significant association was observed between physical activity and waist circumference ($p = 0.05$), but the association was not significant after adjustments for high school specialization and parental body shape ($p = 0.64$).

Conclusions: Self-reported levels of physical activity was not associated with body mass index among adolescents in northern Norway, but was associated with waist circumference for girls.

B17**Associations of leisure-time physical activity and psychological distress with dementia-related mortality: The Cohort of Norway (CONOR)**

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Introduction: Leisure-time physical activity (LPA) has been proposed as a protective factor against dementia, whereas psychological distress (PD) has repeatedly been associated with an increased risk of dementia. Little is known about how LPA is associated with dementia risk among psychologically distressed.

Aims: To investigate the associations of LPA and PD with dementia-related mortality (DRM), and whether the association between LPA and DRM differs according to PD.

Methods: Data from the GENIDEM project was used. 36,945 individuals from the Cohort of Norway (CONOR) aged 50-74 years at baseline in 1994-2002 were included. LPA and PD were assessed through questionnaires, whereas DRM was obtained through the Norwegian Cause of Death Registry, with follow-up time from baseline until January 1st 2015. Adjusted cox regression analyses, with attained age as timescale, were used to estimate hazard ratios (HR) and confidence intervals (CI).

Results: Compared to inactivity, LPA was associated with a decreased DRM risk; light LPA (HR=0.73, 95%CI 0.59-0.89); hard LPA (HR=0.61, 95%CI 0.49, 0.77). A statistically significant difference in DRM risk was observed between light and hard LPA ($p<0.05$). PD was associated with an increased DRM risk (HR=1.45, 95%CI 1.16-1.81). Among non-distressed, LPA was associated with a decreased DRM risk; light LPA (HR=0.77, 95%CI 0.61-0.97); hard LPA (HR=0.65, 95%CI 0.51-0.84). The same applied for those with PD; light LPA (HR=0.57, 95%CI 0.35-0.94); hard LPA (HR=0.42, 95%CI 0.22-0.82). Although the decrease in DRM risk appeared to be larger for the PD group than for the non-PD group, there was no significant interaction between LPA and PD on DRM ($p=0.38$).

Conclusions: Participating in LPA, especially hard LPA, was associated with a reduced DRM risk, whereas PD was associated with increased DRM risk. LPA appears to be equally strongly related with DRM among those with PD and among those without PD, underlining the importance of LPA, even among distressed.

B18

Using metabolic profiling to explore mechanisms that cause LDL cholesterol to decrease following replacement of saturated fat with polyunsaturated fat – a randomized controlled dietary intervention study

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Introduction: Replacing saturated fatty acids (SFA) with polyunsaturated fatty acids (PUFA) reduces the plasma LDL cholesterol (LDL-C) and thereby the risk of cardiovascular disease (CVD). However, molecular links between dietary intake of fatty acids, metabolic dysregulation and CVD remain to be discovered. Recently, comprehensive metabolic profiling or “metabolomics” has emerged as an important field in order to identify new early CVD biomarkers. To date, however, few have applied metabolomics in dietary intervention studies. We recently showed in an 8 week double blind randomized controlled dietary intervention study that exchanging a few commercially available food items with similar food items with improved fat quality (replacing SFA with PUFA) reduced total and LDL-C by 9 and 11 %, respectively compared to the control group, among healthy subjects with moderate hypercholesterolemia (n=99).

Aim: The aim of the present study was to perform a wide-ranging profiling of candidate metabolites that are associated with CVD risk in order to understand further the potential mechanisms of improved fat quality on human health.

Method: We analysed serum by targeted metabolomics using multiple platforms (both NMR and LC-MS technology).

Results: Preliminary results show that among more than 300 metabolites, 166 were differently changed between the groups before and after intervention ($p \leq 0.05$ and $FDR \leq 0.1$). We will present details about which metabolites and how they may associate with LDL-C levels at the meeting.

Conclusion: Applying metabolomics in a randomized controlled dietary intervention trial hold the potential to extend our knowledge intake of fat quality on CVD risk.

C1

Childhood socioeconomic position and behavioral pathways to adult health

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Introduction: The last decades there has been a growing interest in the influence of biological, environmental, behavioral, and psychosocial exposures in early life on adult health outcomes. In utero, childhood and adolescent risk factors are investigated, with a particular focus on birth weight, according to coronary heart disease, respiratory disease, and diabetes. Risk of certain cancer sites has also been linked to early life experiences.

Aims: To examine the association between childhood socioeconomic position (CSEP) and self-reported health status (SRH) at study enrolment among middle-aged women, and to explore the potential mediating effect of adult socioeconomic position (SEP) together with some corresponding childhood and adult lifestyle factors. SEP was measured as years of education, gross household income, and marital status.

Methods: We used data from 90,901 women enrolled in The Norwegian Women and Cancer Study between 1996 and 2003. Multinomial logistic regression models were applied to estimate the relative risk ratios (RRR) with 95% confidence intervals (CI) of reporting very poor or poor self-reported health status compared to good, by CSEP adjusted for SEP and life-course lifestyle factors. The indirect effect of the potential mediating factors was computed by the method developed by Karlson, Holm and Breen.

Results: For very poor SRH as the outcome, both very good (RRR=1.92), poor (RRR=1.36) and very poor (RRR=4.78) CSEP showed increased risk compared to good CSEP in the multivariable models. The J-shaped association with CSEP was also evident for poor SRH. The strong adverse effect of very poor CSEP was significantly mediated by both adult SEP, adult lifestyle, and childhood lifestyle in both SRH outcomes.

Conclusions: We observed a clear J-shaped association between childhood socioeconomic position and poor/very poor self-reported health status at study enrolment, still after taking into account the mediating effect of adult socioeconomic position and life-course lifestyle factors.

C2

What are good priorities for local health promotion in the elderly population? Choices based on a county survey in southern Norway

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Introduction: To ensure well-being in the elderly population and decrease pressure on health services, health promotion and illness prevention should be on the political agenda.

Aims: To identify areas of priority for health promotion amongst the elderly on a local and regional level based on a short county survey.

Methods: A cross-sectional survey was conducted in three southern Norwegian counties in 2015/2016. 22702 adults, 18 years and over, were invited to participate. A public health questionnaire with 36 questions was utilised. The overall response rate was 42.7%, but for those aged 67-79 and over 80 years, 62.8% and 43.9%, respectively. This included 2393 women and 1942 men. Collected data were merged with socioeconomic variables from central registers at Statistics Norway.

Self-reported health on a dichotomous scale, excellent/good versus fair/poor/very poor, was used as dependent variable in a logistic regression model. Independent variables included in the model included sense of coherence, Oslo 3-item Social Support, frequency of participation in activities, regular physical activity, eating habits, alcohol use, and access to various facilities like public buildings and local services, cultural and sport venues, the neighbourhood, outdoors and nature areas. The model was controlled for gender, education, and continuous age and income.

Results: For good/excellent health among elderly people the analyses identified five variables (OR, 95 % CI) with significant association ($p < 0.05$): sense of coherence (3.04, 1.97-4.67), physical activity (2.30, 1.70-3.07), access to outdoors/recreational areas (2.20, 1.24-3.95), social support (1.68, 1.09-2.60), and fish consumption (1.46, 1.03-2.07). Several of the non-significant variables had a high correlation with health initially, likely still of interest in this context.

Conclusions: Main areas of priority for health promotion amongst the elderly identified were social support, access to the outdoors and physical activity.

C3

Major health-related behaviors and subjective wellbeing in the chronically ill individuals

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Introduction: Major behavioral risk factors are known to affect overall subjective wellbeing (SWB). Comprehensive analyses of the association between health behaviors and overall individuals' wellbeing can enable decision-makers to take early policy interventions that minimize costs and the burden of illness. The main aim of this study was to examine variations in SWB as a result of changes in health behaviors in chronically ill individuals.

Methods: Data were obtained from the Multi-Instrument Comparison (MIC) study, which was based on an online survey administered in six OECD-countries – Australia, Canada, Germany, Norway, UK and the US. Data on seven disease-groups has been used: arthritis, asthma, cancer, diabetes, depression, hearing and heart problems (N=6173). A model with an instrumental variables estimation using heteroscedasticity-base instruments was conducted to explore the effect of health and health behaviors on SWB. This method is appropriate to tackle the problem of unobserved omitted variables.

Results: All levels of physical activity was beneficial to wellbeing for chronically ill individuals when health is assumed to be the same. However, only a maximum of 30 minutes moderate-intensity physical activity had an effect on SWB ($p < 0.01$) after adjusting for health. Smokers had 1.6-percentage point lower SWB than non-smokers ($p < 0.05$). Alcohol drinking had no significant effect on SWB. The adverse effect of BMI was trivial and only significant at 10% level. This effect disappears if health is assumed constant across respondents.

Conclusions: Health protective behaviors were generally associated with high well-being while health-risk behaviors were associated with low well-being. The important conclusion is that behavioral risk factors influence subjective well-being mainly through the intervening health.

C4

Disordered eating in Sami and non-Sami Norwegian populations: The SAMINOR 2 Clinical Survey

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Introduction: Very little knowledge exists concerning disordered eating amongst the Sami population. Increased awareness with regards to prevalence and associated risk factors could assist with preventive early intervention efforts in this population with increasing obesity problems.

Aims: The aim of this study was to investigate disordered eating (DE) amongst Sami compared to non-Sami residing in northern Norway.

Methods: Adults aged 40–69 years; 1811 Sami (M: 844, F: 967) compared to 2578 non-Sami (M: 1180, F: 1398) individuals originating from the SAMINOR 2 Clinical Survey (2012–2014) based on the population of 10 municipalities in northern Norway. In a cross-sectional design, stratified on sex and ethnicity, associations were tested between DE (Eating Disturbance Scale, EDS-5) and factors such as age, education level, BMI category, anxiety and depression, physical activity, and consumption of snacks.

Results: No overall significant ethnic difference in DE was identified, although comfort eating was reported more often by Sami individuals ($p=0.01$). Regardless of ethnicity and sex, symptoms of anxiety and depression were associated with DE ($p<0.001$). Furthermore, DE was more common at lower age and higher BMI and education levels were protectively associated with DE among Sami men ($p=0.01$). DE was associated with low physical activity in men and in non-Sami women (Sami men: OR=2.4, CI 95% 1.4-4.0, non-Sami men: OR=2.2, CI 95% 1.4-3.6 and non-Sami women: OR=1.8, CI 95% 1.2-2.9) and so was the consumption of snacks (Sami men: OR=2.6, CI 95% 1.3-5.0, non-Sami men: OR=1.9, CI 95% 1.1-3.1 and non-Sami women: OR=2.1, CI 95% 1.3-3.4).

Conclusions: There were no significant differences with regards to overall DE comparing Sami with non-Sami although comfort eating was reported more often by Sami. There were significant sex- and ethnic differences related to DE and physical activity, snacking and education level.

C5

Burden of disease in Norway in 2015 – results from GBD 2015

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Introduction: Burden of disease estimates describes how different diseases, injuries and risk factors affect a population in terms of non-fatal health loss (morbidity) and mortality. The international Global Burden of Disease project (GBD) publishes yearly updates of disease burden in 195 countries and territories.

Aims: Describe disease burden in Norway in terms of number of deaths, years of life lost (YLL), years lived with disability (YLD) and disability-adjusted life-years (DALY). Further, examine the degree of mortality disease burden attributable to risk factors.

Methods: The GBD database consist of more than 80,000 data-sources collected worldwide. Cause of death registries are primary data-sources for mortality estimations. Published and unpublished health data and scientific reports are main sources for morbidity estimation. YLLs are based on expected remaining life years when a death occurs. YLDs are products of disease prevalence and associated health loss. DALYs are the sum of YLLs and YLDs for a given disease. Burden of disease is calculated for 249 causes of death, 315 disease and injuries, and 79 risk factors.

Results: Non-communicable diseases dominated the Norwegian disease burden in 2015. Three of four deaths occurred in the population above 70 years. Thus, the largest causes of deaths were diseases most common in the older population, namely cardiovascular diseases and dementia. Cancers were also important causes of deaths. Because cancers also affects the population younger than 70 years, these were the largest cause of YLLs. Musculoskeletal disorders and mental disorders were the dominating causes of YLDs. Cancers caused the highest number of DALYs (204 212 DALYs), followed by musculo-skeletal disorders (163 455 DALYs), cardiovascular diseases (163 061 DALYs) and mental disorders (146 882 DALYs). Smoking, unhealthy diet and high blood pressure were the most important risk factors for premature mortality (YLLs).

Conclusion: The importance of the non-fatal diseases musculoskeletal disorders and mental disorders on the Norwegian disease burden are similar to the importance of the large killers cardiovascular diseases and cancers. Several thousands premature deaths could be avoided by reducing smoking, unhealthy diet and blood pressure in the Norwegian population.

C6

Intake of sugar-sweetened beverages in adolescents from Troms, Norway

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Introduction: High intake of sugar-sweetened beverages (SSB) leads to dental decay, and has been associated with weight gain and chronic disease.

Aims: The objective of this paper was to study the intake of SSB and predictors of SSB intake in adolescents from Troms, Norway.

Methods: A cross-sectional analysis from the Tromsø Study – *Fit Futures* (93% participation rate). Descriptive statistics and logistic regression analyses were performed.

Results: We included 426 female and 444 male students aged 15-17 years. 31.8% of the girls and 61.0% of the boys drank at least one glass of SSB per day. The adjusted OR of daily SSB drinking for boys vs. girls was 3.74 (95% CI 2.68-5.22). In the sex-specific multivariable analyses, other dietary habits such as eating snacks weekly or more often (OR 3.67, 95% CI 2.03-6.64 in girls, OR=2.03, 95% CI 1.29-3.19 in boys), and drinking >1 glass of artificially sweetened beverages daily vs. seldom/never (OR 4.05, 95% CI 2.22-7.36 in girls, OR=2.20, 95% CI 1.30-3.72 in boys) were associated with daily SSB drinking. The same was seen for fruit juice. Girls seldom/never eating breakfast had an OR for daily SSB drinking of 4.03 (1.88-8.63) compared to daily eaters, OR in boys was 2.02 (0.97-4.22). Daily snuffing was also associated with daily SSB drinking, OR=4.93 (2.40-10.14) in girls and 2.18 (1.14-4.16) in boys. Similar tendencies were found for smoking. Students in vocational studies, particularly boys (OR 1.59, 1.03-2.46) tended to be more likely to be daily SSB drinkers.

Conclusion: Particularly boys were frequent consumers of SSB, despite efforts at reducing consumption in recent years. In both sexes, prevalence of daily drinking was higher than in national studies. Socioeconomic factors, dietary factors and other health related factors contributed to explaining the variation in daily SSB drinking.

C7

Nutrient intake in the 7th survey of the Tromsø Study 2015-16, and comparison with Norwegian national dietary recommendations

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Introduction: Diet accounts for most of the disease burden in Norway according to the Global Burden of Disease project. The Norwegian dietary recommendations are evidence-based and built on the Nordic Nutrition Recommendations from the Nordic Council of Ministers. To ensure adequate nutrient intake, enhance health and reduce the risk of non-communicable diseases, recommendations are provided for both macro- and micronutrients.

Aim: We aim to study nutrient intake and adherence to the national recommendations in a population-based study.

Methods: A total of 21083 women and men aged 40 years and older living in the Tromsø municipality participated in the 7th survey of the Tromsø Study in 2015-16. Data collection included questionnaires, biological sampling and clinical measurements. A validated food frequency questionnaire (FFQ) (13 pages, 261 questions regarding numerous foods items, meals and drinks) were used to collect dietary information. The individual nutrient intake was estimated using the food and nutrient calculation system KBS at the University of Oslo. We will compute nutrient intake and compare with current national nutrient recommendations, stratified by age, sex and socioeconomic status.

Results: A total of 15146 participants completed the FFQ (72% of the subjects attending the survey, 46% of the originally invited sample). Preliminary results will be presented. A combination of information from the FFQ, other self-report data, biological samples, clinical measurements, and later disease endpoint registries, offers extensive opportunities for future research collaborations.

Conclusion: This study will map the adherence to the national nutrient guidelines in a general adult population. It will contribute with new knowledge to prevent non-communicable diseases. Research opportunities combining information from the comprehensive data collection in the Tromsø Study goes far beyond the ongoing research projects.

C8

The typical Norwegian fishmeal – a study of the specific way of preparing and eating fish and its potential health risks or benefits

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Introduction: The Norwegian Woman and Cancer (NOWAC) study have had a special interest in fish consumption; thus, the questionnaire has quite detailed questions about fish. This made it possible to divide between lean and fatty fish, and between poached and fried lean fish when analysing the data. Results from analysis of fish consumption and risk of colon cancer revealed an increased risk of colon cancer with high consumption of poached lean fish. More details about the Norwegian fish consumption are required to be able to explain the results from that study.

Aims: The aim of the project is to identify the different preparation methods for fish and the composition of a typical fishmeal, in order to later investigate possible associations with disease.

Methods: The standard NOWAC questionnaire was extended with more detailed questions about fish consumption (preservation method, what kind of side dishes eaten along with the fish, cooking methods of side dishes, etc) and sent to 12 272 Norwegian women.

Results: The results identified differences in the way Norwegian women eat and prepare their fish.

Conclusions: Since poached lean fish is most widely used in Norway, it is of importance to reveal whether it is the fish itself that increases the risk of cancer, or if it is other foods or drinks consumed together with the fish, or perhaps the preservation method like salting or smoking that gives the increase. This will also have impact on the nutrition advice given to the public in the future.

C9

Effects of krill oil and lean and fatty fish on lipoprotein subclasses, plasma metabolites and gene expression in peripheral blood mononuclear cells

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Introduction: Nutrigenomics is research focusing on how nutrients affect health by altering the expression of genes and ultimately metabolism. Observational studies and randomized controlled trials (RCTs) show that intake of omega-3 fatty acids reduce cardiovascular disease risk. These fatty acids affect several different pathways, including lipid metabolism and inflammation by acting directly and indirectly by altering gene expression. Omega-3 fatty acids from different dietary sources, such as fish or krill oil, may have different effects because they exist in different lipid forms.

Aim: To study the effect of intake of omega-3 fatty acids from different dietary sources on low-molecular weight metabolites (LMWM), lipoprotein subclasses and transcription of genes in peripheral blood mononuclear cells (PBMCs) to understand the underlying mechanisms behind the beneficial effect of omega-3 fatty acids.

Methods: In an eight-week randomised parallel study, 36 healthy adults with slightly elevated fasting triglycerides were randomised to receive either fish, krill oil or control oil. Subjects in the fish group consumed fish according to dietary guidelines, while the control and krill group received 8 capsules/day. The weekly intake of marine omega-3 fatty acids were 4103 mg in the fish group and 4654 mg in the krill group. We analysed LMWM and lipoprotein subclasses using nuclear magnetic resonance spectroscopy. Gene expression in PBMC was measured using real-time quantitative polymerase chain reaction.

Results: Krill oil altered the lipoprotein subclass profile compared to the intake of fish and control oil by increasing phospholipids and cholesterol in the smallest VLDL subclass. There were no changes in LMWM. Results on gene expression effects will be presented.

Conclusion: By applying a nutrigenomic approach in an RCT we show that metabolic profiling and PBMC gene expression analysis may extend our knowledge of CVD risk after intake of krill oil and fish.

C10

Host characteristics, sun exposure, and site-specific risk of melanoma: a large prospective cohort study in Norway

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Introduction: Cutaneous melanoma is ranked among the leading cancers in Norwegian men and women. The association between melanoma and host characteristics and pattern and amount of sun exposure may differ according to the anatomic site of melanoma, which suggests different causal pathways responsible for melanoma at different anatomic sites.

Aim: To prospectively investigate whether melanomas arising on the trunk, head/neck, and limbs, differ in relation to the strength of their associations with personal characteristics and sun exposure.

Method: We used data from the Norwegian Women and Cancer study, a large population-based cohort study established in 1991. The cohort includes self-reported information on hair, eye and skin colour, and number of large asymmetric nevi as well as information on weeks per year spent on sunbathing vacations and annual number of severe sunburns in different age decades. Multivariable incidence rate ratios (IRRs) and 95% confidence intervals (CIs) were estimated using Poisson regression, with time dependent variables.

Results: During follow-up of 161,829 women, to December 2015, 1382 cases of invasive melanoma were diagnosed. The lower limb was the most common tumour site (n=521), followed by the trunk (n=466), upper limb (n=220), and head/neck (n=111). Risk estimates for skin and hair colour and number of asymmetrical nevi did not significantly differ by anatomic site of melanoma ($0.08 \leq P$ for heterogeneity ≤ 0.69). Highest tertile of sunbathing vacations was associated with higher risk of trunk and lower limb, compared to upper limb tumours, and inversely associated with head/neck tumours (P for heterogeneity = 0.007). More than one week of sunbathing annually during childhood and adolescence was associated with increased risk of lower limb tumors, compared to the other sites.

Conclusions: This large population-based prospective study of northern European women with long-term follow-up, sheds further light on the different aetiological pathways of melanoma development.

C11

Epigenetic changes predate melanoma diagnosis

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Introduction: Melanoma account for a disproportionately large amount of deaths among skin cancers patients. Therefore, early detection of melanoma is crucial for a good prognosis. A perfect biomarker would ideally be non-invasive and predictive of future events. This would for example include epigenetic modifications, such as DNA methylation, in either skin or blood.

Aim: To find association between DNA methylation markers and time until diagnosis of melanoma.

Material: All incident cases of melanoma in the Norwegian Women and Cancer study (NOWAC) with a pre-diagnostic blood sample stored (n = 183). DNA methylation were measured on 850000 CpG positions with Illumina HumanMethylaiton EPIC chip.

Statistical Methods: Robust linear regression with adjustment for multiple testing.

Results: After quality control, 158 cases with complete information remained. Of which 51 had more than 6 years until diagnosis and 35 had less than 2 years between sampling time and date of diagnosis. We plan to look for distinct epigenetic profile associated with time until diagnosis.

Conclusion: Methylation changes may be found in melanoma patients years before the clinical diagnosis of the disease.

C12

Lifestyle predictors for non-participation and outcome in the second round of faecal immunochemical test in colorectal cancer screening

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Background: To reduce colorectal cancer (CRC) mortality through population-based screening programs using faecal tests, it is important that individuals continue to participate in the repeated rounds of screening.

Aim: To identify lifestyle predictors for discontinuation of faecal immunochemical test (FIT) screening after the first round, as well as lifestyle predictors for colorectal neoplasia detected in the second-round FIT screening.

Methods: In this longitudinal study, we invited 6959 individuals aged 50–74 years from south-east Norway for a first round of FIT screening and to complete a self-reported lifestyle questionnaire on demographic factors, body mass index (BMI, kg/m²), smoking habits, physical activity, consumption of alcohol and dietary items. Two years later, we estimated the associations between these factors, non-participation and screening results in the second round of FIT screening using adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Of the 3114 responders to the questionnaire who completed the first-round FIT and who were invited to participate in second-round FIT screening, 540 (17%) did not participate. The OR and (95% CI) for discontinuation of FIT screening after the first round was 1.61 (1.24–2.10) for current smoking compared with non-smoking; 2.01 (1.25–3.24) for BMI ≥ 35 kg/m² compared with BMI 16.9–24.9 kg/m² and 0.70 (0.52–0.94) for physical activity in the third quartile vs the first. Among participants, smoking, high BMI and high alcohol consumption were associated with an increased odds of detecting colorectal neoplasia (n=107).

Conclusions: These results may indicate that Norwegian FIT screening participants who discontinue after the first round have lifestyle behaviors associated with increased risk of CRC.

C13

Significantly increased penile squamous cell cancer incidence in Norway from 1956 to 2015

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Introduction: Penile cancer is a rare disease, reported to occur at rates around 1/100,000 men in several Western countries. The most common morphology type is squamous cell carcinomas (SCC). 48% of penile cancers are HPV positive, while the most common HPV types are HPV 16, 18 and 6/11. Boys might be included in the HPV vaccination program from 2018.

Aims: To describe penile SCC incidence, mortality and survival trends in Norway 1956-2015.

Methods: Penile cancer data 1956–2015 was extracted from Cancer Registry of Norway. We calculated penile SCC age-standardised incidence and mortality rates per 100,000 man-year. 5-year relative survival (RS) was calculated with cohort and period approach and were age-standardised using International Cancer Survival Standard weights. By stage, only penile SCC localized and regional spread cases were included into the 5-year RS analysis. Penile SCC incidence, mortality and survival trends were assessed with joinpoint regression, and the annual percentage changes (APC) were calculated.

Results: In total, 1596 cases of penile cancer were diagnosed in Norway during the period 1956-2015. Penile cancer diagnosed among men below age 55 was relatively rare. SCC was by far the most common histological type and accounted for 92.4% of the total penile cancer cases. The age-standardised incidence rate of penile SCC has been steadily increased from 1956, APC=0.80% (95%CI: 0.46;1.15). The penile SCC age-standardised mortality rates were quite stable over the 60-year period investigated but still showed statistically significant increase, APC=0.47% (95%CI: 0.10;0.85). The age-standardised 5-year RS trend over the whole 60-year study period was increasing, but fell short of statistical significance, APC=0.08% (95%CI: -0.19; 0.36).

Conclusions: Penile SCC incidence and mortality have increased significantly from 1956 to 2015. This rise may be explained by increased HPV prevalence in the population.

C14

Lifetime sunburns and melanoma risk

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Aims: To identify trajectories of sunburns over lifetime and assess the effect of the trajectories identified on melanoma risk.

Methods: We used data from the Norwegian Women and Cancer Study (NOWAC), a population-based prospective cohort with complete 25 years of follow-up on melanoma. We used the average number of sunburns/year for seven age-decades (from 0-9 to 60-69) in a group-based trajectory model to identify clusters of individuals following similar progressions of sunburns over time. Bayesian Information Criterion (BIC) was used to choose the best model. The identified trajectories were used as baseline risk in a Cox model to estimate their effect on melanoma incidence, adjusting for age, birth-cohort, hair colour, region of residence, sunbathing, and follow-up time.

Results: We identified five trajectories for women at ages 0-39 years: 1) *never sunburn* (n=19'500), 2) few sunburns in childhood and adolescence and *increasing* numbers in adulthood (n=31'784), 3) about one sunburn/year in childhood and adolescence and *decreasing* numbers in adulthood (n=21'399), 4) *always about one* sunburn/year (n=49'322), and, 5) *always high* (2-3) numbers of sunburns/year (n=5'875). The Cox model showed a clear trend in the melanoma risk across the trajectories from 1 (reference) to 5 with a hazard ratio (HR) of 1.40 (95% confidence interval (CI)=1.02-1.94) for the *increasing* group (2), HR=1.73 (CI=1.24-2.4) for the *decreasing* group (3), HR=2.12 (CI=1.58-2.86) for the *always about one sunburn/year* group (4), and, HR=2.55 (CI=1.72-3.79) for the *always high* group (5).

Conclusions: Our results support the role of sunburns in melanoma causation. The comparison of the *increasing* and *decreasing* trajectories with similar areas under the curve supports the theory of a higher susceptibility in early life. Comparison of the *decreasing* and the *always about one sunburn/year* trajectories, that diverge in adulthood only, suggests that a person can decrease his/her melanoma risk by starting UV-protective-behaviour in adult life.

C15

Hormonal contraceptive use and *Staphylococcus aureus* nasal and throat carriage in a Norwegian youth population. The Tromsø Study Fit Futures 2

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Introduction: *Staphylococcus aureus* is both a major human pathogen causing a wide range of infections and part of the normal flora of healthy individuals. Sex steroid hormones regulate the host immune response to pathogens, and one study found higher *S. aureus* nasal carriage rates among women using hormonal contraceptives (HC).

Aims: to examine whether use of HC is associated with *S. aureus* nasal and throat carriage in a healthy young population.

Methods: Fit Futures 2 is a large, cross-sectional, population-based study of high school students in Tromsø and Balsfjord, Norway, with 77% participation rate. This analysis includes 436 female participants aged 17-21 with swab samples from anterior nares and throat for the assessment of *S. aureus* carriage, interview about medication (HC use) and disease, as well as clinical examinations, blood samples, and questionnaires on lifestyle and health. We studied the associations between HC use and *S. aureus* nasal and throat carriage in separate multivariable logistic regression models adjusted for potential confounding factors.

Results: In this young female population, 60.8% of the users of HC containing oestrogen derivate in combination with progestin were nasal carriers, compared to 41.8% within the non-user group and 34.2% in the progestin-only group. There was a positive association with higher oestrogen dosage. Women using combination HC with both oestrogen derivate and progestin were more likely to be nasal carriers (OR=2.31, 95%CI=1.43-3.74) than non-users, while no such association was found for throat carriage. Use of progestin-only contraceptives tended to be negatively associated with both nasal and throat carriage, but the estimates did not reach statistical significance.

Conclusions: Use of combination HC was associated with a more than doubled odds for *S. aureus* nasal carriage, and may facilitate a larger reservoir and potential for transmission of the microbe in the general population.

C16

To which extent can variations in spine surgery rates be explained by variations in needs?

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Introduction: By using Small Area Variation (SAV) analysis, researchers have documented regional variation in utilization rates of health care services for more than 40 years. Yet, there is a substantial knowledge gap on the association between utilization rates and patient reported health.

Evidence for positive correlation between health and treatment-volume is ever increasing, but larger volume does not necessarily correspond to per capita rates. It is worth questioning whether health gains would not be greater if resources per capita were equally distributed across regions, resulting in less variation.

Aim: By considering regional utilization rates in relation to patients' health at time of treatment and twelve months after treatment, for 10 686 patients, the aim is to provide more insight into the association between increasing healthcare utilization rates and patients' health.

Methods: Data provided by Norwegian Quality Register for Spine Surgery (NORspine) on patients who underwent lumbar disc herniation surgery in the period 2010 – 2015. Socioeconomic and demographic information, as well as patient reported health (EQ-5D and ODI) was gathered through a questionnaire at time of treatment and twelve months after treatment. Norwegian Patient Registry (NPR) provides data for construction of utilization rates.

We used quantile regression in order to establish whether patients' health differed at time of treatment and after twelve months. Further, we used GEE modeling (Poisson link) to investigate the relation between patient health and utilization rates.

Results: Preliminary results show a clinically important difference in patients' health between regions at time of treatment, but not after twelve months.

GEE model show a positive correlation between health at treatment and utilization rates, but not for health at twelve months. More testing is necessary for robust results.

Conclusion: Yet to be made.

C17

Do new generations of older adults have stronger grip than previous generations? Results for three cohorts of 66-84 year olds in the Tromsø Study: 1994-2016

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Background: The world population is ageing rapidly but evidence pertaining to whether generations of adults reaching old age now have better health and capability than previous generations and how future generations of older adults will compare is scarce and inconclusive.

Aims: Investigate if new generations of older adults have stronger grip than previous generations.

Methods: We included multiple, partly overlapping, birth cohorts (1910-29, 1923-42, 1931-49); all assessed for grip strength using a Martin Vigorimeter (bar) at the same ages (66-84 years) in one of the Tromsø study waves 4 (1994/5), 6 (2007/8) or 7 (2015/16). The study population comprised 5,482 men and women (54% women).

Results: Grip strength among increased significantly in a step-wise pattern between the three study waves, with largest increase in the latest wave, for both men and women. Male grip strength (age standardized using European standard population) was 0.69 bar (95% CI 0.69, 0.70) in T4; 0.71 (0.71, 0.72) bar in T6; and 0.76 (0.75, 0.77) bar in T7. Corresponding numbers for women were 0.62 (0.61, 0.62), 0.63 (0.63, 0.63) and 0.66 (0.65, 0.67). In a model adjusted for age, gender, height, weight, education and smoking the difference in grip strength between T7 and T4 was reduced by 62% compared to an age and gender adjusted model. Male grip strength at 80 years in T7 corresponded to grip strength at 75 years in T4. Likewise, female grip strength at 80 years in T7 corresponded to the average for a 77 year old female in T4.

Conclusion: Our findings suggest better grip strength in more recent birth cohorts, which can be partly attributed to increased body size, higher education and reduced smoking. The new generation of 80 year olds have similar grip strength as 75-77 year olds one generation ago. This improved physical capability among older adults, might have impact on future forecasting of health and social care costs.

C18

General practice consultations and use of prescription drugs after changes to school absence policy

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Introduction: New rules with stricter requirements for documentation of absence were introduced in upper secondary schools in the autumn of 2016.

Aim: To investigate the use of general practice services and dispensing of prescription drugs among 16–18-year-olds in the autumn of 2016 and compare with equivalent figures for the period 2013–15.

Methods: We retrieved information on consultations in general practice (GP) and dispensing of prescription drugs to 15–18-year-olds in the period 2013–16 from the Directorate of Health's system for control and payment of health reimbursements (KUHR) and the Norwegian Prescription Database respectively. The number of consultations and the number of dispensing of drugs were compared to previous years using Poisson regression (reference year 2015). The incidence rate ratio (IRR) was used as an outcome measure.

Results: The number of GP consultations for 16–18-year-olds was 30% higher in the autumn of 2016 than in the autumn of 2015 (IRR 1.30, 95% confidence interval (CI) 1.29–1.31). In the same period, the dispensing of drugs to this age group increased by 8% (IRR 1.08, 95% CI 1.08–1.09). Among the diagnosis groups, respiratory tract infections had the largest increase (IRR 2.21, 95% CI 2.17–2.25). The largest increase in drug dispensing was found for remedies for coughs and colds (IRR 1.73, 95% CI 1.65–1.80).

Conclusions: The increase in consultations in general practice and dispensing of drugs to 16–18-year-olds coincided in time with the introduction of new rules for absence from school. We hold it to be highly likely that the changes were caused by the stricter rules for documentation of absence from school.

P1

Prevalence of self-reported myocardial infarction in Sami and non-Sami populations at two time points: The SAMINOR 1 Survey and the SAMINOR 2 Clinical Survey

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Introduction: Updated knowledge concerning the burden of myocardial infarction in Sami and non-Sami populations is needed.

Aims: To estimate and compare the prevalence of self-reported myocardial infarction (SMI) at two points in time in Sami and non-Sami populations living in the same municipalities.

Methods: The SAMINOR 1 Survey (2003–2004) and the SAMINOR 2 Clinical Survey (2012–2014) are cross-sectional, population-based surveys including Sami and non-Sami inhabitants. The present study is based on data from participants aged 40–79 years in 10 municipalities in rural Northern Norway. In both surveys, data was collected through self-administered questionnaires, clinical examinations and blood sampling. The present study included 6385 and 5908 participants, i.e., 55.4% and 47.4% of the invited samples, respectively.

Results: The prevalence of SMI was stable over time. In women, the total age-standardised prevalence was 2.9% and 2.5% in SAMINOR 1 and 2, respectively. In men in the same surveys, the prevalence was, respectively, 7.8% and 7.5%. Regardless of sex and ethnicity, the burden of disease increased markedly by age. In both men and women, no statistically significant ethnic difference in the prevalence of SMI was found in age-specific groups or in total when controlling for age. Furthermore, small to no ethnic difference in selected risk factors for ischaemic heart disease was found.

Conclusions: In both men and women, no statistically significant difference in the age-standardised prevalence of SMI in Sami and non-Sami was observed. The prevalence over time was stable in both sexes and ethnic groups.

P2

Hypertensive pregnancy disorders and risk of cardiovascular disease in 613,996 Norwegian women: comparison of gestational hypertension and preeclampsia

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Introduction: Preeclampsia has been linked to increased risk of cardiovascular disease (CVD), but a similar association for gestational hypertension has not been established.

Aims: We aimed at exploring the association between gestational hypertension alone or in combination with small for gestational age (SGA) infant and/or preterm delivery and subsequent CVD, and compare the association with that of preeclampsia.

Methods: We linked data from the Medical Birth Registry of Norway with the CVDNOR project and the Norwegian Cause of Death Registry. Hazard ratios (HR) and 95% confidence intervals (CI) were computed using Cox proportional hazard regression, comparing women with and without gestational hypertension or preeclampsia in their first and/or second pregnancy.

Results: We included all women with a first delivery from 1980 through 2009 (n=613,996) and followed them for (median, (Q3-Q1)) 14.3 (21.5-6.9) years. When compared to women with gestational hypertension in their first pregnancy (n=11,197), preeclamptic women (n=28,648) had higher proportion of SGA infants (23.6 % vs. 16.3 % (p <0.001)) and preterm deliveries (20.2 % vs. 6.9 % (p <0.001)). The risk of CVD after gestational hypertension or preeclampsia was similar when the hypertensive disorder occurred in the first or second pregnancy; but with recurrent disease, women with gestational hypertension had a significantly lower risk of CVD compared to women with preeclampsia (HR, 0.6; 95 % CI, 0.4-0.8 without SGA/preterm delivery: HR, 0.7; 95 % CI, 0.5-0.9 with SGA and/or preterm delivery).

Conclusion: Women with gestational hypertension in their first or second pregnancy had a risk of CVD similar to that observed after experiencing preeclampsia. For recurrent disease, women with preeclampsia showed higher CVD risk compared to women with gestational hypertension.

P3

Plasma saturated fatty acid to polyunsaturated fatty acid ratio affects peripheral blood mononuclear cell gene expression related to lipid metabolism: a cross-sectional study in healthy subjects

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Introduction: Nutrigenomics focus on how nutrients alter gene expression and ultimately the metabolic phenotype. Saturated fatty acids (SFAs) and n-6 and n-3 polyunsaturated fatty acids (PUFAs) can directly or indirectly alter gene expression. Dyslipidemia, including elevated levels of serum total- and LDL-cholesterol and triglycerides, is a major risk factor for cardiovascular disease (CVD). Solid evidence indicates that replacement of SFAs with PUFAs reduces serum total- and LDL-cholesterol, and that marine n-3 PUFAs reduces serum triglycerides. However, the underlying mechanisms causing these cardio metabolic effects of SFAs and PUFAs are not completely elucidated.

Aim: To investigate if genes related to cholesterol- and triglyceride metabolism is differentially expressed among subjects with high n-6 PUFA level versus low n-6 PUFA level, high n-3 PUFA level versus low n-3 PUFA level, and high SFA to PUFA ratio versus low SFA to PUFA ratio.

Methods: Fifty-four healthy subjects were divided into tertiles (n=18) based on plasma n-6- and n-3 PUFA levels and SFA to PUFA ratio, and peripheral blood mononuclear cell (PBMC) gene expression levels among subjects in the highest versus the lowest tertiles were compared. 150 genes related to cholesterol- and triglyceride metabolism and defined as expressed in PBMCs were selected for this exploratory study.

Results: The SFA to PUFA ratio was associated with the highest number of differentially expressed genes (25 genes), followed by n-6 PUFA level (15 genes), and n-3 PUFA level (8 genes). Several of the differentially expressed genes associated with the SFA to PUFA ratio were opposite differentially expressed when comparing subjects in the highest versus the lowest n-6 PUFA tertile. More details of the differentially expressed genes will be presented at the poster.

Conclusions: Using a targeted approach to look for differentially expressed genes may increase our understanding of how diet influence lipid metabolism on a molecular level.

P4

Early adulthood weight, subsequent weight change and the risk of cardiovascular disease, a register based study from Norway

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Introduction: Trajectories of weight over the life course has been linked to cardiovascular (CVD) mortality. Being obese at several time points, or weight gain during life, may increase the risk.

Aims: To elucidate the importance of weight trajectories from early adulthood to midlife for CVD mortality.

Methods: Data from Norwegian health surveys (1985-2003), conscript data, tuberculosis screenings and the cause of death registry were linked using the personal identity number. Participants with data on body mass index (BMI) both in early adulthood and midlife, as well as CVD risk factors, were included, n=148 994.

Results: Those who had lost weight from early adulthood to midlife had higher HR of CVD mortality compared to those with a stable weight (HR 1.55 (95 % CI 1.12, 2.15)), also when adjusted for BMI in early adulthood (1.35 (1.08, 1.67)), however not when adjusted for CVD risk factors. Participants being overweight or obese in early adulthood had higher HR for CVD mortality than those being normal weight, also when adjusted for weight change between early adulthood and midlife, and for cardiovascular risk factors (HR 1.37 (1.17 1.60) for overweight, 2.84 (2.07 3.91) for obese). In midlife, those underweight (2.55 (1.52, 4.28)) and obese (1.78 (1.49, 2.13)) had higher HR for CVD mortality than those normal weight, after adjustment for weight change and risk factors.

Conclusion: Obesity in early adulthood is a risk factor for CVD, independently of later weight change. Obesity in midlife is associated with higher risk of CVD mortality, and more strongly among those who was obese also in early adulthood.

P5

Trends in use of oral anticoagulants for stroke prophylaxis in Norway, 2010-2015

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Introduction: Since 2011, several direct-acting oral anticoagulants (DOACs) have been introduced as alternatives to warfarin to prevent strokes in atrial fibrillation.

Aim: To describe the utilization patterns of oral anticoagulants for atrial fibrillation in Norway following the introduction of three DOACs (dabigatran, rivaroxaban and apixaban).

Methods: Using the Norwegian Prescription Database, we identified all adults with pharmacy dispensings for warfarin, dabigatran, rivaroxaban or apixaban between January 2010 and December 2015 in Norway, and used ambulatory reimbursement codes to identify atrial fibrillation as indication. We defined incident use by a 1-year washout period. We describe trends in prevalent and incident use of warfarin and DOACs between 2010 and 2015, as well as patterns of treatment switching for incident users.

Results: 129 285 individuals filled at least one prescription for an oral anticoagulant for atrial fibrillation. The yearly number of incident users increased by 60% (262 to 421 per 100,000 person-years), and the number of prevalent users increased by 50% (1366 to 2044 per 100 000 population). The yearly share of incident users who initiated a DOAC increased to 82% and half the prevalent users were on a DOAC by 2015. Within a year of drug initiation, 6, 12, 16 and 20% of incident users of apixaban, rivaroxaban, warfarin and dabigatran, respectively, switched oral anticoagulant.

Conclusions: Use of DOACs for prophylactic anticoagulation in atrial fibrillation became more prevalent between 2010 and 2015 in Norway, at the expense of warfarin.

P6

Monitoring health and social inequality in North Norway: The Tromsø Study

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Introduction: In the mid-1970s, one in five Norwegian men died from myocardial infarction before the age of 75, and the situation in North Norway was even worse. Since then, cardiovascular mortality has decreased dramatically. However, previous studies showed great social differences in cardiovascular disease (CVD) risk factors and mortality in Tromsø and Norway.

Aims: To investigate changes in social gradients in risk factors over the last 30 years.

Methods: The Tromsø Study collected data on CVD risk factors among adults through seven surveys (Tromsø 1–7) from 1974 to 2016. All surveys comprise questionnaire data, measurements, biological material and clinical examinations. Age group 40–49 years was included in all surveys. Men and women aged 40–49 years who participated in surveys from 1986 to 2016 (Tromsø 3, 4, 6, and 7) were included in this study. Number of years of education was used as a proxy for socioeconomic group, and was self-reported. In age group 40–49 years, the use of antihypertensive medication and lipid lowering drugs was low (< 10% in all surveys).

Results: Among the Tromsø Study participants, major CVD risk factors (blood pressure, blood cholesterol, smoking prevalence) declined, while body mass index (BMI) increased in all socioeconomic groups. Social gradients in risk factors were observed, with more favorable levels observed in all risk factors by increasing length of education. Between 1986 and 2016, social gradients in BMI increased in both sexes. Social gradients in blood cholesterol decreased. Percentage of daily smoking decreased in all educational groups. However, large between-group differences in smoking prevalence were seen in both men and women, and the social gradients persisted during the 30 years of observation.

Conclusion: Persisting and large social gradients in smoking prevalence call for group directed preventive strategies and actions.

P7

Birth weight of offspring and mortality in their parents and aunts/uncles: a population based cohort study

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Introduction: The link between suboptimal foetal growth and a higher risk of cardiovascular disease (CVD) has been demonstrated in several populations. Shared environmental and genetic factors may be responsible for explaining this association.

Aim: To investigate the association between offspring birth weight and CVD mortality among parents and among their siblings (aunts/uncles).

Methods: A cohort was created by linking the Medical Birth Registry, the Cause of Death Registry and National Education Registry, Norway. A multigenerational database was used to identify the siblings of parents by using the unique personal identity number. The final dataset comprised of 1, 353, 968 births (1967-2012) linked to both parents and their siblings (aunts/uncles). The association between offspring birth weight and CVD mortality among parents and aunts/uncles was measured by hazard ratio estimated in Cox regression. Follow up started at the date of offspring birth and continued up to death or at the end of study (30.12.2014).

Results: An inverse association between offspring birth weight and mortality from CVD was observed among parents and their siblings (aunts /uncles). Per quintile increased in birth weight was related to 0.82 (0.79-0.84) hazard ratio from CVD in mothers and 0.93 (0.92-0.94) in fathers. In aunts/uncles, the effects were 0.94 (0.90-0.97) (maternal aunts), 0.94 (0.92-0.96) (maternal uncles), 0.95 (0.92-0.97) (paternal aunts), 0.95 (0.94-0.97) (paternal uncles). Adjustment for education attenuated the associations in parents as well as in all four aunts and uncles. Adjustment for maternal smoking in pregnancy in a subgroup attenuated the associations in mothers and in paternal aunts.

Conclusion: Our results suggest genetic susceptibility on the birth weight and CVD mortality association. However, the role of shared environmental factors cannot be completely excluded and should be assessed in the future studies.

P8**Levonorgestrel-releasing IUD prevents ovarian and endometrial cancer, with no increased risk of breast cancer. The NOWAC Study****Mie Jareid¹, Jean-Christophe Thalabard², Morten Aarflot¹, Hege Bøvelstad¹, Eiliv Lund¹, Tonje Braaten¹**

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Introduction: It has proven difficult to improve the survival rate among women with ovarian cancer, and primary prevention is therefore important. Combined oral contraceptives prevent ovarian cancer, but are not recommendable for women without need for contraception. It is well known that the levonorgestrel-releasing intrauterine system (LNG-IUS) prevents endometrial cancer, and recent studies suggest that LNG-IUS use additionally prevents ovarian cancer. However, they also suggest an increased risk of breast cancer.

Aim: To study the association between ovarian, endometrial and breast cancer in a prospective cohort study that included information on a range of other hormonal exposures.

Methods: Our study cohort consisted of 104 380 women from the Norwegian Women and Cancer Study, of which 9146 were LNG-IUS users and 95 234 were non-users. Exposure information was taken from self-administered questionnaires, and cancer cases were identified through linkage to the Cancer Registry of Norway. Relative risks (RR) and their 95% confidence intervals (CI) were estimated with Poisson regression using a robust error estimate.

Results: Mean follow-up time was 12.5 (3.7) years for a total of 1 305 949 person-years. Among LNG-IUS users there were 18 cases of ovarian cancer, 17 cases of endometrial cancer and 297 cases of breast cancer. For LNG-IUS users compared to nonusers, the multivariable relative risk (RR) of ovarian cancer was 0.47 (95% CI: 0.29,0.78), for endometrial cancer the RR was 0.25 (95% CI: 0.15, 0.43), and the RR of breast cancer was 0.96 (95% CI: 0.85,1.09). The age adjusted RRs were similar.

Conclusion: These results suggest that LNG-IUS use may lower the risk of ovarian and endometrial cancer in the general population.

P9

Coffee consumption and whole-blood gene expression in the Norwegian Women and Cancer Post-Genome Cohort

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Introduction: Norwegians are the second highest consumers of coffee (in kg per capita) in the world, with only Finland consuming more. Lately, there has been a surge in research suggesting several beneficial health effects from coffee consumption. By looking at gene expression, we want to further the understanding of the molecular markers linking coffee consumption to these health effects.

Aims: To evaluate if categories of coffee intake is associated with differential whole-blood gene expression profiles in the Norwegian Women and Cancer Post-genome Cohort.

Methods: Gene expression profiles (Illumina Expression BeadChip) from the whole-blood of 960 women were analysed using *limma* and *clusterProfiler* in R, to identify associations between coffee consumption and gene expression profiles.

Results: Out of 960 healthy women, 132 were considered low coffee consumers (<1 cup of coffee per day), 422 moderate coffee consumers (1-3 cups of coffee per day), and 406 were high coffee consumers (4+ cups of coffee per day). At a false discovery rate (FDR) < 0.05, no difference in gene expression was found between low- and moderate consumers or between moderate- and high consumers of coffee. Between low- and high consumers, 138 genes were differentially expressed. When looking at the non-smokers only, 414 genes were found to be differentially expressed.

Conclusions: Results indicate significantly differentially expressed genes between high and low consumers of coffee.

P10

Cancer risk and all-cause mortality among civilian women in the Royal Norwegian Navy

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Introduction: Civilian personnel are employed at all land-based Royal Norwegian Navy installations. Typical jobs among the women are cleaning, clerical work, catering, and provisioning. Cleaners, who may be exposed to hazardous chemicals inclusive of respiratory irritants or sensitizers from cleaning agents, have been reported as having a heightened cancer risk.

Aims: To investigate cancer incidence and all-cause mortality in a cohort of 3231 civilian women employed by the Royal Norwegian Navy during 1950–2005.

Methods: We followed the cohort from 1960 through 2015 for cancer incidence and all-cause mortality. Standardized incidence ratios for cancer (SIR) and mortality (SMR) were calculated from national rates. SIRs were also calculated in a subgroup of 770 cleaners.

Results: We observed increased risks of all cancers combined (SIR=1.11), lung cancer (SIR=1.35) and ovary cancer (SIR=1.38) in the cohort as a whole. All-cause mortality was close to the national rates (SMR=0.94). In the subgroup of cleaners, the risk of bladder cancer was significantly elevated (SIR=2.32), while a 61% increased risk of lung cancer was not statistical significant.

Conclusion: No healthy worker effect for all-cause mortality was seen in our cohort, and the overall cancer risk was elevated. The observed excess in bladder- and lung cancer among the cleaners is in line with other studies. These cancers are strongly associated with smoking. However, as we have no data on smoking habits of our cohort members, nor on their exposure to hazardous chemical in the workplace, the cancer-causing factor(s) remains unknown.

P11

Blood gene expression changes before breast cancer diagnosis – Predicting metastasis in the Norwegian Women and Cancer (NOWAC) Post-genome Cohort

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Introduction: Metastasis is the major cause of death in breast cancer patients, but little is known of the systemic, time-dependent changes leading up to metastatic cancer.

Aim: Our aim was to explore the dynamic mechanisms of the metastatic process, by using transcriptomic data from blood samples in conjunction with analytical methods that include time as a continuous variable.

Methods: We developed a new statistical method, Local In Time Statistics (LITS), based on calculating statistics in moving windows, and randomization. The method was applied to blood transcriptomic data from the Norwegian Women and Cancer (NOWAC) Post-genome cohort, consisting of 467 case-control pairs and covering the time period up to eight years prior to diagnosis. We used LITS to test whether the transcriptomic profiles in blood vary between cases and controls, with time, or between cases with and without metastatic breast cancer.

Results: We identified transcriptomic differences between cases and controls, as well as time-dependent changes, and differences between cases with and without metastatic cancer. Also, differences were found between those cancers detected in the screening program versus those detected clinically. The probability of correctly predicting metastasis status was the highest one year prior to diagnosis for those attending screening, and 3-4 years prior to a clinically detected cancer.

Conclusion: The new LITS method allowed us to identify previously unseen variation in transcriptomic profiles in blood samples of women who later develop breast cancer. If confirmed by future studies, the findings may serve as new biomarkers of metastatic disease, and as an important contribution to understanding the late stages of human carcinogenesis.

P12

Fit for fight – Self-reported health in military women

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Introduction: In Norway, all young women are called to military service. The health and well-being of women in the military are of vital importance to safe and efficient military operations, and for public health.

Aims: To present preliminary analyses of self-reported health and health behaviour in military women, and to compare this group with military men and women working in civilian positions for the Norwegian Armed Forces.

Methods: The data was collected in January 2017 in an internet based survey among employees in the Norwegian Armed Forces. The questionnaire was developed by the Norwegian Armed Forces Medical Services, and calibrated to the CONOR study (Cohort of Norway). Near 800 military women participated, and were compared with ~6000 military men and ~800 civilian women for three different age-strata (20-29 years; 30-39 years; and 40-70 years).

Results: Overall, military women reported medical conditions and injuries quite equal to the military men. Physical exercise, smoking, and drinking habits were similar between military women and men, but the military women used less snuff. However, young military women (20-39 years) seemed to express more symptoms of mental health problems and they used more medications than military men. Compared to women who had civilian positions in the Norwegian Armed Forces, military women reported less frequently about medical problems, and used less medications. There were no differences in mental health symptoms between military and civilian women. Military women exercised more than civilian women, but seemed to use more snuff. In women aged 30-39 years, the differences between military and civilian women in self-perceived poor health and use of medications were not significant.

Conclusion: Preliminary analyses suggest that military women assess their physical health and health behaviours quite equal to military men. Compared to civilian women, military women exercise more and report less medical conditions.

P13

Life course trajectories of cardiovascular risk factors in women with and without hypertensive disorders in pregnancy. The HUNT Study

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Introduction: Women with a history of hypertensive pregnancy disorders have adverse levels of cardiovascular risk factors. It is unclear how these risk factors evolve during adult life.

Aims: To examine life course trajectories of cardiovascular risk factors in women with and without hypertensive pregnancy disorders.

Methods: We linked information on cardiovascular risk factors from the HUNT Study (1984-2008) with pregnancy information from the Medical Birth Registry of Norway (1967-2012). Life course trajectories of cardiovascular risk factors were drawn using mixed effects linear spline models in 22 308 women with normotension, 1092 with preeclampsia, and 478 with gestational hypertension in first pregnancy.

Results: Women with a preeclamptic first pregnancy had higher blood pressure, BMI, waist and hip circumference, heart rate, and non-fasting serum levels of non-HDL cholesterol, triglycerides, and glucose than women with a normotensive first pregnancy even prior to pregnancy, at age 20. Changes from pre- to post-first pregnancy were similar between the groups, except that BMI increased more and diastolic blood pressure decreased less in women with preeclampsia. After first pregnancy, cardiovascular risk factors developed with age in similar and largely parallel ways in both groups of women, with a time lag of ≥ 10 years between mean levels observed between women with preeclamptic versus normotensive pregnancies. The differences in blood pressure, adiposity, and glucose between the groups were still present at age 60, whereas differences in serum lipids and heart rate largely attenuated after age 50. Risk factor trajectories among women with gestational hypertension were similar to those observed for preeclampsia.

Conclusions: Women with hypertensive disorders of pregnancy had more adverse cardiovascular profiles prior to pregnancy. These differences persisted beyond age 50. Women with hypertensive pregnancy disorders may benefit from early life-style modification to reduce cardiovascular risk factors.

P14

Association between Physical Activity and Experimental Pain Tolerance in a General Population: The Tromsø Study

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Introduction: Several studies have found that physical activity (PA) is associated with pain tolerance. This relationship has mostly been examined in small convenience samples and generalizability to the general population remains unclear.

Aims: To describe associations between levels of PA in leisure time and experimental pain tolerance in a population-based study.

Methods: We used data from the Tromsø 6 Study 2007-08 (N=12,985, attendance rate 66%), including self-reported data on PA and experimental pain tolerance assessment with the cold-pressor test (CPT: 3°C, maximum time limit of 106s). PA was classified as sedentary, low, moderate, or vigorous based on response to a previously validated questionnaire item on leisure time PA. Cox proportional hazards models will be used to compare CPT tolerance time between PA groups, controlling for age, sex and education level.

Results: Complete data are available for 9,773 participants (51% women) aged 30-87 (mean = 55.8) years. Reported PA levels among participants were: sedentary 19%, low 60%, moderate 19%, vigorous 2%. In CPT, 69% of participants reached the maximum time limit. Results from the Cox proportional hazards models are pending.

Conclusion: Our results will demonstrate to what extent levels of PA are associated with CPT pain tolerance. This will enhance our understanding of mechanisms underlying pain sensitivity, which is thought to be a major contributor to the development, persistence, and severity of chronic pain. A subsequent prospective study will aim at exploring the temporal relationship between PA and pain sensitivity.

P15

The association between anemia and falls in community-living women and men aged 65 years and older from the fifth Tromsø Study 2001-02: A replication study

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Introduction: Falls are common among elderly people, and the risk increase with age. Falls are associated with both health and social consequences for the patient, and major societal costs. Identification of risk factors should be investigated to prevent falls. Previous studies have shown anemia to be associated with accidental falls, but the results are inconsistent, and further studies are needed.

Aims: The aim of this study was to investigate the association between anemia and self-reported falls among community-living elderly people. The study is a replication study of Thaler-Kall and colleagues from 2014, who studied the association between anemia and self-reported falls among 967 women and men 65 years and older in the KORA-Age study from 2009.

Methods: We included 2441 participants (54% women) 65 years and older from the population-based Tromsø 5 Study 2001-02. Logistic regression models were used to investigate the association between anemia (hemoglobin <12 g/dL in women and <13 g/dL in men) or hemoglobin level and self-reported falls last year, adjusted for sex, age, medication use and disability. Further, associations between combinations of anemia and frailty or disability, and falls, were investigated.

Results: No statistical significant associations were found between anemia and falls (OR, 95% CI: 0.83, 0.50-1.37) or hemoglobin level and falls (OR, 95% CI: 0.94, 0.81-1.09), or with combinations of anemia and frailty or disability, and falls (OR, 95%: CI: 0.94, 0.40-2.22 and 0.78, 0.34-1.81, respectively). Possible time-gaps between the measured hemoglobin level and the event of falling is a general study limitation.

Conclusions: In this replication analysis, in accordance with the main results from the original study, no statistically significant association between anemia or hemoglobin and falls was found among community-living women and men aged 65 years or older. A limitation yielding both the current and the KORA-Age analysis is the cross-sectional design.

P16

The frailty phenotype as a predictor of all-cause mortality in community- living individuals aged 70 years and older: The Tromsø Study 2001-2016

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Introduction: An important and challenging manifestation of the aging population is the clinical condition of frailty. Frailty is an age-related syndrome of increased vulnerability to stressors due to declines in several physiologic systems. There is a lack of data on frailty prevalence and studies of the association between frailty and mortality in a Norwegian general population.

Aims: To investigate the ability of the frailty phenotype to predict all-cause mortality in a Norwegian population.

Methods: We followed 712 participants (52% women) aged 70 years and older participating in the fifth population-based Tromsø Study in 2001-2002 for all-cause mortality until 2016. The frailty status at baseline was defined by a modified version of Fried's frailty criteria. Cox regression models, combined and stratified by sex, were used to analyse the association between frailty and mortality with adjustment for age, disability, comorbidity, smoking status and years of education.

Results: Among the participants 4% (n=27) were frail and 38% (n=271) were pre-frail. Adjusted hazard ratios (HR) indicated an increased risk of mortality for frail elderly (HR 3.72 (95% CI 2.12, 6.54)) compared to non-frail elderly. This association was also significant in the sex-stratified analysis, with adjusted HR of 6.33 (95% CI 2.68,14.94) for frail men and 2.79 (95% CI 1.29, 6.03) for frail women. The results for pre-frailty showed an overall weaker association with mortality.

Conclusion: Frailty was strongly associated with mortality. The findings suggest that the risk could be higher for frail men than frail women.

P17

Prevalence of Chronic Obstructive Pulmonary Disease in 1995-1997 and 2006-2008: The HUNT Study, Norway

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Introduction: COPD is a major cause of morbidity and mortality across the world and new estimates of prevalence is of great importance.

Aim: To estimate the prevalence of COPD in 1995-1997 and 2006-2008 in Norwegian adults.

Methods: This study based on Nord-Trøndelag Health Study (HUNT), including adults aged ≥ 20 years. COPD was assessed using a fixed-ratio and lower limit of normal (LLN) criteria. Pre-bronchodilator COPD was assessed during 1995-1997 and 2006-2008. Post-bronchodilator COPD (only rural population) was also assessed in 1995-1997. The study included 5304 women and 4845 men in 1995-1997 and 6425 women and 5284 men in 2006-2008. However, the main analysis included participants aged ≥ 40 years. The prevalence of COPD was estimated by weighting on the inverse probability of selection and predicted probability of response. Generalized Estimation Equation (GEE) models were used to assess the change in prevalence from 1995-1997 to 2006-2008.

Results: The prevalence of pre-bronchodilator COPD was 16.6 in 1995-1997 and 14.8 in 2006-2008 with fixed-ratio criteria (OR=0.94; 95%CI: 0.83-1.06), and 10.4 in 1995-1997 and 7.3 in 2006-2008 with LLN criteria (OR=0.69; 95%CI: 0.59-0.80). The prevalence of LLN COPD was higher among men (13.0% in 1995-1997, 7.7% in 2006-2008) than women (7.9% in 1995-1997, 6.9% in 2006-2008). From 1995-1997 to 2006-2008, the prevalence decreased among men but remained approximately stable among women. Among rural residents, the prevalence of post-bronchodilator LLN COPD in 1995-1997 was 9.3 among men and 6.5 among women.

Conclusions: The prevalence of COPD and its trend depended on diagnostic criteria, however overall the prevalence declined from 1995-97 to 2006-08 and was consistently higher among men than women.

P18

Does the usual activities dimension in EQ-5D-5L measure what it intend to measure?

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Introduction: The EQ-5D is the most widely used generic preference-based health-related quality of life measure. It has a wider application in clinical and economic evaluations as well as population studies. It comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The usual activities dimension asks respondents to indicate the severity of problems in their usual activities, such as work, study, housework, family or leisure activities. The aim of this study is to investigate whether the EQ-5D-5L usual activities dimension captures activities described to reflect this dimension; that is, its relationship with measures of variables related to work or study, housework, social and leisure activities.

Methods: Data include 7933 respondents from six countries. The sample constitutes two groups that reported their health along several measures of HRQoL: non-diagnosed healthy group (n=1760) and seven disease groups (n=6173). A regression model investigates the relationship between the predictors and the usual activities dimension. We have controlled for social economic status (age, gender, education, marital status, income, employment status) as well as disease and country dummies. A Shapley value decomposition method was applied to measure the relative importance of each predictors (work/study activities, housework, social activities, and leisure activities).

Results: Leisure, housework, work or study, and social activity measures were all significant ($p < 0.001$) determinants of usual activities, in that order. For instance, one standard deviation decrease in housework activities lead to 0.35 decrease in usual activities dimension of EQ-5D-5L. The Shapley value decomposes the total explained variation (61%). Housework, work or study, leisure, and social activities contribute 30.8%, 22.7%, 21.7%, and 17.1% of this total explained variation in usual activities dimension, respectively.

Conclusions: The usual activities dimension reflect the specific activities described to respondents. Therefore, the usual activities dimension in EQ-5D-5L measures what it really intend to measure.

P19

Parental socioeconomic status and risk of cerebral palsy in the child: Evidence from two Nordic national birth cohorts

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Introduction: Cerebral palsy (CP) is the most common physical disability in children and affects about 2 per 1000 live born. It is unclear whether there is a socioeconomic gradient in CP and whether it has changed in the last generation given changes in income, educational attainment and health behaviors and improvements in antenatal and neonatal care.

Aims: Our aim was to investigate risk of CP in the child by parents' socioeconomic status.

Methods: The study population consisted of almost 1.3 million children born in Denmark during 1981-2007 and 2.4 million children born in Norway during 1967-2007. Data on the births from the Danish and Norwegian Birth registries were linked to Statistics Denmark and Norway to retrieve information on parents' education, and in Denmark also income. In Denmark, the diagnoses of CP were collected from the Cerebral Palsy Registry and in Norway from the National Insurance Scheme and the Norwegian Patient Registry. We used log-binomial regression models to estimate relative risk (RR) of CP according to parental socioeconomic status.

Results: Higher parental educational attainment was associated with decreased risk of CP in children. Compared with primary education, a mother with a master degree or higher had a 30-40% decreased risk of having a child with CP (relative risk (RR) 0.58 (95% confidence interval (CI) 0.50-0.69) in Denmark and 0.66 (95% CI 0.58-0.76) in Norway). An almost identical association was observed for paternal education. The educational gradients remained after excluding children born preterm and appeared stable over time. Compared to single mothers, mothers with partners had lower risk of having a child with CP. No association was found between household income and CP risk in the Danish cohort.

Conclusions: Risk of CP in children decreased with increasing parental educational attainment and was lower in mothers with partners compared to single mothers.

P20

Tinnitus and comorbidity

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Introduction: Tinnitus is defined as the sensation of sound without external stimulation. It is a relatively common health nuisance. International studies indicate a tinnitus prevalence of 8-15% in the general adult population. Tinnitus perception varies greatly when it comes to both manifestation and degree of suffering. It is known that tinnitus can significantly influence mental health and quality of life, but little is known about how comorbidity in general is associated with nuisance and degree of disability.

Aims: The study aims to investigate comorbidity with tinnitus in the general population.

Methods: Using the Tromsø study, Tromsø 7, combined with data from the KUHR (control and disbursement of health refunds) registry, we will investigate the associations between tinnitus and coronary heart disease and pain. We will further examine tinnitus symptom intensity and subjective annoyance and their associations with general health status, work capability and use of health services. Standard multivariate techniques, i.e. linear and logistic regression and analysis of variance, will be used for analysis.

Results: Among 20 558 respondents, 21.0% had experienced ringing in their ears lasting more than 5 minutes within the last 12 months. As the project has only recently started, additional results will be ready later.

Conclusions: The high prevalence of tinnitus makes it a public health issue. Hence, it is useful to examine relationships between tinnitus and other diseases, in order to uncover possible causes for development of debilitating tinnitus. The Tromsø study is thorough and of wide scope and is therefore well suited for this kind of research. The tinnitus prevalence in the Tromsø study is somewhat higher than in other general population studies. However, since tinnitus prevalence increases with age and the participants in the Tromsø study are of age 40 and above, this is only to be expected.

P21

County Public Health Survey – web based surveys only?

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Introduction: The Norwegian Institute of Public Health (NIPH) in collaboration with the County Councils of Vestfold, Aust-Agder and Vest-Agder conducted a survey during 2015-16 of factors related to public health, wellbeing and living conditions. The Ministry of Health has asked NIPH to present plans for future county surveys, which will encompass all counties and repeated every 4 years. Before concluding, NIPH will run a County Public Health Survey in Hordaland which will help determine if web-based methods only are sufficient.

Aims: What are the implications of using only web-based data collection for large scale county public health surveys? Data will be collected through helsenorge.no and NIPH web based survey solution. Helsenorge.no, a primary online access point to Norwegian health services, also offers a private health archive and uses a secure logon and is a trusted service which offers two-way communication with citizens. Thus, helsenorge.no or other web-based solutions are of potential interest as a means to conduct health surveys – and being web-based only, at a fraction of the cost of more traditional methods. The salient point is response rates and non-response bias. Are they low generally for web based surveys, and does secure logon, in the case of helsenorge.no influence response rates? Therefore two independent samples from the general population in Hordaland will be drawn. One will be invited to complete the survey through helsenorge.no and the other through NIPH web-based survey solution. This allows us to investigate differential response rates and potential bias for the two samples. A further aim is to link data with several health and socioeconomic registries and conduct a thorough analysis of potential bias and issues related to validity due to non-response.

P22

Vision-related selection data in the Norwegian Armed Forces Health Registry

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Introduction: The Norwegian Armed Forces Health Registry (FHR) includes a large body of historical data from medical examinations and fitness testing of young Norwegians obtained in the course of selection for national military service. Through the years 1980-2016, overall visual function for over a million conscripts has been scored using a categorical variable with value labels 1, 4, 5, 6, 7, and 9. The score is based on a simple evaluation of the visual acuity of each eye and information on any eye disease. The formal criteria for assigning the highest score (9) have remained essentially unchanged over the years, while the criteria for assigning the second highest score (7) were relaxed slightly in 2008.

Aims: To investigate the quality of vision-related conscript-selection data in the Norwegian Armed Forces Health Registry.

Methods: Vision assessment data, available in electronic records for 1980 onwards, were examined in terms of the frequency of the two highest scores, 7 and 9. These frequencies were stratified by year of assessment, by age group and by testing site.

Results: On a national level, the frequencies of the two scores fluctuated from one year to the next without any reliable trend. This was seen whether age groups were combined or examined separately. A stratification by testing site revealed large inter-site differences in score frequencies, as well as differences in frequency trends over time.

Conclusion: While the Norwegian Armed Forces' assessment of visual function in conscripts may be fully adequate for selection purposes, the limitations of the resulting data must be given careful consideration in the context of any epidemiological studies.

P23

Metabolically healthy obesity and risk for atrial fibrillation

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Introduction: Atrial fibrillation (AF) is the most prevalent arrhythmia and has been described as a global epidemic. Many studies suggested that, metabolically healthy obesity is a relatively benign condition regarding the risk for myocardial infarction. However, little is known about the association between metabolically healthy obesity and AF.

Aims: The present study aimed to assess the risk for AF among metabolically healthy obese individuals.

Methods: In a population-based prospective cohort study, a total of 50,804 men and women free of AF were classified according to body mass index (BMI) and metabolic status at baseline. BMI also was measured 10, 20 and 40 years before baseline for 15,311 participants.

Results: During a median follow-up of 8.1 years, 1,813 participants had AF. Compared to metabolically healthy individuals with a normal weight (BMI <25 kg/m²), the multivariable-adjusted hazard ratio (HR) was 1.6 (95% confidence interval [CI]: 1.2 to 2.1) among obese (BMI ≥30 kg/m²) and metabolically healthy participants and 1.6 (95% CI: 1.3 to 1.9) among obese and metabolically unhealthy participants. We found similar results for class I obese, class II obese, long-term and abdominal obesity stratified for metabolic status.

Conclusions: Metabolically healthy obese individuals had similar AF risk as metabolically unhealthy obese individuals. AF risk was higher for severe obesity and long-term obesity.

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