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Utgis vanligvis med to regulære temanummer pr. år. I tillegg kommer supplement med sammendrag fra Norsk forening for epidemiologis årlige konferanse.

DEN 26. NORSKE EPIDEMIOLOGIKONFERANSEN

OSLO,

13.–14. NOVEMBER 2019

The 26th Norwegian Conference on Epidemiology
Oslo, November 13–14, 2019

We would like to welcome you to Oslo and the 26th conference of the Norwegian Epidemiological Association (NOFE). Our annual conference continues to be an important meeting place for the epidemiological community in Norway.

The theme of this year's conference is *Life course epidemiology – from cradle to grave*. We are delighted to have three keynote speakers who will address different aspects of life course epidemiology from etiology to data analysis in their lectures; Professor Deborah Lawlor (UK), Associate professor Ruth Keogh (UK) and Professor Gita Mishra (Australia). Their short biographies are presented on page 5.

We have received 82 abstract submissions for poster or oral presentations. Our parallel sessions cover topics from reproduction to mortality and a wide range in between, reflecting the diversity of the ongoing epidemiological research in Norway. This year we have included a special session for Norwegian cohort studies. This session was proposed by the Cohort of Norway (CONOR) as an opportunity to come together, present and discuss the potential for future research. The response has been positive with 11 contributions, including new data linkage possibilities; the County Public Health Surveys and the Norwegian Registry for Primary Health Care.

In an academic life-course perspective, our national research school in population based epidemiology – EPINOR – has an important role in securing the next generation of epidemiologist. We will hear more about the status and future of EPINOR in a plenary presentation and it is great to see that a number of EPINOR students are joining us for the conference in conjunction with their annual meeting. We hope that NOFE will continue to be a venue for interaction and collaboration between our senior and younger epidemiologists.

In keeping with tradition, we will award two prizes: "Paper of the year" and "NOFE honorary membership". The latter is awarded to a senior epidemiologist who has made a significant contribution to epidemiological research in Norway.

If you have a thematic suggestion for upcoming issues of *Norsk Epidemiologi – the Norwegian Journal of Epidemiology,* use the opportunity to talk to editor Trond Peder Flaten or NOFE leader Linda Ernstsen during the conference.

We hope to see many of you at the NOFE annual meeting and please join us for a welcome drink at 7 pm at restaurant DS Louise where we will have dinner at 7.30 pm.

We thank the Cancer Registry of Norway for their financial support to the conference.

Welcome to Oslo and NOFE 2019!

The NOFE Board
&
The organizing committee for the NOFE 2019 Conference

Christine L Parr, Karin Magnusson
Maria C Magnus, Nathalie C Støer, Morten Valberg

The Norwegian Institute of Public Health, Diakonhjemmet Hospital, Oslo University Hospital, the Cancer Registry of Norway

The 26th Norwegian Conference on Epidemiology

Oslo, November 13–14, 2019

Programme Overview

Wednesday, November 13th

09:00	**Registration** at Nationaltheatret Konferansesenter, KS Agenda Poster mounting
09:45	**Welcome and opening**: NOFE leader Linda Ernstsen
09:55	**Keynote speaker: Prof. Debbie Lawlor, MRC Integrative Epidemiology Unit, University of Bristol, UK** *"Exploring causal effects of early life exposures on health and development"* Chair: Maria C Magnus
10:45	**Coffee break** with refreshments
11:00	**Oral presentations of submitted abstracts – 1:** *Cohort session A1-A6 (Nordkapp)* *Cardiovascular diseases B1-B6 (Finse, Færder og Fredriksten)* *Infectious diseases C1-C6 (Stiklestad)*
12:30	**Lunch**
13:30	**Publication of the year award and Honorary membership award** Chairs: NOFE secretary Marie Wasmuth Lundblad and NOFE leader Linda Ernstsen
14:30	**Coffee break**
14:45	**Oral presentations of submitted abstracts – 2:** *Cohort session (cont.) A7-A11 (Nordkapp)* *Cancer B7-B11 (Finse, Færder og Fredriksten)* *Pregnancy C7-C11 (Stiklestad)*
16:00	**Coffee break** with refreshments
16:15	**EPINOR – National research school in population based epidemiology (2013-2020)** Prof. Torkjel Sandanger, EPINOR scientific coordinator Chair: NOFE leader Linda Ernstsen
16:30-17:30	**NOFE annual meeting**
19:00	**Welcome drink** at DS Louise, Aker Brygge, Stranden 3, 0250 Oslo
19:30	**Conference dinner** at DS Louise

Thursday, November 14th

09:00-09:50	**Keynote speaker: Prof. Gita Mishra, School of Public Heath, University of Queensland, Australia** *"Visualization and modelling changes in categorical variables in longitudinal studies"* Chair: Bjørn Heine Strand
10:00	**Oral presentations of submitted abstracts – 3:** *Lifestyle: A12-A15 (Nordkapp)* *Mental health: B12-B15 (Finse, Færder og Fredriksten)* *Methods: C12-C15 (Stiklestad)*
11:00	**Poster viewing** and coffee break with refreshments *Posters P1-P8 (outside Nordkapp)*
11:30	**Oral presentations of submitted abstracts – 4:** *Skin cancer: A16-A19 (Nordkapp)* *Early life and adolescence: B16-B19 (Finse, Færder og Fredriksten)* *Musculoskeletal: C16-C19 (Stiklestad)*
12:30	**Lunch**
13:30	**Keynote speaker: Associate prof. Ruth Keogh, Dept. of Medical Statistics at the London School of Hygiene & Tropical Medicine, UK** *"Estimating long-term treatment effects in observational data"* Chair: Nathalie C Støer
14:20	**Coffee break** with refreshments
14:35	**Oral presentations of submitted abstracts – 5:** *Cancer (cont.): A20-A24 (Nordkapp)* *Reproductive epidemiology: B20-B24 (Finse, Færder og Fredriksten)* *Various topics: C20-C24 (Stiklestad)*
15:50	**Closing of the conference by NOFE leader Linda Ernstsen**

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Keynote speakers' biographies

Deborah Lawlor

Deborah Lawlor was born in Bradford and studied medicine at Bristol University before working as a doctor in Bradford and Mozambique. She moved back to Bristol in 2000 to study for a PhD. She is now a Professor of epidemiology in the Medical Research Council Integrative Epidemiology Unit at the University of Bristol. Her research is concerned with developing and applying novel causal methods to better understand the causes of adverse reproductive, perinatal and cardio-metabolic health, and the links between those conditions.

Gita Mishra

Gita Mishra is a National Health and Medical Research Council (NHMRC) Principal Research Fellow and Professor of Life Course Epidemiology at the School of Public Heath, University of Queensland. She is Director of the Australian Longitudinal Study on Women' Health (ALSWH), a major national study running since 1996. Previously, while in the UK, she held positions as Senior Research Scientist and as Program Leader at Medical Research Council units at Cambridge and University College London (UCL). Her academic/professional qualifications include a PhD in Statistics (1997) from the University of Auckland, NZ, and she is currently recognised as a Chartered Statistician (Royal Statistical Society) and a Chartered Scientist (UK Science Council). She is internationally recognised for her contribution to research on life course epidemiology and women's health. Her specific focus is on the factors that affect reproductive health from menarche to menopause, and the influence of reproductive health across the life course. She has more than 300 peer-reviewed scientific papers and book chapters, including co-editorship of a key academic textbook on Family Based Studies. In 2017, she was presented an honorary membership of Sigma International, a global nursing organisation, for her contribution to women's health and was elected as a Fellow of the Australian Academy of Health and Medical Sciences (FAHMS). Most recently she was the presented with "2018 Leader of the Year" award by the Faculty of Medicine, The University of Queensland.

Ruth Keogh

Ruth Keogh is an Associate Professor in the Department of Medical Statistics at the London School of Hygiene & Tropical Medicine. Ruth studied Maths and Statistics at the University of Edinburgh, before studying for a master's degree and DPhil at the University of Oxford. She joined the London School of Hygiene & Tropical Medicine in 2012, following previous positions in Oxford and Cambridge. Ruth is interested generally in statistical methodology for the analysis of longitudinal observational data, including for prediction and causal inference. She has worked in several areas of application in epidemiology and is now particularly focusing on research in cystic fibrosis. Ruth's recent work has been funded by a UK Medical Research Council Fellowship. In 2018 she received a Suffrage Science Award for women working in maths and computing.

The 26th Norwegian Conference on Epidemiology

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Scientific Programme for Parallel Sessions

Oral presentations of submitted abstracts – 1

Nordkapp			
Time	**No.**	**Cohort session** **Chairs: Per M Magnus, Inger Njølstad**	**Presenters**
11:00	A1	The Cohort of Norway (CONOR) – past, present and future	Magnus, Per M
11:15	A2	The Tromsø Study 1974-2016	Grimsgaard, Sameline
11:30	A3	The HUNT Study since the 1980s, an expanding success	Krokstad, Steinar
11:45	A4	The Population-based Study on Health and Living in Regions with Sami and Norwegian Populations – the SAMINOR Study	Broderstad, Ann Ragnhild
12:00	A5	The Norwegian Women and Cancer Cohort (NOWAC)	Sandanger, Torkjel M
12:15	A6	Healthy Choices and the Social Gradient – research possibilities arising from collaboration between large population studies on health	Njølstad, Inger

Finse, Færder og Fredriksten			
Time	**No.**	**Cardiovascular diseases** **Chairs: Gerhard Sulo, Øyvind Næss**	**Presenters**
11:00	B1	Secondary prevention of cardiovascular disease needs improvement in men and women, with and without diabetes: The Tromsø Study 2015-16	Hopstock, Laila Arnesdatter
11:15	B2	Antibodies to specific oral bacteria differ in predicting cardiovascular disease mortality	Håheim, Lise Lund
11:30	B3	Management of modifiable cardiovascular risk factors (blood pressure and lipids) following diagnosis of Myocardial Infarction, Stroke and Diabetes: Comparison between Russia and Norway	Cook, Sarah
11:45	B4	Prevalence and incidence rates of atrial fibrillation in Norway 2004-2014 – a CVDNOR study	Ariansen, Inger
12:00	B5	Weight and weight change and risk of atrial fibrillation – the HUNT Study	Feng, Tingting
12:15	B6	Risk of coronary heart diseases and stroke in the Sami and non-Sami populations in rural Northern Norway – the SAMINOR Study	Siri, Susanna Ragnhild Andersdatter

Oral presentations of submitted abstracts – 1 (continued)

		Stiklestad	
Time	**No.**	**Infectious diseases** **Chairs: Anne-Sofie Furberg, Lars Christian Stene**	**Presenters**
11:00	C1	Smokeless Tobacco and Carriage of *Staphylococcus aureus*; The Tromsø Study – Fit Futures 1	Karlsen, Anna
11:15	C2	Atopic disease in relation to *Staphylococcus aureus* carriage and spa type distribution in a subarctic adult population	Devold, Jonas Arvola
11:30	C3	Quantifying the transmission dynamics of MRSA in the community and healthcare settings in a low-prevalence country: a modelling study	Di Ruscio, Francesco
11:45	C4	Parechovirus infections and increased risk of coeliac disease: nested case-control study within the MIDIA longitudinal birth cohort	Tapia, German
12:00	C5	Hospitalization with pandemic influenza and mortality in people with and without type 2 diabetes	Ruiz, Paz LD
12:15	C6	Genomic definition of the global pneumococcal population to contextualise disease, vaccine impact and antibiotic resistance	Gladstone, RA

Oral presentations of submitted abstracts – 2

Nordkapp			
Time	**No.**	**Cohort session (continuing)** **Chairs: Sameline Grimsgaard, Per M Magnus**	**Presenters**
14:45	A7	The Norwegian Mother, Father and Child Cohort Study, an infrastructure for research	Vejrup, Kristine
15:00	A8	The Norwegian Environmental Biobank	Thomsen, Cathrine
15:15	A9	Population based Regional Health Studies – a ground for harvesting	Ariansen, Inger
15:30	A10	County Public Health Surveys – new resource for research?	Nilsen, Thomas
15:45	A11	The Norwegian Patient Registry and the Norwegian Registry for Primary Health Care: Research potential of two nationwide healthcare registries	Jensberg, Heidi
Finse, Færder og Fredriksten			
Time	**No.**	**Cancer** **Chairs: Tom Grotmol, Nathalie C Støer**	**Presenters**
14:45	B7	Does the increased risk of colorectal cancer (CRC) due to cigarette smoking differ by sex for the right – and left colon cancer as well as rectal cancer?	Gram, Inger T
15:00	B8	Body fatness and type 1 and type 2 endometrial cancer: The Norwegian Women and Cancer Study	Rylander, Charlotta
15:15	B9	Reproductive factors, exogenous hormone use and risk of pancreatic cancer – The Norwegian Women and Cancer Study	Borch, Kristin B
15:30	B10	A Healthy Lifestyle Index and associated risks of breast, lung and colon cancers in the Norwegian Women and Cancer study	Chen, Sairah L
15:45	B11	Urinary tract cancer incidence among males in the Norwegian Offshore Petroleum Workers (NOPW) cohort	Shala, Nita K
Stiklestad			
Time	**No.**	**Pregnancy** **Chairs: Anne Lise Brantsæter, Liv G Kvalvik**	**Presenters**
14:45	C7	Women's risk of miscarriage according to chronic underlying conditions	Magnus, Maria Christine
15:00	C8	Introduction of fetal diagnostic technology: the impact on fetal death rates in Norway	Eskild, Anne
15:15	C9	Placental weight and risk of neonatal death	Dypvik, Johanne
15:30	C10	The Norwegian birthweight "hump" 1992-2007	Carlsen, Ellen Øen
15:45	C11	Associations between maternal vitamin D status in second and third trimester of pregnancy and offspring enamel hypomineralisation at 7-9 years: a longitudinal study	Børsting, Torunn

Oral presentations of submitted abstracts – 3

Nordkapp			
Time	**No.**	**Lifestyle** **Chairs: Nicolai A Lund-Blix, Marie Wasmuth Lundblad**	**Presenters**
10:00	A12	Salt intake estimated from 24-hour urine and spot urine collection in the Tromsø study 2015-16	Meyer, Haakon E
10:15	A13	Compliance to five-a-day in a Norwegian population. Daily intake of vegetables, fruits and berries and comparison with the Norwegian nutrition recommendations – The Tromsø Study 2015-16	Nilsen, Linn
10:30	A14	Is the ongoing overweight/obesity epidemic partly explained by concurrent decline in cigarette smoking? The Tromsø Study 1994–2016	Løchen, Maja-Lisa
10:45	A15	Physical activity and gene expression in the Norwegian Women and Cancer Post-genome Cohort	Lukic, Marko
Finse, Færder og Fredriksten			
Time	**No.**	**Mental health** **Chairs: Ann Ragnhild Broderstad, Linda Ernstsen**	**Presenters**
10:00	B12	Are psychosocial working conditions associated with suicide and deliberate self-harm? A register-based study of 420,895 Norwegians	Mehlum, Ingrid S
10:15	B13	Associations between human service work and mental disorders: causal or not? A registry-based study of Norwegians born 1967-1976	Kristensen, Petter
10:30	B14	Weight underestimation linked to anxiety and depression in a cross-sectional study of overweight individuals in a Sami and non-Sami Norwegian population: The SAMINOR Study	Kvaløy, Kirsti
10:45	B15	Insomnia prevalence varies substantially dependent on classification criteria: The Tromsø Study 2015-2016	Hopstock, Laila Arnesdatter
Stiklestad			
Time	**No.**	**Methods** **Chairs: Morten Valberg, Christian M Page**	**Presenters**
10:00	C12	Landmark estimation of transition probabilities – with an application to registry data on sickness absence and work	Maltzahn, Niklas
10:15	C13	Exploring the individually-randomised stepped wedge design for trials where all patients eventually receive the intervention	Olsen, Inge Christoffer
10:30	C14	Hypothetical interventions and risk of myocardial infarction in a general population of adults. Application of parametric g-formula to the Tromsø Study	Wilsgaard, Tom
10:45	C15	Towards a composite index for socioeconomic position when studying health inequalities	Lindberg, Marie Hella

Oral presentations of submitted abstracts – 4

Nordkapp			
Time	**No.**	**Skin cancer** **Chairs: Marit B Veierød, Trude Robsahm**	**Presenters**
11:30	A16	Skin cancer incidence among males and females in the Norwegian offshore petroleum workers (NOPW) cohort	Liu, FC
11:45	A17	Use of antidepressants and risk of cutaneous melanoma: A prospective case-control study	Berge, LAM
12:00	A18	DNA methylation profiles in blood in relation to melanoma in the Norwegian Women and Cancer study	Page, Christian M
12:15	A19	Sunscreen use and subsequent risk of cutaneous squamous cell carcinoma	Lergenmuller, Simon

Finse, Færder og Fredriksten			
Time	**No.**	**Early life and adolescence** **Chairs: To be determined**	**Presenters**
11:30	B16	Parent-offspring recurrence of attention-deficit/hyperactivity disorder	Solberg, Berit S
11:45	B17	Gluten intake in early life and risk of type 1 diabetes	Lund-Blix, Nicolai A
12:00	B18	Adolescent body composition in relation to birth weight and childhood growth patterns. The Tromsø study: Fit Futures	Evensen, Elin
12:15	B19	The association between objectively measured physical activity and longitudinal changes in body composition in adolescents; The Tromsø Study Fit Futures Cohort	Aars, Nils Abel

Stiklestad			
Time	**No.**	**Musculoskeletal health** **Chairs: Kristin Holvik, Anne Johanne Søgaard**	**Presenters**
11:30	C16	Midlife bone mineral density loss in the distal forearm and subsequent mortality: findings from the population based Tromsø Study	Hauger, Annette V
11:45	C17	Individual Variation in Adaptive Immune Responses and Risk of Hip Fracture – A NOREPOS Population-Based Cohort Study	Dahl, J
12:00	C18	Hand-arm vibration syndrome: A 22-year follow-up study	Aarhus, Lisa
12:15	C19	Sickness absence duration in young adults with musculoskeletal and psychological diagnoses: impact of the Norwegian Agreement for a More Inclusive Working Life	Hasting, Rachel L

Oral presentations of submitted abstracts – 5

Nordkapp			
Time	**No.**	**Cancer** **Chairs: Bettina Kulle Andreassen, Anette Hjartåker**	**Presenters**
14:35	A20	Associations between lifestyle factors and risk of bladder cancer, in a large population-based Norwegian cohort	Hektoen, Helga H
14:50	A21	Asthma, asthma control and incidence of lung cancer: the HUNT Study	Jiang, Lin
15:05	A22	Serum 25-Hydroxyvitamin D levels predict cancer survival: A prospective cohort with measurements prior to and at the time of cancer diagnosis	Robsahm, Trude E
15:20	A23	Cisplatin treatment of testicular cancer introduces long-term changes to the epigenome, possibly associated with metabolic syndrome	Wojewodzic, Marcin W
15:35	A24	The clone war of cancer clones of immune cells versus clones of cancer cells	Lund, Eiliv
Finse, Færder og Fredriksten			
Time	**No.**	**Reproductive epidemiology** **Chairs: Siri Håberg, Maria C Magnus**	**Presenters**
14:35	B20	Inadequate iodine intake is associated with subfecundity in mild-to-moderately iodine deficient Norwegian women	Brantsæter, Anne Lise
14:50	B21	Hearing impairment and gender specific patterns of fertility – evidence from the HUNT study in Norway	Skirbekk, Vegard
15:05	B22	Temporal trends in age at menarche and age at natural menopause: a population study of 312 656 women in Norway	Gottschalk, Marthe S
15:20	B23	The association of birthweight with age at natural menopause. A population study of women in Norway	Bjelland, Elisabeth K
15:35	B24	Growth in children conceived by assisted reproductive technologies: the Norwegian Mother and Child Cohort Study	Magnus, Maria C
Stiklestad			
Time	**No.**	**Various topics** **Chairs: Charlotta Rylander, Laila Hopstock**	**Presenters**
14:35	C20	Evaluating exposure to environmental contaminants across past decades in the context of effect studies today	Nøst, Therese Haugdahl
14:50	C21	Relationship between periodontitis and Alzheimer's disease: A bidirectional Mendelian randomization study	Sun, Yi-Qian
15:05	C22	Trends in disability free life expectancy in the older Norwegian population: it is getting better	Strand, Bjørn Heine
15:20	C23	Air pollution and mortality in Norway – using NORCOHORT	Oftedal, Bente
15:35	C24	Are compensation claims from patients associated with 30-day mortality? A longitudinal analysis of health trusts in Norway	Skyrud, Katrine Damgaard

The 26th Norwegian Conference on Epidemiology
Oslo, November 13–14, 2019

Submitted abstracts

EPINOR – National Research School in Population based epidemiology (2013-2020)

Torkjel M Sandanger[1], Tom Ivar Lund Nilsen[2], Bente Evjen Schøning[1]
(on behalf of the steering committee EPINOR)

1) Department of Community Medicine, UiT the Arctic University of Norway, Tromsø, Norway
2) Department of Public Health and nursing, NTNU, Trondheim, Norway

EPINOR is one of the national research schools that received funding from the National Research Council for eight years. The partners of EPINOR are UiB, UiO, NTNU, UiT, UiS, FHI and STAMI and we are currently 150 PhD students. The external four-year evaluation confirmed that we have been successful in a number of our activities, including strengthening the national network of PhD students and the student's interaction with other research groups. Our main activities have been a yearly Summer School and fall meetings in conjunction with the NOFE conference. Our activities have also included funding of students attending courses abroad, development of new courses nationally, supervisor seminars and funding of international and national guest lecturers.

As we now are in our last two years of the funding period, we would like to present what has been achieved so far, our activities in the last period, and some of our plans for future activities and follow-up of this effort.

One key effort for the future is a stronger collaboration with NOFE. We encourage everyone to talk to us during the NOFE conference, about the field of epidemiology training and suggestions for activities in 2020 and beyond.

A1

The Cohort of Norway (CONOR) – past, present and future

Per Magnus[1], Steinar Krokstad[2], Inger Njølstad[3], Øyvind Næss[4], Grethe S. Tell[5], Thomas S. Nilsen[1]

1) Norwegian Institute of Public Health, Oslo, Norway
2) HUNT Research Centre, Department of Public Health and Nursing, Norwegian University of Science and Technology, Trondheim, Norway
3) Department of Community Medicine, University of Tromsø – The Arctic University of Norway, Tromsø, Norway
4) Department of Community Medicine and Global Health, University of Oslo, Oslo, Norway
5) Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

CONOR – the early days: In the years 1987-1992, the Research Council of Norway (RCN) had a programme to strengthen epidemiology as an academic discipline in Norway. One of the suggestions from the steering group of this programme was to set up a large nation-wide cohort, collecting standardized exposure data, including biological samples, and later link to endpoints in health registries. The main intention was to detect causes of rare, but serious diseases, using nested case-control designs. After discussions, the initiative was transformed into a collaborative effort between the major epidemiology centres in Norway. The data collection started with the Tromsø IV study in 1994, followed by the HUNT II study in 1995-97. Other important parts were the HUSK study in Hordaland (1997-99) and the HUBRO study in Oslo (2000-01). The aim was to include more than 200 000 participants in the cohort. CONOR was coordinated by a steering group set down by the Ministry of Health. The biobank for CONOR was established together with the HUNT biobank in Levanger.

CONOR – present status: The different cohorts that have contributed data and biological samples are run by the universities in Tromsø, Trondheim and Bergen and by the Norwegian Institute of Public Health (NIPH). A steering committee evaluates applications for access to data. A series of studies have been performed. CONOR has benefitted from infrastructure grants from the RCN to BIOHEALTH as well as BIOBANK I and BIOBANK II. This has paid for the extraction of DNA from blood samples. The legal status of CONOR is being consolidated through new agreements in 2019. More information on the present status and publications from CONOR can be found at www.fhi.no/conor.

CONOR – future: Modern developments in informatics and genomics have made large, population-based cohorts even more useful than envisaged by the early pioneers. The possibilities to link CONOR to a series of other Norwegian data sets opens for new research initiatives across many disciplines. CONOR is becoming more valuable as time passes. The aim of the presentation is to encourage further use of this great, Norwegian resource.

A2

The Tromsø Study 1974-2016

Sameline Grimsgaard, Laila Arnesdatter Hopstock, Inger Njølstad

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

Introduction: The Tromsø Study is Norway's most longstanding and comprehensive population-based cohort study. From 1974 to 2016, we have conducted seven surveys with high attendance rates (65-79%) in the municipality of Tromsø. The Fit Futures youth cohort has been surveyed twice and with high attendance in 2010-11 (93%) and 2012-13 (77%). We plan the third survey in 2020-21.

Aims: The Tromsø Study was initiated to study incidence, prevalence, risk factors and prevention of cardiovascular disease (CVD). It has expanded to cover a wide range of chronic diseases, risk factors and endpoints. The Tromsø 7 survey (2015-16) is the most comprehensive to date. New focus areas are antimicrobial resistance, physical activity, diet, ageing, dental health, mental health, substance abuse and social inequality in health.

Methods: The database comprises data from *questionnaires* (work, disease, well-being, use of health care services and medications, sleep, reproduction, smoking, alcohol and more); *physical measurements* (anthropometry, blood pressure, heart rate); *clinical examinations* (echocardiography, electrocardiography, carotid ultrasound, body composition, bone density, pain sensitivity, dental examinations, lung function, cognitive and physical function, eye examination, accelerometry); and *biological samples* (blood, urine, hair, saliva, nasal swabs and faeces). *Endpoint registries* cover CVD, venous thromboembolism, diabetes, fractures and annual updates to the Norwegian Cancer and Death Registries.

Results: 45,473 women and men participated at least once, and 18,510 participated ≥ 3 times. The study forms basis for 800 scientific publications, > 140 Ph.D.'s and 220 ongoing research projects. The cohort is recruitment base for several intervention studies.

High CVD-mortality in the 1970ties was attributed to high total cholesterol, blood pressure and smoking. The Tromsø Study shows that two thirds of the CVD-mortality reduction is attributed to decline in these three major risk factors. Well known findings are that boiled coffee increases total cholesterol, whereas HDL-cholesterol protects against CVD. Recent findings are that men who quit smoking and increase physical activity before 55 years have significantly improved survival to 90 years.

Conclusions: The Tromsø Study has rich data from questionnaires, measurements, clinical examinations, biological samples and endpoint registries, offering unique possibilities to study secular and longitudinal trends in risk factors and chronic disease.

A3

The HUNT Study since the 1980s, an expanding success

Steinar Krokstad[1,2], Arnulf Langhammer[1], Marit Næss[1], Bjørn Olav Åsvold[1,3], Vegar Rangul[1,4], Kristian Hveem[1], Erik R Sund[1]

1) HUNT Research Centre, Department of Public Health and Nursing, NTNU
2) Levanger Hospital, Nord-Trøndelag Health Trust
3) St. Olavs Hospital
4) Nord Universitet

Introduction: The HUNT Study has followed a Norwegian county population since 1984 covering people aged 13 to 103 years in four decennial data collections. Materials from interviews, questionnaires, clinical examinations and biological samples (blood and urine, saliva and faeces in the latest survey) are quality assured and available from HUNT databank and biobank for research. Big data can be analysed in HUNT Cloud.

Aims: To present an overview of the HUNT Study assets and material, and present some highlights from health statistics and research.

Methods: The data collection in HUNT is based on a decentralized structure by establishing temporary examination stations in all municipalities in the county (23 municipalities in HUNT4), and in classrooms and nurse offices in all secondary schools and high schools (60 schools in Young-HUNT4). The total population of adults was invited in HUNT1 (1984-86), HUNT2 (1995-97), HUNT3 (2006-08) and HUNT4 (2017-19), and the total population of adolescents in Young-HUNT1 (1995-97), Young-HUNT3 (2006-08) and Young-HUNT4 (2017-19), establishing cohorts to be followed for decades. All adults participating in HUNT2 and HUNT3 are genotyped. The data can be linked to several population-, family-, health- and administrative national registers covering alle participants, providing unlimited research opportunities.

Results: In total 144.000 participants have attended. The attendance rate was approx. 90% (HUNT1), 70% (HUNT2), 54% (HUNT3) and 54% (HUNT4), 90% (Young-HUNT1), 78% (Young-HUNT3) and 75% (Young-HUNT4). More than 19.000 adults have participated four times. Approx. 100 scientific papers are published annually, and about 200 PhDs are completed from a broad range of scientific environments, both nationally and internationally.

Conclusions: The HUNT Study has followed a Norwegian general population for more than three decades, describing changes in population health over time, generating knowledge and insight in disease development and treatment, and are contributing to innovations and targeted improvements in preventive medicine and health care.

A4

The Population-based Study on Health and Living in Regions with Sami and Norwegian Populations – the SAMINOR Study

Ann Ragnhild Broderstad[1,2], Marita Melhus[1]

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Introduction: The Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations – The SAMINOR Study consist of three separate surveys; the SAMINOR 1 Survey (2003–2004), the SAMINOR 2 Questionnaire Survey (2012) and the SAMINOR 2 Clinical Survey (2012–2014).

Aims: The main objectives are to assess associations between lifestyle factors and risk factors for disease in relation to the different ethnic groups.

Methods: In SAMINOR 1 inhabitants aged 30, 35–79 yr in 24 selected municipalities were invited. Participation rate was 61%. The SAMINOR 2 Questionnaire Survey, was performed in the same areas as SAMINOR 1. The invitees was in the age range 18–69 yr. The participation rate was low (27%). The SAMINOR 2 Clinical Survey was done in 10 selected SAMINOR municipalities. The age range was 40–79 yr, with a participation rate of 49%. The 11 questions regarding ethnicity were identical in all three surveys.

Results: The definition of ethnic groups is a core question in the SAMINOR Study and can be defined in different ways, depending on the selected criteria. The questions include both objective and subjective criteria. Self-reported ethnicity information enables comparisons between Sami and non-Sami participants. Selected results from all of the three surveys, will be presented with focus cardiovascular diseases, type 2 diabetes mellitus and mental health.

Conclusions: The study design with both objective and subjective criteria on Sami language and self-perceived ethnicity and identity, makes it possible to categorize the participating sample into indigenous versus non-indigenous groups. This has resulted in valuable information about lifestyle and diseases in high north.

A5

The Norwegian Women and Cancer Cohort (NOWAC)

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The Norwegian Women and Cancer Study (NOWAC) is a randomly sampled, nationally representative prospective cohort study, that was initiated in 1991 by Prof Eiliv Lund. The main aim was to study associations between lifestyle and cancer among women. Currently, more than 170,000 women have been enrolled. The study participants were enrolled in batches in the period 1991-2005. At entry, the women were 30-70 years. The questionnaires have been between 2-8 pages and include detailed information about reproductive factors, anthropometry, smoking habits, alcohol intake and includes information on SES and childhood conditions as well as validated food frequency questionnaires. Cancer outcomes and mortality is updated yearly. A sub-cohort of the NOWAC study constitutes the Norwegian sub-cohort of the European Prospective Investigation into Cancer and Nutrition coordinated at the International Agency for research on Cancer (IARC).

The majority of the participants has filled in at least two follow-up questionnaires, and the last follow up was in 2016. In addition to answering questionnaires, 50,000 of the women donated blood, including preserved mRNA in PAX tubes, white blood cells (buffy coat), and plasma. During the last decade, several studies within the cohort have demonstrated the feasibility of obtaining good quality data for gene expression and epigenetics in this prospective cohort. Through a number of externally funded projects, the cohort has accumulated a substantial amount of data on molecular markers in blood for a number of cancer types.

The detailed and repeated information for each participating woman in a nationally representative study, gives a unique opportunity to estimate population attributable fractions (PAFs) for possible single and/or combined risk factors for cancer and other non-communicable disease endpoints.

A6

Healthy Choices and the Social Gradient – research possibilities arising from collaboration between large population studies on health

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Introduction: In modern welfare states like Norway, all citizens have in principle equal access to education and health services. Yet social inequalities in health are increasing. What kind of actions and interventions can successfully reduce these inequities? The current understanding of behaviour, biological markers and socioeconomic status is based on a simplistic understanding of their relationship and future risk of disease. As a result, intervention efforts at the individual and societal level have been of limited value. Our project has access to unique data sources that enable the combination of these factors, by applying cutting-edge analytical methods and technology. We will address current challenges in public health by exploring systematic differences in lifestyle and health over the life course and across generations and socioeconomic groups, using existing population studies with follow-up data on health and disease.

Aims: We aim to increase our understanding of determinants that shape people's health trajectories and their interplay: prenatal and childhood circumstances, socioeconomic position, health related behaviour and social relationships. Our ultimate goal is to increase knowledge about how policy and interventions can improve population health and reduce health inequities between groups and geographical areas.

Methods: Supported by the Research Council of Norway, the *Healthy Choices* project includes research on health behaviour and social inequalities in health carried out at UiT the Arctic University of Norway in collaboration with national and international partners. We will use large longitudinal population based studies in the Northern region (SAMINOR, The Tromsø Study, The Finnmark Study) and Norway (Norwegian Women and Cancer Study), with up to 45 years' follow-up and with self-reported information on health related behaviour, quality of life and wellbeing, and (for some) childhood living conditions. Results from clinical tests and biomarkers, including epigenetic data, are available from several studies. Datasets will be linked with national health registries. We will use intervention trials and social media platforms to test the effect of actions that aim to reduce health inequalities. *Healthy choices* will be implemented in UiT educational programs, enabling active student involvement in all phases of research including the planning of a new student survey.

B1

Secondary prevention of cardiovascular disease needs improvement in men and women, with and without diabetes: The Tromsø Study 2015-16

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Introduction: Cardiovascular disease (CVD) secondary prevention guidelines emphasise treatment targets and lifestyle modification to decrease the risk of recurrent events. Patients with diabetes are at particularly high risk of disease progression and premature death.

Aims: Investigate treatment and lifestyle target achievement after CVD among women and men with and without diabetes, in a population-based sample.

Methods: Among 21083 participants from the seventh wave of the Tromsø Study 2015-2016 (attendance 65%), CVD prevalence (self-reported and/or validated myocardial infarction and/or stroke) was 6% (n=1245), of whom 14% had diabetes. We used logistic regression models adjusted for age to investigate current treatment guidelines target achievement for blood pressure (<140/90 mmHg, <130/80 mmHg if diabetes), LDL cholesterol (<1.8 mmol/L) and HbA1c (<7.5% if diabetes) levels, body mass index (<25 kg/m^2), abdominal obesity (waist circumference <80 cm in women, <94 cm in men), smoking (non-smoking), physical activity (self-reported >sedentary, accelerometer-measured moderate-to-vigorous ≥150 min/week), diet (fruit intake ≥200 g/day, vegetable intake ≥200 g/day, saturated fat intake <10% of total energy intake) and medication use (antihypertensives, lipid-lowering drugs, antidiabetics if diabetes), in women and men aged 40-95 years, by diabetes status.

Results: Prevalence of target achievement for risk factors and medication use varied in participants both with and without diabetes; blood pressure (32% vs 58%, p<0.001), LDL cholesterol (13% vs 9%, p=0.066), body mass index (11% vs 25%, p<0.001), abdominal obesity (6% vs 19%, p<0.001), smoking (88% vs 89%, p=0.806), self-reported (65% vs 81%, p<0.001) and accelerometer-measured (10% vs 12%, p=0.666) physical activity, fruit- (61% vs 66%, p=0.410), vegetable- (39% vs 38%, p=0.791), and saturated fat- (14% vs 22%, p=0.099) intake, and use of antihypertensives (76% vs 62%, p<0.001) and lipid-lowering (83% vs 74%, p=0.020) drugs. Among participants with diabetes, 59% achieved the HbA1c level target and 85% used antidiabetics. Target achievement was more prevalent in men compared to women, except for HbA1c, body mass index and fruit- and vegetable intake. Further, all medication use was more prevalent in men compared to women.

Conclusions: Secondary prevention of CVD was suboptimal both in participants with and without diabetes.

B2

Antibodies to specific oral bacteria differ in predicting cardiovascular disease mortality

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Introduction: An infection hypothesis in cardiovascular disease has been discussed over the years. We have investigated if, which, and how oral bacteria may predict cardiovascular disease (CVD). From the oral cavity more than 700 bacterial species have been identified. Our choice of which bacteria to include in our study were based on clinical and microbiological knowledge. They comprised *Aggregatibacter actinomycetemcomitans* (AA), a facultative bacteria, and three anaerobes *Tannerella forsythia* (TF), *Porphyromonas gingivalis* (PG), and *Treponema denticola* (TD). The latter three are termed collectively 'The red complex'.

Aim: To study antibody levels to the four oral bacteria AA, TF, PG, and TD as predictors for CVD mortality, adjusting for known confounders.

Methods: This analysis originates from the Oslo II–study on men that was performed in 2000. The participants had previously been invited and most had participated in the health survey called the Oslo–study 1972/73. In the Oslo II health survey was registered questionnaire information on different health aspects including oral health as infections and tooth extraction, serum analyses for total cholesterol, triglycerides, HDL, glucose, body measurements of blood pressure and anthropometic measurements. Full blood and remaining serum after the analyses were stored at –80 °C. From frozen serum was later analysed hs-CRP and antibody measurements by the ELISA technique of the four bacteria mentioned. Cox proportional hazards regression analyses were used in prediction models for mortality. Information on cause specific deaths were supplied by Statistics Norway.

Results: Different prediction models were tried out for the antibody measurements. Using quartile values and trend worked the best. These measurements showed that there were differences among the bacteria. AA, a common oral bacteria closer linked to gingivitis, behaved different from the other three that are causal to severe periodontitis. This could be due to their different requirements as anaerobes versus facultative anaerobes. 'The red complex' bacteria predicted mortality differently for cases versus controls.

Conclusions: Antibody measurements to oral bacteria provides more knowledge linking oral infections to a major systemic disease, cardiovascular disease.

Manuscript submitted.

B3

Management of modifiable cardiovascular risk factors (blood pressure and lipids) following diagnosis of Myocardial Infarction, Stroke and Diabetes: Comparison between Russia and Norway

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Introduction: Cardiovascular disease (CVD) is the leading cause of death worldwide. CVD mortality is particularly high in Russia, much higher than in neighbouring Norway. Following diagnosis of CVD, secondary prevention through management of modifiable risk factors such as elevated blood pressure and lipids is crucial to improve long-term prognosis.

Aim: To compare use of medications for reducing blood pressure and lipids and subsequent levels of control between Russia and Norway in those with existing CVD.

Methods: The study population was adults aged 40-69 years reporting a diagnosis of myocardial infarction (MI), stroke and/or diabetes participating in cross-sectional population-based studies in Russia (Know Your Heart (KYH) 2015-18 N=626) and Norway (seventh wave of the Tromsø Study 2015-16 (Tromsø 7 N=1353). Reported medications were coded in line with the Anatomical Therapeutic Chemical classification system (2016). Targets for control of blood pressure and low-density lipoprotein (LDL) cholesterol were defined using the 2016 Joint European Societies guidelines for CVD prevention in clinical practice.

Results: Age- and sex-standardized prevalence of use of lipid-lowering medications was higher in Tromsø 7 for those reporting all three diseases but with a disproportionately large difference in those reporting MI (+48% (95% CI 39%, 57%)). Control of LDL cholesterol was poor in both studies. Use of blood pressure medication was higher in KYH for stroke (+40% (95% CI 30%, 50%)) and diabetes (+27% (95% CI 19%, 34%)) groups but approximately equal for the MI group (-1% (95% CI -1%, 1%)). Despite higher use of blood pressure medication, blood pressure control was poorer among the Russian participants (age- and sex-standardized prevalence of blood pressure controlled to treatment guidelines: MI 51.8% vs 76.3%, stroke 49.5% vs 69.6%, diabetes 51.9% vs 63.9%).

Conclusions: We identified several differences in the management of blood pressure and lipids in people with CVDs participating in population-based surveys in Russia and Norway. Of particular note were differences in lipid-lowering medication use in participants reporting MI, with substantially lower levels of use in the Russian study despite similar levels of use of blood pressure lowering medications. This suggests a fundamental difference in prescribing practices to be explored further.

B4

Prevalence and incidence rates of atrial fibrillation in Norway 2004-2014 – a CVDNOR study

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Aim: To study time trends in incidence of atrial fibrillation (AF) in the entire country of Norway from 2004-2014, by age and sex, and to estimate the prevalence of AF at the end of the study period.

Methods: The CVDNOR Project provided nationwide records of inpatient admissions with AF as primary or secondary diagnosis and deaths with AF as underlying cause of death for adults (≥18 years of age) in 1994-2014, in addition to outpatient visits 2008-2014 with AF as primary or secondary diagnosis. We defined incident AF as inpatient admission or out-of-hospital death due to AF, with no inpatient admission for AF during the previous 10 years. We estimated age-standardized incidence rates (IR) with 95% confidence intervals (CIs) and age-adjusted average yearly change in incidence measured as incidence rate ratios (IRR) with 95% CIs, using Poisson regression. AF prevalence was based upon all cases identified through inpatient admissions (1994-2014) and outpatient visits (2008-2014) and alive (2014).

Results: We identified 175,979 incident AF cases (30% with AF as primary diagnosis at inpatient admission, 69% as secondary diagnosis; 0.6% as out-of-hospital AF deaths). IRs of inpatient admission or death from AF per 100,000 person years were stable at 433 (426-440) in 2004 and 440 (433-447) in 2014. IRs were stable or declining over time across strata of sex and age with the exception of an estimated increase in 18-44 year-olds (IRR 1.02, 95% CI 1.01-1.03). In 2014, the prevalence of AF was 3.4% in the adult population.

Conclusion: For the adult population in Norway, we found overall stable incidence rates of AF from 2004 to 2014. The prevalence of AF was 3.4% at the end of 2014, which is higher than reported in previous studies. Signs of increasing incidence of early-onset AF (<45 years) are worrying and need further investigation.

B5

Weight and weight change and risk of atrial fibrillation – the HUNT Study

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Introduction: Although obesity has been associated with risk of atrial fibrillation (AF), the associations of long-term obesity, recent obesity and weight change with AF risk throughout adulthood are uncertain.

Aims: To explore the associations of long-term obesity, recent obesity and weight change with AF risk throughout adulthood are uncertain.

Methods: An ambispective cohort study was conducted which included 15,214 individuals. The cohort was created from 2006-2008 (the baseline) and was followed for incident AF until 2015. Weight and height were directly measured at baseline. Data on previous weight and height were retrieved retrospectively from measurements conducted 10, 20, and 40 years prior to baseline. Average body mass index (BMI) over time and weight change was calculated.

Results: During follow-up, 1149 participants developed AF. The multivariable-adjusted hazard ratios were 1.2 (95% CI: 1.0-1.4) for average BMI 25.0-29.9 kg/m^2 and 1.6 (1.2-2.0) for average BMI ≥ 30 kg/m^2 when compared to normal weight. The association of average BMI with AF risk was only slightly attenuated after adjustment for most recent BMI. In contrast, current BMI was not strongly associated with the risk of AF after adjustment for average BMI earlier in life. Compared to stable BMI, both loss and gain in BMI were associated with increased AF risk. After adjustment for most recent BMI, the association of BMI gain with AF risk was largely unchanged while the association of BMI loss with AF risk was weakened.

Conclusions: Long-term obesity and BMI change are associated with AF risk. Obesity earlier in life and weight gain over time exert cumulative effects on AF development even after accounting for most recent BMI.

B6

Risk of coronary heart diseases and stroke in the Sami and non-Sami populations in rural Northern Norway-the SAMINOR Study

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Introduction: There are conflicting results regarding coronary heart diseases (CHD) mortality in Sami, however, Sami might have lower risk of myocardial infarction (MI), and higher mortality and risk of stroke compared to non-Sami living in the same geographical area. There is a need for more knowledge on incidences and risks in these populations. Height is inversely associated with stroke and MI, and Sami have on average lower height than non-Sami.

Aim: Compare the risk of acute myocardial infarction (AMI), CHD, stroke and ischemic stroke (IS), and a composite endpoint (AMI or stroke), in Sami and non-Sami populations in rural Northern and Mid-Norway, and identify intermediate factors of potential ethnic differences in risk.

Methods: Participants in the SAMINOR 1 Survey (2003–2004) aged 30 and 36–79 years were followed to the 31st December 2016. The five defined endpoints were fatal or non-fatal events of AMI, CHD, stroke, IS and a composition cardiovascular endpoint including the four conditions. We compared hazard ratios (HR) with 95% confidence intervals (CI) in Sami and non-Sami populations using Cox regression models and adjusting consecutively for sex, height and conventional risk factors.

Results: Sami and non-Sami had similar adjusted risk of AMI (HR 0.95, 95% CI 0.79, 1.15), CHD (HR 0.97, 95% CI 0.87, 1.09) and the composite endpoint (HR 1.05, 95% CI 0.90, 1.21). Sami ethnicity was associated with increased adjusted risk of stroke (HR 1.24, 95% Cl 1.00, 1.52) and IS (HR 1.32, 95% Cl 1.05, 1.67). Height explained the ethnic difference in stroke and IS observed in women.

Conclusions: Sami and non-Sami had similar risks of AMI, CHD, and the composite endpoint, but the risk of stroke and IS was higher in Sami. Height explained the increased risk of stroke and IS in Sami women.

C1

Smokeless Tobacco and Carriage of *Staphylococcus aureus*; The Tromsø Study – Fit Futures 1

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Introduction: *Staphylococcus aureus* is both a potent human bacterial pathogen causing serious infections and part of the normal bacterial flora in nose and throat. Nasal- and throat carriage of *S. aureus* is found in more than 50% of healthy adolescents. Therefore, identification of modifiable risk factors for *S. aureus* carriage in youth is important for limiting this bacterial reservoir and prevent infections. Smoking has been inversely associated with *S. aureus* nasal carriage in adults. Snuff use is increasing among adolescents in Norway, yet studies on how snuff use affects health are largely lacking.

Aims: To examine whether there is an association between snuff use and nasal and throat carriage of *S. aureus* in adolescents.

Methods: The Tromsø Study – Fit Futures 1, 2010-2011, invited all first-year upper-secondary school students in Tromsø and Balsfjord to an examination of health and lifestyle; 1038 participated (93% attendance). This analysis includes 457 boys and 445 girls, age 15-19 years, with data on self-reported snuff use and two consecutive nasal and throat swab cultures for the assessment of *S. aureus* carriage. We studied the association between snuff use (sometimes or daily) and nasal and throat carriage in multivariable logistic regression models adjusted for known risk factors.

Results: Prevalence of snuff use was 33% in girls and 39% in boys. Girls who used snuff, had 86% higher odds for *S. aureus* nasal carriage (OR, 95% CI = 1.18-2.94; carriage defined as one or two positive cultures) and 59% higher odds for throat carriage (OR, 95% CI = 1.01-2.50; carriage defined as two positive cultures) compared with non-users. In the total population, snuff use was associated with a 48% higher odds for nasal carriage (OR, 95% CI 1.09-1.99; carriage defined as one or two positive cultures). There were no associations between snuff use and *S. aureus* throat or nasal carriage among boys. Test for interaction between sex and snuff use was not statistically significant.

Conclusions: Snuff use was associated with higher *S. aureus* nasal and throat carriage among adolescent girls. Our novel findings suggest that smokeless tobacco may be a determinant of the bacterial reservoir in the population.

C2

Atopic disease in relation to *Staphylococcus aureus* carriage and spa type distribution in a subarctic adult population

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Introduction*:* Atopic diseases are common, and the atopic epidemic has ravaged through the westernized countries and is heading for the developing countries too. Despite being a common disease, however, treatment and diagnostic options are still lacking. The immune system and development of atopic disease are interconnected with the environment through exposures or lack thereof. The microbiota of the mucosal membranes and skin throughout the body have been purposed serving a sentinel role in this interplay.

Aims: In this study, we investigated if atopic disease is associated with *Staphylococcus aureus* nasal colonization and carriage in adults. Furthermore, we wanted to test whether the distribution of *S. aureus* spa types differs in adults with atopic disease compared to adults without atopic disease in a general population of men and women.

Material and methods: The Tromsø Staph and Skin is a sub-study of Tromsø 6, a population-based cohort with high attendance rate (65.7%). Out of a total of 4,026 participants who had nasal swab sample taken, 3,367 and 2,485 participants were enrolled in our study of *S. aureus* colonization and carriage, respectively. The study included questionnaires on lifestyle and disease, clinical examination, and blood samples. In order to investigate the association between atopic disease and *S. aureus* independently of known risk-factors we used multivariable logistic regression analysis.

Results: In the Tromsø Staph and Skin study, the lifetime prevalence for asthma, atopic dermatitis, recurrent hand eczema and pollen allergy were 9.4%, 12.5%, 13.8% and 19.7% respectively. In the total population, *S. aureus* colonization and carrier rate was 29.5% and 26.1%, respectively. *S. aureus* colonization and carriage was most frequent in males; colonization and carrier rates were 38.0% and 34.7%, accordingly. In females the corresponding rates of colonization and carrier were 19.6% and 22.9%. We found pollen allergy to be associated with 45% [odds ratio OR= 1.45, 95% CI, 1.11 to 2.52] and 55% [OR=1.55, 95% CI, 1.06 to 2.24] higher risk of *S. aureus* colonization and carriage in males, respectively. Furthermore, among males, having one atopic disease was associated with a 67% [OR=1.67, 95% CI, 1.11 to 2.52] higher risk of *S. aureus* carriage.

Conclusion: *S. aureus* colonization and carriage is associated with pollen allergy in males. This cross-sectional study cannot define causality, but our data provide some evidence that support the hypothesis of *S. aureus*' role in modulation and maintenance of atopic disease and pollen allergy, even in adults.

C3

Quantifying the transmission dynamics of MRSA in the community and healthcare settings in a low-prevalence country: a modelling study

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Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common pathogen in healthcare settings that in the last two decades has become increasingly frequent in the general population. The growing circulation of MRSA in the society, heightened by an increasing human mobility, generates a pressure on hospitals that represents a potential challenge for the containment of MRSA infections, even in those countries characterized by a low prevalence of MRSA, such as Norway, and implementing strict infection-control policies.

Aims: The study aims to obtain a clearer understanding of the epidemiological connections between healthcare and community settings as well as of the main drivers of the MRSA transmission in Norway.

Methods: We developed a stochastic individual-based model reproducing the real socio-demographic structure of Norway, explicitly representing households, hospitals and nursing homes, and including the observed increase of cases imported from abroad. The transmission model was calibrated using time series of symptomatic infections reported in the Norwegian national registry (2008-2015) and published household prevalence data.

Results: We estimated an effective reproductive number (Re) of 0.68 (95% CI 0.47-0.90), excluding the hypothesis of an ongoing epidemic in Norway as the explanation for the observed rise of MRSA infections. The growth in the number of positive cases was rather attributed to the increasing acquisitions abroad. As a result of more frequent importations, the prevalence of carriage has almost doubled over the study period, reaching in 2015 a value of 0.37% (0.25-0.54%) in the community and 1.11% (0.79-1.59%) in hospitalized patients. About half of the colonization events occurred within households. However, nosocomial acquisition was still a primary source of symptomatic disease, with 44% (32-53%) of infections developed after transmission in hospital. Transmission in the community was responsible for 12% of symptomatic infections developed in hospitals.

Conclusion: Our results recognize households as a potential target of preventive strategies in the community and re-emphasize the central role of hospitals in the transmission dynamics and, thus, the importance of implementing control measures in these settings. Moreover, the drive exerted by the growing importation and the global circulation highlights the need for coordinated initiatives to reduce the spread of antibiotic resistance worldwide.

C4

Parechovirus infections and increased risk of coeliac disease: nested case-control study within the MIDIA longitudinal birth cohort

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Introduction: Recent work by our group has shown an association between *Enterovirus A-B* infections and later development of coeliac disease (CD).

Aims: We aimed to test whether a related virus, Human parechovirus (HPeV), was associated with later CD in a longitudinal birth cohort.

Methods: During 2014-16, 220 children with HLA-DQ2/DQ8 from the longitudinal birth cohort MIDIA consented to CD screening. 25 children were diagnosed with CD and included in a nested case-control study. For each study case, two random controls were matched for duration of follow-up, date of birth and county of residence. We retrospectively analysed stored (collected at ages 3, 6, 9, 12 months, and annually thereafter) plasma samples for CD antibodies and identified the seroconversion interval. We investigated presence of HPeV by quantitative real-time RT-PCR in 2005 stool samples collected monthly from ages 3-36 months.

We analyzed the data using a mixed effects logistic regression model with faecal sample virus positivity before CD seroconversion as the dependent variables and CD status as an independent variable. We adjusted for sex, age, age squared, calendar month of sampling, number of siblings, and family history of CD.

Results: HPeV was detected in 222 of 2005 samples (11.1%), and was more frequent in stool samples prior to CD seroconversion in cases (adjusted odds ratio [aOR] 1.69,95%CI 1.16-2.46,p=0.01). This estimate was increased if diarrhea was reported (aOR 3.72, 95%CI 1.03-13.42, p=0.045). Estimates were essentially unchanged when restricted to infections after gluten exposure (not shown). Samples concurrently positive for HPeV and enterovirus prior to CD were more frequent in cases (aOR 4.58,95%CI 1.25-16.69,p=0.02).

Conclusions: Our findings suggest that human parechovirus, and enterovirus, in early life are associated with later CD. These enteric infections may contribute to the development of CD.

C5

Hospitalization with pandemic influenza and mortality in people with and without type 2 diabetes

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Introduction: There is limited evidence linking type 2 diabetes (T2D) to influenza-related complications.

Aims: To test whether people with type 2 diabetes had higher risk of hospitalization with pandemic influenza during 2009-2010, and higher subsequent relative mortality, compared to people without type 2 diabetes. We also investigated pandemic influenza vaccination uptake, and its associations with influenza hospitalization and mortality.

Methods: In this population-based cohort study, we linked individual-level data from several national registers for all Norwegian residents aged 30 years or older as of January 2009. People with or without T2D at baseline were followed until December 2013. We used Cox regression to estimate adjusted hazard ratios (aHRs).

Results: Among 2,992,228 individuals 149,432 (5.0%) had type 2 diabetes at baseline, and 206,747 (6.9%) died during follow-up. Vaccination coverage varied with age but was consistently higher in people with T2D than in those without (overall 59.5% vs 38.9% overall), Figure 1. Pandemic influenza hospitalization was more common in individuals with T2D (aHR 2.46, 95%CI 2.04–2.98). The mortality hazard ratio associated with hospitalization for pandemic influenza was lower in people T2D with T2D (aHR 1.82, 95%CI 1.21–2.74) than in those without T2D (aHR 3.89, 95%CI 3.27–4.62). The same pattern was observed when restricting to 90 days mortality (aHR 3.89, 95%CI 1.25–12.06 among those with T2D and aHR 10.79, 95%CI 7.23–16.10 among those without T2D). The rate of hospitalization for pandemic influenza was 78% lower in those vaccinated compared to non-vaccinated among people with T2D (aHR 0.22, 95% CI 0.11–0.39), while the corresponding estimate for those without T2D was 59% lower (aHR 0.41, 95%CI 0.33–0.52). Mortality was 25% lower in those vaccinated compared to non-vaccinated among people with T2D (aHR 0.75, 95% CI 0.73–0.77), while the corresponding estimate for those without T2D was 9% (aHR 0.91, 95%CI 0.90–0.92).

Conclusions: There may have been a lower threshold for pandemic influenza hospitalization for people with T2D, rather than more severe influenza infection. Our combined results support the importance of influenza vaccination among people with T2D, especially during pandemics.

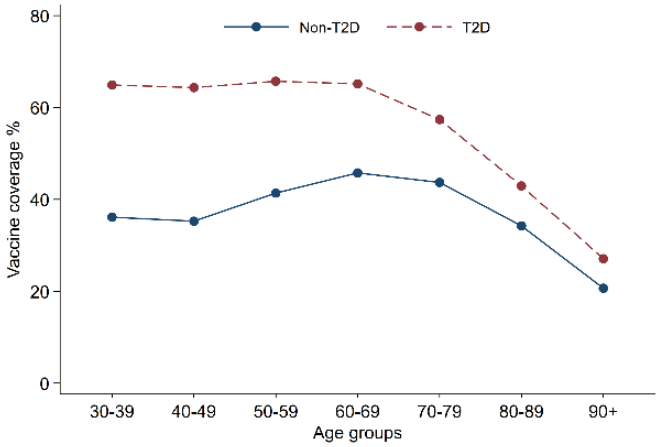

Figure 1. Pandemic influenza vaccination coverage in Norway by age-group among individuals with and without prevalent type 2 diabetes during the 2009-2010 pandemic.

C6

Genomic definition of the global pneumococcal population to contextualise disease, vaccine impact and antibiotic resistance

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Introduction: Pneumococcal conjugate vaccines (PCVs) have reduced the total incidence of invasive pneumococcal disease, however non-vaccine-types are increasing in incidence.

Aims: We used whole genome sequencing to study the role of pneumococcal population structure on vaccine-type replacement, antibiotic resistance and invasiveness.

Methods: 20027 pneumococcal genomes representing: Africa (40%), Asia (25%), Europe (19%), North (12%) and South America (5%), were used to define Global Pneumococcal Sequence Clusters (GPSCs) with PopPUNK. We inferred resistance from genetic determinants, and measured invasiveness using odds ratios, relating prevalence in disease to that in carriage. A pooled incidence rate of non-vaccine-type invasive pneumococcal disease post-PCV by GPSC was calculated for Israel, South Africa, and USA.

Results: Thirty-five GPSCs were represented by >100 isolates. 22/35 (63%) of these lineages expressed non-vaccine serotype variants in the years before PCV introductions. Vaccine-type replacement was mediated by expansion of existing non-vaccine serotypes within GPSCs. GPSC3, was the most common lineage causing non-vaccine-type invasive pneumococcal disease post-PCV13. The relatedness of GPSC3 sub-clades prevalent in post-PCV13 disease from USA, Israel and South Africa were not previously realised.

Resistance was unevenly distributed across the population, with a significantly higher proportion ($p > 0.05$) of multi-drug resistant isolates found in 9/35 common GPSCs. In the non-vaccine-types, we detected significant increases in the prevalence of resistance to penicillin ($p=0{\cdot}0016$) and erythromycin ($p=0{\cdot}0031$) after PCV13. Finally, we detected, serotype-independent, increased invasiveness of six genetic backgrounds.

Conclusions: Existing non-vaccine-serotypes in most GPSCs preclude the removal of these lineages by pneumococcal conjugate vaccines, and such variants are selected for by vaccination. A subset of GPSCs have increased resistance and/or serotype-independent invasiveness. Global genomic surveillance of the pneumococcal population provides powerful data for optimising future vaccine design to limit invasiveness and antimicrobial resistance.

A7

Population based Regional Health Studies – a ground for harvesting

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Introduction: Norway has large and comprehensive data from population based long-term prospective cohorts and mandatory national registers and biobanks. Thus, we can elucidate a wide range of public health challenges by joining forces on accumulated knowledge and existing data and research infrastructure. We can also do comparable analyses to test similar hypotheses in independent datasets with individual data.

Aims: To describe the unique data sources and scientific potentials of the Norwegian population based health examinations and health surveys conducted from 1972 through 2006.

Methods: Norway has numerous national and regional population based health surveys including data from questionnaires, clinical examinations, biological specimens and anthropometric measures. HUNT and Tromsø are large ongoing studies comprising a total county population examined in several waves. In addition, abundant data are available from various population based regional health surveys throughout Norway from 1972 through 2006 including about 600 000 participants with overall participation rates of up to 88%. Furthermore, height and weight data is available from about 1.9 mill Norwegians who participated in the nationwide mandatory mass tuberculosis screening program 1963-1975.

There is a unique potential in these data sources for high-quality research at the population level by linking data from existing population-based health surveys, nationwide mandatory registers and biobanks.

Results: Several large ongoing and planned national and international research projects are based on individual-level linkages of data from health studies in Norway combined with register and biobank data, covering the population of Norway. These projects provide knowledge about risk factors and protective factors of diseases, health and ill health at the population level, as an essential source of information needed for primary prevention at the population level. The research areas include cardiovascular disease, osteoporosis and hip fractures, diabetes, chronic obstructive pulmonary diseases, cancer, multimorbidity and polypharmacy, social inequalities, physical activity, smoking and body weight. Examples of ongoing and planned research projects using the data from the health studies will be given, along with an overview of further research potentials, strengths and limitations.

Conclusions: National collaboration across research areas and institutions including a linkage of Norwegian population based health surveys and mandatory registers is a unique ground for harvesting.

A8

The Norwegian Mother, Father and Child Cohort Study, an infrastructure for research

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Introduction: MoBa is a large ongoing prospective population-based cohort aimed at studying causes of disease.

Aims: The Norwegian Mother, Father and Child Cohort Study investigates a number of different risk factors such as environmental toxins, infections, diet, workloads or genetic factors that can lead to impaired health. This is linked to information about illnesses (mental and physical) in children, mother and father.

Methods: During the period 1999–2008, pregnant women in Norway were invited to participate in the study at the time of the routine ultrasound examination at 17 weeks of pregnancy. Fathers / partners were also invited. Around 95,000 mothers, 75,000 fathers and 114,000 children are now participating. Participants answer questions about several risk factors often before illness has developed, and have so far responded to 11 questionnaires from the time of pregnancy, through the child's first year of life and until the children are 14 years old. By linking information from MoBa with health registries such as the Cancer Registry, the Patient Register or the Prescription Register, further information can be obtained on diseases that develop in the participants.

Blood samples were collected from both parents during pregnancy and from the child's umbilical cord at birth. This provides unique opportunities to investigate genetic conditions (DNA) in mother, father and child trios.

Results: MoBa is one of the largest surveys of its kind in the world. Because MoBa contains data from multiple generations and from relationships, such as parents, siblings and cousins, it may be used to distinguish between inheritance and environmental causes of disease and to determine whether exposure is a true causal factor and not just incidentally associated with the disease.

Conclusions: As a birth cohort MoBa offers a unique frame for studying exposure during pregnancy and adolescence, and the effect on child development and health status. MoBa has been used in more than 500 research projects and has resulted in >650 publications, and as the cohort is maturing new research opportunities are arising.

A9

The Norwegian Environmental Biobank

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Introduction: Human biomonitoring (HBM) of nutrients and environmental contaminants is emerging as an important tool to gain information about exposures to essential and toxic substances. In 2016, the HBM4EU project (https://www.hbm4eu.eu/) was launched with the aim to coordinate and advance human biomonitoring in Europe. Norway participates in the project with The Norwegian Institute of Public Health (NIPH) as a national coordinator. Following the HBM4EU initiative, NIPH started The Norwegian Environmental Biobank nested within the Norwegian Mother and Child Cohort study (MoBa).

Aims: The Norwegian Environmental Biobank aims particularly at biomonitoring nutrients and environmental contaminants in pregnant women and their children. The main goal is to obtain an overview of the population's exposure to environmental pollutants and nutritional status over time and assess the impact on a number of health outcomes. The biobank will be a future resource of stored human biological specimen (blood and urine) and thus an important tool in the national and international effort to reduce exposure to environmental pollutants.

Methods/design: The Norwegian Environmental Biobank includes biomarker data from n=3000 blood samples donated by pregnant women in MoBa (collected 2002 to 2008), and recently collected biospecimen from family triads (mother, father, child, n≈600). A range of biomarkers have already been analyzed, including nutrients (e.g. vitamins A, D, E), essential elements (e.g., Se, Zn, Cu, Mn in blood, Na, I, K in urine), heavy metals (e.g., Cd, Hg, Pb), and biomarkers of health status (e.g., CRP, HbA1c, TSH, fT3, fT4). Biomarker data from the Norwegian Environmental Biobank can be linked to numerous questionnaires already collected in MoBa, as well as to national health registries. Pregnancy and birth records from the Medical Birth Registry of Norway (MBRN) are already linked to the MoBa database.

In addition to the participation in HBM4EU, The Norwegian Environmental Biobank is integrated in several ongoing research projects, such as NON-PROTECTED and CATCH-UP.

A10

County Public Health Surveys – new resource for research?

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Introduction: Norwegian counties are required by law to monitor public health status in their respective counties. In 2012, The Norwegian Institute of Public Health was tasked with developing a County Public Health Survey (CPHS) aimed at providing public health relevant measures not covered by other registries and useful at policy level.

Aims: Develop content and survey methods for CPHS.

Methods: In 2015/16, a first CPHS was conducted in Vestfold and Agder, using mixed models. In 2018, an online only survey was conducted in Hordaland. Additionally, a small sample was followed up with telephone interviews for comparison with the online only sample. From 2019, online only surveys were conducted in Sogn og Fjordane and Troms and Finnmark. CPHS invitations are sent by e-mail and SMS using the ID-porten log on solution. Participants consent to registry linkages and follow up studies. Since online surveys are scalable at marginal costs, sample sizes for online only surveys were substantially increased, using simple random sampling. In Bergen, estimates with 5% error margin were provided for all city districts. In Sogn og Fjordane the final sample represent 10% of the adult population.

Results: At present the CPHS include 56,744 respondents. Response rate for the online only surveys are 40-45%. Despite being an online survey, the response rate for those 66+ is 45% for men and women. The response rate for men 18-25 is <30%. The questionnaire accommodates county specific interests, but a core module contains information on BMI, health behaviour, physical activity, mental health, perceived financial situation, social support, loneliness, local environment and access to public and private services, injuries and demographics. Due to (national/local) political initiatives to employ Quality of Life (QoL) measures as steering tools for policy development, a QoL module was added in 2019

Conclusions: Large samples provide results on small geographical units. Future surveys will increasingly focus on smaller geographical units due to demand from local authorities. The database is growing rapidly as data from new counties and follow-up surveys are added. The questionnaire will regularly be revised, but conservatively in order to have time series for key interest areas.

A11

The Norwegian Patient Registry and the Norwegian Registry for Primary Health Care: Research potential of two nationwide healthcare registries

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Introduction: The Norwegian Directorate of Health is responsible for two nationwide registries. These registries, the Norwegian Patient Registry (NPR) and the Norwegian Registry for Primary Health Care (NRPHC), together cover all governmental-funded health care.

Aims: To present the NRPHC as possible future research tool

Methods: The NPR (specialist health care) was established in 2008, while the NRPHC (primary health care) was established in 2017. Data from the NPR are extensively used in a large variety of epidemiological studies. Data from the NRPHC will increase its importance when the registry covers a longer time period. In this presentation, the NRPHC is presented as a possible future research tool.

Results: There are no results since this is a presentation of a new health register as a future research tool.

Conclusion: There is no conclusion since this is a presentation of a new health register as a future research tool.

B7

Does the increased risk of colorectal cancer (CRC) due to cigarette smoking differ by sex for the right – and left colon cancer as well as rectal cancer?

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Introduction: Colorectal cancer (CRC) is the third most common cancer among men and women in the United States. Smoking was established as a causal factor for CRC by the International Agency for Research on Cancer in 2012 and by the US Surgeon General in 2014. The majority of the studies reviewed did not examine possible sex differences and also considered CRC as a single disease. Neither of the two expert reports commented on possible differences between men and women, in the relationship between smoking and the three anatomical (right colon, left colon, and rectum) subsites of CRC.

Aims: To examine if the increased risk of colorectal cancer (CRC) due to cigarette smoking differed by sex for the right and left colon cancer and rectal cancer in the Multiethnic Cohort study.

Methods: We analyzed data from 188,052 participants (45% men, ages 45-75), who were enrolled in the Multiethnic Cohort study in 1993-1996. We identified CRC cases via linkage to the Hawaii and California Surveillance, Epidemiology, and End Results Program cancer registries through December 2013. We used Cox proportional hazards regression to estimate multivariable-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: During a mean follow-up of 16.7 years, we identified 4,879 incident cases of invasive colorectal adenocarcinoma. In multivariate Cox regression models, compared with never smokers of the same sex, male ever smokers had a 39% [hazard ratio (HR) =1.39; 95% Confidence interval (CI): 1.16,1.67] higher risk of left, but not of right (HR=1.03; 95% CI: 0.89,1.18) colon cancer, while female ever smokers, had a 20% (HR=1.20; 95% CI: 1.06,1.36) higher risk of right, but not of left (HR=0.96; 95% CI: 0.80,1.15) colon cancer. Compared with male smokers, female smokers had a greater increase in risk of rectal cancer with number of pack-years ($P_{heterogeneity} = 0.03$).

Conclusions: Our results suggest that male smokers are at increased risk of left colon cancer and female smokers at increased risk of right colon cancer. Our study also suggests that female who smoke may have a higher risk of rectal cancer due to smoking than their male counterpart.

B8

Body fatness and type 1 and type 2 endometrial cancer: The Norwegian Women and Cancer Study

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Introduction: Body fatness has been associated with increased risk of 13 cancer types and is a particular strong risk factor for endometrial cancer (EC). Only a few previous studies have assessed the relationship between body fatness and EC subtypes.

Aim: To assess the association between body fatness, measured a**s** body mass index (BMI), and incidence of type 1 and type 2 EC in a representative sample of Norwegian women.

Methods: We used data from 151 537 participants in the Norwegian Women and Cancer (NOWAC) cohort of which 935 were diagnosed with type 1 and 263 with type 2 EC during follow-up. Height and body weight were self-reported and BMI was categorized into four groups; underweight (BMI<18.5 kg/m^2), normal-weight (18.5 ≤ BMI <25.0 kg/m^2), overweight (25.0 ≤ BMI <30.0 kg/m^2), and obesity (BMI≥30 kg/m^2). Multivariable Cox proportional hazard regression was used to assess the effect of BMI on type 1 and type 2 EC.

Results: Compared to women in normal-weight, women with overweight had 35% increased risk of type 1 EC (Hazard Ratio [HR] =1.35, 95% confidence interval [CI]: 1.07, 1.69), but no increased risk of type 2 EC (HR=1.06, 95% CI: 0.71, 1.60) ($p_{heterogeneity}$ = 0.317). Women with obesity had almost three times higher risk of type 1 EC (HR=2.94, 95% CI: 2.24, 3.85) and 95% higher risk of type 2 EC (HR=1.95, 95% CI: 1.15, 3.34) ($p_{heterogeneity}$ = 0.185). There were linear trends in risk estimates of type 1 (p_{trend}<0.001) and type 2 EC (p_{trend}=0.033). For every 2 units increase in BMI, the risk of type 1 EC increased by 21% (HR=1.21, 95% CI: 1.17, 1.25.) and the risk of type 2 EC by 11% (HR=1.11, 95% CI: 1.03, 1.20) ($p_{heterogeneity}$ = 0.060).

Conclusions: Body fatness was associated with both type 1 and type 2 EC in a dose-dependent manner and there was no statistically significant difference in effect estimates across subtypes. However, the association seems to be stronger in type 1 EC, which could support the idea that estrogen plays a more important role in the development of type 1 ECs than in type 2 EC.

B9

Reproductive factors, exogenous hormone use and risk of pancreatic cancer – The Norwegian Women and Cancer Study

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Introduction: Pancreatic cancer accounts for less than 4% of all cancer prevalence in Norway, but is the fourth leading cause of cancer-related death as the survival rate is extremely low. The pancreatic cancer incidence has increased from 7.5 per 100 000 women in 1965 to 13.1 per 100 000 women in 2017. Reproductive factors and use of exogenous hormones have been associated with several types of cancer. However, few studies have investigated the relationship between exogenous hormone use, parity, breastfeeding and pancreatic cancer risk.

Aims: To investigate the relationship between reproductive factors, use of exogenous hormones and pancreatic cancer risk, in a large prospective cohort of women in Norway.

Methods: Among 165 424 women enrolled in the nationally representative Norwegian Women and Cancer Study, 499 incident pancreatic cancer cases were identified. Multivariable cox proportional hazard models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI).

Results: We found that breastfeeding for more than 24 months was associated with decreased risk of pancreatic cancer (HR=0.54; 95% CI= 0.34-0.86) compared to no breastfeeding. Among parous women, age at first birth was negatively associated with pancreatic cancer risk (HR=0.97 per year; 95% CI= 0.94–1.00). There were no associations between parity, age at menopause, or hormonal therapy use and duration and pancreatic cancer incidence.

Conclusions: Our study suggests that breastfeeding and older age at first birth decrease the risk of pancreatic cancer, while no associations were found for menopausal age, parity or hormonal therapy use.

B10

A Healthy Lifestyle Index and associated risks of breast, lung and colon cancers in the Norwegian Women and Cancer study

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Introduction: There is substantial evidence to support the strong influence of lifestyle exposures on the risk of major cancer types among women such as breast, lung, and colon cancers. However, only a small number of studies have examined the combined impact of these exposures; and never in a Scandinavian population.

Aims: To examine the combined association of lifestyle risk factors assessed though an *a priori* defined healthy lifestyle index (HLI) score with the risks of breast, lung, and colon cancers.

Methods: This prospective study included approximately 80 000 women from the Norwegian Women and Cancer (NOWAC) cohort. Lifestyle and diet were assessed at baseline through questionnaires from 1996 to 2004. The HLI was derived from five lifestyle risk factors (smoking, diet, alcohol, physical activity, and body mass index), with each component assuming 0-4 points summing to a possible score of 0-20, where higher scores represented healthier behaviours. Cox proportional hazard regression models were used to estimate hazard ratios (HR) for risks of breast, lung, and colon cancers (95% CI).

Results: Please note that our analysis has not been completed. However, results for breast, lung, and colon cancers will be available by the day of the event.

Conclusions: n/a

B11

Urinary tract cancer incidence among males in the Norwegian Offshore Petroleum Workers (NOPW) cohort

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Introduction: Urinary tract (kidney and bladder) cancers are common and have several well-known and suspected risk factors. In industrialized countries, it has been estimated that as much as 20% of bladder cancers in men can be attributed to occupational carcinogens.

Aims: Prospective follow-up of cancer incidence to examine the overall and subgroup risk of urinary tract cancers among male offshore workers compared to the general Norwegian population.

Methods: The NOPW cohort was established in 1998, and nearly 26,000 male workers completed a baseline questionnaire. The current follow-up ran from 30 June 1999 through 31 December 2017. Information on incident cancers was obtained via linkage with the Cancer Registry of Norway. Standardized Incidence Ratios (SIRs) with 95% confidence intervals (CI) were calculated by period of first employment (1965–85 and 1986–98) and by four main job categories, based on expected numbers from national, 1-year age- and 1-year time-specific incidence rates for men.

Results: Overall, 359 incident urinary tract cancers were identified during 439,275 person-years of follow-up, suggesting an increased risk when compared to the general male population (SIR 1.38, CI 1.24–1.53). The total number of observed kidney cancers was slightly elevated (SIR 1.10, CI 0.92-1.30). For bladder cancer, the incidence rate was 60% higher (SIR 1.63, CI 1.42-1.86). We found the same above-mentioned risk pattern for both the early and late periods of first employment. For all of the four main job categories the observed kidney cancers were close to expected. However, the risk of bladder cancer was increased for workers in production (SIR 2.00, CI 1.27–3.00), maintenance (SIR 1.51, CI 1.24–1.83), catering/administration (SIR 1.81, CI 1.29–2.47), and suggestively so in drilling (SIR 1.48, CI 0.86–2.37). The same risk pattern was seen for the earliest period of first employment. For the more recently employed, bladder cancer was only increased for maintenance workers (SIR 1.69, CI 1.12–2.44).

Conclusions: We found an overall elevated risk of urinary tract cancers, most pronounced for bladder cancer. Further studies with exposure data and confounder control are needed to address whether the observed excess can be attributed to offshore work.

C7

Women's risk of miscarriage according to chronic underlying conditions

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Introduction: There are sporadic reports that women with some chronic conditions have an increased risk of miscarriage. Most previous studies have only evaluated single conditions, and have not attempted to look at patterns across different groups of diseases.

Aims: To systematically evaluate the risk of miscarriage among women with different chronic diseases prior to becoming pregnant.

Methods: We conducted a national registry study including all registered pregnancies in Norway between 2010 and 2017 (n=688,011). This study used information from the birth registry, the national patient registry and the general practitioner database to identify all live births, stillbirths, miscarriages and induced abortions. We classified women as having chronic conditions based on the coding system used in the patient and general practitioner databases (International Classification of Diseases and the International Classification for Primary Care), requiring two registrations of the condition prior to the conception date. We used logistic regression to estimate the associations of interest, adjusting for maternal age, and correcting for the competing risk due to induced abortions by including 50% of induced abortions in the denominator.

Results: The preliminary analysis conducted indicate an overall risk of miscarriage of about 13.3% when excluding induced abortions from the denominator, and 12% when including 50% of the induced abortions in the denominator. We observed an increased risk of miscarriage among women with a history of various cardiometabolic diseases, such as hypertension (adjusted OR 1.22; 95% CI: 1.13, 1.31), chronic kidney disease (adjusted OR 1.74; 95% CI: 1.19, 2.56), type 2 diabetes (adjusted OR 1.35; 95% CI: 1.21, 1.50) and ischemic heart disease (adjusted OR 2.18; 95% CI: 1.32, 3.63). Furthermore, we also observed an increased risk of miscarriage among women with mood disorders, with an adjusted odds ratio of 1.52 (95% CI: 1.40, 1.44).

Conclusions: Our findings indicate that various underlying chronic conditions might increase the risk of miscarriage. Cardiometabolic diseases seem to pose a specific risk.

C8

Introduction of fetal diagnostic technology: the impact on fetal death rates in Norway

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Introduction: Since 1970 there has been an almost 80% overall decline in the fetal death rate in Norway, and the decline in fetal deaths has been most prominent in term (≥ 37 weeks of pregnancy) and postterm pregnancies (≥ 42 weeks of pregnancy). Since the 1980s, fetal ultrasonographical examinations have been introduced in antenatal care. The impact of introducing such technologies on the fetal death rates has not been known.

Aim: We studied the impact of introducing the fetal diagnostic technologies; regular ultrasound and Doppler ultrasound, on fetal death rates.

Methods: We included all pregnancies in the Medical Birth Registry of Norway during the years 1967-2015, and we made individual linkages to the Central Person Registry and the Education Registry of Norway to obtain information about potential confounding factors. Information about the introduction of regular ultrasound and Doppler ultrasound was obtained by questionnaires to all maternity wards in Norway (n=44), in 2004 and in 2016. The data were analyzed using a hospital fixed□effects regression with fetal mortality as the outcome measure. The key independent variables were the introduction of ultrasound at each maternity ward. Hospital□specific trends and risk factors of the mother were included as control variables. The richness of the data allowed us to perform several robustness tests.

Results: Regular fetal ultrasound was gradually introduced at maternity wards after1980, and by 1995, regular fetal ultrasound was routinely used in antenatal care. The introduction of regular fetal ultrasound explains 20% of the overall decline in the fetal death rate. Regular fetal ultrasound had no effect on preterm fetal deaths, but explained 50% of the decline in postterm pregnancies.

Doppler ultrasound was gradually introduced after 1992. By 2015, 95 percent of all pregnant women delivered at a maternity ward that could offer such examination. The introduction Doppler ultrasound explained 30 percent of the decline in the fetal death rate in preterm pregnancies (28-36 pregnancy week), but had no effect on term pregnancies.

Conclusion: The effects of regular ultrasound, is likely to be explained by improved estimations of the gestational age of the fetus. It is known that postterm pregnancy is a risk factor of fetal death. By introducing reliable estimates for gestational age, pregnancies that have lasted longer than 41-42 weeks can be identified and timely interventions can be performed. The effect of Doppler ultrasound is likely to be explained by improved identification of pregnancies with impaired fetal-placental circulation.

C9

Placental weight and risk of neonatal death

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Introduction: Low placental weight has previously been associated with increased risk of fetal death and with cerebral palsy in infants. By contrast, in preterm born children also high placental weight and high placental weight relative to birthweight increased the risks. These previous findings suggest that placental weight may be associated with neonatal death, and that associations may differ by gestational age at birth.

Aims: We studied the association of placental weight with the risk of neonatal death.

Methods: We used data from the Medical Birth Registry of Norway during 1999–2015, including all singleton infants in Norway without congenital malformations (n=868 617) and all singleton infants with congenital malformations (n=38 229).We grouped the distribution of placental weight (in grams) into quartiles, within two-week intervals of gestational age at birth. The associations of low (1st quartile) and of high (4th quartile) placental weight with neonatal death were estimated as crude and adjusted odds ratios (aOR) with 95% confidence intervals (CI). The 2nd and 3rd quartile combined was used as the reference category.

Results: In total, 0.06% (492/ 868 617) of the infants without congenital malformations died during the neonatal period. Among the infants born preterm (gestational weeks 29-36), both high (aOR 2.31, 95% CI 1.63-3.27) and low placental weight (aOR 1.56, 95% CI 1.05-2.32) increased the risk of neonatal death. Among the infants born at term, placental weight was not associated with neonatal death. In total, 1.22% (467/ 38 229) of the infants with congenital malformations died during the neonatal period. Among the preterm born infants, the associations of placental weight with neonatal death displayed similar patterns as for infants without congenital malformation. However, in term born infants with congenital malformations, low placental weight increased the risk of neonatal death (aOR 1.96, 95% CI 1.48-2.60).

Conclusions: We found that preterm born infants with either high or low placental weight had increased risk of neonatal death. In term born infants, low placental weight increased the risk of neonatal death among infants with congenital malformations. These findings may help to identify infants at increased risk of neonatal death.

C10

The Norwegian birthweight "hump" 1992-2007

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Introduction: Mean birthweight is often regarded as a marker of population health. Norway experienced an unusual and distinctive rise of mean birthweight from 1992-1996, peaking in 1997-2003, and declining to its earlier level in 2003-2007.

Aims: To describe and understand this observed rise-and-fall pattern of birthweight in Norway, and possible underlying or accompanying factors or outcomes.

Methods: Our initial study population included all livebirths registered in the Medical Birth Registry of Norway for the years 1982-2016. Mean birthweight was calculated for each year. We first looked at neonatal mortality and other birth outcomes to explore corresponding health changes during this period. The birthweight "hump" was seen only among term births, so we restricted our remaining analysis to term births. We stratified births by variables known to be associated with birthweight (including maternal age, parity, sex ratio, cigarette smoking, seasonality) in a search of possible contributing factors. We conducted quantile regression analysis of birth weight, adjusting for maternal age, parity, gender and gestational age.

Results: We found an increase in mean birthweight of ~60 grams from 1992-1996 and a subsequent decrease of similar magnitude from 2003-2007. The proportion of children with a birthweight >4500 grams showed the same "hump" pattern, whereas the proportion of children with a birthweight <2500 grams remained steady, while neonatal mortality rates declined. The rise-and-fall pattern in birthweight was not observed among children of mothers born outside of Norway. A very similar pattern was seen in Sweden but not in other Nordic countries. Quantile regression analysis showed that the change in birthweight by year of birth was consistent after adjusting for covariates.

Conclusions: The "hump" pattern in the birthweight of term births in Norway was robust for adjustment for known influencers of birthweight. Its source remains unknown, but seems to be restricted to women born in Norway, with a similar pattern in Sweden. The pattern was not accompanied by reciprocal changes in rates of neonatal mortality or low birthweight, showing that birthweight can be a marker of fetal health, but not an infallible predictor.

C11

Associations between maternal vitamin D status in second and third trimester of pregnancy and offspring enamel hypomineralisation at 7-9 years: a longitudinal study

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Introduction: Enamel hypomineralisation, and particularly Molar Incisor Hypomineralisation (MIH), have received increasing attention in the oral health field over the last two decades. The condition can have a considerable impact on oral and general health, including an increased risk of caries, infection and tooth extraction. The aetiology is disputed and may be multifactorial. Although vitamin D plays an important role in the development of teeth, few studies have addressed the relation between maternal vitamin D levels in pregnancy, and enamel hypomineralisation in their offspring.

Aims: To investigate associations between maternal vitamin D levels during pregnancy and enamel hypomineralisation in their offspring at 7-9 years of age.

Methods: From 2007-2009, 855 pregnant women participated in a randomised controlled study investigating the effects of exercise. At the latest follow-up (2016-17), we invited the children to a dental examination, which included registration of caries experience and enamel hypomineralisation. The exposure variable was maternal serum 25(OH)D at second and third trimester of pregnancy. We used logistic regression and hurdle models in the analyses, with adjustment for potential confounders.

Results: Among the participants, 44.3% (n=78) had at least one permanent tooth with enamel hypomineralisation and 31.8% (n=55) had MIH (at least one permanent first molar with enamel hypomineralisation). Children in the group with the highest (>75 nmol/l) level of maternal 25(OH)D in second trimester, were more likely to have at least one permanent tooth with enamel hypomineralisation, than those in the group with middle (50-75 nmol/l) level of maternal 25(OH)D (fully adjusted OR (aOR)=2.49, 95% CI 1.12 to 5.51). When looking specifically at MIH, those in the highest maternal 25(OH)D group at second trimester were also more likely to be affected, however, the association was not statistically significant (aOR=2.06, 95% CI 0.87 to 4.88). In addition, no statistically significant associations were found between maternal 25(OH)D in third trimester and enamel hypomineralisation.

Conclusions: Children in the group with maternal 25(OH)D levels >75 nmol/l in second trimester were more likely to have at least one permanent tooth with enamel hypomineralisation compared to those with maternal levels between 50 and 75 nmol/l.

A12

Salt intake estimated from 24-hour urine and spot urine collection in the Tromsø study 2015-16

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Introduction: As advocated by the World Health Organization, a reduction of salt intake is a public health priority in numerous countries including Norway. On this background, the surveillance of salt intake at the population level is important. However, the validity of salt intake assessed by dietary surveys is generally low.

Aims: To estimate salt intake by 24-hour urine collection. In addition, we aimed to assess the usefulness of spot urine collection for surveillance purposes by employing prediction models previously used in other populations.

Methods: In the population-based Tromsø Study 2015–2016, 24-hour urine was collected by 493 men and women aged 40–69 years, of whom 475 also collected spot urine. Sodium and potassium excretions were calculated by multiplying respective urinary concentrations by the total volume of urine. Based on the sodium concentration in spot urine, we also estimated 24-h sodium excretion by three different equations.

Results: Mean sodium excretion was 4.09 ± 1.60 g/24-hour in men and 2.98 ± 1.09 g/24-hour in women, corresponding to a daily salt intake of 10.4 and 7.6 g. Potassium excretion was also higher in men compared to women, resulting in a sodium to potassium molar (Na/K) ratio of approximately 1.8 in both genders. Of the three equations based on spot urine, estimated mean 24-h sodium excretion was closest for the INTERSALT formula (4.29 g/24-hour in men and 2.96 g/24-hour in women). Expressed as salt intake, the mean difference between spot urine and 24-hour urine was 0.4 g/day for men and −0.1 g/day for women.

Conclusions: In this population-based study, we found that salt intake estimated by 24-h urine excretion was higher than the officially recommended intake, especially among men. On the other hand, urine potassium excretion was rather high resulting in a favourable Na/K ratio. We also found that sodium concentration in spot urine predicted the mean sodium excretion reasonably well in the Tromsø population when using the INTERSALT equation.

Ref: Meyer HE, Johansson L, Eggen AE, Johansen H, Holvik K. Sodium and potassium intake assessed by spot and 24-hour urine in the population-based Tromsø Study 2015-2016. Nutrients. 2019 Jul 16;11(7).

A13

Compliance to five-a-day in a Norwegian population. Daily intake of vegetables, fruits and berries and comparison with the Norwegian nutrition recommendations – The Tromsø Study 2015-16

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Introduction: Non-communicable diseases contributed to 73% of total deaths globally in 2017 and an unhealthy diet is among the most significant risk factors. Intake of vegetables, fruits and berries is associated with beneficial health effects and reduced risk of non-communicable diseases. The Norwegian nutrition recommendations suggests an intake of at least five portions (500 grams (g)), of vegetables, fruits and berries daily (potatoes excluded) of which half should be vegetables.

Aims: To study the intake of vegetables, fruits and berries and compliance to the Norwegian nutrition recommendations in a Norwegian general population.

Methods: We included participants from the seventh survey of the population-based Tromsø Study (2015-16) who completed a validated food frequency questionnaire (n=11,425, age 40-96 years). Food intake were calculated using the food and nutrient calculation system KBS (Kostberegningssystemet, University of Oslo). Intake of vegetables and fruits/berries and proportion of participants above and below the recommended intake was investigated in strata of sex. Probability of compliance to the recommended five-a-day were investigated with logistic regression analysis in groups of age (10-year age-groups), body mass index (BMI) (normal <25, overweight 25-29.9 or obese ≥30 kg/m^2), self-reported leisure-time physical activity (sedentary, low, moderate or vigorous) and educational (primary, secondary, low or high tertiary) level (with mutual adjustment) in strata of sex.

Results: Median intake (25th – 75th percentile) of vegetables was 228 (148-330) and 168 (103-251), and fruit/berries 292 (180-445) and 268 (155-426) g/day, in women and men, respectively. In total, 44% and 60% of women, and 25% and 54% of men, met the recommended minimum intake of 250 g/day of vegetables and fruits/berries, respectively. Probability of compliance was positively associated with physical activity – and educational level ($p<.05$). Older women were more likely to comply with recommendation for vegetables, and older women and men were more likely to comply with recommendation for fruit/berries, compared to age-group 40-49 ($p<.05$). Participants with obesity were more likely to comply with recommendation for vegetables, but not fruits/berries, compared to those with normal BMI ($p<.05$).

Conclusions: A low proportion met the recommended intake of vegetables and fruits/berries, and intake varied with sex, physical activity, and educational level.

A14

Is the ongoing overweight/obesity epidemic partly explained by concurrent decline in cigarette smoking? The Tromsø Study 1994–2016

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Introduction: The widespread increase in overweight and obesity in the Norway coincides with a substantial cigarette smoking decline. Many ex-smokers report unwanted weight gain following smoking cessation.

Aim: Can the population overweight/obesity epidemic be partly attributed to smoking cessation?

Methods: Data were collected from the Tromsø Study among 10,945 women and men aged 25-54 years who participated in the 1994-95 survey (attendance 72%) and then 22 years later (attendance 65%). We studied changes in mean body mass index (BMI, kg/m^2) and weight in subgroups by self-reported cigarette smoking status, 10-year age groups and gender. We included subjects with smoking habits qualifying for the following sub-groups: Smoker (persistent daily smoker), Quitter (daily smoker in the first, but not in the second survey), Ex-smoker (non-smoker in both surveys who reported being a previous smoker), Never-smoker (non-smoker in both surveys who never smoked daily).

Results: Smoking prevalence decreased from 36% to 15% between 1994 and 2016. BMI increased in all subgroups ($p<0.001$); higher in quitters than in persistent smokers and non-smokers. BMI increased more in women than in men, except among persistent smokers (p=0.06). BMI increase was substantial among the youngest, exemplified by mean (SD) increase of 4.5 (3.6) BMI units in women and 4.2 (2.8) BMI units in med aged 25-34 years who quit smoking between surveys. This is equivalent to a weight gain of 12.2 (10.2) kilograms in women and 13.3 (9.2) kilograms in men.

Table. Change in mean BMI (SD) by age-group, smoking status and gender.

Smoking status	Quitter	Smoker	Ex-smoker	Never-smoker
Women (N = 5851)	n=1311	n=854	n=1500	n=2186
25-34 yr	4.5(3.6)	3.5(3.5)	3.3(3.2)	3.2(3.1)
35-44 yr	4.3(3.3)	2.4(3.1)	2.7(2.9)	2.7(2.9)
45-54 yr	3.9(3.3)	1.3(2.9)	2.0(2.9)	2.0(2.9)
Men (N=5094)	n=1171	n=624	n=1306	n=1993
25-34 yr	4.2(2.8)	3.2(2.7)	2.6(2.6)	2.9(2.6)
35-44 yr	3.6(2.7)	1.9(2.4)	2.2(2.3)	2.0(2.0)
45-54 yr	2.8(2.9)	0.8(2.2)	1.6(2.4)	1.2(2.1)

Conclusions: Over 22 years, mean BMI increased considerably in men and women aged 25-54 years, regardless of smoking status. Weight gain was most prominent among quitters and the youngest. Public health interventions should be targeted at weight loss and weight maintenance, particularly among those who quit smoking.

A15

Physical activity and gene expression in the Norwegian Women and Cancer Post-genome Cohort

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Introduction: Physical activity (PA) is one of the major modifiable risk factors for diseases including cancer, along with other lifestyle factors. The physiological and molecular mechanisms of the association between PA and health are not fully understood. In recent years, the influence of PA on the immune system has emerged as a new field of research. Regular PA may promote an anti-inflammatory state in the body, thus contributing to the down-regulation of pro-inflammatory processes related to the onset and progression of multiple disease states.

Aims: We aimed to assess whether PA levels were associated with differences in the gene expression signatures in blood samples collected in the Norwegian Women and Cancer (NOWAC) Post-genome Cohort, a nationally representative, population-based cohort of middle-aged women.

Methods: Questionnaire data on self-reported PA levels and other variables were extracted from the NOWAC database. Final sample size included data from 850 healthy women. Blood samples were collected using the PAXgene Blood RNA collection system, and gene expression profiles were measured using Illumina HT-12 Expression Bead Chip microarrays. After data preprocessing, we tested for differences in gene expression between groups with low and high PA levels, using limma for the single-gene level, and global test for a targeted gene set analysis using 48 gene sets that were manually curated from the literature, or from relevant molecular databases (ArrayExpress and MSigDB). Statistical analyses were adjusted for BMI, smoking, and medication use. P-values were adjusted using the false discovery rate (FDR), significance threshold was set to $p<0.05$.

Results: Mean age of our study population was 54.3 years, mean BMI was 25.3kg/m^2, and 25% were current smokers (Table 1). When comparing low versus high self-reported PA levels, we did not identify any significantly differentially expressed genes or gene sets. Equally, analyzing PA as a continuous variable did not reveal any significantly differentially expressed genes or gene sets. A volcano plot shows the low level of significance in the dataset (Figure 1).

Conclusion: In our cross-sectional analysis of healthy, middle-aged Norwegian women, self-reported PA was not associated with any differences in blood gene expression profiles. To our knowledge, this is the first cross-sectional study aiming to assess the association between gene expression and PA levels in a general population.

B12

Are psychosocial working conditions associated with suicide and deliberate self-harm? A register-based study of 420,895 Norwegians

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Introduction: Poor psychosocial working conditions are associated with increased risk of mental health disorders. Some studies suggest that work factors may also increase the risk of suicidal behaviour. However, these studies mostly measured suicidal ideation, rarely completed suicides, and hardly ever used longitudinal data.

Aims: To examine the relationship between selected psychosocial work factors and suicide death, as well as hospital treated deliberate self-harm (DSH) and similar diagnoses.

Methods: Data on all persons born in Norway 1967-1976, employed in 2007 (N=420,895), were retrieved from national registers. Outcomes were the gender-specific four-year risk (2008-2011) of suicide death (Cause of Death Registry) and hospital treated DSH (Norwegian Patient Registry). Binary psychosocial work exposures were obtained from a job-exposure matrix (a tool used to assess occupational exposure at the group level) for job demands, job control and leader support. Based on these, we constructed job strain (high demands, low control), and isostrain (high demands, low control, low support) as exposure variables. These were linked to occupation in 2007, registered using the ISCO88 four-digit code. We estimated associations (Risk Ratios, RRs) between the psychosocial work factors and risk of DSH and suicide in binomial regression models, adjusted for year of birth, education level, marital history and current family pattern.

Results: During 2008-2011, 884 had a diagnosis of DSH (annual rate 53 per 100,000; women 56, men 49), while 164 suicided (annual rate 9.7; women 4.5, men 14.5). DSH was associated with all work factors, except job demands and leader support among men. Associations were strongest for high isostrain, adjusted RR 1.5 (95% confidence interval (1.2-1.7) and high job strain RR 1.3 (CI; 1.2-1.5), similar in women and men. Associations with suicide were positive only among men, with strongest associations for high job strain, RR 1.5 (1.0-2.1).

Conclusions: Deliberate self-harm was associated with psychosocial work factors, similarly in both sexes, but suicide was only associated among men. Strongest associations were with high isostrain and high job strain. Reasons other than work-related causes cannot be excluded, particularly health-related selection of people with mental illness into worse jobs (reverse causality).

B13

Associations between human service work and mental disorders: causal or not? A registry-based study of Norwegians born 1967-1976

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Introduction: Depression and stress-related disorders have been associated with human service work and psychosocial job exposures. Some studies suggest heterogeneity across gender and specific occupations, e.g., high risks for men in female-dominated occupations. An alternative to work-related causes could be health selection (reverse causality).

Aims: To examine a broader diagnostic range of mental disorders, to assess if occupational characteristics could support non-causal explanations for depression and stress-related mental disorders.

Methods: Totally 568 970 national residents 1st Jan 2008, born in 1967-76, were followed in national registries through 2014. We classified 2007 ISCO-88 occupational codes into five exposure categories: no customer or client contact (reference), customer contact, and three client contact categories (health, education, social/security). Mental and behavioural disorders 2008-2014 were retrieved from the Norwegian Patient Registry (NPR). Associations for depression (ICD-10 F32-33) and reactive stress disorder (F43) were compared with adult personality disorders (F60-69) and disorders with usual onset early in life (F90-98) where we assumed that associations could represent health selection. Ratios between seven-year disease odds and exposure categories were estimated in gender-stratified, covariate-adjusted logistic regression models with 99% confidence intervals (CI).

Results: Nine percent (N=51 767) experienced any of the four study outcomes. The most remarkable finding was increased ORs for all four outcomes among men in health sector occupations: F32-33: 2.0 (CI, 1.8-2.3); F43: 2.1 (1.8-2.5); F60-69: 2.1 (1.7-2.6), and F90-98: 2.3 (1.8-2.9). Men in female-dominated occupations within the health sector had increased ORs for depression and reactive stress, but contrary to non-professionals, professionals (psychologist, head nurse, midwife) had low OR estimates for personality and early onset disorders. Results for women and other client and customer occupations for men showed moderately increased OR estimates for most exposure and outcome categories. Differences between crude and adjusted exposure-outcome associations were small.

Conclusions: Depression and stress-related disorders were associated with customer and client contact. In spite of the obvious problem with lack of outcome data prior to the establishment of NPR in 2008, the results indicate that occupations with psychosocial challenges are influenced by health selection, particularly for men in non-professional positions with client contact in the health sector.

B14

Weight underestimation linked to anxiety and depression in a cross-sectional study of overweight individuals in a Sami and non-Sami Norwegian population: The SAMINOR Study

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Introduction: Underestimation of overweight and obesity may prevent weight loss attempts resulting in further weight gain and maintenance of overweight. There is, however evidence of potential mental health benefits of weight underestimation that may surpass the negative consequences.

Aims: The main aim was to study the association between underestimation of overweight/obesity and symptoms of anxiety and depression in Sami and non-Sami populations in Northern Norway. Secondary aims were to investigate weight perception in general in overweight/obese Sami compared to non-Sami.

Methods: The study design was population-based cross-sectional and the setting was the SAMINOR 2 Clinical Survey in which participants from 10 rural municipalities in Northern Norway were enrolled between 2012 and 2014. The study included 3266 adult Sami and non-Sami with overweight/obesity (body mass index ≥25) whereof 1384 underestimated their weight (42%). The main primary outcome measure was symptoms of anxiety and depression and secondary outcome measures were BMI and the demographic variables: sex, age, education and marital status.

Results: When comparing the ethnic groups, a higher number of Sami compared to non-Sami men were obese, and a greater proportion reported symptoms of anxiety and depression. Additionally, more men than women, and a higher proportion of Sami women compared to non-Sami women, underestimated their weight. Multivariable-adjusted analyses showed that women were less likely to underestimate their weight compared to men (OR=0.43, 95% CI: 0.33-0.55 in Sami and OR=0.33, 95% CI: 0.26-0.42 in non-Sami), slightly higher odds of weight underestimation were observed with increasing age in both ethnic groups (OR=1.03, 95% CI: 1.01-1.05 in Sami and OR=1.02, 95% CI: 1.00-1.03 in non-Sami), while higher education lowered the odds in non-Sami (OR=0.69, 95% CI: 0.55-0.87). Weight underestimation was protectively associated with anxiety and depression in Sami men (OR=0.48, 95% CI: 0.27-0.84) and in non-Sami women (OR=0.44, 95% CI: 0.25-0.78) adjusted for age, BMI, education and marital status.

Conclusions: Independent of ethnicity, more men than women underestimated their weight. Underestimation of weight was protectively associated with anxiety and depression symptoms in Sami men and non-Sami women. The association between weight perception and mental health needs to be considered in public health strategies aimed at preventing further obesity increase in the population.

B15

Insomnia prevalence varies substantially dependent on classification criteria: The Tromsø Study 2015-2016

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Introduction: Insomnia is the most common sleep disorder, but studies report varying prevalence in the general population. It is not clear whether this is due to differences in classification or true variation in prevalence.

Aims: To investigate insomnia prevalence, symptoms and the association with use of hypnotics and self-reported health in the general population using the three main diagnostic disease classifications.

Methods: In the seventh Tromsø Study (2015-2016) 21,083 women and men (participation proportion 65%) completed an online general questionnaire including the Bergen Insomnia Scale (BIS), an insomnia scoring tool based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV diagnostic criteria. We coded the BIS items (sleep onset latency, wakeup after sleep onset, early morning awakening, non-restorative sleep, daytime impairment, dissatisfaction with sleep) and duration of sleep problems, into the three main diagnostic classifications in use; DSM (edition IV and 5), International Classification of Sleep Disorders 3rd Edition (ICSD-3), and International Statistical Classification of Diseases 10th Revision (ICD-10). We investigated the prevalence of insomnia across the four sets of diagnostic criteria, insomnia symptoms, and the association between insomnia and self-reported use of hypnotics, and with self-reported health, stratified by sex and age-groups.

Results: Insomnia prevalence varied between 8.2% for DSM-5, 9.6% for ICD-10, 19.4% for ICSD-3 and 23.0% for DSM-IV. Sleep onset latency (21.2%), wakeup after sleep onset (18.9%), early morning awakening (22.9%), non-restorative sleep (33.1%), daytime impairment (12.8%) and dissatisfaction with sleep (27.4%) were all common complaints. Insomnia was more common in women than in men, and had an overall inverse association with age. Participants with insomnia reported higher use of hypnotics and lower self-reported health. Findings were consistent across all diagnostic criteria.

Conclusions: The prevalence of insomnia varies substantially with different diagnostic criteria, but is consistently higher in women compared to men, in younger age compared to old age, among users of hypnotics compared to non-users and among participants with low self-reported health compared to those with higher self-reported health. To compare insomnia prevalence across populations, a standard classification is needed.

C12

Landmark estimation of transition probabilities – with an application to registry data on sickness absence and work

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Introduction: Multi-state models are increasingly used in biomedical research and the standard estimation procedure for the probability of transitioning from one state to another relies on the assumption that the future is independent of the past given the present; the so-called Markov assumption. In many practical applications this assumption might fail, for example when modelling transitions between states of sick leave, disability, education, work and unemployment for Norwegian adults. Modelling the transitions between such states properly are key, for example when aiming to learn more about withdrawal from the labor market and on the effects of interventions made to improve return-to-work after sickness absence.

Aims: Improving the Landmark Aalen-Johansen method for estimation of transition probabilities in non-Markov multistate models developed by Putter and Spitoni in 2018 and to better utilize the detailed data available on sickness absence and work participation from Norwegian registries.

Methods: We propose a testing procedure for transition specific violations to the Markov assumption and exploit this test to construct a hybrid Landmark Aalen-Johansen estimator for transition probabilities. The methods are applied and evaluated in a simulation study and subsequently used on a subsample of individuals from a Norwegian birth cohort of all Norwegians born between 1967 and 1976 (n=626 928), followed until 2012. Data on sick leave, disability, education, work, unemployment and more collected from FD-trygd and various other national registries.

Results and conclusions: The results show that the hybrid approach can improve statistical power and that this can prove vital when studying multi-state models where certain transitions are less traveled than others. Furthermore, using that the test depends on the landmark time point, an investigative plot against a landmark time grid is presented. In the simulation study the plot seems to reveal details about the nature of the non-Markov behavior i.e. whether it is due to time dependence or a simple frailty.

C13

Exploring the individually-randomised stepped wedge design for trials where all patients eventually receive the intervention

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Introduction: When planning a randomised controlled trial (RCT) to assess the effect of losartan (the intervention) on patients with glioblastoma, we faced interesting study design challenges. Glioblastoma is a rare disease, resulting in a small target population and ethical reasons require that all patients eventually receive the intervention during the study. The stepped wedge cluster RCT design is an increasingly used method to evaluate e.g. hospital policy interventions. Each cluster (usually hospital or medical centre) is randomised to initiate the intervention at different timepoints. Over time, all clusters contribute to observations under both control and intervention. [1]

Aims: To investigate the efficiency of modifying the stepped wedge cluster RCT design to randomize individuals instead of clusters.

Methods: In the case of the losartan-glioblastoma trial, only one treatment centre is available and cannot be cluster randomised. We therefore modified the usual stepped wedge design to randomize individual patients instead of clusters sequentially, a so called individually-randomised stepped-wedge design. Simulations were used to compare the power of the new design to that of the standard parallel group design, under different sample-size calculation assumptions and design options.

Results: The required sample size for the new design was 50-60% lower than that of the standard parallel group design, confirming the analytical results by [2]. The efficacy gain compared to the parallel design depended on the intra-subject correlation coefficient.

Conclusions: The individually-randomised stepped wedge design can be an efficient alternative to other individually-randomised designs. It is particularly useful when there is an ethical requirement that all patients receive the intervention.

C14

Hypothetical interventions and risk of myocardial infarction in a general population of adults. Application of parametric g-formula to the Tromsø Study

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Introduction: The population impact of lifestyle interventions on the risk of myocardial infarction (MI) should ideally be estimated using pragmatic randomized trials, but in practice answers need to be inferred from population based cohort studies.

Aims: To use the parametric g-formula to estimate the 19 year risk of MI under hypothetical interventions on six cardiovascular risk factors.

Methods: We estimated the relative and absolute risk reduction under feasible and intensive risk reduction strategies for smoking, physical activity, alcohol drinking, body mass index, total serum cholesterol, and systolic blood pressure in 14,965 men and women from the population-based Tromsø Study with 19 years of follow-up (1994-2013).

Results: The estimated 19-year risk of MI under no intervention was 7.5% in individuals with baseline mean age 49.3 years (range 25-69). This risk was reduced by 30% (95% confidence interval: 19%, 39%) under joint feasible interventions on all risk factors, and 69% (59%, 77%) under a set of more intensive interventions. The most effective interventions were a lowering of total cholesterol in serum to 5.18 mmol/l (33% lower MI risk) and lowering of systolic blood pressure to 120 mmHg (37% lower MI risk). The absolute risk reductions were significantly larger in men, in older participants, in smokers, and in those with low education.

Conclusion: Modification of population levels of cardiovascular risk factors could have prevented close to one third of the cases of MI in the municipality of Tromsø during 19 years of follow-up.

C15

Towards a composite index for socioeconomic position when studying health inequalities

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Introduction: Studies on social inequalities in health apply alternative measures of socioeconomic position (SEP): education, occupation and income, and to a lesser extent, neighbourhood. As compared to the use of separate indicators, a composite SEP index has the potential to account for multiple aspects of relevance when determining individuals' social standing.

Aim: to develop a composite SEP index based on weighted combinations of education, occupation and income, and examine how well this index performs in predicting inequalities in health-related quality of life (HRQoL).

Methods: We use data from two waves of a comprehensive health survey of the adult population resident in the city of Tromsø conducted in 2007/08 (N=13,000, aged 30 +) and in 2015/16 (N=21,000, aged 40 +). HRQoL is measured by EQ-5D. A composite index for SEP is developed using adjacent-category logistic regression analyses, as a function of three commonly used socioeconomic indicators: education, occupation, and income. Weights are derived based on the relative contribution of each of these three indicators in explaining variations in respondents' subjective assessment of the social status associated with their current occupation. An alternative, simplified index is also developed, based on education and income only. We test the validity of the two indexes in predicting variation in HRQoL, compared to the SEP indicators separately.

Results: Analyses show that occupation is the main SEP driver, and that income adds weight only for the highest income category. When removing occupation, education level turns out to be the major determinant of SEP, again with income being of importance only in the highest category. Comparisons across genders show that men consider income as relatively more important for their subjective status, while women consider education as relatively more important.

Conclusions: We demonstrate a novel method for analysing the association between SEP and HRQoL. A simple composite index, based on weighting of education, occupation and income levels, proved to validly predict variation in HRQoL. Our results suggest that a composite SEP index should get increased attention when studying the links between SEP and inequalities in health.

A16

Skin cancer incidence among males and females in the Norwegian offshore petroleum workers (NOPW) cohort

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Introduction: Exploration and test-well drilling for oil and gas on the Norwegian continental shelf began in the late 1960s. Subsequent production from operating wells on the Ekofisk field was initiated in 1971. Skin cancer incidence in relation to hydrocarbon exposure and ultraviolet radiation (UVR) has only been studied among male offshore workers, but not among females.

Aims: We aimed to examine the incidence of cutaneous melanoma and squamous cell carcinoma (SCC) in general and by UVR exposure, among male and female offshore workers compared to background rates of the Norwegian population.

Methods: The Norwegian Offshore Petroleum Workers (NOPW) cohort (n=27,917) with information on work history and lifestyle factors was linked to the Cancer Registry of Norway (CRN) for prospective follow-up of melanoma and SCC 1999–2017. Background rates (sex-, age- and period-specific) were extracted from the CRN and standardised incidence ratios (SIRs) were computed with 95% confidence intervals (CIs) by sunburns, solarium use, sunny vacations, sunscreen use and education.

Results: After 490,790 person-years of follow-up, 246 cases of melanoma (males = 214, females = 32) and 143 cases of SCC (males = 133, females = 10) were diagnosed. Increased incidences were found for melanoma in females (SIR 1.72, 95% CI: 1.18–2.43) and for SCC in males (SIR 1.21, 95% CI: 1.01–1.44). For melanoma, the incidence was increased among females who reported low UVR exposure. For SCC, the increased incidence was found mainly in males across all levels of UV related activities. Workers with a college/university degree had excess risk of melanoma, and correspondingly among males for SCC. Significant increase of melanoma/SCC incidence were not found at lower educational levels.

Conclusions: The results suggest that Norwegian female and male offshore workers have higher melanoma and SCC incidence than the general Norwegian population, respectively. Dose-response relationships between UVR exposure and melanoma/SCC risk, will be studied by survival analyses in the NOPW cohort, enabling adjustment for possible confounding factors and interaction effects.

A17

Use of antidepressants and risk of cutaneous melanoma: A prospective case-control study

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Introduction: The incidence of cutaneous melanoma is increasing worldwide and is the most rapidly growing malignancy in Norway. Increased exposure to ultraviolet radiation (UVR) is the major risk factor, but other factors could also be involved. Antidepressant drugs are shown to have cancer promoting and inhibiting side effects and the prescription rates have experienced a parallel increase with the melanoma incidence. However, studies on the association between use of antidepressants and melanoma incidence are lacking.

Aims: We aimed to prospectively examine the association between use of antidepressant drugs and melanoma risk.

Methods: Using Norwegian nationwide registries (the Cancer Registry of Norway, the Norwegian Prescription Database and the National Registry), we identified all men and women aged 18-85 with a first primary melanoma between 2007—2015 (n=11 055) and matched each case to 10 population controls (n=107 055) by sex and year of birth using risk-set matching. We obtained information on prescribed antidepressant drugs, as well as potentially confounding drug use. Information about region of residence served as a proxy for residential ambient UVR exposure. Conditional logistic regression models were used to estimate adjusted risk ratios (RRs), and 95% confidence intervals (CIs) for the association between overall and class-specific antidepressant drug use and melanoma.

Results: Compared with 0-1 prescriptions, ≥8 prescriptions of antidepressants overall was negatively associated with melanoma incidence (RR 0.80, CI 0.74-0.86). Significantly reduced RRs were found for selective serotonin reuptake inhibitors (RR 0.83, CI 0.74-0.93) and other types (RR 0.77, CI 0.61-0.95), but not for tricyclic antidepressants (RR 0.84, CI 0.68-1.02). A negative association was found for all histological subtypes, trunk, upper and lower limb sites, local disease, both sexes, ages >50 years and residential regions with medium and high ambient UVR exposure. The association was most prominent for long-term antidepressant use (>5 years).

Conclusions: The negative associations found between use of antidepressants and melanoma incidence may result from reduced exposure to UVR, although we cannot rule out cancer-inhibiting actions induced by the drugs.

A18

DNA methylation profiles in blood in relation to melanoma in the Norwegian Women and Cancer study

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Introduction: Cutaneous melanoma accounts for a majority of deaths from skin cancer, and the incidence of this cancer is increasing in Norway. The molecular basis for cancer onset is not fully understood for melanoma. Better predictors for the melanoma prognosis, such as tumor thickness, histological subtype, and location may help the clinical community to provide more targeted interventions.

Material: All incident melanoma cases with a DNA sample in the Norwegian Woman and Cancer (NOWAC) cohort, matched with cancer free controls. The matching was done based on age at blood sampling and time in freezer. DNA methylation was measured in over 850 000 CpG sites in 183 incident melanoma cases and 183 matched controls using the Illumina EPIC methylation array.

Methods: A genome wide analysis of differences between cases and controls is carried out with conditional logistic regression. We also analyze epigenetic patterns in relation to tumor thickness, histological subtype, and location; using appropriate methods for high dimensional statistical analysis.

Significance: Discovery of biomarkers for predicting melanoma and/or features related to melanoma histology and pathology. In particular; melanoma risk, tumor thickness, subtype and location.

A19

Sunscreen use and subsequent risk of cutaneous squamous cell carcinoma

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Introduction: Although it has been shown that sunscreen use decreases the risk of sunburns, melanoma and actinic keratosis, few studies investigated the association between sunscreen use and risk of cutaneous squamous cell carcinoma (SCC). It is a challenge in observational studies that the determinants for sunscreen use are essentially the same as for SCC. Methods such as inverse probability weighting might help to better control confounding and imbalances in analyses of the association between sunscreen use and SCC.

Aim: We aimed to estimate the effect of sunscreen use on SCC risk.

Methods: We use the Norwegian Women and Cancer cohort study with complete follow-up of cancer data from the Cancer Registry of Norway until end of 2015. We estimate the (marginal) effect of sunscreen use on SCC risk using inverse probability of treatment weighting to control for confounding and correct for imbalances between sunscreen users and non-users. Adjustments were based on directed acyclic graphs, and effect estimates were produced using Aalen additive hazard regression models to estimate the cumulative regression coefficients and Cox proportional hazard regression models to estimate hazard ratios and 95% confidence intervals.

Results: We included 148,725 women (born 1927-1963), of whom 558 were diagnosed with SCC in the period 1991-2015 (mean follow-up = 13.4 years). Sunscreen use was less common in women with lower educational level, darker skin color, and in smokers. Women using less sunscreen tended to go on fewer sunbathing vacations and had fewer sunburns. Further results will be presented at the conference.

B16

Parent-offspring recurrence of attention-deficit/hyperactivity disorder

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Introduction: A strong recurrence risk of attention-deficit/hyperactivity disorder (ADHD) from parent to offspring has been reported, but the mechanisms and patterns of recurrence from each parent to male and female offspring are not known.

Aims: To examine the recurrence risk by parental and offspring sex and whether reproduction influences recurrence risks.

Methods: The nationwide Medical Birth Registry of Norway (MBRN) was used to identify individuals born 1967-2011. Those born 1967-1968 were followed to 2011 for their own reproduction. Individuals diagnosed with ADHD were identified using the Norwegian Prescription Database (2004-2015) or the Norwegian patient registry (2008-2015). We used Poisson regression to calculate the relative risk (RR) and adjusted prevalence for ADHD in offspring by maternal ADHD only (n=20,032; 0.8%), paternal ADHD only (n=16,952; 0.7%) or ADHD in both parents (n=1,545; 0.06%). Offspring with neither paternal nor maternal ADHD served as the reference group (n=2,447,559; 98.5%). Reproduction (the percentage of individuals born 1967-68 with offspring registered in the MBRN) were calculated for men and women with and without ADHD.

Results: Parental and offspring ADHD were strongly related. Maternal ADHD had a stronger association with offspring ADHD than paternal ADHD ($RR_{maternal}$ 8.4; 95% confidence interval (CI) 8.2-8.6 versus $RR_{paternal}$=6.2; 95% CI 6.0-6.4). The highest recurrence risk was when both parents were diagnosed with ADHD (RR_{both}=11.7; 95% CI 11.0-12.5). Further, the adjusted prevalence of offspring ADHD when both parents had ADHD was 41.5% in male offspring and 25.1% in female offspring. Recurrence risks from both maternal and paternal ADHD were higher in female than in male offspring. Men diagnosed with ADHD had lower reproduction than women with ADHD (75.2% versus 90.4%, respectively) and were generally older at childbirth.

Conclusions: Transgenerational ADHD recurrence risk was high and higher from maternal than paternal ADHD, regardless of offspring sex. Our results may prove helpful for health-care professionals when it comes to the identification of children at high risk of ADHD.

B17

Gluten intake in early life and risk of type 1 diabetes

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Introduction: No studies have investigated the relation between the amount of gluten intake by both the mother during pregnancy and the child in early life and risk of developing type 1 diabetes in childhood.

Aims: To examine the association between the maternal gluten intake during pregnancy, child's gluten intake at age 18 months, and the risk of type 1 diabetes in the child in a Norwegian population-based nation-wide study.

Methods: We included 86,306 children in The Norwegian Mother and Child Cohort Study born from 1999 through 2009, followed to April 15, 2018. The outcome was clinical type 1 diabetes, ascertained in a nation-wide childhood diabetes registry. Hazard ratios were estimated using Cox regression for the exposures maternal gluten intake during pregnancy and child's gluten intake at 18 months. We derived the amount (g/day) of gluten intake from a semi-quantitative food frequency questionnaire at week 22 of pregnancy and from a questionnaire completed by the guardian when the child was 18 months old.

Results: During a mean follow-up of 12.3 years (range 0.7-16.0), 346 children (0.4%) developed type 1 diabetes (incidence rate 32.6 per 100,000 person-years). The average gluten intake was 13.6 grams/day for mothers during pregnancy, and 8.8 grams/day for the child at 18 months of age. Maternal gluten intake in mid-pregnancy was not associated with the development of type 1 diabetes in the child (adjusted hazard ratio 1.02 (95% confidence interval 0.73 to 1.43) per 10 grams/day increase in gluten intake). However, the child's gluten intake at 18 months of age was associated with an increased risk of later developing type 1 diabetes (adjusted hazard ratio 1.46 (95% confidence interval 1.06 to 2.01) per 10 grams/day increase in gluten intake).

Conclusions: This study suggests that the child's gluten intake at 18 months of age, and not the maternal intake during pregnancy, could increase the risk of type 1 diabetes in the child.

B18

Adolescent body composition in relation to birth weight and childhood growth patterns. The Tromsø study: Fit Futures

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Introduction: Body composition, especially fat mass, fat distribution and central obesity, is associated with cardio-metabolic risk factors also in adolescents. High birth weight as well as childhood overweight/obesity are related to overweight/obesity later in life. More research is requested on the relationship between birth weight and early growth and later body composition and fat distribution.

Aims: To explore how birth weight, childhood body mass index (BMI) and growth are related to body composition measures in late adolescence.

Methods: We used data from 907 adolescents (52% boys) in the Tromsø Study, Fit Futures, a population-based cohort study conducted in 2010-2011 and 2012-2013 in Tromsø, Norway. Anthropometric data were retrospectively obtained from the Medical Birth Registry of Norway and childhood health records at (mean age) 2.5 and 6.0 years of age. Body composition was measured by dual X-ray absorptiometry at 15-18 and 18-20 years of age. In sex specific analyses, conditional growth models and linear mixed models were used to assess associations between birth weight, childhood BMI, BMI gain, with fat mass index (FMI, kg/m^2), fat-free mass index (FFMI, kg/m^2) standard deviation scores (SDS), as well as android:gynoid fat mass ratio (FMR), at 15-20 years as outcomes.

Results: In adjusted analyses, a 1-SD (585 g) higher birth weight was associated with higher FMI and FFMI in adolescence, FMI SDS: β= 0.19, (95% Confidence Interval: 0.08, 0.31), FFMI SDS: 0.18 (0.07, 0.29): FMI SDS: 0.09 (-0.03, 0.21), FFMI SDS: 0.15 (0.04, 0.25) in girls and boys, respectively. Conditional BMI gain in childhood was associated with higher FMI, FFMI and central overweight/obesity with the strongest associations seen between age 6-16.5 years: FMI SDS: 0.67 (0.63, 0.71), FFMI SDS: 0.46 (0.39, 0.52), android:gynoid FMR: 0.05 (0.05, 0.06) in girls, FMI SDS: 0.80 (0.75, 0.86), FFMI SDS: 0.49 (0.43, 0.55), android:gynoid FMR: 0.06 (0.06, 0.07) in boys.

Conclusions: Compared to birth weight and early childhood, a high BMI as well as greater BMI gain at later ages was more strongly linked to FMI and central obesity at 15-20 years. The magnitude of the associations increased with age, so preventive efforts should address both childhood and adolescence.

B19

The association between objectively measured physical activity and longitudinal changes in body composition in adolescents; The Tromsø Study Fit Futures Cohort

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Introduction: Physical activity may play an important role in preventing excess adiposity, but there is a lack of studies using robust measures of both physical activity and body composition to ascertain an association in adolescents.

Aims: Our aim was to study the effect of objectively measured physical activity on two-year changes in five different measures of body composition in a cohort of Norwegian adolescents.

Methods: In 2010-11 The Fit Futures Study invited all students in their first year of upper secondary high school from the neighboring municipalities of Tromsø and Balsfjord to a health examination, with 1,038 of the eligible participating (93%). A follow-up study was performed in 2012-13, of which 870 (77%) participated. We included participants <18 years of age at baseline with a valid recording of objectively measured physical activity, as well as valid measurements of body weight, body height, waist circumference, fat mass and lean mass in both studies (n = 435, 60.5% girls). The impact of baseline physical activity on 2-year changes in body mass index, waist circumference, fat mass index, lean mass index and appendicular lean mass index was explored using linear regression, and adjusted for potential confounders.

Results: Boys had significantly higher physical activity volume, indicated as counts per minute (CPM) ($p=0.01$) and on average more minutes in moderate physical activity (MVPA) than girls ($p <0.01$). There was no association between CPM and change in fat mass index in neither sex. In girls there was a weak positive relationship between counts per minute and change in lean mass index and appendicular lean mass index ($p=0.04$), but the relationship was attenuated after adjustments ($p=0.09$ and 0.06, respectively). Time spent in MVPA at baseline was not significantly associated with change in either measure of body composition between baseline and follow-up in neither sex.

Conclusions: Objectively measured physical activity was not associated with 2-year changes in objectively measured body composition in this cohort of Norwegian adolescents.

C16

Midlife bone mineral density loss in the distal forearm and subsequent mortality: findings from the population based Tromsø Study

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Introduction: Decreasing bone mineral density (BMD) is a part of the ageing process in both women and men. Low BMD is known to be associated with both increased risk of fractures and increased mortality. Whether the rate of bone loss starting in midlife is associated with mortality is not yet established.

Aims: To investigate if rate of BMD change in the distal forearm over seven years can predict mortality.

Methods: 1 627 postmenopausal women and 1 759 men aged 50-74 who participated in the longitudinal Tromsø Study waves 4 (1994-95) and 5 (2001-2002) were included. Cox regression models adjusted for lifestyle- and health related variables were used to assess associations between BMD change over seven years (continuous and in quartiles) and mortality during 17 years of follow-up in participants with normal BMD, osteopenia and osteoporosis at baseline.

Results: Baseline BMD decreased and seven-year bone loss increased with increasing age. Mortality rates were higher at lower BMD and at higher bone loss rates. In Cox regression, continuous BMD change was associated with increased mortality only in men with normal baseline BMD. In this group, the quartile (Q1) with the largest reduction in BMD had significantly higher mortality (HR 1.61, 95% CI 1.23, 2.11) than the quartile (Q4) with increased or unchanged BMD. Women with normal baseline BMD who experienced the largest bone loss (Q1) had significantly higher mortality than women in Q3 (moderate BMD reduction), but not Q4 (increased / unchanged BMD). BMD change was not associated with mortality in participants with osteopenia or osteoporosis at baseline.

Conclusions: BMD loss of the distal forearm was associated with increased mortality only in those with normal BMD at baseline, and the association was linear only in men.

C17

Individual Variation in Adaptive Immune Responses and Risk of Hip Fracture – A NOREPOS Population-Based Cohort Study

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Introduction: T-cell mediated immune responses may affect bone homeostasis, and subsequently the risk of fracture, through multiple pathways. Tuberculin skin tests (TST) are likely one of the few tests directly reflecting in vivo T-cell responses to have been conducted on a population-scale.

Aim: To estimate the impact of individual variation in these immune responses on the risk of hip fracture in the general population. The hypothesis was that individuals with a tendency towards pro-inflammatory responses have an increased risk of fracture.

Methods: We used data from the compulsory nationwide Norwegian mass tuberculosis screening and BCG vaccination programme during 1963-1975, which covered an estimated 80-85% of the population. This data included results from standardized TST. Individuals aged 14-30 years at the time of TST measurement and born 1940-1960 were included in the current analysis. All included individuals had a negative TST followed by BCG vaccination in the past, and had no signs of tuberculosis upon examination. TST results at the screening were recorded in millimetres, and later categorized according to clinical guidelines (positive/negative).

Our cohort constitutes 248 551 individuals who were alive and living in Norway at the start of the NORHIP database in 1994. This database includes records on all hospitalizations due to hip fractures in Norway during 1994-2013 (follow-up). Risk estimates were adjusted for county, BMI, age and time between BCG-TST, using Cox regression models.

Results: There were 3580 incident hip fractures during follow-up (first fractures), with a median age at the time of fracture of 61 years (range 36-73). Men with a positive TST had a 22% (HR 1.22, 95% CI 1.02-1.44) increased adjusted risk of hip fracture compared to men with a negative TST. This association was strengthened in sensitivity analyses limited to either those born 1945-1960 (post WW2) or aged 11-14 years at BCG vaccination (school vaccination). No clear association was observed in women.

Conclusion: We conclude that men with a negative tuberculin skin test after BCG vaccination have a reduced risk of hip fracture decades later. Women do not demonstrate similar associations, potentially due to sex specific differences in immune responses.

C18

Hand-arm vibration syndrome: A 22-year follow-up study

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Introduction: Hand-arm vibration syndrome (HAVS) is associated with hand numbness and painful attacks of white fingers. Little is known about the long-term course and prognostic factors.

Aims: To study the long-term course of HAVS.

Methods: Forty male sheet metal workers (mean age 60 years at follow-up) were examined with a test battery in 1994 and 2017. At baseline, the sample comprised 27 workers with HAVS symptoms and 13 workers without HAVS symptoms. Among the 27 workers, 25 workers reported work-related hand-arm vibration during follow-up (mean 3639 hours). In 2017, the mean time since vibration stopped was 8.4 years.

Results: The 27 workers with HAVS in 1994 showed no statistically significant change in hand numbness, white finger attacks, shoulder/arm pain or finger pain from 1994 to 2017. Isolated hand numbness (without white finger attacks) was more common at baseline than at follow-up. Vibration exposure during follow-up was associated with increased finger pain, whereas smoking predicted a poorer score at a cold provocation test. Alcohol consumption (s-CDT), diabetes (HbA1c) and folate deficiency did not influence the course. A diagnosis of HAVS in 1994 did not predict poor hand strength (measured by dynamometry and pinch grip) 22 years later. The manual dexterity (measured by the Grooved Pegboard test) declined during 22 years of follow-up in agreement with published reference values when allowing for aging.

Conclusion: This 22-year follow-up study indicates a tendency toward irreversibility of hand numbness, finger pain and white finger attacks in workers with HAVS. Continued vibration exposure seems to predict increased finger pain. Our findings highlight the importance of HAVS prevention.

C19

Sickness absence duration in young adults with musculoskeletal and psychological diagnoses: impact of the Norwegian Agreement for a More Inclusive Working Life

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Objectives: The Norwegian Agreement on a More Inclusive Working Life (the IW Agreement) was introduced in 2001 to reduce sickness absence (SA) and increase work participation. Little research has been done on the effects of this agreement. The study's aim was to compare SA duration before and after introduction of the IW Agreement among adults aged 24-38.

Methods: Data from several national registries were combined for 380,857 individuals born in Norway 1967–1976. Individuals' SA was classified into musculoskeletal (code L) and psychological (code P) diagnosis groups using ICPC-2 codes. A difference-in-differences method using negative binomial regression compared the difference in duration (days) of first SA lasting >16 days in individuals working in IW companies relative to non-IW companies in 2000 and 2005. Analyses were stratified by gender, industry, and gender within industry. Standard errors were clustered at the individual level and average marginal effects were calculated with 95% confidence intervals.

Results: The IW Agreement was associated with a statistically significant reduction in duration of first musculoskeletal-related SA (-0.94 days, CI -1.55,-0.33). After stratifying by gender, only women had a statistically significant reduction (-1.38 days, CI -2.23,-0.53). A statistically significant reduction in musculoskeletal SA duration was also found in the manufacturing industry both overall (-1.72 days, CI -3.42,0.18) and for men (-2.41 days, CI -4.32,-0.50). The agreement was not associated with duration of first psychological-related SA overall or in gender-specific analyses, but a significant increase in duration was found in the mining/quarrying industry (2.90 days, CI 0.88,4.93). Women in the wholesale/retail industry showed a reduced duration in both diagnosis groups (musculoskeletal: -4.78 days, CI -9.52,-0.04; psychological: -2.67 days, CI -5.21,-0.14).

Conclusions: Among young adults, the IW Agreement was associated with a reduced duration of first musculoskeletal SA episode overall and among women. Such reductions were not found for psychological diagnoses. However, some industry and gender specific effects of the IW Agreement were found. Diagnosis, gender, and industry therefore seem to influence the relationship between the IW Agreement and SA. The effect sizes were small and it is uncertain how much impact on SA this would have in practice.

A20

Associations between lifestyle factors and risk of bladder cancer, in a large population-based Norwegian cohort

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Introduction: Bladder cancer is the 9th most common cancer worldwide, with nearly 550 000 new cases in 2018. The incidence rates are higher in more developed countries, and the rates are 3-4 folded in men compared to women. The dominant cause of bladder cancer seem to be related to environment and lifestyle, with cigarette smoking being the most important risk factor. Lifestyle factors, including overweight and a low level of physical activity, are associated with increased risk of several cancers, but for bladder cancer the results are inconsistent.

Aims: We aimed to examine the association between lifestyle factors (body mass index, physical activity, blood pressure, and blood lipid levels) and risk of bladder cancer, in a large population-based Norwegian cohort.

Methods: The Janus Cohort comprises 292,851 Norwegians enrolled in 1972-2003. Linkage to the Cancer Registry of Norway, identified bladder cancer cases through 2016. Cox regression was used to estimate hazard ratios of bladder cancer risk with 95% confidence intervals. Analyses were stratified by sex and adjusted for attained age, smoking status (never, former, current smoker), smoking intensity (packyears), education, high risk occupation, body mass index and physical activity.

Results: Over the mean follow-up time of 29 years, 1978 primary bladder cancers were diagnosed. In men, high blood pressure was positively associated with bladder cancer risk, and the association was most pronounced in never smokers. Among women, no associations were found between the lifestyle factors and risk of bladder cancer. However, when stratified by smoking status, an inverse relation was seen for physical activity in never smokers, while a positive relation was found for current smokers.

Conclusion: Our study suggests that high blood pressure is a risk factor for bladder cancer in men, which might be more important among never smokers. In women, physical activity might be related to the risk of bladder cancer, however, dependent on smoking status.

A21

Serum 25-Hydroxyvitamin D levels predict cancer survival: A prospective cohort with measurements prior to and at the time of cancer diagnosis

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Introduction: Circulating 25-hydroxyvitamin D (25-OHD) levels have been inversely associated with cancer death, but the nature of this relationship is unclear. At least two explanations are possible: (A) High circulating 25-OHD inhibits cancer processes via biological mechanisms; (B) The processes and/or consequences of cancer cause serum 25-OHD levels to fall (i.e. reverse causality).

Aims: We aimed to investigate the association between levels of 25-OHD and cancer-specific death (case fatality) using repeated serum samples, obtained at different time points with respect to the time of cancer diagnosis, to shed light on the nature of this relationship.

Patients and methods: Pre-diagnostic serum samples were collected in population health surveys in Norway (1973-2004). Participants who subsequently developed cancer (1984-2004) provided a second serum sample at the time of cancer diagnosis. All samples were stored in the Janus Serum Bank. Repeated samples existed from 202 breast cancers, 193 lung cancers, 124 lymphomas and 37 colon cancers. Serum 25-OHD was measured via competitive radioimmunoassay. Cox regression models assessed associations between 25-OHD and case fatality through 2012, given as hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: The median time between pre-diagnostic and diagnostic samples was 14.4 years. The median 25-OHD levels were 63.3 and 62.5 nmol/L, respectively. During follow-up, 313 cancer deaths occurred. Compared to low pre-diagnostic 25-OHD levels (<46 nmol/L), higher levels (≥46 nmol/L) had significantly lower HRs (39-54%) of case fatality. This result was also seen for the diagnostic samples. Donors who had both samples at ≥62 nmol/L, had 59% lower HR of case fatality, compared to those for whom both samples were <46 nmol/L. Furthermore, vs. a decline in serum 25-OHD (median -22.4 nmol/L) from pre-diagnostic to diagnostic samples, a rise (median 22.3 nmol/L) was associated with lower case fatality (HR 0.57, 95% CI 0.43−0.75).

Conclusion: Our study demonstrates that 25-OHD levels <46 nmol/L, both several years prior to and at the time of cancer diagnosis, were associated with higher case fatality, and indicate benefits of maintaining sufficient 25-OHD levels over a lifetime. All results support explanation A; a causal relationship between higher vitamin D and reduced cancer case-fatality.

A22

Asthma, asthma control and incidence of lung cancer: the HUNT Study

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Introduction: Large prospective studies on asthma in relation to the incidence of lung cancer are limited. It is also unclear if the association is explained by smoking, chronic bronchitis or allergy as these conditions commonly occur in asthma individuals. The aim of this prospective cohort study was therefore to explore the association between asthma, levels of asthma control and lung cancer incidence, taking into account the commonly occurring conditions.

Methods: We followed 63,103 adults who participated in the second survey of the HUNT Study in Norway from 1995-97 to 2017. None of the participants had known cancer at the time of inclusion. Ever asthma (9.0%), doctor-diagnosed asthma (5.5%) and doctor-diagnosed active asthma (3.7%) were defined based on self-reported information at baseline. Among individuals with doctor-diagnosed active asthma, levels of asthma control were categorized into controlled and partly controlled. Incident lung cancer cases were ascertained from the Cancer Registry of Norway. Cox regression models were used to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for incident lung cancer in relation to asthma status.

Results: In total, 1,013 participants developed lung cancer during a median follow-up of 21.1 years. After adjustment for smoking (classified into detailed categories based on information of smoking status and pack-years), chronic bronchitis, allergy and other confounders, increased overall incidence of lung cancer was associated with ever asthma (HR 1.32, 95% CI 1.09-1.61), doctor-diagnosed asthma (HR 1.32, 95% CI 1.04-1.67) and doctor-diagnosed active asthma (HR 1.40, 95% CI 1.08-1.82). Individuals with ever asthma only and without current smoking, chronic bronchitis or allergy appeared to have an increased incidence of lung cancer compared with those with no ever asthma and no such common condition. Partly controlled doctor-diagnosed active asthma was associated with an increased incidence of lung cancer (HR 1.57, 95% CI 1.14-2.16), whereas no clear association between controlled doctor-diagnosed active asthma and lung cancer was observed (HR 1.16, 95% CI 0.65-2.06).

Conclusions: Our study suggested that asthma, in particular partly controlled asthma, was associated with an increased lung cancer incidence. Smoking, chronic bronchitis and allergy did not seem to explain the association.

A23

Cisplatin treatment of testicular cancer introduces long-term changes to the epigenome, possibly associated with metabolic syndrome

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Introduction: Testicular cancer (TC) survival rates have increased over the last decades, largely due to the introduction of cisplatin-based chemotherapy (CBCT). CBCT is part of standard treatment of several cancers. In TC survivors, an increased risk of developing metabolic syndrome (MetS) is observed.

Aims: In the epigenome-wide association study we investigated if CBCT relates to epigenetic changes, and if epigenetic changes render individuals susceptible for developing MetS later in life.

Methods: We analyzed DNA methylation, using the MethylationEPICBeadChip, in samples collected ~16 years after treatment from 279 Norwegian TC survivors with known MetS status. Among the CBCT treated (n=176) and non-treated (n=103), 61 and 34 developed MetS, respectively. We used linear regression models to identify if i) CBCT results in epigenetic changes, and ii) epigenetic changes play a role in development of MetS. Then we investigated if these changes in i) and ii) link to genes, functional networks and pathways related to MetS.

Results: We identified 35 sites that were differentially methylated when comparing CBCT treated and untreated TC survivors. The PTK6 - RAS - MAPk pathway was significantly enriched with these sites and infer a network of 13 genes with *CACNA1D* (involved in insulin release) as a network hub (gene with highest amount of interactions). We found nominal MetS-associations and a functional network with *ABCG1* and *NCF2* as network hubs. The *ABCG1* is involved in cholesterol and phospholipids transport, and regulates lipid homeostasis. The NCF2 codes Neutrophil Cytosolic Factor 2, forms an enzyme complex called NADPH oxidase, which plays an essential role in the immune system.

Conclusion: Our results suggest that CBCT has long-term effects on the epigenome. Since we identified differential methylation occurring in genes associated with conditions pertaining to MetS, we hypothesize that epigenomic changes may also play a role in development of MetS in TC survivors.

A24

The clone war of cancer clones of immune cells versus clones of cancer cells

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Introduction: Over several decades many theories have been proposed to explain carcinogenesis. Knowledge of the carcinogenic process is limited to reductionist experiments mainly in mice in non-pathogenic environment and with standardized lifestyle. For epidemiologists the main research directions have been to search for risk factors for cancer using prospective design of human biobanks and questionnaire information.

Aim: Here I propose that the carcinogenic process is a war, a clone war, between two biological processes.

Discussion: The clone war is between the aggressors, carcinogens mainly consequences of lifestyle, resulting in clones of cancer cells. The defense is the immune system consisting of clones of immune cells. The cancer cells can develop partly as a consequence of immune evasion. The power of the immune system has been known for more than hundred years and rediscovered as immune therapies today. Thus, the effects on the immune system has been neglected. In our systems epidemiology approach we have used the postgenome biobank of NOWAC to study the interactions between carcinogenesis and the immune system over time. The immune effects have been studied by conserved gene expression profiles taken from immune cells in buffered blood samples collected before, at and after diagnosis. For the first time we can look at changes in exposures to carcinogens over time and simultaneously study the changes in gene expression profiles in circulating immune cells in blood. These changes or trajectories demand new, non linear statistics. The clone war of breast cancer has been illustrated by the linear changes in gene expression levels explaining the protection of parity i.e. number of children on breast cancer. The theory might explain provocatively why not all smokers get lung cancer. An important challenge is to avoid analogical fallacies from reductionist experiments for the interpretation of the explorative epidemiological analyses.

B20

Inadequate iodine intake is associated with subfecundity in mild-to-moderately iodine deficient Norwegian women

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Introduction: Iodine is an essential micronutrient and an integral part of thyroid hormones. In women of childbearing age, the estimated average iodine requirement is 95 µg/day and the recommended daily intake is 150 µg/day. While severe iodine deficiency poses reproductive risks, the impact of mild-to-moderate iodine deficiency on subfecundity is unknown.

Aims: To examine whether iodine intake was associated with risk of subfecundity (i.e. >12 months trying to get pregnant) in the Norwegian Mother, Father and Child Cohort Study (MoBa).

Methods: Women enrolled in MoBa were asked to report whether the pregnancy was planned and how many months the couple had sexual relations without any contraception before getting pregnant. Information about time to pregnancy, maternal characteristics and iodine intake was available for 56,416 planned pregnancies. The median (interquartile range) time to pregnancy was 1.5 (0.5-6.0) months and the prevalence of subfecundity was 10.8% (n=6078). We used iodine intake assessed by a validated food frequency questionnaire administered in pregnancy as a proxy for long-term (pre-pregnancy) intake. We used logistic regression to estimate the association between iodine intake and subfecundity, using flexible modelling with restricted cubic splines, and adjusted for relevant confounders.

Results: The median calculated iodine intake was 121 µg/day and median urinary iodine concentration (UIC) was 69 µg/l (adequate intake in non-pregnant adults when median UIC>100 µg/l).The adjusted prevalence of subfecundity was low for iodine intakes at or above 100 µg/day but increased at lower intakes (*P*-overall=0.005). Compared to an intake of 100 µg/day (reference), an intake of 75 µg/day was associated with 5% (95%CI: 1-9%) higher prevalence and an intake of 50 µg/day with 14% (95%CI: 4-26%) higher prevalence of subfecundity. Use of dietary supplements was recorded only for the last 6 months prior to conception and women were included in the analysis regardless of their reported supplement use. In a sensitivity analysis, we excluded women who reported iodine-containing supplement use before conception and the results remained unchanged. We also modelled time to pregnancy by Cox regression and the result was consistent with that for subfecundity.

Conclusions: This study indicates that insufficient habitual iodine intake is associated with subfecundity.

B21

Hearing impairment and gender specific patterns of fertility – evidence from the HUNT study in Norway

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Introduction: Declining fertility coincide with a rise in the prevalence of hearing loss. Both changing family patterns and hearing loss (HL) relate to social activities, economic outcomes and length of life. The relationship between hearing loss and fertility have received insufficient research attention.

Aims: We employ data from HUNT, a population level longitudinal survey that incorporates hearing tests in Norway (baseline N=50,462 individuals).

Methods: Restricted cubic spline regressions. Air conduction hearing threshold levels were obtained by pure-tone audiometry at eight frequencies from 0.25 to 8 kHz in accordance with ISO 8253–1 (1989) as described in an earlier publication in NTHLS (Engdahl et al. 2005) and in SHINT according to according to the Norwegian standards at the time (Aarhus et al. 2019). Adult and childhood hearing thresholds were defined as pure-tone average (PTA) of four frequencies (0.5, 1, 2, and 4 kHz) in the better ear measured in dB HL. Hearing loss was defined as PTA greater than 25 dB HL. We further considered all subjects born between 1941 and 1977 (being in primary school age during SHINT) and not registered with a hearing loss in SHINT as normal hearing in childhood.

Results: We find that both women and men with hearing impairment have considerably fewer children (among women 2.18 children ever born for HL vs 2.50 children for normal hearing and among men 2.17 children for HL vs 2.31 children for normal hearing).

Conclusion: The negative effects of HL on fertility are more evident for later born cohorts. The relative decline in fertility has been particularly strong among hearing impaired men. The effects are also more pronounced when hearing loss was present in childhood.

B22

Temporal trends in age at menarche and age at natural menopause: a population study of 312 656 women in Norway

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Introduction: In the Western world, age at menarche decreased across birth cohorts from the early 1800s until the 1950s. Whether mean age at menarche has continued to decrease in birth cohorts after the 1950s remains uncertain. It is also uncertain whether mean age at natural menopause has changed across birth cohorts.

Aims: To study temporal trends in age at menarche, age at natural menopause, and the number of years between menarche and menopause.

Methods: We performed a retrospective population study of 312 656 women who were born in Norway during the years 1936-1964. Data were obtained by two self-administered questionnaires from women who participated in BreastScreen Norway during the years 2006-2014. We used flexible parametric survival models with restricted cubic splines to estimate mean age at menarche, mean age at menopause and mean number of years between menarche and menopause according to the women's year of birth.

Results: The mean age at menarche was 13.42 years (95% confidence interval 13.40-13.44 years) among women born during 1936-1939, and it was 13.24 years (95% confidence interval 13.22-13.25 years) among women born during 1960-1964. The mean age at natural menopause increased from 50.31 years (95% confidence interval 50.25-50.37 years) among women born during 1936-1939 to 52.73 years (95% confidence interval 52.64─52.82 years) among women born during 1960-1964. The mean number of years between menarche and menopause increased, from 36.83 years (95% confidence interval 36.77-36.89 years) to 40.22 years (95% confidence interval 40.11-40.34 years).

Conclusions: Our study of 312 656 women born in Norway, suggest minor changes in age at menarche across birth cohorts from 1936 to 1964. However, age at menopause and also the time interval between menarche and menopause have increased by approximately three years.

B23

The association of birthweight with age at natural menopause. A population study of women in Norway

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Introduction: The mechanisms underlying the timing of natural menopause are not well understood. Previous studies suggest that birthweight may influence age at natural menopause, but the evidence remains inconclusive.

Aims: To estimate the association of birthweight with age at natural menopause.

Methods: A retrospective population study of 164 608 women in Norway, aged 48-71 years. Data were obtained by two self-administered questionnaires among participants in BreastScreen Norway during 2006-2014. We used Cox proportional hazard models to estimate hazard ratios and logistic regression models to estimate odds ratios of menopause according to birthweight. Restricted cubic splines were applied to allow for possible non-linear associations, and adjustments were made for year of birth and country of birth.

Results: Women with birthweight < 2500g were median 51 years at menopause (interquartile range 49-54 years), whereas women with birthweight 3500-3999g were median 52 years at menopause (interquartile range 49-54 years). The hazard ratio of menopause decreased with increasing birthweight up until 3500g. At birthweights above 3500g, we estimated no further decrease (*P* for non-linearity = 0.007). Birthweight at 2500g increased the odds ratios of menopause before the age of 45 (1.20; 95% CI: 1.14-1.25) and the age of 40 (1.26; 95% CI: 1.15-1.38) compared to birthweight at 3500g. At birthweights 4000g and 4500g, the odds ratio estimates were very similar to the reference group (birthweight 3500g) and the CIs overlapped 1.00.

Conclusions: We found a non-linear dose-relationship of birthweight with age at natural menopause, and low birthweight was associated with early natural menopause. Our findings suggest that growth restriction during fetal life may influence the timing of natural menopause.

B24

Growth in children conceived by assisted reproductive technologies: the Norwegian Mother and Child Cohort Study

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Background/Aims: Studies indicate that children conceived by assisted reproductive technologies (ART) have altered growth patterns. The role of parental subfertility and freezing of embryos in the growth among these children remain unclear. The aim of this study was to describe growth patterns among children conceived by ART, and to evaluate the role of both parental subfertility and frozen versus fresh embryo transfer.

Method: This study included singletons participating in the Norwegian Mother and Child Cohort Study (n=81,492) who had at least two weight and length measurements. We first compared children conceived after frozen (n=155) and fresh (n=777) embryo transfer with in vitro fertilization (IVF), and children conceived by frozen (n=84) and fresh (n=574) embryo transfer with intracytoplasmic sperm injection (ICSI), to all spontaneously conceived children. Subsequently, we compared these groups of children conceived by ART to spontaneously conceived children of parents who had tried to conceive for more than 12 months (n=5,281). We examined differences in growth between the groups by adding interaction terms with linear spline terms reflecting growth periods using mixed effects linear regression, adjusting for maternal age, parity, smoking, and education, in addition to parental body-mas index, parental height, offspring sex and gestational age. The mean number of anthropometric measurements available was 8 (minimum 2, maximum 12) between birth and 7.5 years of age.

Results: Children conceived after fresh embryo transfer IVF (adjusted β -120 grams; 95% CI: -220, -30) or ICSI (adjusted β -90 grams; 95% CI: -200, 21) had smaller birthweight compared to children born spontaneously. Fresh embryo IVF offspring showed a greater increase in both weight (adjusted β 8 grams/week; 95% CI: 2.3, 14) and length (adjusted β 0.19 mm/week; 95% CI: 0.09, 0.29) between 3 and 8 months of age, as compared to spontaneously conceived offspring. Children conceived by frozen embryo transfer IVF had birthweights similar to spontaneously conceived offspring (adjusted β 7 grams; 95% CI: -203, 204), and also experienced a greater weight gain (adjusted β 1.2 grams/week between 16 months and 7 years; 95% CI: 0.2, 2.3). We observed an attenuation of the difference in size at birth and childhood growth when ART children were compared to spontaneously conceived children of subfertile parents.

Conclusion: Our findings indicate an altered growth in ART children, which varies according to the procedure and whether the embryo transfer is fresh or frozen, and might be partly explained by factors related to parental subfertility.

C20

Evaluating exposure to environmental contaminants across past decades in the context of effect studies today

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Introduction: Studies of environmental contaminants in humans, as assessed by monitoring in blood, have demonstrated decreasing concentrations of legacy compounds in recent decades whereas the concentrations of compounds in use during the same period has increased. Many studies aiming to elucidate effects of contaminants on human health today rely on blood samples but the exposure measurements do not necessarily reflect early-life exposures.

Aims: To increase our understanding of contemporary exposure measurements, by summarizing several monitoring studies targeting contaminants in blood samples in combination with an emission-based human exposure model.

Methods: A wide range of contaminants were measured in two sample sets with repeated blood samples in the Tromsø Study and several cross-sectional samples of blood samples in Norwegian cohorts. An emission-based mechanistic model was used to predict concentrations in blood at the time of sample but also earlier in each person's life.

Results: Five repeated measurements within the same persons (median of 40 years in 1979, 68 in 2007) demonstrated decreasing concentrations of legacy compounds like PCBs and pesticides since 1980s but that per- and polyfluorinated substances increased until the sampling year 2001 in the Tromsø Study. Monitoring results of the same substances in four cross-sectional samples of serum from 30 year olds in Norway during the same years indicated that declines in cross-sectional samples of younger persons were larger than in repeated samples from older persons in the same years. Median summed POP concentrations in men and women of fertile ages decreased by −86% 1986-2007.

The time trends of PCB-153 in blood derived from the prediction model agreed well with those observed although individual variation could not be captured in individual predictions in cross-sectional sample sets. Still, this indicates the high level of understanding of emissions, environmental fate and human bioaccumulation of these compounds.

Conclusions: The observed time trends of contaminants in blood could largely be explained by time trends in emissions, and our mechanistic environmental fate and human bioaccumulation model was largely capable of reproducing measured concentrations of PCB-153. These findings are of great value for our understanding of human exposure to these compounds.

C21

Relationship between periodontitis and Alzheimer's disease: A bidirectional Mendelian randomization study

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Introduction: Recent experimental studies indicated that a periodontitis-causing bacterium might be a causal factor for Alzheimer's disease (AD).

Aims: We applied a two-sample Mendelian randomization (MR) approach to examine the potential causal relationship between chronic periodontitis and AD bidirectionally in the population of European ancestry.

Methods: We used publicly available data of genome-wide association studies (GWAS) on periodontitis and AD. Six single-nucleotide polymorphisms (SNPs) were used as instrumental variables for periodontitis. For the MR analysis of periodontitis on risk of AD, the causal coefficient and confidence interval (CI) were derived from the GWAS of periodontitis including 34,615 individuals (12,289 cases vs. 22,326 controls) in the Gene-Lifestyle Interactions in Dental Endpoints (GLIDE) consortium and from the GWAS of AD (17,008 cases vs. 37,154 controls) in The International Genomics of Alzheimer's Project (IGAP). Twenty-one SNPs were used as instrumental variables for AD. For the MR analysis of AD on risk of periodontitis, the causal coefficient was derived from the GWAS of AD including 25,580 cases and 48,466 controls in the IGAP and from the GWAS of periodontitis in the GLIDE (n=34,615). We employed multiple methods of MR, including MR-PRESSO (pleiotropy residual sum and outlier), inverse-variance weighted (IVW), weighted median, and MR-Egger.

Results: No outliers in the bidirectional MR were detected with MR-PRESSO (global test $P>0.60$). No substantial evidence for horizontal pleiotropy was observed in the MR-Egger regression analyses ($P>0.77$). Based on the IVW method, there was no evidence of genetically predicted periodontitis being associated with a higher risk of AD (coefficient -0.02, 95% CI -0.17 to 0.13, $P=0.78$). There was no clear causal effect of genetically predicted AD on risk of periodontitis either (coefficient -0.01, 95% CI -0.04 to 0.02, $P=0.58$). These findings were supported by other MR methods.

Conclusions: There was limited evidence to suggest that genetic liability to periodontitis increases the risk of AD or vice versa in the population of European ancestry. Prevention and/or treatment of periodontitis might not reduce the risk of AD in humans.

C22

Trends in disability free life expectancy in the older Norwegian population: it is getting better

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Introduction: Knowledge on trends in disability free life expectancy (DFLE) among older adults in Norway is limited.

Aims: We aimed to estimate life expectancy (LE) and DFLE in the older Norwegian population during the last three decades for men and women and across educational strata.

Methods: Cross-sectional data on functional ability for 70+ year olds from HUNT2 and HUNT3 initiated in 1995 and 2006 (N=14,421) was combined with life table data by gender and education from microdata.no. Functional ability to perform practical everyday tasks was assessed using Personal ADL (PADL) items such as washing, dressing and eating and Instrumental ADL (IADL) items such as paying bills, going out, and shopping. DFLE was estimated using the Sullivan method.

Results: Overall, there was a reduction in years lived with disability from 1995 to 2006 for both men and women. At age 70 in 1995, women could expect to live for 15.4 years, of which 8.8 years were without disabilities and 6.6 years were with disabilities. In 2006, DFLE increased to 12.1 and years with disabilities decreased to 4.8 years. In men, DFLE increased from 8.3 to 11.2 years, and disabilities decreased from 4.2 to 3.4 years. Especially, the years spent in high degree of disability decreased in women (1.2 years), while the years spent in lower degree of disability were equally reduced in men and women (0.5-0.6 years). DFLE increased in all educational groups, but more in the higher than in the lower educational groups. The educational gap in LE decreased slightly from 2.2 to 2.1 years in women, and increased from 1.6 to 1.8 years in men, while the educational gap in DFLE increased in both genders (from 1.5 to 2.0 years in women and 1.3 to 1.6 years in men).

Conclusion: During 1995-2006, both LE and DFLE improved in the older Norwegian population in both genders and across educational strata. However, educational inequalities in DFLE increased.

C23

Air pollution and mortality in Norway – using NORCOHORT

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Introduction: Long-term exposure to air pollution is associated with natural cause mortality. However, there is still uncertainty about the shape of the relationship at low concentrations. These concentrations are present in Norway, which makes Norwegian data highly relevant to gain more knowledge about health risks at low concentrations.

Aims: To investigate the association between air pollution and natural cause mortality in Norway.

Methods: Norway participates in the multicentre *Effects of Low-Level Air Pollution: A Study in Europe* (ELAPSE) study with the new national cohort NORCOHORT. The NORCOHORT consists of all Norwegian citizens 30 years or older having home address in Norway per 1.1.2001, about 2.6 mill individuals. Data from several national registers were linked to the NORCOHORT population, including the population register, the mortality register, the cancer register, the patient register, the KUHR register, the CVDNOR project, socioeconomic data from Statistics Norway and the CONOR cohort. Annual averages of air pollutants (fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2), black carbon (BC) and ozone) were modelled by IRAS in The Netherlands, using hybrid land use regression with 100m spatial resolution. These concentrations were linked to the NORCOHORT population using the individual home addresses. We used Cox proportional hazard models with increasing levels of adjustment for area- and individual-level confounders. Flexible approaches were used to capture non-linearity in the air pollution-mortality association.

Results: We estimated significant associations between $PM_{2.5}$, NO_2 and BC with mortality, with hazard ratios (HRs) of 1.08 (95% confidence interval (CI): 1.07, 1.09), 1.06 (1.05, 1.07) and 1.05 (1.04, 1.06) per increments of 5, 10 and 0.5 $\mu g/m^3$ in the three pollutants, respectively. Adjusting for other pollutants the estimate of NO_2 was stable, while $PM_{2.5}$ and BC decreased somewhat in two-pollutant models. The association with ozone was negative, but changed to a positive significant association after adjusting for NO_2. We found associations even at rather low concentrations, e.g. well below WHO guidelines.

Conclusions: This study suggests that even at the low Norwegian concentration levels, air pollution may have an effect on mortality. Still, the study lacks smoking information on individual level, which likely would have influenced the estimated associations.

C24

Are compensation claims from patients associated with 30-day mortality? A longitudinal analysis of health trusts in Norway

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Introduction: The Norwegian System of Patient Injury Compensation is a government agency under the Ministry of Health and Care Services and deals with patient reported complaints about incorrect treatment in the public and private healthcare services. The quality indicator 30-day mortality may be associated with better clinical quality. How these two parameters relate to each other, has not been evaluated previously in Norway.

Aims: To test if compensation claims from patients are associated with existing measures of quality indicators (e.g 30-day mortality).

Methods: Data on compensation claims (total number of claims received and number of granted claims) were obtained from The Norwegian System of Patient Injury Compensation. 30-day mortality were collected from the national quality indicator system. All measures were given for each health trust annually from 2010 to 2017. The annual national trends were plotted, and the Pearson correlation coefficient was used to calculate the association between 30-day mortality and compensation claims at the trusts level (total number of claims and granted claims).

Results: Preliminary results show that both the rate of 30-day mortality and of granted claims have declined over time. Moreover, 30-day mortality were significantly correlated with total number of claims, with correlation coefficient of 0.51 with p=0.025. For granted claims, the correlation coefficient was 0.43 with p= 0.068.

Conclusions: Results from the present study indicate an association between compensation claims from patients and 30-day mortality, suggesting that both parameters capture similar aspects of the latent quality of the health trusts.

P1

Mild-to-moderate iodine deficiency is associated with lower birthweight and increased risk of preterm delivery in the Norwegian Mother, Father, and Child Cohort Study

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Introduction: Severe iodine deficiency is associated with foetal growth restriction and preterm delivery. Less is known about the potential impact of mild-to-moderate iodine deficiency on these outcomes.

Aim: To investigate whether maternal iodine intake in pregnancy was associated with birth weight (BW) z-score (i.e. BW adjusted for gestational length and sex) and preterm delivery (before week 37).

Methods: The study population included 77,995 singleton pregnancies from The Norwegian Mother, Father and Child Cohort Study recruited in 2002-2008. Habitual iodine intake was calculated from a validated food frequency questionnaire covering the first half of pregnancy. Use of supplements was reported in questionnaires. Urinary iodine concentration (UIC) was measured in gestational week 18 in a subsample of n=2795 women. 5.0% were born before gestational week 37. Associations were modelled flexibly by use of restricted cubic splines, and adjusted for age, parity, pre-pregnancy BMI, education, smoking in pregnancy, energy intake, and fibre intake.

Results: Median iodine intake from food was 121 µg/day and median UIC was 69 µg/L. Median UIC<150 µg/L is considered insufficient in pregnant women. In non-users of iodine-containing supplements (n=48,958), a low habitual iodine intake from food (lower than about 150 µg/day) was associated with a lower mean BW z-score ($p<0.001$). Compared to an intake of 150 µg/day (reference), mean z-score was 0.04 SD lower at 100 µg/day and 0.12 SD lower at 75 µg/day. Results were similar when using UIC as the exposure (n=2795, $p=0.017$). Any use of iodine containing supplements in pregnancy was associated with 0.03 (95% CI: 0.01, 0.04) SD increase in BW z-score compared to no use (n=77,949, $p<0.001$).

A low habitual iodine intake from food (lower than about 100 µg/day) was associated with increased risk of preterm delivery ($p=0.003$). Compared to an intake of 100 µg/day (reference), 75 µg/day was associated with 10% increased risk, and 50 µg/day with 28% increased risk. Use of an iodine-containing supplement was not associated with the risk of preterm delivery (OR: 0.97 (95%CI: 0.91, 1.04, $p=0.42$)).

Conclusions: Our results indicate that mild-to-moderate iodine deficiency in pregnancy is associated with restricted foetal growth and increased risk of preterm delivery.

P2

Environmental toxicants in breast milk of Norwegian mothers and gut bacteria composition and metabolites in their infants at one month

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Introduction: Early disruption of the microbial community may influence life-long health. Environmental toxicants can contaminate breast milk and the developing infant gut microbiome is directly exposed. A few experimental studies suggest exposure to persistent organic pollutants can affect the gut microbiome.

Aims: To investigate whether environmental toxicants in breastmilk affect the composition and function of the infant gut microbiome at one month.

Methods: We measured environmental toxicants in breastmilk, fecal short-chain fatty acids (SCFAs), and gut microbial composition from 16S rRNA gene amplicon sequencing using samples from 267 mother-child pairs in the Norwegian Microbiota Cohort (NoMIC). We tested 28 exposures: polychlorinated biphenyls (PCBs), polybrominated flame retardants (PBDEs), per- and polyfluoroalkyl substances (PFASs), and organochlorine pesticides. We assessed chemical exposure and alpha diversity/SCFAs using elastic net regression modelling and generalized linear models, adjusting for confounders; variation in beta diversity (UniFrac), taxa abundance (ANCOM), and predicted metagenomes (PiCRUSt) in low, medium and high exposed groups.

Results: PBDE-28 and surfactant perfluorooctanesulfonic acid (PFOS) were associated with less microbiome diversity. Some sub-OTUs of Lactobacillus, an important genus in early life, were lower in abundance in samples from infants with relative "high" (>80th percentile) vs. "low" (<20th percentile) toxicant exposure. Breast milk toxicants were associated with microbiome functionality, explaining up to 34% of variance in acetic and propionic SCFAs, essential signalling molecules. Per one standard deviation of exposure, PBDE-28 was associated with less propionic acid (-24% [95% CI: -35% to -14%] relative to the mean), and PCB-209 with less acetic acid (-15% [95% CI: -29% to -0.4%]). Conversely, PFOA and dioxin-like PCB-167 were associated with 61% (95% CI: 35% to 87%) and 22% (95% CI: 8% to 35%) more propionic and acetic acid, respectively.

Conclusions: Environmental toxicant exposure may influence infant gut microbial function during a critical developmental window and these novel findings require replication.

P3

Cord blood metabolites and risk of type 1 diabetes in childhood

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Introduction: Several small studies have investigated the possible association between metabolites and type 1 diabetes, but it is still unclear if there is any association between metabolites and later disease.

Aims: We aimed to study if metabolite concentrations measured in cord blood taken at birth could predict later type 1 diabetes.

Methods: We quantitatively measured 17 metabolites (Table 1), using a targeted metabolomics LC-QQQ-MS platform, in 166 children who later developed type 1 diabetes, and 177 random control children who did not develop type 1 diabetes. We present preliminary results analysed by logistic regression. We report the odds ratio (OR) per z-score increase, and analysed the metabolites divided into tertiles to test for linearity. As a sub-analysis we attempted to cluster the metabolites (four clusters) and investigated if these were associated with later type 1 diabetes.

Results: No metabolite reached statistical significance (Table 1). Phenylalanine showed signs of non-linearity, which means the estimate reported must be interpreted with caution. No cluster was statistically associated with type 1 diabetes.

Table 1: Metabolites studied	OR, 95% CI	p-value
Asymmetric dimethylarginine	1.04 (0.83 - 1.31)	0.72
Alanine	1.10 (0.90 - 1.36)	0.34
L-3 Hydroxybutyric acid (ß)	0.81 (0.64 - 1.03)	0.08
L-Citrulline	1.04 (0.84 - 1.29)	0.71
Glycocholic acid	1.02 (0.81 - 1.27)	0.88
Glycochenodeoxycholic & Glycodeoxycholic acid	1.01 (0.84 - 1.21)	0.91
Glutamine	0.88 (0.71 - 1.08)	0.22
Glutamic acid	1.18 (0.93 - 1.48)	0.17
Glycine	0.97 (0.79 - 1.19)	0.78
L-Kynurenine	0.90 (0.73 - 1.11)	0.31
Leucine & Isoleucine	1.00 (0.81 - 1.23)	0.99
Phenylalanine	0.93 (0.75 - 1.15)	0.49
Taurine	0.95 (0.76 - 1.19)	0.67
Taurocholic acid	1.08 (0.83 - 1.39)	0.57
Taurochenodeoxycholic & Taurodeoxycholic acid	1.13 (0.96 - 1.34)	0.15
Tryptophan	0.86 (0.66 - 1.11)	0.24
Tyrosine	1.01 (0.82 - 1.25)	0.92

Conclusions: In this preliminary analysis, we found no support for the hypothesis that metabolites measured in cord blood could predict later type 1 diabetes.

P4

Early parent-reported signs of cerebral palsy in Denmark and Norway

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Introduction: Cerebral palsy (CP) is a group of non-progressive motor disorders and a major cause of childhood disability. Even though the underlying brain damage is most often present at birth, the disease may takes years to diagnose. Parents are often the first to observe deviance in their children's development.

Aim: To investigate the associations between early developmental and behavioral characteristics reported by parents and later diagnosis of CP.

Methods: We analyzed prospectively collected data from the Mother, Father and Child Cohort study, and the Danish National Birth Cohort. 149 978 term born singletons, including 203 children with CP, participating in the study at 6 months of age were included. Information on early characteristics were retrieved from questionnaires (Norway) and structured interviews (Denmark) reported by the parents when the child was 6 months old. We used log binominal regression models to estimate relative risk for a diagnosis of CP by each exposure.

Results: Children later diagnosed with CP were less likely to be exclusively breastfed, peaking in the third month of life (RR (relative risk) 0.6, 95% CI (confidence interval) 0.4-0.8). They had increased risk for several indicators of motor delay at six months, including not stretching out for a toy (RR 47, 95% CI 30-74), not grabbing a toy (RR 224, 95% CI 141-356) and not holding a toy with both hands (RR 165, 95% CI 112-243). Parents more frequently reported the child to be inconsolable (RR 3.3, 95% CI 1.4-6.7) and suffer from colic (RR 2.1, 95% CI 1.5-6.7) and more often experienced the child to be very difficult to care for (RR 5.3, 95% CI 2.8-3.0). Children later diagnosed with CP were also at increased risk for experiencing pneumonia (RR 1.8, 95% CI 1.1-3.0), febrile seizures (RR 24, 95% CI 14-40) and non-febrile seizures (RR 26, 95% CI 15-48) and had more frequent visits to the Mother and Child Health Care Centres.

Conclusions: Parents reported less breastfeeding, more frequent indicators of motor delay, and more health problems the first 6 months of life in term born singletons later diagnosed with CP.

P5

The Tromsø Study 1994-95: Is grip strength in men and women aged 50-79 years associated with non-vertebral osteoporotic fracture during 15 years follow-up?

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Introduction: Norway has the world's highest hip- and forearm fracture incidence rates. The causes of osteoporotic fractures are multifactorial, but low bone mineral density (BMD) and falls are the most important predictors. As neuromuscular strength and control are associated with several of the shared risk factors for osteoporosis and falls, we wanted to explore the association between a simple physical measure like grip strength with fracture. Handgrip strength is a powerful predictor of disability, morbidity and mortality, and might be an indicator of sarcopenia and thus a predictor of fall-risk.

Aims: To explore whether low grip strength was associated with increased risk of non-vertebral osteoporotic fracture in the population-based Tromsø Study 1994-95.

Methods: Grip strength was measured by a Martin Vigorimeter and incident non-vertebral osteoporotic fractures (distal forearm (distal radius, distal ulna), hip (femoral neck, trochanter), pelvis and proximal humerus) occurring during 1994-2010, were retrieved by linkage to the x-ray archives at the University Hospital of North Norway. At baseline, weight and height were measured, whereas information on the other covariates were obtained through self-reported questionnaires. Cox regression was used to estimate the hazard ratio (HR) of fracture in age- and gender-specific quintiles of grip strength, and per 1 SD lower grip strength. Adjustments were made for age, height, body mass index (BMI), marital status, education, smoking, physical activity, use of alcohol, self-perceived health and self-reported diseases.

Results: In 2,889 men and 3,900 women aged 50-79 years, 1,099 non-vertebral osteoporotic fractures, were sustained during median 15 years follow-up. Risk of non-vertebral osteoporotic fracture increased with declining grip strength: Hazard ratios per SD lower grip strength was 1.22 (95% confidence interval 1.05-1.43) in men and 1.09 (95% confidence interval 1.01-1.18) in women. HR for osteoporotic fracture in lower vs. upper quintile was 1.58 (95% confidence interval 1.02-2.45) in men and 1.28 (95% confidence interval 1.03-1.59) in women.

Conclusions: In men and women aged 50-79 years, lower hand grip strength was associated with higher risk of non-vertebral osteoporotic fractures during 15 years follow-up.

P6

Comparison of overall rates for cancer incidence and cancer mortality for vessel crews and land-based personnel in the Royal Norwegian Navy

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Introduction: A cohort was established comprising 28 300 Royal Norwegian Navy military servicemen who served between 1950 and 2004. A previous study followed the cohort through 2007 for mortality and through 2008 for cancer incidence. While it showed a "healthy soldier effect" in terms of lowered all-cause mortality it also revealed an elevated cancer incidence. Compared to land-based personnel, vessel crews had approximately 60% higher risk of lung cancer and alcohol-related cancers, as well as higher mortality from non-neoplastic alcohol diseases.

Aims: To investigate overall cancer incidence and cancer mortality in vessel crews and land-based personnel. We also looked at the relative rates for the two groups.

Methods: We followed the cohort from 1953 through 2017 for cancer incidence and from 1951 through 2017 for cancer mortality and calculated standardized incidence (SIR) and mortality ratios (SMR) for cancer from national rates. Poisson regression analysis was used to compare rates according to personnel group. Relative risks expressed as rate ratios (RRs) were calculated for vessel crews using land-based personnel as reference. Ninety-five percent confidence intervals (CIs) were computed.

Results: Among vessel crews, we observed increased ratios for total cancer incidence (SIR=1.13) and mortality (SMR=1.10), while in the land-based group total cancer incidence was identical to the population average (SIR=1.00) and cancer mortality lower than the reference (SMR=0.83). When we compared the two groups, vessel crews had 13% higher risk of being diagnosed with cancer (RR=1.13), and a substantially higher mortality (RR=1.36).

Conclusion: Vessel crews had a higher risk of being diagnosed with, and dying from, cancer than did the land based personnel. When comparing the vessel crews with the land-based group, the risk elevation for cancer death (36%) is greater than the risk elevation for a cancer diagnosis (13%). This means that the vessel crew more often die from their cancer, which is indicative of higher incidence of cancers with poorer survival rate. One such cancer is lung cancer, which was more frequent in the vessel group (RR=1.72).

P7

Post-diagnostic blood gene expression profiles in breast cancer – a clinical follow-up in the NOWAC Post-genome cohort

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Introduction: Metastases are the major cause of death among breast cancer patients. Analyses of gene expression from immune cells in blood could potentially improve the understanding of the immune response during the carcinogenetic and metastatic processes.

Aims: We used the Norwegian Women and Cancer (NOWAC) Post-genome cohort to explore gene expression profiles from immune cells in blood, in the first 8 years *after* breast cancer diagnosis.

Methods: A random sample of NOWAC participants were invited to donate blood samples for the Post-genome cohort, irrespective of disease status. Linkage to the Cancer Registry of Norway revealed 445 incident cases of breast cancer among the Post-genome participants, during the 10 years before blood sampling. Age-matched controls were drawn from the Post-genome cohort, and the final study sample included 415 case/control pairs, and 137 (33%) of the cases had metastatic cancer. Gene expression profiles were analyzed using the Illumina HumanHT-12 v.4 bead chip array, and R was used for statistical analyses. Analyses were stratified on cancer stage and vital status at the end of follow-up (15 years).

Results: There was 2849 differentially expressed genes when comparing all cases to controls. Compared to in situ, invasive, or metastatic cases who survived, the metastatic cases who died within the follow-up time, had the largest number of differentially expressed genes, with a transient peak around 3 years after their initial breast cancer diagnosis.

Conclusions: The strong, transient signals in the blood of women with metastatic cancers who died during follow-up, could offer the potential for development of predictive tests of survival. Even more important, we might increase our understanding of the last stage of carcinogenesis as a balance between the driving forces of tumor progression, and the defense of the body through the immune system.

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Whole Genome Bisulfite Sequencing from The Janus Serum Bank opens door for Epigenome-Wide Association Studies

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Introduction: DNA methylation is an epigenetic mark involved in the regulation of gene expression and development. There is increasing recognition that aberrant DNA methylation plays an important role in cancer development. Methylation analysis on biobanked serum samples is challenging due to limited DNA amounts extracted from such samples.

The Janus Serum Bank is a population based biobank reserved for cancer research. The specimens are collected between 1972-2004. The biobank contains blood samples from 318628 Norwegians, and is internationally unique regarding size and number of cancer cases. We aim to study associations between the methylome and testicular cancer (TC). However, the developed protocols will be applicable to other methylation profiling studies.

Aims: Our goal was to establish Whole Genome Bisulfite Sequencing (WGBS) of Janus Serum Bank samples yielding a few nanogram of DNA. The main goal is to perform a hypothesis free epigenome-wide association study (EWAS) to identify relevant CpGs.

Methods: Differential DNA methylation will be studied in pre-diagnostic archived blood samples from 82 cases and 82 matched controls. Here we present details from our pilot experiment done on 5 samples, sequenced on NovaSeq instrument.

Results: We have conducted the pilot study that demonstrates rich genome wide DNA methylation profiles from archived samples. We obtained 820GB of data, including 2.5 billion reads of good quality. Average coverage of the samples was 20x, evenly distributed across human genome. Average alignment to human genome was 83.3%. 81.6% of Cs were methylated in CpG context. Other C context (CHG, CHH) were very low (0.0034, 0.0035).

Conclusion: Epigenome-Wide Association Studies of the Janus Serum Bank samples are possible. Our findings may provide increased understanding of the underlying epigenetic architecture of TC and thereby identification of targets for early diagnosis. These studies will be important for biomarker discoveries and understanding the biology of many cancer types.