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DEN 27. NORSKE EPIDEMIOLOGIKONFERANSEN

BERGEN,

3.–4. NOVEMBER 2021

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The 27th Norwegian Conference on Epidemiology
Bergen, 3–4 November 2021

We wish you all a very warm welcome to Bergen and the 27th conference of the Norwegian Epidemiological Association (NOFE). Last year, we had to postpone the conference due to the covid-19 pandemic. We are therefore very pleased that the NOFE conference could be arranged in 2021.

The theme of the 27th NOFE conference is *Organization, opportunities and challenges with using health surveys in research*. We have invited several speakers from Norway and are delighted also to have two international keynote speakers, Professor Janet Rich-Edwards (Harvard School of Public Health, US) and Professor Nicholas J. Timpson (University of Bristol, UK).

During the conference, there will be 60 oral presentations in parallel sessions, covering a wide range of epidemiological themes, and 29 posters will be available for viewing. We are delighted to see the large number of abstracts submitted this year and we thank you all for your important contributions to the conference!

EPINOR, the national research school in population-based epidemiology, plays an important role in securing the next generation of epidemiologists and we hope that NOFE will continue to serve as a venue for interaction and collaboration between our senior and younger epidemiologists.

At the conference, NOFE will be awarding the two prizes – 'Paper of the Year' and 'NOFE Honorary Membership' – and we look forward to celebrating these with you during the first day of the conference.

If you have a thematic suggestion for upcoming issues of *Norsk Epidemiologi – the Norwegian Journal of Epidemiology,* please contact NOFE by e-mail (post@nofe.no).

We hope to see many of you at the NOFE annual meeting on Wednesday 3 November.

Finally, we wish to express our gratitude to the Norwegian Institute of Public Health, the Western Norway University of Applied Sciences and the University of Bergen for their financial support for the NOFE conference.

Welcome to Bergen and NOFE 2021!

The NOFE Board
&
The organizing committee for the NOFE 2021 Conference

Ragnhild B. Strandberg, Anne Kjersti Daltveit, Marjolein M. Iversen, Kari Klungsøyr, Roy M. Nilsen and Hilde Kristin R. Riise

The 27th Norwegian Conference on Epidemiology

Bergen, 3–4 November 2021

International keynote speakers' biographies

Janet Rich-Edwards

Janet Rich-Edwards, ScD, is a world-leading epidemiologist on the topic of taking a life course approach to women's health, examining childhood and early adult predictors of later cardiometabolic health. She works with a variety of data sources: Longitudinal cohort studies (such as the Nurses' Health Studies and the HUNT study), vital statistics registries (including linked Norwegian birth and mortality data), and randomized trials. She is an associate professor at Harvard Medical School and the Harvard Chan School of Public Health.

Nicholas J. Timpson

Nicholas J. Timpson is the principal investigator (PI) of ALSPAC/Children of the 90s, being responsible for the day-to-day running of the study and chairing the ALSPAC Executive. This role as PI requires him to oversee research infrastructure, lab infrastructure, cohort maintenance, record linkage, new data collection (clinic and remote), and the maintenance of data/data access. Alongside this, his research focuses on the application of genetic epidemiology to revealing potentially causal relationships between modifiable risk factors and complex health outcomes. He is a Wellcome Trust Investigator focusing on understanding body mass index (BMI) as a risk factor. He leads work applying these methods to questions on the aetiology of cancer (CRUK and H2020 supported), cardiovascular health (NIHR supported) and the role of the environment in cardiometabolic health (H2020 supported). Most recently he has become substantially involved in the strategic deployment of population-based resources in a coordinated manner to address population health. This has been most clearly demonstrated in the case of the current pandemic, where through collaboration with the UK Coronavirus Immunology Consortium, Wellcome Longitudinal Population Studies COVID-19 Questionnaire Research Group, National Core Studies (Longitudinal Health and Wealth) and NIHR/UKRI non-hospitalised long COVID group "CONVALESCENCE", he is part of the population-based study contribution to understanding COVID-19 and the pandemic. Nic also co-leads a Wellcome PhD programme in Bristol.

The 27th Norwegian Conference on Epidemiology

Bergen, 3–4 November 2021

Abstracts

A1

Can we trust the hazard ratio? – Causal consequences of observed proportional hazards

Morten Valberg[1], Mari Brathovde[1,2] and Odd O Aalen[2]

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Introduction: The hazard ratio (HR) is by far the most frequently used effect measure in applied time-to-event analyses. However, the causal interpretation of the HR is not necessarily simple, even in the context of randomized controlled trials (RCTs).

Aims: To demonstrate that the HR has a built-in selection bias, even when all assumptions of Cox' proportional hazard model are satisfied. Furthermore, to investigate the direction of the bias in both a single time-to-event setting and in a competing risks setting.

Methods: We use a frailty modelling approach to investigate the implications of observed proportional hazards on the causal interpretability of the HR.

Results: We show that an observed, time-constant HR will be an attenuated version of the treatment/exposure effect in individuals, even in a simple two-armed RCT. In the competing risk setting, the causal interpretation of the observed HR is even more challenging. If the same underlying factors affect the different competing risks, then we show that the observed cause-specific HR can be both overestimating and underestimating the treatment/exposure effect. Thus, treatments that are harmful or beneficial, respectively, may appear as having the opposite effect if the observed cause-specific HRs are used as the measures of effect.

Conclusions: Making causal conclusions based on HRs are challenging, even in RCTs and even when all assumptions of the Cox model are satisfied.

A2

Separable effects of baseline exposure in multi-state models

Niklas Nyboe Maltzahn[1,2], Jon Michael Gran[2] and Mats Julius Stensrud[3]

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Introduction: In the context of competing events, identification of causal effects of exposure on a particular event is a long-standing problem. By considering exposure as consisting of components targeting different events, the framework of separable effects has provided a solution to this identification problem. This solution has important practical consequences for epidemiological research with application to a wide range of problems from estrogen therapy in prostate cancer research to specific policy goals of public policy interventions such as the IA-agreement.

Aims: To show how the discrete time theory of separable effects can be extended to continuous time m ulti-state models.

Methods: By choosing a specific formulation of Multistate models we are able to make the link between discrete time separable effects model and the continuous time equivalent clear and precise.

Results: The extension is subsequently used to estimate separable effects of baseline exposure in continuous time multi-state models. To achieve this extension, we provide a counter factual causal framework focusing on counterfactual probability measures rather than counter-factual random variables.

Conclusions: The extension of the separable effects framework to Multistate models show the utility and potential of the framework as originally stated. The extension also explores a possible way of connecting interventions in discrete time to interventions in continuous time.

A3

Diving into registry data: enhancing epidemiology with bioinformatics and experiments

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Introduction: Usually, the process of designing new drug takes even up to 10 years, costs millions of dollars (https://en.wikipedia.org/wiki/Cost_of_drug_development), and has a fail rate of 80-90% (see references in https://en.wikipedia.org/wiki/Drug_development#Clinical_phase). However, more than thousand drugs are already on the market being used by many Norwegians. Each prescribed medication, each clinical visit, and much more information is being registered in the Norwegian national registries. There lies a huge potential in these data in the search of drug repurposing.

Aims: To find new treatment for neurological diseases using drugs already available on the market (drug repurposing).

Methods: We develop an algorithm that harnesses data from Norwegian national registries (Norwegian Patient Registry, NPR, Norwegian Prescription Database, NorPD, and Statistics Norway, SSB) to search for new treatments without the need of a costly and timely drug design process. Our project DRONE (Drug Repurposing for Neurological diseases, https://www.uib.no/en/epistat/139849/drone-drug-repurposing-neurological-diseases) combines advanced statistical methods of epidemiology with bioinformatics, machine learning, and sophisticated in vitro and in vivo experiments to search for drugs that are associated with a risk change of developing neurological diseases, such as Parkinson's disease (PD), multiple sclerosis, or amyotrophic lateral sclerosis.

Results: We have tested various statistical methods to estimate the change of risk of having PD associated with each of ca.800 drugs that were used by PD patients before they could be defined as having the disease. We found that approximately 30 drugs not prescribed for PD gave significantly reduced disease risk and about 100 drugs significantly increased the risk for PD. These results will provide a starting point for further analyses in the lab and bioinformatics post-processing.

Conclusions: When properly established, our method can aid finding new treatment for these chronic diseases, but also pinpoint the molecular processes that underlie disease genesis and/or progression. Moreover, the idea behind our project can be adapted and applied to other diseases.

A4

Causal inference in survival analysis using longitudinal observational data: Sequential trials and marginal structural models

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Introduction: Longitudinal observational patient data can be used to investigate the causal effects of time-varying treatments on time-to-event outcomes. Several methods have been developed for controlling for the time-dependent confounding that typically occurs. The most commonly used is inverse probability weighted estimation of marginal structural models (MSM-IPTW). An alternative, the sequential trials approach, is increasingly popular, in particular in combination with the target trial emulation framework. This approach involves creating a sequence of 'trials' from new time origins, restricting to individuals as yet untreated and meeting other eligibility criteria, and comparing treatment initiators and non-initiators. Individuals are censored when they deviate from their treatment status at the start of each 'trial' (initiator/noninitiator) and this is addressed using inverse probability of censoring weights. The analysis is based on data combined across trials.

Aims/methods: We show that the sequential trials approach can estimate the parameter of a particular MSM, and compare it to a MSM-IPTW with respect to the estimands being identified, the assumptions needed and how data are used differently. We show how both approaches can estimate the same marginal risk differences. The two approaches are compared using a simulation study and in an application to data from the UK Cystic Fibrosis Registry to estimate the effect of dornase alfa on survival.

Results and conclusions: The sequential trials approach, which tends to involve less extreme weights than MSM-IPTW, results in greater efficiency for estimating the marginal risk difference at most follow-up times, but this can, in certain scenarios, be reversed at late time points. The sequential trials approach can be an intuitive alternative for estimating the effect of time-varying exposures, explicitly answering to the target trial framework for causal inference.

B1

Birthweight, consecutive pregnancies, and long-term maternal mortality: at term and beyond

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Introduction: Low offspring birthweight is found to be associated with parental cardiovascular disease (CVD) mortality. Knowledge of the association between large offspring and maternal mortality, however, shows inconsistency. Most of these conclusions are based on first-born infants while not considering women's consecutive births.

Aims: To assess long-term CVD mortality in women with term deliveries by trajectories of offspring birthweight by gestational age.

Methods: Population-based cohort study, Norway, 1967-2020. Women with first and second (438,818) singleton term births in the Medical Birth Registry of Norway between 1967-2013, were followed up till 2020 by linkage to the Norwegian Cause of Death Registry. Birthweight (grams) adjusted for each gestational week was categorized into quartiles (Q) for women's first and second pregnancy. Exposure trajectories were made by combining Q1, Q2/Q3 and Q4 from first and second pregnancy, keeping women with both first and second offspring in Q2/Q3 quartile as the reference group. Risk of CVD (40-69 years) mortality was estimated by cox regression model and expressed as hazard ratios (HR) with 95% confidence interval (CI), adjusting for women's age at first birth and year of delivery.

Results: The risk of CVD mortality was highest in women with two consecutive births in Q1 (HR 1.7, 95% CI 1.5-2.0), compared to the reference population. Mortality was lower for women with first birth in Q2/Q3 and second birth in Q4 (HR 0.7, 95% CI 0.6-0.9) and for women with two consecutive births in Q4 (HR 0.8, 95% CI 0.7-0.9). Having an offspring in Q1 carried a higher risk of mortality if it happened in women's last pregnancy than in the first.

Conclusion: Women with large offspring have lower risk of CVD mortality while risk is higher for women with consecutive low birthweight infants. Maternal mortality risk is modified by birthweight of the successive offspring.

B2

How is birth weight affected in the next singleton birth following a first singleton or twin birth?

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Introduction: Birth weight of offspring have been recognized as a marker of maternal short and long-term health. Previous studies suggest that the fetus is larger in the subsequent singleton birth compared to the first singleton birth. However, the parity effect of plurality on birthweight in the second singleton birth has not been well described.

Aims: To determine the parity effect of plurality on birthweight in subsequent singleton birth after a first singleton or twin birth.

Methods: This was a population-based cohort study with data from the Medical Birth Registry of Norway (1967-2020). The study population included 936 448 first singleton birth and 5 767 first twin birth followed by a subsequent singleton birth. Birth weight (in grams) for second singleton birth following a first singleton or twin birth were evaluated by analysis of variance using STATA. Mean birthweight for twins were based on the sum of the twin pairs.

Results: The mean birthweight in a second singleton birth was higher after a twin birth (3603g; SD:607) than after a first singleton birth (3587g; SD:579), p=0.03. When restricted to strict term weeks (39-41) in the first birth, mean birthweight in a second singleton birth was also higher (3899g; SD:524) after a twin birth above the mean birthweight (5763g) than after a first singleton birth (3821g; SD:525) above the mean birthweight (3545g), p=0.0006. These are crude results, and we intend to adjust for maternal age, maternal education and year of delivery.

Conclusion: The size of the twin in the first pregnancy affects the birthweight of the subsequent singleton birth. Women who had given birth to large term twins in the first pregnancy had larger subsequent singleton birth than women with a large first term singleton birth.

B3

Epigenome wide association study of folate levels in pregnancy

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Introduction: Folate is a water-solute vitamin that represent a key source of methyl-donors through the one-carbon metabolism cycle by participating in the conversion of homocysteine to methionine. Folic acid supplements are recommended to women planning pregnancy, and during the first trimester to prevent neural tube defects in the offspring. Maternal folate levels are associated with DNA methylation (DNAm) in offspring cord blood. However, whether maternal serum folate levels are associated with maternal DNAm in white blood cells (WBC) is currently not known.

Aims: To perform an epigenome-wide association study (EWAS) of serum folate levels in maternal blood samples.

Methods: The Epigenetics in pregnancy (EPIPREG) study includes nearly all European and South Asian women participating in the STORK Grorudalen cohort. We quantified DNA methylation in maternal WBC collected in gestational week 28 (±2 SD) by Illumina's Infinium Methylation EPIC BeadChip. Of 480 women, 472 passed the EWAS quality control filters and were considered for analysis. Serum folate was measured by Roche's Electrochemiluminescence (ECLIA) assay, and folate data was available for 463 women, whereof 302 were European and 161 South Asian. A linear mixed model using ethnicity as a random intercept was used to perform the association analysis with the M-values. We adjusted for WBC composition, age and smoking as fixed effects. An FDR<0.05 was accepted as significant.

Results: Two CpG sites were associated with maternal serum folate; cg19888088 in the gene body of *EBF3* gene (Beta= -0.006, p=5.9E-08), and cg10871182 which is unannotated (Beta= -0.019, p=7.8E-08).

Conclusions: We found two CpG sites associated with maternal folate in pregnancy. One of the sites is in *EBF3* gene, which plays a role in neural development and migration. The two sites have not been previously reported in EWAS of maternal folate in offspring cord blood. However, in line with our results, other CpG sites in *EBF3* gene have shown a negative relationship with maternal serum folate and DNAm in cord blood. Hence, maternal serum folate is associated with DNAm in *EBF3* gene in both the mothers and the offspring.

B4

Preconception leisure-time physical activity and family history of cardiovascular disease as they relate to preterm delivery

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Introduction: Preterm birth is associated with health consequences such as cardiovascular disease sequelae for mother and child. Several risk factors for preterm birth have been explored and established. However, studies are lacking investigating possible associations between family history of cardiovascular disease and risk factors, such as physical activity, as they relate prospectively to risk of delivering preterm.

Aims: To investigate whether prepregnancy past-year weekly leisure-time physical activity or a family history of stroke or of myocardical infarction prior to age 60 years in first degree relatives associated, with subsequent preterm delivery.

Methods: Health survey baseline data from Cohort of Norway (CONOR, 1994-2003) were linked to the Medical Birth Registry of Norway for identification of all subsequent births (1994 – 2012). Log-binomial regression models provided relative risks (RR) and 95% confidence intervals (CI) for preterm delivery (<37 weeks gestation). Multinomial logistic regression provided odds ratios (OR) for early preterm (<34 weeks) and late preterm (>34 to <37 weeks gestation) relative to term deliveries.

Results: The mean (SD) length of time from baseline CONOR health survey participation to subsequent delivery was 5.6 (3.5) years. A family history of myocardial infarction associated with increased risk of early preterm deliveries (OR 1.66; CI 1.11-2.49), whereas a family history of stroke associated with increased risk for late preterm deliveries (OR 1.62; CI 1.07-2.47). Adjustment for known medical risk factors for preterm delivery did not alter the results. Sensitivity analyses, removing high-risk pregnancies gave similar results. Light physical activity of three or more hours per week relative to less activity was not associated with early, late, or total preterm deliveries. However, vigorous physical activity of three or more hours relative to less than one hour per week associated with increased risk of early preterm delivery, but not late or total preterm deliveries.

Conclusions: A family history of cardiovascular disease may help identify women at risk for preterm delivery. Additional research is needed regarding the potential risks of vigorous leisure-time physical activity immediately prior to and during early pregnancy.

C1

Norwegian County Public Health Surveys – Cohort Update

Thomas Nilsen, Marit Knapstad, Leif Edvard Aarø, Jens Chr. Skogen, Marianne Abel Hope, Rune Johansen, Øystein Vedaa, Ragnhild Bang Nes and Ole Trygve Stigen

Norwegian Institute of Public Health (NIPH)

Introduction: Norwegian counties are mandated by law to monitor public health status in their respective counties. Starting with the first pilot survey in 2015, the Norwegian County Public Health Survey (NCPHS) has rapidly expanded to become one of Norway largest surveys. NCPHS is aimed at providing public health relevant measures not covered by other registries and useful at policy level. NCPHS also has the flexibility to add questions and modules of special interest for the counties or of national interest, e.g. topics concerning the Covid-19 pandemic.

Aims: Describe NCPHS as of today, give an overview of research opportunities, some results and present projects.

Methods: NCPHS invitations are sent by e-mail and SMS using the ID-porten log on solution. Participants consent to registry linkages and follow up studies. Stratified sampling is used to provide reliable results on municipal level. On average 25 % of the adult population is invited to NCPHS.

Results: 10 Counties have so far conducted NCPS (old county structure). 185.000 respondents, aged 18+, are in the database. Autumn 2021, Vestfold/Telemark and Viken will be added, with an expected new 140 000 respondents. 26 000 have participated in the NCHPS Covid-19 surveys, a follow up of respondents from Nordland and Agder Counties, and new samples from Oslo and Vestland. In 2019 NCPHS included a Quality of Life (QoL) instrument. There is increased interest in QoL measures, and new local and governmental initiatives are exploring how to implement QoL measures as policy tools. A major QoL report (published 2020) was largely based on NCPHS data. NCPHS will play a pivotal role in QoL measurements on county and municipal level. NCPHS has provided data for numerous projects, ranging from housing needs for the elderly to adverse childhood experiences and health related outcomes. County specific modules have provided useful data, e.g. a report on National Ethnic Minorities in Troms and Finnmark.

Conclusions: NCPHS is rapidly expanding, in both content and number of respondents. NCPHS data are accessible for research, also with the possibility registry linkages and conducting new data collections on sub-populations.

C2

Quality of life, psychological distress, sleeping problems and global subjective health after injuries. A study among adults in three Norwegian counties

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Introduction: Studies examining impacts of injuries on outcomes like quality of life and psychological distress are important to understand a broader range of consequences of injuries for the health of populations.

Aims: The aims of this study were to examine associations between being injured (self-report questions) and quality of life, psychological distress, sleeping problems, loneliness, and global subjective health.

Methods: Data were collected among adult populations (18+ years) in three Norwegian counties in 2019-2020 (response rate 45.3%, n = 74,030). Data were analysed with General Linear Modelling in SPSS Complex.

Results: Reporting to have been injured once during the last 12 months was associated with slightly elevated levels of psychological distress, sleeping problems, and loneliness, and lower mean scores on quality-of-life indicators and global subjective health. Reporting being injured twice or more showed more pronounced contrasts to the reference group on the same outcomes, with Cohen's *d*-values (absolute numbers) ranging from 0.17 to 0.54. For having been victim to violence *d*-values ranged from 0.30 to 1.01. Moderate functional impairment due to injuries was associated with less favourable scores on all outcomes (*d* ranging from 0.15 to 0.71). For strong functional impairment *d*-values ranged from 0.35 to 1.17 (all values reported as absolute numbers).

Conclusions: Elevated levels of distress and reduced levels of quality-of-life outcomes are particularly associated with multiple injuries (two or more), being victim to violence, and functional impairment due to injuries. Although injuries are reported retrospectively and cover 12 months or more, and questions related to outcomes are measured with reference to study participants' situation at present (or last week), the direction of causal processes remains uncertain. Previous studies with other research designs (retrospective reporting to establish pre-injury baseline values or comparison with normative population data) have, however, provided support for the hypothesis that being injured has serious impact on psychological distress and health-related quality of life. Strengths of the present study includes a broad selection of outcome variables measured with well tested instruments, large community-based samples, and more detailed exposures such as being injured twice or more, and functional impairment due to injuries.

C3

Psychological distress before and nine months into the COVID-19 pandemic: a longitudinal study from The Norwegian Counties Public Health Surveys

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Introduction: Longitudinal population-based samples that includes pre-pandemic baseline data are called for to examine the mental health impact of the COVID-19 pandemic.

Aims: Using a longitudinal design, we examined a) whether self-reported psychological distress changed from before to three and nine months into the pandemic among Norwegian adults (18+ years), and b) whether changes were moderated by baseline socio-demographic factors (gender, age, educational attainment, economic difficulties, relationship status and work status).

Methods: A random sample (n=20,196) of participants in the ordinary rounds of The Norwegian Counties Public Health Survey in Nordland and in Agder counties (t1) were invited to additional surveys in June 2020 (t2, response rate 59 %) and November 2020 (t3, response rate 44 %). Psychological distress was measured by The Hopkins Symptom Checklist-5 (HSCL-5). We examined change and evidence of effect moderation in mixed-effects maximum likelihood regression models.

Results: Overall temporal trends in psychological distress were found, with a decline in mean distress score from t1-t2 (adjusted z-score -0.16) and oppositely an increase from t1-t3 (adjusted z-score 0.08). We found evidence of effect moderation for all variables examined ($p<.001$). While both men and women showed a similar decline in psychological distress from t1 to t2, only women had deteriorated beyond the t1 level at t3. Moreover, the t1-t3 increase was relatively larger in the youngest (18-39) and oldest (70+) age groups, among those with higher education, those *not* having difficulties in making ends meet, those in a relationship and those reporting to be a student at baseline than their comparison groups.

Conclusion: Our data suggests some variation in psychological distress over the course of the pandemic in the general adult population, but also that the degree of change differed across sociodemographic groups. The variation in temporal trends by socio-demography did not all follow “expected” patterns, with for instance stronger increase in psychological distress among the higher than the lower educated. Pre-pandemic inequalities in mental health did, however, clearly remain.

C4

The National Health Survey from the Norwegian Institute of Public Health – Establishing a new data source for surveillance and research

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Introduction: Currently, there is a lack of nationally representative data on many health and lifestyle factors not covered in the national registries, as for example prevalence of sleep problems, Musculo-skeletal pain and trends in dietary habits. The National Health Survey was piloted by the Norwegian Institute of Public Health (NIPH) in 2020, and will be established as a yearly web-based survey in adults (age 18+) possibly including collection of biologic material from a nationally representative subsample.

Aims: To present the National Health Survey and results from the 2020 pilot.

Methods: Every year, a random sample of 2600 people from each of Norway's 11 counties will be drawn from the National Population Register and invited via e-mail and sms to participate in a web-survey on health and lifestyle habits. The questionnaire covers a broad range of topics on somatic and mental health, and lifestyle factors, including sleep, diet, physical activity, alcohol, and tobacco. Additionally, questions can be added covering contemporary issues. A random sample of participants will be invited to donate biological samples via a "do it yourself-kit" aiming at 500 samples in year 1 and subsequently 100 samples/year. Data analyses are performed on weighted data compensating for design and self-selection (by sex, age, and in the future, education). Survey data can be linked with registry data.

Results: In the pilot survey (2020), electronic contact information was available for 88% of the original sample, mainly missing for elderly people (age >75). The participation rate was 38.1% of the invited (n=8852), and highest in middle-aged women (57% at age 56-65). Participation was lowest (<20%) in younger men (<25 years) and older women (>85 years). Self-reported education may indicate that participants with higher education were overrepresented.

Conclusions: This new survey facilitates close monitoring of trends and associations in health and health-related behaviours, both at national and county level, and establishes a framework for collection of nationally representative biological material. Overall, the participation rate in the pilot study was acceptable, but results from the study will at varying degree be affected by selection bias.

D1

Pigmentary characteristics and melanoma survival in Norwegian women

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Introduction: The increased risk of cutaneous melanoma in individuals with lighter pigmentation is well documented. However, less is known about the role that pigmentary characteristics play in prognosis after melanoma diagnosis. Current research is inconclusive with regards to the potential direction of association between pigmentary characteristics and well-known prognostic factors such as tumor thickness at diagnosis. Additionally, where a protective effect has been found, it is unclear if improved survival stems from diagnosis at an earlier stage due to increased melanoma awareness in these individuals or biologically from genetic variants associated with these characteristics.

Aim: To investigate the association between patient pigmentary characteristics and overall and melanoma-specific survival in women.

Methods: We used the Norwegian Women and Cancer cohort study with complete follow-up through 2018 from the Cancer Registry of Norway. We performed Cox regression to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between pigmentary characteristics (hair color, eye color, skin color, freckling, and a pigmentary score) and overall and melanoma specific survival, adjusting for age and Breslow thickness at diagnosis. Additionally, the association between skin reaction to acute (degree of redness after short term sun exposure) and long-term sun exposure (skin color after repeated sun exposure) and survival were assessed on a subsample of the cohort.

Results: We included 1603 women (born 1927-1964) who were diagnosed with an incident primary invasive melanoma between 1991-2018 (233 deaths, 134 melanoma deaths, mean follow-up=7.9 years). Preliminary results show that after adjusting for age at diagnosis and tumor thickness, neither lighter pigmentary characteristics, nor a lighter overall pigmentary score were associated with overall or melanoma-specific survival. Adjusted HRs (95% CIs) for melanoma death were 0.91 (0.38-2.16) and 1.04 (0.43-2.56) for dark vs medium and dark vs fair pigmentary score, respectively (P_{trend}=0.73).

Conclusion: Our results do not suggest an association between pigmentary characteristics and survival after melanoma diagnosis. Thus, education about sun protection habits and skin self-examination should be emphasized for both those with lighter and darker pigmentary characteristics.

D2

Cohort profile: The Clinical and Multi-omic (CAMO) cohort, part of the Norwegian Women and Cancer (NOWAC) study

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Introduction: Breast cancer is the most common cancer worldwide and the leading cause of cancer related deaths among women. The high incidence and mortality of breast cancer calls for improved prevention, diagnostics and treatment, including identification of new prognostic and predictive biomarkers for use in precision medicine.

Aim: To compile a cohort amenable to integrative study designs for precision medicine.

Methods: We included a subset of participants from the prospective, population-based Norwegian Women and Cancer (NOWAC) study, who were diagnosed with breast cancer in North Norway before 2013 according to the Cancer Registry of Norway. For these patients, who constitute the Clinical and Multi-omic (CAMO) cohort, prospectively collected questionnaire data on lifestyle and reproductive factors as well as blood samples were extracted from the NOWAC study. Furthermore, clinical and histopathological data were manually curated from medical records and tumor biopsies.

Results: The lifestyle and reproductive characteristics of the study participants in the CAMO cohort (n=388) were largely similar to those of the breast cancer patients in NOWAC (n=10356). The majority of the cancers in the CAMO cohort were tumor grade 2 and of the luminal A subtype. Approx. 80% were estrogen receptor positive, 13% were HER2 positive, and 12% were triple negative. Lymph node metastases was present in 31% at diagnosis. The epidemiological dataset in the CAMO cohort is complemented by mRNA, miRNA and metabolomics analyses in plasma, as well as miRNA profiling in the tumor tissue. Additionally, histological analyses at the level of proteins and miRNAs in tumor tissue are currently ongoing.

Conclusion: The CAMO cohort provides data suitable for epidemiological, clinical, molecular and multi-omics investigations, thereby enabling a systems epidemiology approach to translational breast cancer research and precision medicine.

D3

The Norwegian Women and Cancer study (NOWAC)

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Introduction: The Norwegian Women and Cancer study (NOWAC, or Kvinner og kreft in Norwegian) is a national prospective cohort study with 172 000 participants born from 1927 to 1965. Initially, the research project focused on hormonal factors and risk of breast cancer. Over the years, the scope has broadened, and today we are studying a variety of exposures and outcomes, though still most of the research is cancer-related. Given the broadened scope and recent changes in legislation, we are currently in the process of turning the NOWAC study into a health registry.

Methods: The first data were collected in 1991, and most of the data collection has been done by mail. Participants have filled in a questionnaire on e.g. reproductive factors, anthropometry, smoking habits, physical activity, socio-economic factors, childhood conditions, and dietary intake, at one to four occasions at least six years apart. During the years 2003-2006, the NOWAC study was expanded to collect plasma, buffy coat, and blood samples for gene expression profiling using the PAXgene Blood RNA system. The resulting NOWAC Post-genome cohort comprises ~50 000 of the NOWAC participants. In collaboration with Norwegian hospitals, archived breast cancer tissue was collected along with clinical data from ~400 of the Post-genome cohort participants, resulting in the Clinical and Multi-omic (CAMO) cohort. Annual linkages with the Cancer Registry of Norway and the Norwegian Cause of Death Registry have ensured good quality outcome information. Data from NOWAC are included in many international collaborations, most notably the European Prospective Investigation into Cancer and Nutrition.

Conclusion: 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. This is now a mature cohort with ample opportunities for studying various diseases including also multi-morbidity. We are currently discussing how to ensure sustained use of the data in the future. As a part of this we have started to develop a multi-generation study.

D4

Childhood cancer risk among individuals with major birth defects: A Nordic collaborative study

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Introduction: Worldwide, about 400,000 new childhood cancer cases are diagnosed each year. Still, the underlying causes of childhood cancer are largely unknown. Population-based studies have previously found that children with birth defects have an excess childhood cancer risk, suggesting that birth defects and childhood cancer share a common etiology. Increased cancer risk is observed both for chromosomal and non-chromosomal birth defects. Few have investigated potential differences in this association by sex, but recent research suggests that birth defects is a strong mediator of the association between sex and childhood cancer.

Aims: To examine the risk of cancer among children with birth defects, overall and by sex.

Methods: A population-based nested case-control study was performed in four Nordic countries, including children born between 1967 and 2014. Cases were defined as children with a cancer diagnosis in the cancer registries before the age of 20. Controls were frequency sampled and matched on country and birth year (case-control ratio 1:10). The primary exposure was major birth defects diagnosed in the medical birth-, patient- or malformation registries. We used logistic regression models to estimate the odds ratio of cancer. We evaluated birth defects as a mediator of the association between sex and childhood cancer by using a counterfactual framework.

Results: More than 20,000 children were diagnosed with cancer during the study period. The three most common cancers were leukemia, central nervous system tumors, and lymphomas. Approximately 5% of the cases and 2% of the controls were born with major birth defects, the most common being congenital heart defects, limb defects, and genital defects. The OR of cancer was higher for chromosomal defects (10-fold) than for non-chromosomal (2-fold), and higher among females (3-fold) than males (2-fold). Male sex was an independent risk factor for childhood cancer and very little of the association between sex and childhood cancer was mediated through birth defects (<5%).

Conclusion: We found increased cancer risk among individuals with birth defects and sex differences for some birth defect-cancer associations. Birth defects did not act as a strong mediator for the effect of sex on childhood cancer risk.

E1

Understanding long-term symptoms after covid-19: Results from MoBa

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Introduction: Physical, psychological and cognitive symptoms have been reported as post-acute sequelae for covid-19 patients, but are also common in the general uninfected population. It is unclear whether long-covid can be described as one syndrome, or a mix of symptoms caused by different mechanisms.

Aims: To calculate the excess risk and identify patterns of 22 symptoms up to 12 months after covid-19 using a large population-based cohort study.

Methods: More than 70,000 participants were followed in an ongoing cohort study, the Norwegian Mother, Father and Child Cohort Study (MoBa) during the covid-19 pandemic. Infected and non-infected cohort participants registered presence of 22 different symptoms in March 2021. A covid-19 diagnosis was obtained by linkage to The Norwegian Surveillance System for Communicable Diseases (MSIS). We estimated associations between covid -19 status and symptoms reported in March 2021 using log-binomial regression models. Associations were reported as excess risk (risk differences, RD) and relative risks (RR). Symptom patterns among covid-19 cases were derived from exploratory factor analysis using the tetrachoric correlation matrix.

Results: One year after the initial infection, 12 of 22 symptoms were associated with SARS-CoV-2 infection, based on relative risks between infected and uninfected subjects. For instance, 17.4% of SARS-CoV-2 infected cohort participants reported fatigue that persisted 12 months after infection, compared to new occurrence of fatigue that had lasted less than 12 months in 3.8% of non-infected subjects (excess risk 13.6%). The relative risk for fatigue was 4.6 (95 % CI 3.2 to 6.3). Three main underlying factors explained 57% of the variance in the 12 symptoms. Poor memory, fatigue, brain fog and heart palpitations had high loadings on the first factor, shortness-of-breath, cough and reduced lung function had high loadings on the second factor, while headache and dizziness loaded high on the third factor. Lack of taste and smell showed low to moderate correlation to other symptoms. Anxiety, depression and mood swings were not strongly related to a covid-19 diagnosis.

Conclusions: These results suggest that there are clusters of symptoms after covid-19 due to different mechanisms and question whether it is meaningful to describe long-covid as one syndrome.

E2

COVID-19 vaccination in Norway – using nationwide individual level data to identify distribution and overlap of prioritized groups

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Introduction: The Norwegian COVID-19 vaccine program prioritized certain high-risk groups and professions. Old age and underlying chronic diseases are known risk factors for severe COVID-19 (hospitalizations and deaths), and vaccination of healthcare workers is crucial to ensure care capacity and reduce SARS-CoV-2 transmission. Estimation of prevalence and overlap of prioritized groups at the population level is critical for planning and vaccine distribution, although challenging.

Aims: To provide proportions and quantify the overlap of medical risk conditions and healthcare worker status in the total adult population in Norway.

Methods: Beredt C-19, the emergency preparedness register for COVID-19, includes data on all Norwegian residents. We included data on all residents ≥18 years (~4.2 million individuals) and used ICD-10 and ICPC-2 diagnostic codes from consultations in primary and specialist care from January 2017 to December 2020 to identify medical risk conditions. The information covered all hospitalizetions, outpatient visits and consultations at general practitioners and emergency rooms for all patients in the Norwegian healthcare system. Healthcare workers were identified through the International Standard Classification of Occupations. Individual-level information was linked using the unique personal identification number. We calculated the proportion (%) of the adult population with each condition and the percentage with overlapping conditions.

Results: In December 2020, 4,259,495 residents were ≥18 years, 50.2% men and 946,931 (22.2%) ≥65 years. 20.6% of all adults, and 47.3% of those ≥65y, had at least one risk condition. The most frequent medical risk conditions were cardiovascular disease (8.8%), chronic pulmonary disease (6.2%) and diabetes (5.5%). Among all residents aged 18-64y, 352,138 (8,3%) were healthcare workers (19,623 physicians, 83,966 nurses and 201,505 auxiliary nurses), of whom 11.5% had at least one risk group diagnosis.

Conclusion: In Norway, 20.6% of all adults and 47.3% of those ≥ 65y, have at least one medical risk condition for severe COVID-19. 8.3% of residents aged 18-64y are healthcare workers, among whom 11.5% were in at least one medical risk group. Access to and use of individual-level data to identify people in risk groups, and overlap between groups, has been important for planning, distribution, and surveillance of the COVID-19 vaccine program.

E3

Short-term safety of SARS-CoV-2 vaccination in the elderly population in Norway

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Introduction: In January 2021, the Norwegian Medicines Agency was notified about 23 deaths after SARS-CoV-2 vaccination of frail elderly people in Norway. The information received international attention, raising the question of vaccine safety in the elderly population.

Aims: To assess short-term safety of SARS-CoV-2 vaccination with respect to all-cause mortality in the elderly population in Norway and to explore whether safety varies across different types of health services (none, home-based, short-term stay at nursing home, and long-term stay at nursing home).

Methods: We used individual-level data from the Emergency Preparedness Register for COVID-19 (Beredt C19), which is based on Norwegian health and administrative registries. The original data set comprised 967,786 individuals aged 65 years and older by the start of the Norwegian vaccination campaign on December 27, 2020. In order to explore the effect of vaccination, we used 1:1 matching of vaccinated individuals (vaccinees) and unvaccinated individuals (controls). The final study sample included 168,140 matched pairs. The individuals in each pair were followed for up to three weeks from the day of first-dose vaccination of the vaccinee until death, emigration, first-dose vaccination of the control, second-dose vaccination (vaccinee only), or end of study on March 1, 2021. The time scale was days since first-dose vaccination of the vaccinee. Kaplan-Meier survival functions were estimated for the vaccinated and unvaccinated groups. We used Cox proportional-hazards regression to estimate crude hazard ratios (HRs) of death between vaccinated and unvaccinated individuals, with associated 95% confidence intervals (CIs), overall and by health-service group.

Results: By March 1, 2021, there were 6,773 deaths, of which 10.5% occurred within three weeks after vaccination. We observed a small absolute reduction in mortality risk during the first three weeks after vaccination, with an overall HR of 0.29 (95% CI: 0.25–0.34). Similar results were observed for all four health-service groups.

Conclusions: We found no evidence of increased short-term mortality among vaccinated individuals. The reduced mortality risk observed immediately after first-dose vaccination is most likely a healthy-vaccinee effect resulting in residual confounding, as immunity against the coronavirus is not expected to develop until the end of the three-week period after vaccination.

E4

Sex differences in incidence of bloodstream infections and the mediating role of known risk factors. Results from the population-based HUNT study in Norway

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Introduction: Previous studies indicate sex disparities in incidence and severity of bloodstream infections (BSI). It remains unclear whether the observed sex differences arise from differences in biology, medical conditions, health behaviours, lifestyle, and exposure to different pathogens.

Aims: To examine the effect of *sex* on risk of BSI and to assess to what extent known risk factors for BSI mediate this association in the general population.

Methods: In the prospective, population based HUNT2 Survey (1995-97) including 65,237 participants, whereof 46.8% were men, we investigated sex differences in risk of first-time BSI. Using an inverse odds weighting procedure we estimated the excess risk of BSI mediated by known risk factors as potential mediators between sex and BSI; health behaviours (smoking, alcohol consumption), education attainment, cardiovascular risk factors (systolic blood pressure, non-HDL cholesterol, body mass index) and comorbidities. In secondary analyses we assessed BSI mortality (death within first 30 days after a BSI), and BSI caused by the most frequent bacteria.

Results: We documented a first-time BSI for 1,840 (2.9%) participants (51.3% men) during a median follow-up of 14.8 years. Of these, 396 (0.6%) died (56.6% men). Men had 41% higher risk of any first-time BSI (95% confidence interval (CI), 28-54%) than women. An estimated 34% of the excess risk of BSI in men was mediated by known BSI risk factors. The hazard ratio (HR) of BSI mortality was 1.87 (95% CI, 1.53-2.28) higher in men compared to women. The HR with 95% CI for BSI due to *S. aureus* was 2.09 (1.28-2.54), *S. pneumoniae* 1.36 (1.05-1.76), and *E. coli* 0.97 (0.84-1.13) in men vs women.

Conclusions: This large study show that men have higher risk of BSI than women. One-third of this effect was mediated by known risk factors for BSI. BSI represents an important global burden of disease and our findings raise important questions regarding sex-specific approaches to prevent BSI in both men and women.

A5

Body mass index and incidence of lung cancer in The HUNT Study: Using observational and Mendelian randomization approaches

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Introduction: Observational studies have shown an inverse association between body mass index (BMI) and lung cancer risk. Mendelian randomization (MR) analysis using genetic variants as instruments for BMI may clarify the nature of the association.

Aims: We studied the causal association between BMI and lung cancer incidence using observational and MR approaches.

Methods: We followed up 62453 cancer-free Norwegian adults from 1995–97 (HUNT2) until 2017. BMI in HUNT2 was classified as <25.0, 25.0–29.9 and ≥30.0 kg/m^2. Seventy-five genetic variants were included as instruments for BMI (among which 14 also associated with smoking behavior). Incident lung cancer cases were ascertained from the Cancer Registry of Norway. Cox regression models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Multivariable MR was used to examine the effect of BMI after controlling for smoking.

Results: During a median follow-up of 21.1 years, 1009 participants developed lung cancer (327 adenocarcinoma). The HRs and 95% CIs were 0.73 (0.58–0.92) for BMI 25.0–29.9 kg/m^2 and 0.53 (0.37–0.76) for BMI ≥ 30 kg/m^2 compared with BMI <25.0 kg/m^2 (P for trend <0.001). However, multivariable MR suggested a positive association between genetically determined 1 kg/m^2 increase in BMI and the incidence of adenocarcinoma (HR 1.28, 95% CI 1.03–1.58). No associations were found with other lung cancer subtypes.

Conclusions: Our study suggests that the inverse association between BMI and adenocarcinoma in observational analysis may not be causal. More MR studies are needed to confirm our finding of a positive association.

A6

Problems with Power: Unanticipated computational challenges in a large nutritional epidemiology cohort

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Introduction: The Adventist Health Study-2 is a prospective nutritional epidemiology cohort with over 95,000 subjects. The study's primary measurement instrument is a 52-page questionnaire which includes a detailed food frequency questionnaire (FFQ). One key challenge of using FFQ data analytically is the error introduced by recall biases when subjects over- or under-report intake of foods.

To correct for this measurement error, a calibration sub-cohort of 1000 subjects additionally provided six 24-hour dietary recalls. This was then used to perform regression calibration. Unfortunately, the residuals from a calibrated regression cannot be used to estimate confidence intervals. Instead, the preferred approach is to use bootstrap resampling to construct the distribution of the calibrated estimates, from which a confidence interval can then be obtained.

Bias-corrected and accelerated (BCa) confidence intervals are preferred over simpler percentile-based methods as they provide accurate intervals when the bootstrap distribution is skewed. However, the standard function for calculating BCa intervals provided by the "boot" R package exhibited intractable computation times. This was due to its regression-based approach to calculating the acceleration parameter needed to obtain the confidence intervals, given combination of the large number of subjects in the dataset and the number of bootstrap rounds used.

Aims: To implement a method of calculating BCa confidence intervals in a reasonable amount of time when the number of subjects and bootstrap rounds is large.

Methods: We implemented a jackknife-based calculation of the acceleration parameter, where the analysis is performed multiple times on the dataset in which each subject is removed in turn. To further decrease the calculation time, a delete-a-group jackknife approach was implemented, which removes groups of subjects from the dataset at each jackknife round, rather than a single subject each time.

Results: The initial jackknife implementation, when parallelized, reduced the computation time from several days to under two hours. The delete-a-group jackknife implementation further reduced the computation time to several minutes.

Conclusions: The increased statistical power that comes from a large cohort can introduce computational difficulties in certain circumstances. Alternate analytic approaches can be effective in avoiding intractable computation times.

A7

Validation study of the self-reported educational level in the Tromsø Study

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Introduction: Self-report education is much used in epidemiological studies. In the Tromsø Study using self-reported data on education has a long tradition, but the validity is yet to be established.

Aims: To assess the validity of self-reported education in the Tromsø Study by comparing self-report data with national register data, Statistics Norway (SSB).

Methods: In the population-based Tromsø Study 2015-2016 (Tromsø7), self-reported educational level; primary-, secondary-, college/university <4 years-, and college/university ≥ 4 years education from 21083 women and men was compared to educational level from SSB. Sensitivity, positive predictive value (PPV) and weighted kappa were used to measure the validity of self-reported information from Tromsø7 in three different age groups (< 52, 53-62 & ≥ 63), using register information on educational level from SSB as gold standard. Multivariable logistic regression models were used to compare social gradients in self-reported cardiometabolic diseases between self-reported educational level from Tromsø7 and SSB.

Results: Sensitivity of self-reported educational level was highest among those with college/university ≥ 4 years (≥ 96% in all age groups), and lowest among those primary educated (≥ 70% in all age groups). PPV was 66.3% among age group < 52 and 49.6% among age group ≥ 63 primary educated. The lowest PPV was observed among those with college/university ≥ 4 years, aged ≥ 63 years (46%) and those aged < 52 years (51,6%). The agreement was high (86-89%) in all age groups, with substantial kappa values (0.63-0.69). We found a comparable social gradient in cardiometabolic diseases when using either self-reported or registry-based educational data. However, the apparent social gradient was less pronounced when the self-reported variable was used.

Conclusions: The results show that self-reported educational level in Tromsø7 is valid, with high percentage of agreement and substantial kappa values in all age groups. The social gradient, however, was less pronounced for the self-reported education variable compared to the registry-based education variable.

A8

Pizza made healthy – an epidemiological cookbook

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Ingredients (Introduction): Large surveys, multi-cohort studies and sophisticated statistical methods lay the ground for ever-increasing quality in epidemiological research. Still, there is a concern that the quality is deteriorating – rightfully so. A common quality deteriorating practice in epidemiological studies is failure to correct for multiple testing.

Palette (Aims): There are multiple methods to correct for multiple testing, but it seems like the most common approach is to not correct at all. With the no-correction approach, the chances of drawing the wrong conclusion increase for every test you do.

Utensils (Method): *Does pizza protect against cancer?* is an Ig Nobel award winning paper by Gallus et al. (*Int J Cancer*, 2003) and serves as example. The pizza-cancer association was investigated for 5 cancer sites, and the results for several hypothesis tests are presented. Gallus' own conclusion is

> "The ORs for all the cancers considered, and the corresponding trends, were significant, with the exclusion of those for larynx and rectum. The favourable influence of pizza on the risk of several digestive tract neoplasms […]"
>
> *Mediterranean diet and cancer risk*, *Eur J Cancer Prevention*, 2004, Gallus et al.

The significance Gallus' is referring to in the quote has not been subject to correction for multiple testing, but it will now.

Buon Apetito! (Results): The p-value is not a tool for disregarding interesting findings: The pizza-cancer association is present for 8314 people in this study. The question is whether the association would be present if the study were repeated with 8314 different hospitalised Italians. Regardless of the actual existence of a pizza-cancer association, we can expect to find at least one association following the statistical analysis scheme of Gallus', which makes an eventual finding uninteresting.

By applying a simple Bonferroni-correction, the new conclusion would be:

> "None of the ORs were significant, but the corresponding trends for oesophagus and colon were significant."

Nutrition value (Conclusions): The favourable influence of any food item on cancer risk will be found eventually if the statistical analyses are not conducted correctly. With proper use, statistical analysis points research in the right direction.

B5

Hip-IMPACT: Explaining the declining hip fracture rate from 1999-2019. A NOREPOS study

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Introduction: After decades with increasing hip fracture incidence, the age-standardised hip fracture rates have declined since 1999. The causes of the decline are not clear, but the introduction of osteoporosis medication in 1996 and changes in established modifiable lifestyle factors such as increasing body mass index and reduced smoking prevalence may explain parts of the decline.

Aims: This study aimed to quantify how much of the decline in hip fracture rates could be explained by temporal changes in established risk factors for hip fracture and osteoporosis medication uptake using an adaptation of the IMPACT coronary heart disease model methods.

Methods: Hip fractures in 1999 and 2019 were obtained from the NOREPOS hip fracture database (NORHip). Prevalences of osteoporosis medication use and risk factors were obtained from the Norwegian Prescription Database, Statistics Norway, and the literature. We calculated the difference between the observed number of hip fractures in 2019 and the expected number in 2019 given unchanged age- and sex specific fracture rates since 1999. Hip fractures prevented in 2019 attributable to changes in prevalence of risk factors were estimated according to sex and 5-year age groups from 50 to 90+.

Results: Hip fracture rates decreased by 28% from 1999 to 2019 with 2,756 fewer hip fractures observed than expected in 2019. Approximately one-tenth of the decrease was attributed to increased use of osteoporosis medication, while more than half of the decrease was attributed to changes in risk factors, including increased BMI, physical activity, hip replacements, reduced smoking and some fall-risk increasing drugs. Increased use of drugs associated with hip fracture risk that partially offset these effects were taken into account.

Conclusions: The Hip-IMPACT model explained ≈ 70% of the decline in hip fracture rate.

B6

Associations between vertebral fracture and mortality. The Tromsø Study 2007-2020

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Introduction: Vertebral fractures are hallmarks of osteoporosis but only one-third of these receive clinical attention. Vertebral fractures have been associated with mortality, but studies including longer follow-up periods and clinically available equipment are warranted.

Aim: Investigate the association between all-cause mortality and vertebral fracture measured by dual-energy X-ray absorptiometry (DXA) in a general population of older adults.

Methods: Data from the sixth Tromsø Study (Tromsø6; 2007-08) were linked to mortality data from the Norwegian Cause of Death Registry. DXA-based lateral vertebral fracture assessment (VFA) was performed in a randomly selected sub-sample from Tromsø6 to evaluate vertebral deformities (mild, moderate, severe). We included 2476 participants (58% women) aged ≥55 years who were followed from VFA at baseline in 2007-08 throughout 2020. We used Cox regression models to estimate hazard ratios (HRs) for all-cause mortality, and adjusted models included age, sex, body mass index, education, smoking, alcohol intake, hypertension, cardiovascular disease and self-reported health status.

Results: Mean follow-up in the cohort was 11.2±2.7 years. In total, 341 vertebral fractures (13.8%) were detected at baseline, and 636 participants (25.7%) died between baseline and follow-up. The adjusted HR for mortality was non-significant for participants with fracture versus those without. Adjusted HRs were however significant in participants with three or more fractures (HR 2.71, 95% CI 1.69-4.34), and in participants with at least one severe fracture (HR 1.74, 95% CI 1.27-2.38). These results were consistent in sub-sample analyses restricted to > two years of follow-up, or by additional adjustment for self-reported physical activity.

Conclusion: We conclude that individuals above 55 years with three or more vertebral fractures, or at least one severe vertebral fracture, have significantly increased risk for all-cause mortality. DXA-based screening could be a potent and feasible tool in detecting vertebral fractures that are usually “clinically silent”. Future research should investigate the causes of death that are most commonly associated with vertebral fractures to support treatment options.

B7

Cold – a risk factor for osteoporotic fractures and fracture related mortality

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Introduction: Norway is a far-stretched country with large variations in climate and length of winter season. It is also a high-incidence country for osteoporotic fractures, in particular hip fractures, which cause high mortality. Although most hip fractures occur indoors, there is a higher incidence of both forearm- and hip fractures during wintertime, compared to summertime in Norway. In the recent years, there has been a downward trend in hip fracture incidence, but it is not known whether changes in ambient temperature have affected this trend.

Methods: All hospitalized hip fractures (ICD-10 code S72.0-S72.2) and hospitalized/outpatient forearm fractures (ICD-10 code S52 with subgroups) from 2008-2018 were retrieved from the Norwegian Patient Register. Incident fractures were quality-assured using a standardized procedure. Average monthly ambient temperatures (degrees Celsius, °C) for 1046 weather stations in the years 2008-2018 were provided by the Norwegian Meteorological Institute. Statistics Norway provided demographic data and month of death. Poisson models (with person-years as offset) were fitted to estimate the association (Incidence Rate Ratios (IRR), 95% Confidence Intervals (CI)) between temperature and incidence of fracture and mortality.

Results: The temperature ranged from -20.2 °C to 22 °C, with a median of – 2 °C in winter and 14.4 °C C in summer. At low temperatures (≤0 °C) compared to >0 ˚C, there was a 53% higher risk of forearm fracture (IRR = 1.53, 95% CI:1.51, 1.55) and 21% higher risk of hip fracture (IRR = 1.21, 95% CI:1.19, 1.22), when adjusting for age, sex, calendar year, urbanization, residential elevation and distance to coastline. The associations with both forearm- and hip fracture were stronger in the younger age groups (<80 years). There was 9% higher risk of <1-year post-hip fracture mortality when winter temperatures were ≤0 ˚C at the time of the fracture (IRR=1.09, 95%CI:1.05, 1.13). From 2008-2018, winter-temperatures increased by 0.2 °C per year. The downward trend in hip fracture incidence did not change when adjusting for temperature.

Conclusion: There was a higher risk of osteoporotic fractures at low temperatures, and a higher post-hip fracture-mortality at low winter temperatures, but the trend in hip fracture incidence did not seem to be affected by temperature.

B8

Stroke survival and the impact of geographic proximity to first-degree relatives: population-based cohort study

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Introduction: Social support may be important for post-stroke survival, in addition to individual risk factors and medical care.

Aims: To determine if geographical proximity between stroke survivors and their first-degree relatives, as a proxy for familial care, is related to survivor mortality.

Methods: All Norwegians born before 1964 were linked to hospitalisation data from the CVDNOR project to identify those who survived a first stroke hospitalisation between 1 January 1994 and 31 December 2009. The 128,277 survivors were linked to residential and family information from Norwegian national registries and censuses, and the distance between them and their nearest first-degree relatives at the year of hospitalisation was calculated. All-cause mortality of the population was recorded for the period from first stroke hospital discharge to 31 December 2014. Cox proportional hazards models estimated the hazard ratios, with 95% confidence intervals of all-cause mortality associated with the distance to the nearest first-degree relative after adjusting for socio-demographic and clinical covariates.

Results: Of the 128,277 survivors, 51,463 (40.1%) lived in the same basic statistical unit, defined as living in the same household or an immediate neighbourhood, as their nearest first-degree relative. Living up to 30 km from the nearest family member was associated with a higher risk of mortality (hazard ratio 1.04, 95% confidence interval 1.02–1.05) than those living in the same basic unit. The association was more pronounced (1.13, 1.07–1.19 for ≤ 30 km; 1.25, 1.15–1.35 for > 30 km) in young survivors hospitalised at age ≤ 65 years. Having a spouse/cohabitant was strongly associated with lower mortality (0.79, 0.76–0.81) in the overall population, and the impact was higher (0.61, 0.57–0.65) in young survivors.

Conclusions: Stroke survivors living far from their nearest first-degree relatives had a slightly increased mortality than those living in the same basic unit with their family, whereas having a spouse/cohabitant seems to have more influence on the risk of death. The impact of family social support on mortality was more prominent for young survivors than it was for older survivors.

C5

30-day mortality after myocardial infarction in patients with prostate cancer in Norway – A population-wide registry-based study

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Introduction: People with prostate cancer (PCa) are at an increased risk of cardiovascular disease, including myocardial infarction (MI). However, patients with active malignancies have been excluded from trials to evaluate best treatments for MI. As people with PCa become a larger subpopulation of MI patients, clinicians need evidence-based recommendations for treating MI in people with PCa.

Aims: To identify the Norwegian population diagnosed with PCa that had a MI after their cancer diagnosis using routinely collected registry data, describe the rate of invasive treatment, and calculate age-adjusted 30-day mortality.

Methods: We used data from the Cancer Registry of Norway to identify all people diagnosed with PCa between 2013 and 2019, which was linked with the Myocardial Infarction Registry to identify hospitalisations for MI, with supplementary data from the Cardiovascular Disease Registry. We evaluated the first type 1 MI after PCa diagnosis. Invasive treatment for MI was defined as one or more of coronary angiography, percutaneous intervention (PCI) or coronary artery bypass graft (CABG). Death within 30 days was identified by linking with the Norwegian Cause of Death registry and age-adjusted mortality was calculated, adjusted to the Norwegian male population over 18.

Results: We identified 866 type 1 MIs that came after PCa diagnosis from a total of 33,538 diagnosed with PCa. ST elevation was diagnosed in 249 cases (28.8%) and 617 (71.2%) were non-ST elevated. The median age at MI was 73 years and averaged 2 years from PCa diagnosis to MI. 728 (84.1%) patients received invasive treatment, with 491 (56.7%) having angiography, 589 (68%) received PCI and 58 (6.7%) CABG. There were 56 deaths (6.5%) within 30-days of hospitalization, and the age-adjusted 30-day mortality rate was 39.6 per 1000 persons.

Conclusions: Myocardial infarction presents a serious risk of morbidity and mortality for people with PCa, with nearly 40 per 1000 patients dying within 30 days. We intend to carry this research forward to compare the PCa population that experience an MI to the general population to determine if PCa patients are receiving optimal treatment and care for their MIs and if they are having worse health outcomes.

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C6

Trends in melanoma tumour thickness in Norway 1980-2019

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Introduction: Norway ranks fifth in incidence and second in mortality of cutaneous melanoma worldwide. Tumour thickness at diagnosis is the cornerstone of melanoma classification and the most important prognostic factor for clinically localized primary melanoma. Increased incidence of thin tumours may be a result of increased awareness and changes in pathological practice. Recently digitized tumour thickness data (1980-2007) and data from the Melanoma Registry (2008-), enable investigating long-term trends in melanoma thickness.

Aim: To investigate trends in tumour thickness, overall and in important subgroups in a nationwide case series from 1980 to 2019.

Methods: Tumour thickness was categorized in T-categories: T1 (≤1.0 mm), T2 (1.0-2.0 mm), T3 (>2.0-4.0 mm), and T4 (>4.0 mm). Incidence rates were age-standardized using the European standard population. Trends and changes in incidence rate over time were analysed with annual percentage changes (APC) and average APC.

Results: We included 47,439 morphologically verified first primary invasive melanoma cases (52% women) diagnosed in 1980-2019. Median age at diagnosis increased from 58 years in 1980-1999 to 65 in 2008-2019. Throughout the period studied, women were diagnosed at a thinner stage than men. In men, median (interquartile range) tumour thickness decreased from 1.4 mm (0.75-3) in 1980-1999 to 1 mm (0.6-2.3) in 2008-2019, and in women from 1 mm (0.6–2) to 0.9 mm (0.5–1.8). T1 melanoma incidence increased most, and an incidence plateau was found between 1993 and 2006: APC (95% CI) was 17.02 (14.58, 19.51) in 1980-1993, 0.75 (-0.4, 1.91) in 1994-2006 and 6.08 (4.88, 7.3) in 2007-2019. No plateau was found for T2, T3 and T4 melanomas. Although less pronounced, incidence of tumours >2mm also has increased. Average APC (95% CI) of T4 melanomas was 3.04 (2.32, 3.76) for 1980-2019. Results from age-period-cohort analysis are in progress.

Conclusions: T1 melanomas had the largest increase in incidence over time. An increasing trend was also observed in thicker tumours, suggesting that the rise in melanoma incidence is due to not only overdiagnosis/pathological practice.

C7

The Oslo II-study 2000: Low level of antibodies to the oral bacteria *Tannerella forsythia* and *Treponema denticola* predict cancer incidence

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Introduction: The levels of antibodies mirror the level of reaction by the immune system to specific bacterial infections.

Aims: To study whether antibodies to four anaerobic oral bacteria causing chronic periodontitis are associated with incidence of cancer specific diagnoses during 17 ½ years follow-up after the Oslo II-study health screening in 2000.

Methods: Participants were a random sample of men, n=697. Stored serum was analysed for antibodies by the ELISA method to *Tannerella forsythia* (TF), *Porphyromonas gingivalis* (PG), and *Treponema denticola* (TD) all three collectively termed the red complex, and the facultative anaerobe bacterium *Aggregatibacter actinomycetemcomitans* (AA). These bacteria are known to be causal to periodontitis. The prospective analysis of 17 ½ years follow-up was by Cox proportional hazards regression adjusted for known confounders of periodontitis and cancer.

Results: Among the 621 participants with no prior cancer diagnoses, 221 men developed cancer. The ELISA results showed the incidence risk trend was inverse by quartile values. The results are presented by 1st quartile as highest value and 4th as lowest value of antibody levels. TF inversely predicts bladder cancer (n=22) by HR= 1.71 (95% CI: 1.12, 2.61). TD inversely predicts colon cancer (n=26) by HR=1.52 (1.06, 2.19) and bladder cancer (n=22) by HR=1.60 (1.05, 2.43).

Conclusions: Low level of antibodies to *Tannerella forsythia* predict bladder cancer, and low level of antibodies to *Treponema denticola* predict bladder and colon cancer. The study results indicate an immunologic involvement in cancer incidence as shown by the prediction being associated with low levels of antibodies to two oral bacteria. Under review.

C8

Breast cancer related exposures and gene expression profiles in normal breast tissue – The Norwegian Women and Cancer (NOWAC) study

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Introduction: Normal breast tissue is utilized in tissue-based studies of breast carcinogenesis. While gene expression in breast tumor tissue is well explored, our knowledge of transcriptomic signatures in normal breast tissue is still incomplete.

Aims: The aim of this study was to investigate variability of gene expression in a large sample of normal breast tissue biopsies, according to breast cancer related exposures (obesity, smoking, alcohol, hormone therapy and parity).

Methods: We analyzed gene expression profiles from 311 normal breast tissue biopsies from cancer-free, post-menopausal women, using Illumina bead chip arrays. Principal component analysis and *K*-means clustering was used for initial analysis of the dataset. The association of exposures and covariates with gene expression was determined using linear models for microarrays.

Results: Heterogeneity of the breast tissue and cell composition had the strongest influence on gene expression profiles. After adjusting for cell composition, obesity, smoking, and alcohol showed the highest numbers of associated genes and pathways, whereas hormone therapy use and parity were associated with negligible gene expression differences.

Conclusions: Our results provide insight into associations between major exposures and gene expression profiles, and provide an informative baseline for improved understanding of exposure-related molecular events in normal breast tissue of cancer-free, post-menopausal women.

D5

Risk factors and psycho-socioeconomic determinants for cardiovascular diseases according to various living areas with lifestyle factors as mediators. The Tromsø Study

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Introduction: Cardiovascular disease (CVD) is the leading cause of death and disability. Lifestyle factors such as smoking, alcohol, physical inactivity and unhealthy diet are the main risk factors that, in turn, contribute to other modifiable risk factors, such as hypertension, diabetes, raised blood cholesterol and obesity. There is social inequality in CVD risk between and within geographical regions.

Aims: To estimate associations of area level socio-economic status (ASES) with cardiovascular risk factors and other health-related outcomes and the mediating role of lifestyle behaviors.

Methods: We included 19,415 participants (52% women) from the seventh survey of the Tromsø Study (Tromsø7, 2015-16). ASES was the exposure variable, created by aggregating individual SES variables (education, income and housing ownership) at the geographical subdivision level. The data for individual-level SES and geographical subdivision of Tromsø municipality (36 areas) was obtained from Statistics Norway. Variables from questionnaires and clinical examinations obtained from Tromsø7 were used as mediators and outcome variables. The lifestyle factors used as mediators were smoking, alcohol, snuff and physical activity. The outcomes were body mass index (BMI), total/HDL cholesterol ratio, waist circumference, hypertension, diabetes, self-perceived health, insomnia, anxiety and depression. Mediation and mediated moderation analysis were performed with age as a moderator, and the analyses were stratified by sex.

Results: ASES was significantly associated with all the outcome variables except for insomnia in men and anxiety in women. CVD risk decreased with an increase in ASES. These associations were mediated by smoking, physical activity and alcohol. However, the associations between ASES and total/HDL cholesterol ratio (men), hypertension (women), insomnia and anxiety were not mediated by alcohol. The associations of ASES with BMI (women), total/HDL cholesterol ratio, waist circumference and self-perceived health were moderated by age, and the moderating effects were mediated by smoking and physical activity in both sexes. The largest mediated effects were seen in the associations of ASES with depression and total/HDL cholesterol ratio, with the mediators accounting for 44% and 43% of the observed effects.

Conclusions: Living in lower ASES areas is associated with increased CVD risk due to unhealthy lifestyle behaviors, such as smoking, alcohol and physical inactivity.

D6

Modelling unobserved heterogeneity by education level in cardiovascular disease mortality – A frailty analysis of Norwegian population-based health surveys

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Introduction: Smoking, physical inactivity, cholesterol, and systolic blood pressure are established risk factors for cardiovascular disease (CVD), however, there remains a substantial variation in CVD risk that is not accounted for by these factors (unobserved heterogeneity).

Aims: We investigate if the variation in this additional, unexplained risk differs across education levels before and after taking the established risk factors into account.

Methods: We used frailty models to account for unobserved heterogeneity, stratified by three education levels (low, middle, high). We estimated Gini coefficients indicating how the unobserved heterogeneity varied across education level, from the estimated parameters of frailty distributions. The study population (n=506,665) was collected from three Norwegian health surveys (Cohort of Norway, the Age 40 Program and the Counties Study) and linked to National Education Database and the Norwegian Cause of Death Registry.

Results: Different levels of unobserved variation in the risk of CVD deaths was found between education levels. The Gini coefficients, describing the extent of unobserved variation in risk, for low, middle and high education were 0.52, 0.69 and 0.79, respectively. Hazard ratios corresponding to each of the covariates also differed according to education levels.

Conclusions: The unobserved heterogeneity varied according to education levels. We found more individual variation in unobserved risk of CVD among people with high level of education compared to those in the other two groups even after accounting for the established risk factors. The frailty variance was smaller in the low education group, this could be partially explained by the fact that the group was less physical active and contained more smokers compared to other groups.

D7

Time trends and characteristics of heart failure listed (incorrectly) as the underlying cause of death: a thirty-year nationwide study in Norway

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Introduction: The underlying cause of death (UCoD) is the most important information obtained from death certificates and used as endpoint in population-based and clinical studies. In the framework of Global Burden of Disease study, heart failure (HF) should be used only as immediate/intermediate cause of death. When used to describe the UCoD, HF is considered a 'garbage code' (GC) (i.e. not specific enough or not able to cause the death). HF represents the most frequent GC used within cardiovascular diseases chapter and negatively affect the quality of mortality data.

Aim: To describe trends and characteristics of deaths with HF listed as the UCoD (referred to as 'HF deaths') in Norway, 1986-2015.

Methods: Register-based study, linking information from the Cause of Death Registry, the Patient Registry and the National Education Database. We calculated age-standardized proportions of 'HF deaths' (within overall mortality) using the direct standardization method and analyzed them using Joinpoint Regression. We also described changes over time in characteristics of 'HF deaths', and, to put findings into perspective, compared them to those of overall mortality

Results: 'HF deaths' accounted for 3.6% of 1 290 575 deaths registered in Norway. This fraction increased by 3.3%/year during 1986-1999, declined by 3.9%/year during 1999-2007 and stabilized thereafter, with no significant change over the whole study period (AAPC = +0.3; 95% CI:-0.6; +1.1) (Figure 1). Age at death increased over time in both groups, being higher for 'HF deaths' in every period (Figure 2A, red font vs black font). Sex and education distribution among 'HF deaths' followed the pattern of overall mortality (Figure 2B). The proportion of deaths in nursing homes accounted for most 'HF deaths' and was constant over time; in-hospital deaths increased on the 'expense' of deaths occurring at home. This pattern was different for that of overall mortality where the proportion of deaths in nursing homes was smaller but increased substantially over time. The proportion of autopsies was quite low and declined in both groups (Figure 2B).

Conclusion: The use of HF to describe the UCoD in Norway remained constant over time, displaying a different pattern than that of overall mortality.

D8

Prevalence and incidence rates of atrial fibrillation in Denmark 2004-2018 – methodological considerations

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Introduction: Atrial fibrillation (AF) is the most common cardiac arrhythmia. However, the reported occurrence has been inconsistent across countries with varying methodology between studies making comparisons difficult.

Aims: To investigate the prevalence and incidence of AF in the Danish population from 2004 to 2018 and to investigate how methodological issues, such as varying case definitions and types of health care data, influence the observations.

Methods: A register-based study was conducted of all individuals aged ≥18 years living in Denmark during the period of 2004-2018. The cumulative prevalence of AF at the end of the study period was calculated as the number of AF cases alive with at least one inpatient or two outpatient diagnoses from 1994 to 2018 divided by the number of Danish residents in 2018. Incidence rates were calculated as the number of annual AF cases with no previous diagnosis in the past 10 years (i.e., a 10-year washout period) divided by the person-time contributed by the population free of AF on 1 January in the same calendar year. Average annual change was assessed using Poisson regression. Furthermore, the influence of varying methodology was investigated. All statistical analyses were repeated using previously published Norwegian data to explore the estimates' generalizability to a neighbouring country with a comparable health care system.

Results: The cumulative prevalence of AF was 3.0% in the Danish population in 2018. The incidence rate increased from 391 to 481 per 100,000 person-years (PYs) during the period of 2004-2015 (1.7% annual increase), after which it declined to 367 per 100,000 PYs in 2018 (8.5% annual decline). This pattern was observed in both men and women irrespective of age. The Norwegian incidence remained stable and at a higher level during the study period. However, methodological choices — particularly the case definition's strictness and length of washout periods when considering incident cases — influenced both the Danish and Norwegian estimates.

Conclusions: The cumulative prevalence of AF is currently around 3.0% in the Danish population, but the incidence has declined since 2015. As these observations are influenced by methodological choices, future studies should strive for more transparent reporting in their publications.

E5

Feasibility of Twitter text mining as a tool for investigating patterns in antenatal mental health experiences

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Introduction: Many users of Twitter discuss information about their antenatal health and mental health. While large scale health surveys are expensive and time consuming, collecting this information from this online platform can be relatively simple, quick, and free.

Aims: This study investigated the feasibility of using twitter text mining to collect information on individual antenatal mental health experience in a large and diverse population.

Methods: We collected tweets using the free basic API offered by Twitter Fall 2020. Data collection lasted 3 weeks. We conducted two automated tweet mining searches simultaneously. The first search collected a cohort of tweets containing either the words “pregnancy” and “pregnant.” The second cohort collected tweets containing key words about antenatal depression or anxiety. All tweets from the second search cohort and a subset of the first cohort were manually coded as containing content relevant to our study question. The coded data was then used to develop a training dataset of common words and bigrams associated with tweets about antenatal depression but not associated with tweets about pregnancy generally. From this we developed a machine learning model which would identify relevant tweets from the first search cohort.

Results: We collected 5 535 842 tweets for the first search cohort and 1032 tweets for the second cohort. Only 119 tweets from the second cohort and none of the subset of 1000 tweets selected from the first cohort were relevant to our study question. We found that models scored high on performance measures for the training task, but subjectively produced poor results on the larger dataset. While common words and bigrams selected by the learner were relevant to our study question, we determined the wide variety of content associated with the word pregnancy and the small size of our training dataset produced an overfit model with poorly applicable outcomes.

Conclusions: Due to the diverse content shared on Twitter and relatively slow pace of available free APIs, these methods may not be readily applicable as a health survey technique. Despite the large quantity of tweets collected, tweets concerning rich antenatal health data were much fewer than anticipated.

E6

The physical activity paradox – Association between occupational physical activity, leisure time physical activity and chronic pain

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Introduction: Higher levels of leisure time physical activity are associated with cardiovascular health benefits, while higher levels of occupational physical activity are associated with detrimental health outcomes. It is uncertain whether this paradox occurs in chronic pain as well.

Aims: To determine the association between different levels of occupational and leisure time physical activity and chronic pain in different anatomical regions.

Methods: We used data from Tromsø7. Occupational and leisure-time physical activity had four levels: sedentary, walking, walking and lifting and manual labour versus sedentary, low, moderate or vigorous, respectively. Information about pain was obtained through a digital body map, the Graphical Index of Pain (GRIP). Pain characteristics were graded on a 11-point numeric rating scale (NRS). Chronic pain was defined as pain experienced within last 4 weeks with an onset of ≥3 months and rating of >3 in pain intensity, bother and impact of daily activites. We used general linear models to estimate the prevalence and prevalence ratios (PRs) of chronic pain (10 anatomical regions) in different levels of occupational and leisure time physical activity. All models were adjusted for covariates with sedentary level as reference group for both exposures.

Results: A total of 20,844 respondents reported on GRIP (52.5% women). The prevalence of chronic pain in the upper and lower extremities, head and back decreased with increased levels of leisure time physical activity. In contrast, the highest levels of occupational physical activity were associated with higher prevalence of chronic pain across all anatomical regions. For example, PRs for chronic back pain were 1.25 (95% CI 1.06 to 1.44) for walking, 1.31 (95% CI 1.09 to1.54) for walking and lifting and 2.71 (95% CI 1.94 to 3.49) for manual labour. However, they were 0.88 (95% CI 0.73 to 1.03) for low, 0.60 (95% CI 0.47 to 0.73) moderate and 0.39 (95% CI 0.18 to 0.59) vigorous leisure-time physical activity.

Conclusions: Higher levels of occupational physical activity was associated with more chronic pain, as opposed to leisure time physical activity which was inversely related to chronic pain for several anatomical regions.

E7

Effect of physical activity on psychosocial health among adult survivors of childhood cancer – The SURfit study

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Introduction: Childhood cancer survivors (CCS) are at elevated risk of experiencing fatigue, depression, and reduced quality of life. Inadequate physical activity (PA) among CCS may precipitate these conditions. Only a few randomized controlled trials have investigated the effect of PA on quality-of-life, nearly none on fatigue, and zero on psychological distress. Furthermore, none of these included long-term CCS.

Aim: This paper investigated the effects of a one-year individualized exercise intervention on fatigue, mental health, and health-related quality of life (HRQoL) in adult CCS.

Method: We randomized 151 CCS aged ≥16 years, <16 at diagnosis, and ≥5 years since diagnosis, identified through the Swiss Childhood Cancer Registry. The intervention group received personalized exercise counselling to increase intense PA by ≥2.5h/week for one year. Motivational tools included phone calls by physiotherapists, a web-based activity diary, and pedometers. Controls maintained their usual PA levels. Assessments were performed at baseline, 3, 6, and 12 months.

Severity-of-fatigue was measured with the Checklist Individual Strength, psychological distress with the Brief Symptom Inventory (BSI-53), and HRQoL (physical and mental component summary scores) with the Short Form-36 questionnaire. Z-scores were calculated based on representative normative populations. We used generalized linear mixed-effects models with intention-to-treat (ITT, primary), as well as per-protocol allocations whereof compliance was based on increase in cardiopulmonary fitness and daily self-reported PA.

Results: Our primary ITT analysis found significantly lower severity-of-fatigue z-score, ie. less fatigued, by -3.56 (95% confidence interval (CI) -5.69 to -1.43, p=0.001) in the intervention group compared to controls at 12 months; primary analyses showed no other significant effects. Per-protocol analyses showed improved HRQoL-physical component z-scores in the intervention group by 3.06 (95%CI 0.99 to 5.14, p=0.004) and 3.54 (1.13 to 5.96, p=0.004) over the controls at 12 months.

Conclusions: Individualized exercise interventions may effectively improve fatigue and physical health-related quality-of-life among adult long-term survivors of childhood cancer. This is despite no effects on psychological distress. Our effects are greater than an often-suggested minimal clinically important difference (MCID) of 0.5 to 1.0 z-score for psychometric instruments. Future studies should investigate the feasibility of implementing such large-scale PA interventions in follow-up care for CCS.

E8

The association between health anxiety and number of physical diseases in a general population

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Background: Health anxiety (HA) is a condition ranging from mild worry to excessive anxiety about disease, and is associated with both increased healthcare use and the risk of disability benefits. As the prevalence of people living with a physical condition is growing due to increasing age in the general population and improvement of diagnostics and treatment. Therefore, the association between HA and physical disease is of growing interest and relevance.

Aim: To examine the association between HA and burden of disease (measured as the number of physical diseases) in a general population.

Methods: This study used cross-sectional data from the seventh Tromsø study. 18 432 participants aged 40 years or older gave self-reported information whether they had different diseases, previously or present. Participants were categorised according to both the number of present and the number of previous physical diseases: None, one-, two-, three-, or four or more diseases. Participants with no previous or present disease constituted the reference category. HA with a newly revised version of the Whiteley Index-6 (WI-6-R) with a 5-point Likert scale. The total score ranged from 0 (No HA) to 24 (highest possible HA). Associations were explored using exponential regression analysis. Demographics, family history of disease, socioeconomic- and social variables were included as confounders.

Results: The mean level of HA in the reference group was 2.28, and increasing number of physical diseases was associated with increasing levels of HA. For increasing numbers of present diseases, HA levels increased with 42 %, 79 %, 119 % and 125 %, respectively, after adjusting for confounders. For increasing numbers of previous disease, the increase of HA levels was significant, albeit slightly lower (36 %, 68 %, 94 % and 120 % increase).

Conclusion: HA is associated with physical disease, and higher burden of disease was associated with significantly increasing levels of HA. These findings were consistent both in participants stating present as well as previous disease, indicating that HA is persistent also when participants have recovered from disease.

A9

Reproductive factors in relation to incidence of lung cancer in Norwegian women: the HUNT Study

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Introduction: Previous studies have investigated the relationships between female reproductive factors and lung cancer risk with inconsistent findings.

Aims: This prospective cohort study aimed to evaluate if early age at menarche and other female reproductive factors were associated with lung cancer incidence.

Methods: We followed up 33,313 cancer-free women who participated in the second survey of the HUNT Study in Norway from 1995-1997 to 2018. Reproductive factors were self-reported at baseline. Early menarche was defined as menarche at the age of 12 years or before. Other reproductive factors included age at menopause, menopause status (natural/non-natural), reproductive period, parity, age at first birth, as well as oral contraceptive use and hormone replacement therapy. Incident lung cancer cases and histologic types were ascertained from the Cancer Registry of Norway. Cox regression models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) after adjustment for smoking and other confounders.

Results: In total, 467 women developed lung cancer during a median follow-up of 19.9 years, and among them, 169 had lung adenocarcinoma. Early menarche was associated with an increased incidence of lung adenocarcinoma (HR 1.43, 95% CI 1.02-2.03). Similar result was observed among post-menopausal women (n=12,209), and the corresponding hazard ratio was 1.46 (95% CI 0.89-2.39). Other reproductive factors were not associated with the incidence of lung cancer overall or histologic types.

Conclusions: Our findings suggested that early menarche was related to the development of lung adenocarcinoma, but the causal relationship warrants further investigation.

A10

Smoking and subfertility: multivariable regression and Mendelian randomization analyses in the Norwegian Mother, Father and Child Cohort Study

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Introduction: Smoking and subfertility are associated, particularly in women. Nevertheless, this relationship presents some methodological flaws: it is of small magnitude, could be affected by residual confounding and is mainly based on retrospective studies. These limitations could be overcome by prospective studies and complementary methods such as Mendelian randomization (MR).

Aims: To investigate the association between smoking-related traits and subfertility (time-to-pregnancy ≥12 months) by multivariable logistic regression and MR.

Methods: Our population is 34,716 women (average age 30) and 32,739 men (average age 33) with questionnaire and genotype information from the Norwegian Mother, Father and Child Cohort Study. Self-reported information on smoking (having ever smoked [both sexes], age of smoking initiation [women], having quit smoking [women], cigarettes/week in current smokers [both sexes]) was gathered for the observational analyses. Genetically predetermined levels and likelihood of presenting these traits were estimated in MR analyses.

Results: 10% of couples were subfertile. In multivariable regression (covariates: age, education years, body mass index, number of previous pregnancies), a higher smoking intensity in current female smokers was related to greater odds of subfertility (+1 standard deviation [SD, 48 cigarettes/week]: odds ratio [OR] 1.07, 95% confidence interval [95%CI] 0.99-1.15). Delays in smoking initiation (+1SD [3.2 years]: OR 0.90, 95%CI 0.85-0.95) and quitting smoking (versus not quitting: OR 0.90, 95%CI 0.81-1.00) were linked to decreased subfertility odds in women. These relationships, of small magnitude, were not observed in MR. No associations were found for a 1SD increase in the genetically predicted number of cigarettes smoked per week (one-sample MR: OR 0.97, 95%CI 0.90-1.04; two-sample MR: OR 0.68, 95%CI 0.40-1.15), age of smoking initiation (one-sample MR: OR 0.97, 95%CI 0.90-1.04; two-sample MR: OR 0.47, 95%CI 0.11-2.01) and likelihood of quitting smoking (one-sample MR: OR 1.03, 95%CI 0.99-1.09; two-sample MR: OR 0.80, 95%CI 0.46-1.38). In men, smoking and subfertility were unrelated in multivariable regression and MR analyses.

Conclusions: Increased tobacco use, earlier smoking initiation, and not quitting smoking were associated with greater subfertility in women in multivariable regressions but not in MR. This discordance could be due to unmeasured residual confounding in multivariable regression, weak genetic instruments, or other biases.

A11

Risk of cardiovascular disease among subfertile women and men: The HUNT Study, Norway

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Introduction: Only a handful of studies have examined the association between subfertility (having tried to conceive for more than 12 months without getting pregnant) and risk of cardiovascular disease (CVD), yielding inconclusive evidence.

Aims: To investigate the association between subfertility and risk of CVD subtypes (stroke, coronary heart disease (CHD), myocardial infarction, and angina) in both women and men.

Methods: We studied 33,065 women (mean age 48 years) and 19,262 men (mean age 49 years) participating in The Trøndelag Health Study (HUNT), focusing on the population-based health surveys from 1995-1997 (HUNT2), 2006-2008 (HUNT3) and 2017-2019 (HUNT4). We assessed the association between self-reported subfertility and CVD subtypes using Cox proportional hazards models adjusted for age, birth year, body-mass index, education, smoking history, and cohabiting partnership. Information on CVD was available by linkage to hospital records.

Results: A total of 17% of women and 15% of men reported subfertility. The mean follow-up time was 14.1 years (SD 8.9) for women and 13.7 years (SD 8.9) for men. The rates of stroke, CHD, myocardial infarction, and angina in the female population were 30, 50, 24 and 31 per 10,000 person years, respectively. Equivalent numbers for men were 41, 93, 51 and 57 per 10,000 person years. In women, subfertility was associated with an increased risk of CHD (hazard ratio [HR] 1.16; 95% confidence interval [CI]: 1.03 to 1.30), angina (HR 1.21; 95% CI: 1.06 to 1.40), and a suggestive increased risk of stroke (HR 1.15; 95% CI: 0.99 to 1.33). We found no association between subfertility and myocardial infarction in women (HR 1.06; 95% CI: 0.90 to 1.26). Equivalent HRs for men were 1.05 (95% CI: 0.87 to 1.26) for stroke, 0.92 (95% CI: 0.81 to 1.04) for CHD, 0.93 (95% CI: 0.78 to 1.10) for myocardial infarction, and 0.95 (95% CI: 0.81 to 1.11) for angina.

Conclusion: Subfertility is associated with CVD in women but not in men. Subfertility, like other indicators of female reproductive health, is a sex-specific CVD risk factor. Future studies should assess whether CVD risk stratification in women can be improved when these are included in prediction algorithms.

A12

Early childhood respiratory tract infections according to parental subfertility and conception by assisted reproductive technologies

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Introduction: Studies have confirmed higher health care use and costs in children born following assisted reproductive technologies (ART). Results on respiratory tract infections remain inconclusive and the contribution of underlying parental subfertility was rarely studied.

Aims: To assess the occurrence, frequency, and hospitalization for upper (URTI) and lower respiratory tract infections (LRTI) according to parental subfertility (time-to-pregnancy 12 or more months) and conception by ART.

Methods: This study based on the Norwegian Mother, Father and Child Cohort Study (MoBa) with data on ART treatment from the Medical Birth Registry (MBRN). Time-to-pregnancy and respiratory infections were self-reported. We examined respiratory tract infections when the child was 0-6, 7-18, and 19-36 months of age. URTI included throat infections with or without streptococci and ear infections, while LRTI included bronchitis, bronchiolitis, RSV, and pneumonia. We used log-binomial regression to examine the risk of occurrence and hospitalisation, and negative-binomial regression for frequency of infection, while accounting for maternal characteristic (age, education, parity, BMI and smoking during pregnancy).

Results: We included 77 075 singletons from fertile parents, 7527 from subfertile and 1946 following ART. The occurrence and frequency of URTI's did not differ between the fertile and subfertile group. ART children had a slight increased frequency of URTI's (incidence rate ratio (IRR)) of 1.20 (95% CI 1.07-1.34) and LRTI's (IRR 1.22; 95% CI 1.02, 1.47) at 19-36 months. ART singletons also had a higher risk for hospitalisation due to URTI between 6-18 months (adjusted relative risk (aRR) 1.75; 95% CI 1.18-2.61) and 19-36 months (aRR 1.54; 95% CI 1.28-1.86), and a modest increased risk for hospitalisation due to LRTI at 19-36 months (aRR 1.36 95% CI 1.02-1.81). A higher risk for hospitalisation due to URTI at 19-36 months remains in ART singletons when directly compared to children born to subfertile parents (aRR 1.41; 95% CI 1.13-1.76).

Conclusions: Our results indicate that children conceived by ART might have a slightly higher frequency and risk of hospitalization for respiratory tract infection during early childhood. These results were not explained by characteristics influencing underlying parental subfertility.

B9

Burden of disease due to transportation noise in the Nordic countries – a NordSOUND study

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Background: Environmental noise is of increasing public health concern and is the second largest environmental risk factor, after air pollution, in terms of estimated disease burden for Europe.

Aims: As part of the Nordic collaborative project NordSOUND (Nordic studies on occupational and traffic noise in relation to disease) we aimed at estimating the burden of disease (BoD) due to road traffic and railway noise in four Nordic countries and their capital cities, in terms of DALYs (Disability-Adjusted Life Years).

Methods: Available data on road traffic and railway noise exposure were used, including data from the strategic noise mapping for 2016 conducted according to the Environmental Noise Directive, END (Directive 2002/49/EC). High degree of noise annoyance (HA), high degree of sleep disturbance (HSD) and ischaemic heart disease (IHD) were included in the analyses based on exposure-response functions from the WHO systematic review (WHO, 2018). Country-specific estimates from the Global Burden of Disease (GBD) study were used as background health data for IHD.

Results: The DALY rates for road traffic noise varied considerably between the Nordic countries, from 72 DALY/100,000 in Finland to 162 DALY/100,000 in Denmark. The burden attributable to railway noise was much lower, with the lowest rate in Denmark (16 DALY/100,000) and the highest in Sweden (53 DALY/100,000).

Conclusions: Since several aspects of the noise exposure modelling vary considerably between the Nordic countries, harmonization of noise exposure modelling is important to assure comparative BoD estimates between the Nordic countries.

B10

Educational and gender differences in duration in work participation and non-participation among older individuals in Norway

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Introduction: Prolonging working life and increasing work participation among older individuals until retirement at age 67 in Norway is required to maintain the welfare state. Gender and educational differences in duration of work participation and non-participation would provide insight into how long older individuals can be expected to work and help to identify groups of individuals that can benefit most from interventions.

Aims: To estimate the duration in employment and working years lost, by gender and highest attained education among older individuals in Norway.

Methods: This prospective registry-based cohort extracted data from FD-Trygd (Statistics Norway). It consisted of a random sample (10%) of all individuals who lived in Norway in January the year they turned 60 between 2000-2005 (n=14,291 men and n=14,109 women). Follow-up was 10 years. The following hierarchy was used to identify precedence in 9 states: death, (early) retirement >50%, disability pensioning >50%, sickness absence >50%, employment, unemployed, education, emigration, and non-employed (no registration in any other state). Average time spent in each state was calculated.

Results: Throughout the 10-year follow-up, individuals spent on average 2y7m in employment, 3y0m in (early) retirement, 2y6m in disability pension, 1y0m in non-employment, 128 days in sickness absence, 42 days in unemployment, two days in education, and zero days in emigration. Men spent more years in work (2y10m) than women (2y2m), and fewer years in disability pension (2y1m and 2y10m for men and women, respectively). There was an educational gradient for women in employment (range 1y5m-4y5m, from lower education to tertiary graduates) and for men (range 2y0m-4y10m). There was an educational gradient for disability pensioning in the opposite direction (range 3y10m-1y1m for women; range 3y4m-0y2m for men).

Conclusions: Considering retirement age at 67, three years spent in (early) retirement may be expected during the 10-year follow-up. Individuals worked on average less than half of the potential time until age 67. Most of the working years were lost to disability pensioning. Employment duration decreased while duration in disability pensioning increased with lower educational attainment. Individuals with lower educational background may benefit most from preventative measures to increase working capacity to prolong working life.

B11

Gender differences in the impact of work exposures on age of withdrawal from paid employment among older workers

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Introduction: With the increase in the non-working age population, extending working life is a key political objective in most industrialised countries. However, to successfully extend working life for both genders among older workers, more knowledge is needed on which work-related factors affect early exit from work differently for men than for women.

Aims: The study aimed to evaluate gender differences in associations between work exposures at age 62 and age of withdrawal from paid employment in Norway.

Methods: The study utilized registry data on individuals born 1949-1953 who were in paid employment when turning 62 (N=145,331). Individuals were followed from the month they turned 62 until either withdrawal from paid employment, 67 years of age, or end of follow-up (June 2016). Information about 8 biomechanical and 7 psychosocial exposures was obtained from a gender-specific job exposure matrix. Gender-specific hazard ratios (HRs) of all-cause withdrawal were calculated for each work exposure separately using Cox regression. Gender differences were examined by calculating the additive difference in the gender-specific HRs (male HR minus female HR). Cause-specific withdrawals were assessed with cumulative incidence curves.

Results: Mean age of withdrawal in the study population during follow-up was 63.5 years for both men and women. Largest gender differences were found for monotonous work (HR difference: 0.26, 95% CI: 0.23-0.29), high psychological demands (HR difference: -0.24, 95% CI: -0.27--0.21) and hands above shoulder height (HR difference: 0.15, 95% CI: 0.11-0.19). The gender differences were primarily driven by early retirement and health reasons.

Conclusions: Gender modified the impact of work exposures on age of withdrawal from paid employment among older workers.

B12

Night shift work and risk of aggressive prostate cancer in the Norwegian Offshore Petroleum Workers (NOPW) Cohort

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Introduction: Prostate cancer is one of the most common cancers and has few established risk factors. A higher rate of prostate cancer in industrialized societies has spurred research into its association with common occupational and environmental exposures. This includes night shift work, which leads to sleep deprivation, stress, vitamin D deficiencies and exposure to artificial light at night. Positive associations have been observed in studies of night shift work exposure and prostate cancer risk, and particularly so for long-term exposure and rotating night shift work.

Aims: Using the nationwide Norwegian Offshore Petroleum Workers cohort, we aimed to study the association between extreme night shift work schedules and aggressive prostate cancer.

Methods: Among 25 347 males who worked offshore 1965–1998, we established a study population of 299 aggressive prostate cancer cases and 2056 non-cases according to a case-cohort design. Work history was recorded as years with day, night and rollover shift. Weighted Cox regression, adapted to a case-cohort design, was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for aggressive prostate cancer risk, adjusted for education and year of first employment. With age as the time scale, person-years were generated from start of follow-up (01.07.1999) to the date of first prostate cancer diagnosis, emigration, death or end of follow-up (31.12.2019). Multiple imputation was used to account for missing covariates.

Results: Day work was the most frequent shift work category, followed by rollover shift work. Comparing cases to non-cases, median duration of rollover shift work was 1.2 years (12%) higher while median duration of day work was 2 years (20%) lower. Compared to day work only, an increased risk of aggressive prostate cancer (HR 1.54, CI 1.04–2.28) was found in persons exposed to ≥16 years of rollover shift work. Compared to day work only, an increased risk was also indicated for ever exposure to any shift work (HR 1.25, CI 0.96–1.63) and rollover shift work only (HR 1.26, CI 0.94–1.69).

Conclusions: Long-term exposure to extreme rollover shift work increases the risk of aggressive prostate cancer in offshore petroleum workers.

C9

Intake of sucrose-sweetened beverages and risk of developing pharmacologically-treated hypertension in women: Cohort study

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Introduction: Recent evidence from human and animal research links sweetened beverages with hypertension development, but the majority of studies evaluate beverages sweetened by high fructose corn syrup and not sucrose-sweetened beverages (SSB).

Aims: To investigate the association between intake of SSBs and risk of developing pharmacologically treated hypertension in a population of Norwegian mothers followed up to 10 years after delivery.

Methods: Women without hypertension at baseline in the Norwegian Mother, Father, and Child Cohort Study (MoBa) (n=60,027) who delivered between 2004-2009 were linked to the Norwegian Prescription Database (NorPD) for identification of antihypertensive medication use after the first 90 days following delivery. Diet was assessed by a validated semi-quantitative FFQ in mid pregnancy. Cox proportional hazard analyses evaluated hazard ratios (HR) for the development of hypertension associated with quintiles of SSB consumption as percent energy.

Results: A total of 1,480 women developed hypertension within 10 years of follow-up. The highest relative to the lowest quintile of SSB intake was associated with an elevated risk for hypertension after adjusting for numerous covariates in multivariate models [HR: 1.20 (95% CI: 1.02, 1.42)]. Consistency in results was observed in sensitivity and stratified analyses.

Conclusions: This study provides evidence that beverages sweetened by sucrose associate with an increased risk of hypertension in women.

C10

Intake of fermented dairy products and associations with blood lipid concentrations – The Tromsø Study: Tromsø7

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Introduction: Dairy fat is rich in saturated fatty acids known to increase serum low-density lipoprotein cholesterol (LDL-C) concentration, which is an important risk factor for atherosclerosis and cardiovascular disease (CVD). Nevertheless, prospective cohort studies do not provide a clear picture of dairy consumption and cardiovascular risk, as intake of fermented dairy products has been associated with reduced risk. How intake of fermented dairy products is associated with blood lipid concentrations may provide a possible explanation for the suggested reduced CVD risk.

Aim: To examine the associations between total intake of fermented dairy products, intake of yoghurt and cheese, and blood lipid concentrations in a population-based study.

Methods: In 11,377 adult and elderly women and men participating in the population-based Tromsø Study 2015-2016, we used multivariable linear regression to examine the associations between total intake of fermented dairy products, intake of yoghurt and cheese, and serum concentrations of total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), and triglycerides. Dietary data was collected using a validated food frequency questionnaire, and blood lipid concentrations were analyzed with enzymatic colorimetric methods based on non-fasting blood samples. Analyses were adjusted for potential confounding factors, and cheese intake analyses were stratified by self-reported use of lipid-lowering drugs (LLD) as a statistically significant interaction was found.

Results: Cheese intake was positively associated with HDL-C (regression coefficient 0.07 mmol/l (95% CI 0.04, 0.11)) and inversely associated with LDL-C (regression coefficient -0.10 mmol/l (95% CI -0.18, -0.02)) and triglyceride concentrations (relative change -5.25 % (95% CI: -8.84 %, -1.49 %)) per 100 g/day among participants not using LLD, while no significant associations were found among those using LLD. Total intake of fermented dairy was inversely associated with triglyceride concentrations (relative change -0.44 % (95% CI: -0.78 %, -0.09)) per 100 g/day, while no associations were found for yoghurt intake.

Conclusion: The associations between intake of fermented dairy products and blood lipid concentrations seem to be dependent on the type of dairy product. Cheese intake showed the most favorable associations being positively associated with HDL-C and inversely associated with LDL-C and triglyceride concentrations among subjects not using LLD.

C11

BMI and waist circumference as predictors of frailty/prefrailty among elderly people

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Introduction: Unintentional weight loss is widely acknowledged as an important indicator of frailty. However, growing evidence suggests an association between obesity among elderly and the risk of frailty. Body mass index (BMI) and Waist Circumference (WC) can be assessed easily and act as simple indicators of general and abdominal obesity, respectively. There have been limited studies exploring the longitudinal relationship of BMI and WC with frailty.

Aim: To examine prospectively the association of BMI and WC with the risk of frailty/prefrailty.

Methods: Data were derived from 4509 men and women aged $\geq$ 45years who participated in the population based Tromsø4 study (1994/95) with follow-up measurements at Tromsø7 (2015/16). Frailty status was determined at Tromsø7 using a modified version of Fried's frailty criteria. Information on BMI and WC were obtained from baseline along with consecutive Tromsø surveys conducted in 2001/02, 2007/08 and 2015/16. Multivariable logistic regression models were used to assess the association of BMI and WC with frailty/prefrailty, both independently and as trajectories over time. Group based trajectory modelling was used to identify BMI and WC trajectories. Analyses were adjusted for age, sex, education, smoking, alcohol, marital status, friends status, physical activity and self-perceived health.

Results: In our study, 28% were prefrail while 1% were frail. Overweight (OR 1.19, 95% CI: 1.02-1.39) and obese (OR 2.41, 95% CI: 1.93-3.02) individuals at baseline had increased risk of becoming prefrail/frail at follow-up compared to individuals with normal weight. Individuals with moderately high (OR 1.57, 95% CI: 1.21-2.03) and high WC (OR 2.14, 95% CI: 1.59-2.87) had higher risk of prefrailty/frailty compared to individuals with low WC. Increased risk of prefrailty/frailty was observed among those in increasing BMI trajectory i.e., overweight to obese or class I obese to class II obese compared to those with stable normal weight. Further, higher risk of prefrailty/ frailty was observed among those with constantly high WC from the baseline till follow-up compared to those in stable low WC trajectory. (Please note that we are still doing further sensitivity analyses, complete results will be available by the day of the event.)

Conclusion: The results suggest an association between obesity and the risk of frailty among elderly.

C12

Intakes of fish and long chain *n*-3 polyunsaturated fatty acid supplements during pregnancy and subsequent risk of type 2 diabetes in a large prospective cohort study of Norwegian women

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Introduction: While seafood is considered an important component of a healthy diet, concerns have been raised related to contaminant exposures and risk of type 2 diabetes (T2D).

Aims: To investigate associations between intakes of total fish, lean fish, fatty fish, and long chain n-3 polyunsaturated fatty acid (LC*n*-3PUFA) supplements and risk of T2D in women after pregnancy. Furthermore, we sought to compare the estimated intakes of methylmercury (MeHg) and sum of dioxins and dioxin-like polychlorinated biphenyls (*dl*-PCBs) to tolerable weekly intakes (TWI).

Methods: Women free of diabetes at baseline (n=60,831) who participated in the population-based Norwegian Mother, Father, and Child Cohort study (MoBa) were prospectively evaluated for incident T2D, identified on the basis of medication usage >90 days after delivery, ascertained through the Norwegian Prescription Database. Dietary intake data were obtained with a validated 255-item food frequency questionnaire (FFQ), which assessed habitual diet during the first 4-5 months of pregnancy. Intakes of MeHg and sum of dioxins and *dl*-PCBs were derived with use of a contaminant database and the FFQ.

Results: Median (IQR) age was 31 (27, 34) years at time of delivery, and follow-up time was 7.5 (6.5, 8.5) years. T2D occurred in 683 (1.1%) participants. Multivariable Cox regression analyses identified lower risk of T2D with increasing energy-adjusted lean fish intake per 25 g/1000 kcal (HR 0.71, 95% CI 0.53-0.95, p=0.022). However, in stratified analyses, a lower risk was found only in women with pre-pregnancy BMI ≥25 kg/m^2. There were no associations between intake of total fish, fatty fish, or LC*n*-3PUFA supplements and T2D. MeHg intake was low, but the sum of dioxins and *dl*-PCBs (pg TEQ/kg bw/wk) exceeded the TWI set by the European Food and Safety Authority (EFSA) for the majority of participants.

Conclusions: Intake of lean fish, but not fatty fish or LC*n*-3PUFA supplements, was associated with lower risk of pharmacologically treated T2D in Norwegian women who were overweight or obese. Fatty fish, which contain dioxins and *dl*-PCBs, did not increase the risk of T2D, but the exceedance of the EFSA TWI for dioxins and *dl*-PCBs is a health concern.

D9

Estimating risk of disease in the presence of "fuzzy" loss to follow-up: type 1 diabetes in the MIDIA birth cohort 2001-2017

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Introduction: Loss to follow-up is often difficult to explicitly define (is "fuzzy") in longitudinal cohort studies with scheduled contact via questionnaires and/or telephone because response may be delayed, and participants developing disease may be more likely to respond. At what time individuals potentially lost to follow-up are censored in survival analysis may severely influence risk estimates.

Aims: We compared risk estimates based on censoring at last contact, ignoring censoring and registry linkage (where loss to follow-up can be ignored).

Methods: The MIDIA study followed over 900 children with increased genetic risk of type 1 diabetes (HLA DQ8/2 genotype) born throughout Norway during 2001-2007. Based on previous studies they were informed that their risk of type 1 diabetes before age 15 years was estimated to be 6-8%. Follow-up via mailed questionnaires (and blood sampling) were scheduled at ages 3, 6, 9 and 12 months and annually thereafter. Participants were contacted via phone if they did not respond to questionnaires. We estimated risk as 1-Kaplan-Meier survival, counting follow-up from birth to type 1 diabetes diagnosis or censoring (at end of 2016 or loss to follow-up). Loss to follow-up was defined as not having responded one year after the last scheduled contact. In 2017, actual disease status and date of diagnosis was obtained via linkage to the Norwegian Childhood Diabetes Registry with nearly complete coverage.

Results: During 2001-2016, we identified 35 cases of type 1 diabetes among 909 high-risk children, and the risk by age 15 years was 4.2% if ignoring loss to follow-up. Censoring at the operationally defined loss to follow-up resulted in a risk estimate at 15 years of 8.0%. Registry linkage in 2017 identified an additional 18 cases, and the risk at age 15 year was estimated to 6.5%.

Conclusions: Ignoring loss to follow-up underestimated the risk, while censoring at our pragmatic definition gave an estimate that was too high. Registry linkage helps reduce problems with loss to follow-up, and we note that we were able to predict the risk for the cohort based on exogenous information before the study start.

D10

Antidepressant fill trajectories in pregnant women with depression and/or anxiety in Norway: results from a registry linkage study

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Background: Antidepressant exposure patterns in pregnant women are more complex than a simplistic classification as continuation or discontinuation.

Methods: We conducted a nationwide, registry-linkage study in Norway using data on antidepressant prescription fills in pregnancies within women with a delivery between 2008 and 2018, having depression/anxiety and antidepressant fills prior to pregnancy. We employed the PRE2DUP method to generate the expected duration of treatment and antidepressant use periods (ADUPs) for each pregnancy. Information from ADUPs (timing and dosage) were used for longitudinal k-means trajectory modelling on antidepressant exposure, number of days of exposure to antidepressant and cumulative dose of each week in the time window including six months prior to pregnancy, eight months into pregnancy and one year after birth. We assessed the association between maternal characteristics and trajectory group membership using multinomial logistic regression.

Results: We included 8,460 pregnancies within 8,092 women. We identified four trajectories of antidepressant prescription fills in the 108-week time window: two distinct discontinuing patterns (one started prior to pregnancy and completely discontinued from the start of pregnancy (30.4%) and one started around the start of pregnancy and completely discontinued from the end of pregnancy (33.8%)), one continuation pattern (20.6%) and one interruption patterns (started decreasing use prior to pregnancy toward the end of pregnancy and increasing use in the postpartum year, 15.2%). Using the dose by week, we identified four dose-dependent trajectories: early discontinuers – low dose, late discontinuers – high dose, and continuers with dose adjustment and continuers without dose adjustment. The strongest predictors of trajectory group membership included: maternal age, marital status, parity, previous miscarriage or stillbirths, pregnancy planning, severity of depression/anxiety prior to pregnancy, comedication (e.g., opioid analgesic), type of antidepressant and average dose prior to pregnancy.

Conclusions: Longitudinal trajectory modelling revealed different antidepressant fill trajectories in pregnant women with depression/anxiety. The predictors of trajectory group membership might be useful to anticipate the potential antidepressant fill patterns in pregnant women.

D11

Association between prenatal analgesic opioid exposure and fifth grade school performance – a MoBa study

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Introduction: Opioid analgesics are used by 3-20% of pregnant women. Prenatal opioid exposure may interfere with normal fetal brain development; however, few studies have examined the long-term neurodevelopmental consequences of this drug exposure.

Aims: To investigate the association between opioid analgesic exposure in pregnancy and school performance among children in fifth grade.

Methods: We used data from the Norwegian Mother, Father and Child Cohort Study (1999-2008) linked to the Medical Birth Registry of Norway and data from Statistics Norway. The study included 64 256 children, born to 54 568 mothers who reported a pain-related disorder during pregnancy. Exposure was self-reported by the mother, and classified according to timing (first, second and third trimester) and duration of use (according to number of four-week intervals, e.g. 1, 2-3, and 4 or more). Women who used opioid analgesics prior to pregnancy (discontinuers) acted as our comparator group. School performance was measured by results of standardized tests in English, math and reading among children in fifth grade. Mean scores were calculated and standardized according to subject and test year. Propensity scores with inverse probability of treatment weights were used to control for measured confounding. Generalized linear models with robust standard errors were used to estimate standardized mean differences in test scores and 95% CI.

Results: Overall, 2.3% of pregnancies were exposed to an analgesic opioid at least once during gestation. Children exposed to opioid analgesics in 1st trimester and for 2-3 four-week intervals during pregnancy scored lower on the Numeracy test (weighted β -0.17, 95% CI: -0.30, -0.05 and weighted β -0.26, 95% CI: -0.45, -0.08, respectively) compared to children of mothers who discontinued. Exposed children did not perform worse on tests in English and reading, regardless of timing and duration of exposure.

Conclusions: In this study, children prenatally exposed to opioid analgesics scored lower on tests in numeracy, compared to children of mothers who discontinued, but not on tests in English or reading. The observed difference is small and may not be of clinical relevance. Residual or unmeasured confounding cannot be ruled out as possible explanations for this finding.

D12

Prenatal triptan exposure and risk of ADHD in childhood: results from the Norwegian Mother, Father and Child Cohort study

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Introduction: Triptans are commonly used in acute treatment of migraine. Prenatal exposure to triptans may be associated with adverse fetal neurodevelopment; however, data on these outcomes is limited.

Aims: To examine the association between exposure to triptans during pregnancy and risk of attention deficit hyperactivity disorder (ADHD) in the offspring.

Methods: The study used data from the Norwegian Mother, Father and Child Cohort Study (MoBa), linked to the Medical Birth Registry of Norway, the Norwegian Patient Registry (NPR) and the Norwegian Prescription Database (NorPD). Use of triptans during pregnancy was self-reported in MoBa. Child ADHD was defined as either a diagnosis of hyperkinetic disorder in NPR or filled prescription of ADHD medication in NorPD. Cox proportional hazard models with inverse probability weights were used to estimate weighted hazard ratios (HR) with 95% confidence intervals (CI).

Results: The study sample consisted of 653 pregnancies where mothers reported triptan use during pregnancy, 3222 pregnancies where mothers reported migraine but no triptan use during pregnancy, and 4169 who reported migraine prior to pregnancy only. There were 25 ADHD cases among the exposed children (3.8%), and 114 (3.5%) and 148 (3.6%) cases in the comparison groups, respectively. Children exposed to triptans had no increased risk of ADHD compared to 1) unexposed children whose mothers had migraine in pregnancy (HR 1.14, 95% CI 0.70-1.84), and 2) unexposed children whose mothers had migraine before pregnancy only (HR 0.91, 95% CI 0.54-1.53).

Conclusions: The results of this study are reassuring, suggesting no increased risk of childhood ADHD associated with prenatal triptan exposure.

E9

The Young-HUNT COVID Survey

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Introduction: Children and adolescents are less at risk for severe COVID-19 disease. Even so, the pandemic has significantly affected adolescent's lives due to instructed social distancing and interruption of school routines to prevent further large-scale disease outbreaks. Fear of disease risk may also generally have affected mental health and well-being. In addition to direct effects on mental health and well-being, there have been concerns that children and adolescents with fewer resources would be especially vulnerable with further adverse effects on mental health and quality of life.

Aims: Collect data to study changes in mental health, life satisfaction, well-being, healthcare utilization and lifestyle related to the COVID-19 restrictions in adolescents aged 16-20 years in Trøndelag, including previously participants in the Young-HUNT4 Survey (2017-19).

Methods: Senior High School students (32 schools) in the county of Trøndelag were in spring 2021 invited to participate in the electronic questionnaire survey, The Young-HUNT COVID Survey.

Results: The strike among teachers, cancelled exams and lock-down at many schools right after survey start resulted in a lower participation rate than anticipated, in total n = 4731, 33%. The participants, 2414 girls and 2317 boys, had a mean age of 18.1 years. Of the 1857 adolescents living in the northern region of the county, 40% had filled in the questionnaire. Of these, 1466 were former Young-HUNT4 participants. The dataset is a valuable source for studying potential health consequences of the COVID-19 pandemic focusing on for instance time trends, regional differences among sub-groups and longitudinal changes in adolescents.

Descriptive characterization and preliminary results will be presented.

E10

Within-host seasonal immunity and seasonal influenza – trajectories of gene expression from immune cells in blood – the NOWAC postgenome biobank

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Introduction: Throughout evolution seasons have been defined by the same photoperiods or by secondary seasonal changes in humidity and temperature. Viruses have over millions of years adapted to these seasons creating different seasonal virus infections. Knowledge of the biological background could be important for the handling of future seasonal covid (corona) pandemics.

Aims: Here we will explore variations in the yearly influenza epidemics towards within-host seasonal immunity changes using trajectories of gene expression from immune cells in blood to test the hypothesis that seasonal within-host changes in gene expression occurs before the season of virus epidemics.

Material: Gene expression analyses were based on the NOWAC postgenome biobank that was created for gene expression analyses by collecting 50 000 blood Rnase buffered samples from a random sample of Norwegian women. As test set 425 samples earlier used as controls for breast cancer in nested case-control series were used and as retest set another 432 samples. Gene expressions were based on Illumina microarrays. We used a sinus function with both a sinus and a cosinus term. Information on seasonal influenza for the years of collecting blood samples, 2003-6, was obtained from the surveillance system of MSIS, as weekly percentages of sickleaves for influenza.

Results: In the test set close to 50% of 6118 genes were significant with 416 with a fold change >0.2. In the retest set 234 genes were significant showing the same seasonality. The significant genes in the test set had two distinct spikes, in august-september and in february-march in a model with both seasonal and flu terms presented as one year. The trajectories of the genes expression over the four years will be analysed together with the yearly flu.

Conclusion: To be drawn when the analyses are finalized.

E11

Association of insomnia symptoms with the risk of bloodstream infections: results from the prospective population-based HUNT Study in Norway

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Introduction: There is evidence of a complex and bidirectional relationship between sleep and the immune system (1). Research suggests a decreased immune function with increasing symptoms of insomnia (2). No other large prospective studies have investigated the associations between insomnia and bloodstream infections in a general population. Insomnia is a common condition in the general population, thus, it may be an important preventable risk factor for bloodstream infections (BSI).

Aims: To assess if symptoms of insomnia are associated with BSIs and mortality due to BSI in a general population.

Methods: Our study consists of 53,536 men and women participating in the second HUNT study (HUNT2 1995-97) and answering the insomnia questionnaire. Data from HUNT2 was linked to prospective information from hospital-based BSI registry in Nord-Trøndelag Hospital Trust (HNT HF) on clinically relevant BSI up until 2011. Using cox regression we estimated hazard ratios and 95% confidence intervals to assess the risk associated with severity of each insomnia symptom and first-time BSI episode as well as BSI mortality defined as death within 30 days of BSI.

Results: We found a modest relative increased risk of BSI with having symptoms of insomnia almost every night/often; Having difficulties maintaining sleep (HR 1.14, 95% CI 0.96–1.34); Difficulties initiating sleep (1.19, 95% CI 1.01–1.18); Having a feeling of non-restorative sleep (HR 1.23, 95% CI 1.04–1.46) and; Cumulative insomnia symptoms (HR 1.39, 95% CI 1.04–1.87). Being troubled by insomnia to such a degree that it affected work performance was associated with a 41% increased risk of bloodstream infections (HR 1.41, 95% CI 1.08–1.84).

Conclusions: We found evidence of a moderately increased risk of BSI among patients with symptoms of insomnia.

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E12

Prevalence of mental disorders and suicidality in the general population before and during the first six months of the COVID-19 pandemic in Norway

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Introduction: Both globally and in Norway there have been concerns that the COVID-19 pandemic will lead to a mental health crisis. As a result, there has been a rapid propagation of surveys exploring mental health issues during the pandemic. A deterioration of population mental health has been found in several of these studies. However, most of these surveys suffers from important limitations in terms of recruitment strategy, representativeness, measures and reference period. Data from an ongoing Norwegian epidemiological diagnostic psychiatric interview survey, conducted from January to September 2020, allowed for comparison of mental disorder and suicidal ideation prevalence from before through different phases of the first six months of the pandemic.

Aims: To compare prevalence of i) current mental disorders, ii) suicidal ideation, and iii) suicide deaths before and during different phases in the first six months of the COVID-19 pandemic in the general adult population and among groups with presumed risk for increased mental health problems during the pandemic.

Methods: Participants from the Trøndelag Health Study (HUNT) in Trondheim were recruited through repeated probability sampling. Using the Composite International Diagnostic Interview (CIDI 5.0) (n=2,154), current prevalence of mental disorders was examined in repeated cross-sectional analyses. Data on suicide was retrieved from the Norwegian Cause of Death Registry and compared with 2014-2018 for the months March-May.

Results: Prevalence of mental disorders decreased significantly from the pre-pandemic phase (January 28th to March 11th 2020; 15.3% [95% CI 12.4-18.8]) to the first pandemic phase (March 12th – May 31st; 8.7% [6.8-11.0]) and was fairly stable through the interim phase (June 1st July 31st; 14.2% [11.4-17.5]) and the second phase (August 1st-September 18th; 11.9% [9.0-15.6]). Suicidal ideation was non-significantly (n.s) increased during the pandemic. Suicide deaths were 15% lower (n.s) in March-May 2020 (n=140) compared with the same months pooled over 2014-2018 (n=165).

Conclusion: We found no increase in mental disorders or suicides during the COVID-19 pandemic up through early autumn 2020. COVID-19 related mortality, transmission rates, intensity and implementation of measures and lockdowns have been less severe in Norway than many other countries and could account for these results.

P1

Evaluation of data consistency extracted from Sri Lankan paper-based pregnancy records

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Introduction: In the Sri Lankan public healthcare system, paper-based pregnancy records are always kept with the pregnant woman so she may receive antenatal health care at any facility with full health information. This record-keeping system may also serve as a promising recruitment tool for researchers conducting antenatal and postpartum health surveys.

Aims: The purpose of this study is to assess the agreement between similar data on the handheld pregnancy records and investigate the utility of handheld pregnancy records for health survey research.

Methods: This was a cross-sectional study including 505 pregnant women in Galle, Sri Lanka visiting 4 local antenatal clinics. We copied information from handheld pregnancy records into a digital server.

Results: We found data for maternal BMI, history of abortion, history of Caesarean section, subfertility, blood type, pre-eclampsia, thyroid health, ectopic pregnancy, and diabetes to be reported on 2 or more sections of the record. Patients with BMI > 25 were not categorized as having high BMI in 65% of cases (85/130), and patients with BMI <20 were not categorized as low BMI in 24% of cases (21/86). Abortion was reported consistently across the record in 82% of cases (50/61). Caesarean section was reported consistently in 79% of records (60/76). Subfertility was reported consistently in 32% of records (12/38). Negative blood type as an antenatal risk factor was denoted for 85% of all reported cases with negative blood type (11/13). Pre-eclampsia was not reported consistently in any of the 31 records indicating pre-eclampsia. Thyroid health problems were reported consistently in 44% of cases (7/16). The only ectopic pregnancy was not consistently reported. Of the 32 records indicating diabetes, only one was reported consistently (3%).

Conclusions: Researchers wishing to use handheld pregnancy records as a health survey tool in Sri Lanka should be aware that inconsistencies are common. Researchers should also take care to understand the meaning of each record section, as some of the very low agreement we found may be attributed to ambiguity regarding what information was requested, such as gestational versus chronic diabetes, or present versus history of pre-eclampsia.

P2

The Centre for Disease Burden at the Norwegian Institute of Public Health

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Introduction: The Centre for Disease Burden at the Norwegian Institute of Public Health (NIPH) was established in 2015. The Centre is responsible for the work with disease burden analyses at NIPH, for maintaining a close collaboration with Institute of Health Metrics and Evaluation (IHME), which coordinates the Global Burden of Disease (GBD) study, and for coordinating a network of national researchers interested in disease burden analyses. The Centre is also an important actor into NIPHs work with forecasting analyses.

Aim: To build network and collaboration between researchers at the Centre and other researchers/ institutions in Norway who are interested in burden of disease and forecasting analyses.

Methods: The Centre has several activities directed towards building up a researcher network around disease burden analyses in Norway; i) coordinating the analyses and writing of research articles and reports describing disease burden in the Nordic countries, Norway and the fylker, ii) giving input to measures to be included in health surveys that can give basis for Norwegian burden of disease estimates, iii) acting as GBDs link to data from Norwegian health surveys and registries, and iv) arranging workshops and seminars on disease burden analyses.

Conclusion: The Centre for Disease Burden at NIPH aims for collaboration with researchers across Norway with an interest in disease burden and forecasting analyses. Interested researchers may contact acting director (ann.kristin.knudsen@fhi.no).

P3

A life-course approach to prevent noncommunicable diseases in an ageing population – NCDNOR

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Introduction: The preventive potential of noncommunicable diseases (NCDs) is traditionally estimated separately for each NCD, but the lifetime risk of NCDs, and how these diseases co-occur are uncertain, as are the role of clustering of life conditions, shared risk factors, biomarkers and mental health throughout the life course. Thus, we need to achieve new knowledge in the prevention of NCDs. The project is a collaboration between The Norwegian Institute of Public Health, The Norwegian University of Science and Technology, The Cancer Registry of Norway and UiT The Arctic University of Tromsø, and a strong group of users and end-user partners such as The Norwegian Health Association, The Norwegian Directorate of Health, The County Council of Trøndelag, and Tromsø and Levanger municipalities.

Aims: Our concept includes consolidation of NCD endpoints across somatic disciplines, examining joint and interacting effects of socioeconomic circumstances, life conditions, health behaviours, biological markers and mental health throughout the life-course to elucidate plausible underlying causal mechanisms with the ultimate goal of identifying targets for prevention.

Main objectives:

1. To quantify patterns of NCD occurrence, multimorbidity and polypharmacy of NCDs to recognise underlying potential causal mechanisms by integrating social contexts and biomarkers and do cost-effectiveness analysis.
2. To elucidate how socioeconomic position ultimately translates into inequalities in health taking shared risk factors among NCDs into account.

Methods: We will use the largest and most comprehensive population-based long-term prospective cohorts, mandatory national registries and biobanks to provide adjusted analyses applicable for the complete Norwegian population.

Results: We will give an overview of the project and some preliminary descriptive results.

P4

Tobacco use and risk of being infected with SARS-CoV-2: Results from MoBa

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Introduction: While several studies show associations between smoking and poorer disease prognoses in covid-19 patients, clear evidence of a higher susceptibility to SARS-CoV-2 infection among smokers has not been established.

Aims: Our primary aim was to investigate associations between cigarette smoking or use of other nicotine-containing products and a positive SARS-CoV-2 test. A secondary aim was to examine associations between tobacco use and having been tested for SARS-CoV-2 in the same period.

Methods: Questionnaires were distributed to participants in the Norwegian Mother, Father and Child Cohort Study every 14 days since March 2020. Tobacco use and testing behavior during the pandemic were recorded by participants (n=78,860). SARS-CoV-2 infection status was assessed by linkage to The Norwegian Surveillance System for Communicable Diseases (MSIS) in May 2021. We examined associations using logistic regression models stratified by gender and adjusted for age, education level, geographical region, number of household members, and work situation.

Results: About 2% were registered with a covid-19 diagnosis and 49% of women and 39% of men reported to have been tested for SARS-CoV-2. Snus use was more common among men (26%) than women (9%), while smoking was less common both among men (5%) and women (7%). We found no clear associations between smoking or snus and a covid-19 diagnosis among men. For women, the associations between tobacco use and a diagnosis were conflicting, indicating that smoking was negatively associated with a diagnosis (adjusted OR 0.65, 95% CI 0.43, 0.94), while increasing snus use up to 5-9 cans per month was associated with higher OR for getting a covid-19 diagnosis among women. For testing behavior, we found no associations with smoking (OR 0.93, 91% CI 0.81, 1.07 for men and OR 1.05, 95% CI 0.96, 1.14 for women), while both male and female snus users had higher OR for having been tested, 1.07 (95% CI 1.01, 1.14) for men and 1.20 (95% CI 1.10, 1.30) for women.

Conclusions: Smoking and snus use were associated with acquiring a SARS-CoV-2 infection, but in opposite directions. This inconsistency was not explained by testing behavior among smokers and snus users.

P5

Digitization of historical military health records – presentations from the first investigations

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Introduction: Military conscription health records are stored as paper records at the National Archives for cohorts born prior to 1957. However, the size and contents of this data source was unknown.

Aims: To estimate the quantity and quality of military health records stored at The Armed Forces section of the National Archives.

Methods: We reviewed all military personnel folders in the 1950 birth cohort and digitized specific health information. This included self-declaration of health, medical examination scheme for conscripts, and cognitive tests. We also searched for other birth cohorts with similar military health information, and reviewed a portion of the documents for around 150 random personnel folders per cohort born between 1918 and 1957.

Results: From the 1950 birth cohort, 17 364 military personnel folders were available at the National Archives. The information from the individual folders were of high quality.

We estimated that folders can be retrieved for approximately 40-60% of the male cohorts born between 1941 and 1957. These health records were consistent and contained detailed health information.

Only a small portion of folders from birth cohorts prior to 1941 have been filed in the National Archives. The health data in these folders is inconsistent and sporadic compared to later born cohorts.

Military personnel folders are also stored at other locations outside the National Archive, such as in local archives within the Armed Forces. These were unavailable for this project. However, these can be included to obtain more complete birth cohorts.

Conclusion: Personnel folders from male birth cohorts 1941-1957 are available at the National Archives and most likely includes 40-60% of the male birth cohorts. This data source may provide useful health information for multiple purposes, including research.

P6

Changes in cancer incidence and cause-specific mortality in Royal Norwegian Navy submariners between two separate follow-up periods

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Introduction: A cohort of 2663 submariners who served in the Royal Norwegian Navy for variable lengths of time between 1950 and 2004 were previously followed up for cancer through 2008 and for mortality through 2007. Compared to the general Norwegian population, there was a statistically significant elevation of overall cancer incidence, bladder cancer and non-melanoma skin cancer by 15%, 53% and 85%, respectively. However, a "healthy soldier effect" was seen in terms of 15% lower total mortality, largely due to a 35% reduction in external cause mortality. We extended the follow-up for cancer and mortality through 2017 and 2019, respectively.

Aims: To investigate possible changes in cancer- and mortality risk between the two follow-up periods.

Methods: Standardized incidence ratios for cancer (SIR) and mortality ratios (SMR) were calculated from national rates for the two follow-up periods separately. Ninety-five percent confidence intervals (CI) were computed on the assumption of a Poisson distribution of the observed cancer cases and deaths.

Results: From the first to the last of the follow-up periods,

- the numbers of cancers and deaths were doubled (to 638 and 634 cases, respectively)
- the overall cancer risk remained elevated (SIR=1.18).
- the risk of non-melanoma skin cancer remained elevated (SIR=2.19)
- melanoma skin cancer incidence developed a statistically significant elevation (SIR=1.66)
- SIR for bladder cancer was no longer statistically significant (1.43)
- the "healthy soldier effect" for total mortality disappeared (SMR=0.94)
- a statistically significantly reduction in mortality from circulatory diseases emerged (SMR=0.77)
- a further reduction in external cause mortality was seen (SMR=0.37)

Conclusions: The elevated overall cancer incidence observed during the previous follow-up was still present at approximately the same level. The "healthy soldier effect" for total mortality was no longer present.

P7

More than 30 years with the Norwegian Arthroplasty Register – a journey from implant to patient focus

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Introduction: The Norwegian Arthroplasty Register (NAR) started registration of total hip arthroplasties in 1987. In 1994, the registration was expanded to include all types of joint arthroplasties. The main purpose of the NAR was to identify poorly performing implants and operation methods as early as possible, and stop the use of these. Identification of poor implants was in general done by using traditional survival analysis. In 2017, registration of patient reported outcomes (PROM) was included making it possible to measure patient function, pain and quality of life after surgery. This expanded the possibility in defining relevant endpoints.

Aims: To present the NAR and the potential to link this data source to other registries and health surveys.

Methods: Data from both primary and revision arthroplasties are reported to the register. Reported data includes details on the surgical procedure and implants with catalogue numbers along with patient related information. The patients report PROM prior to the operation and at 1, 6 and 10 years post-operatively. The results are given as survival time for the implants, adherence with pre-defined quality indicators, and scores from PROM. The register also tracks the performance of implants and operation methods in linkage with other registers or health surveys to view the complete patient history in order to give the patients the best possible treatment.

Results: Each year close to 20,000 operations (10,000 hips) are reported to the NAR. At present there are more than 200,000 hip arthroplasties recorded in the register. The NAR has close to 100% coverage of primary operations. The register produces an annual report including results on hospital level. The register is involved in many research projects, including linkage studies with the Norwegian Patient Registry and the HUNT study. Since 2009, the NAR has been part of The Norwegian National Advisory Unit on Arthroplasty and Hip fractures.

Conclusions: The NAR is a well performing register and has several ongoing linkage projects with other registries and health surveys. There is a high potential in expanding this use of data from the NAR as outcome based on linkage to other registries or projects.

P8

Country of first birth and neonatal outcomes in migrant and Norwegian-born parous women in Norway: a population-based study

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Introduction: With increasing international migration, more knowledge is needed regarding migrant women's pregnancies and births. Migrant families represent great diversity and investigating the risk of adverse neonatal outcomes in sub-groups of migrant women is therefore vital.

Aims: To investigate associations between country of a woman's first birth and adverse neonatal outcomes in migrant and non-migrant women giving birth in Norway.

Methods: Data were retrieved from the Medical Birth Registry of Norway and Statistics Norway. We investigated associations between country of a woman's first birth and adverse neonatal outcomes (very preterm birth (22+0-31+6 gestational weeks), moderately preterm birth (32+0-36+6 gestational weeks), post-term birth (≥42 gestational weeks), small for gestational age, large for gestational age, low Apgar score (≤7 at 5 minutes), stillbirth and neonatal death) in multiparous migrant and non-migrant women (1990-2016). Associations were investigated using multiple logistic regression and reported as adjusted odds ratios (aORs) with 95% confidence intervals (CI).

Results: Multiparous migrant women with a first birth before immigration to Norway had increased odds of adverse outcomes in subsequent births relative to those with a first birth after immigration: very preterm birth (aOR=1.27; CI 1.09-1.48), moderately preterm birth (aOR=1.10; CI 1.02-1.18), post-term birth (aOR=1.19; CI 1.11-1.27), low Apgar score (aOR=1.27; CI 1.16-1.39) and stillbirth (aOR=1.29; CI 1.05-1.58). Similar results were found in births to Norwegian-born women who had their first baby abroad.

Conclusions: The increased odds of adverse neonatal outcomes for migrant and Norwegian-born women who had their first births outside Norway should serve as a reminder of the importance of taking a careful obstetric history in these parous women to ensure appropriate care for their subsequent pregnancies and births in Norway.

P9

Network on the Coordination and Harmonisation of European Occupational Cohorts (OMEGA-NET): Achievements after 4 years of networking, collaboration, and training

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Introduction: OMEGA-NET (2017-2022) is a COST Action network, funded by EU, involving about 200 occupational health researchers in 40 countries, including non-European partners.

Aims: The goal is to create a network to optimize the coordination and use of occupational, industrial, and population cohorts in Europe and beyond, to inform evidence-based interventions and policy.

Methods: A range of networking tools are available for COST Actions, such as meetings, workshops, conferences, training schools, short-term scientific missions (STSMs) and dissemination activities.

Results: Despite COVID-19 restrictions, the network has made great achievements, including two online searchable inventories: the *Inventory of Occupational Cohorts*, with more than 140 cohorts registered, and the *Inventory of Occupational Exposure Tools,* with about 75 tools, of which half are Job-Exposure Matrices. Working groups have discussed and written papers on harmonisation and standardisation of occupational exposure and health outcome information. So far, 15 papers are published, some as editorials or position papers, others are accepted or in progress. A webinar series, available on YouTube, present work of OMEGA-NET. The Action also includes opportunities for networking, leadership, and training for early career researchers in occupational epidemiology and exposure assessment, and visits to other research institutions (STSMs), as well as stakeholder engagement.

Conclusions: OMEGA-NET is the largest coordination activity on occupational health globally and will substantially enhance future European and international research.

P10

Return to work as a long term-outcome measure in sepsis survivors: A systematic review

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Introduction: Return to work (RtW) is a recommended measure of long-term functional level after critical disease. Being a sepsis survivor is associated with new and worsened physical and mental status that can affect RtW.

Aims: The purpose of this review was to conduct a systematic literature search investigating how RtW after sepsis hospitalization is measured, to find RtW rate in sepsis survivors and if any determinants for RtW are identified.

Methods: The literature search and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses Guidelines (PRISMA). The search was conducted in three databases, PubMed, EMBASE and CINAHL. Search was last updated 3 June 2021.

Results: Of 173 articles screened, eight studies (4.6%) met the criteria for critical appraisal. One study was published in USA, one in Australia and six in Europe. The size of the investigated cohorts ranged from N= 21 to N= 5762. Median age for the sample population ranged from 38 to 59 years. Follow-up for RtW varied from 2 months to 60 months. RtW was measured with self-composed non-validated questionaries in six articles, national databases were used to collect data in one study, and one combined income database and self-composed questionnaire. Some studies reported if survivors had RtW, others reported if they partly or fully had RtW, some reported economic consequences and use of government funding. 24 to 86 % of sepsis patients were able to RtW and RtW increased by time after discharge. Length of hospital stay and longer mechanical ventilation seems to be determinants for RtW in sepsis survivors.

Conclusions: There is an increasing level of RtW rate with time after critical illness, but the RTW rates diverge. Use of a validated employment tool is absent, and therefore it is difficult to do a meta-analysis of RtW. It is thus crucial for the knowledge base that critical-care societies finish the work validating RtW instruments. Finding return to work determinants can help care givers to address important multifaceted morbidity after sepsis and improve outcome.

P11

The association of comorbidity clusters with long-term survival and incidence of exacerbation in a COPD cohort. The HUNT Study, Norway

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Background: COPD is a heterogeneous disease often viewed as part of a multimorbidity complex. There is a need for better phenotyping of the disease, characterization of its interplay with other comorbidities and its association to long-term outcomes.

Aims: This study aims to examine how clusters of comorbidities are associated with severe exacerbations and mortality in COPD.

Methods: Participants with potential COPD were recruited from the second (1995–97) and third (2006–08) survey of the HUNT Study and followed until April 2020. Ten objectively identified comorbidities were clustered using self-organizing maps. Severe COPD exacerbations requiring hospitalization were assessed using hospital data. All-cause mortality was collected from national registries. Multivariable Cox regression was used to calculate hazard ratios (HR) with 95% confidence intervals (CI) for the association between comorbidity clusters and all-cause mortality. Poisson regression was used to calculate incidence rate ratios (IRR) with 95% CI for the cumulative number of severe exacerbations for each cluster.

Results: Five distinct clusters were identified, including "less comorbidity", "psychological", "cardiovascular", "metabolic" and "cachectic" clusters. Using the less comorbidity cluster as reference, the psychological and cachectic clusters were associated with all-cause mortality; HR 1.23 (1.04-1.45) and HR 1.83 (1.52-2.20), adjusted for age and sex. The same clusters also had increased risk of exacerbations; unadjusted IRR of 1.24 (95% CI 1.04-1.48) and 1.50 (95% CI 1.23-1.83), correspondingly.

Conclusions: During 25 years of follow-up, individuals in the psychological and cachectic clusters had increased mortality. Furthermore, these clusters were associated with increased risk of severe COPD exacerbations.

P12

Does pain tolerance mediate the effect of physical activity on new onset chronic pain in the general population?

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Introduction: Physical activity (PA) may influence both pain sensitivity and the risk of experiencing chronic pain. The former is increasingly being viewed as a possible predictor of chronic pain development. There is a lack of knowledge regarding the mechanisms acting between PA, chronic pain, and pain tolerance.

Aims: To assess whether PA influences risk of chronic pain through affecting pain sensitivity.

Methods: We will use data from the 6th and 7th surveys of the population-based Tromsø Study. Analyses will include participants with information on baseline leisure-time PA and level of pain tolerance assessed with the cold-pressor test (3°C circulating water for a maximum of 106 seconds). We will investigate possible mediation of pain tolerance between baseline leisure-time PA and chronic pain, using longitudinal log-linear mediation analysis with natural effects. We will also assess the effect of different pain tolerance modalities studied in the 7th survey, i.e. cold-pressor vs. computerized cuff-pressure algometry, as well as different types of chronic pain definitions.

Results: Selection criteria yield 6,250 participants (51% women; mean age: 54 years) eligible for inclusion into analysis.

Conclusions: Our data are uniquely situated for investigating mechanisms of the relationships between physical activity and pain in the general population, accounting for a broad range of covariables. Our analyses aim to disentangle the direct and indirect effect of PA on chronic pain. This has never been done in a sample of this magnitude and generalizability.

P13

Use of ADHD medication in pregnancy in Norway and Sweden, 2010-2019

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Introduction: Use of ADHD medication in adults has increased in the last two decades in the Nordic countries, including among women of childbearing age.

Aims: The objectives of this study were to describe recent trends in ADHD medication use in pregnancy in Norway and Sweden, characteristics of users, and patterns of use.

Methods: We studied pregnancies resulting in births at 22-44 gestational weeks using linked data from the birth and drug registers of Norway (2010-2018; N=524,583) and Sweden (2010-2019; N=1,084,441). We identified pregnancies with ≥1 prescription filled from 3 months before pregnancy to delivery for ADHD medications (amphetamine, dexamphetamine, methylphenidate, atomoxetine, lisdexamfetamine, guanfacine). We compared characteristics of those who used any ADHD medication in pregnancy to no use. Among pregnancies with any ADHD medication use, discontinuation was defined as no use after first trimester and initiation as use only after first trimester.

Results: ADHD medication use in pregnancy increased by 2.9 per 1000 pregnancies in Norway (from 2.6 to 5.5/1000) and by 5.9/1000 in Sweden (from 1.6 to 7.5/1000), mainly driven by methylphenidate and since 2015/2016 by lisdexamfetamine in Sweden. Women who used ADHD medication were younger, less likely to have had a prior birth or to be married/cohabiting, and more likely to smoke and use other psychotropic medication. They had particularly high use of co-medication with antidepressants, anxiolytics/hypnotics, and opioids: 42% in Norway and 64% in Sweden used ≥1 additional class of psychotropic medication. Most women discontinued ADHD medication in pregnancy (85% Norway, 78% Sweden) and very few initiated (0.8% Norway, 1.2% Sweden).

Conclusions: ADHD medication use during pregnancy increased in Norway and Sweden in the last decade, however discontinuation rates during pregnancy are high. Those who used ADHD medication had more risk factors for pregnancy complications including low parity, smoking, and other psychotropic drug use, which is important to account for in future drug safety studies.

P14

Validation of a web-based food frequency questionnaire for dietary intake assessment in the Hordaland Health Study

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Introduction: Valid assessment of dietary intake is essential when exploring associations between dietary factors and disease, as imprecise dietary intake data may reduce our understanding of such associations. All dietary assessment methods inevitably introduce measurement error to some extent, which ideally should be considered during data analysis and interpretation. Being aware of this, methodological studies should be conducted to address how well a given assessment method captures dietary intake, and to highlight the extent and direction of the measurement error.

Aims: Within a sub-group of the community-based Hordaland Health Study (HUSK3), we conduct a validation study of an extensive web-based food-frequency questionnaire (web-FFQ) developed by the Department of Nutrition, University of Oslo. We compare dietary intake registered by the web-FFQ with dietary intake from repeat administrations of 24-hour dietary recall interviews (24-HDRs).

Methods: The validation study is based on data from HUSK3 which included 2192 men and women born 1950-51. All HUSK3 participants were requested to complete the web-FFQ as a part of the health survey. For the present sub-study, 175 participants granted their consent to be contacted for repeated 24-HDRs via telephone. A total of 120 participants completed at least two 24-HDRs while 67 participants completed three 24-HDRs. Information on intake of foods, energy and nutrients was generated through Kostberegningssystemet (KBS), a software developed at the Department of Nutrition, University of Oslo.

Results: Preliminary analyses in participants completing three 24-HDRs, show that intakes of energy, protein, fat, carbohydrates, fiber and micronutrients were higher in the FFQ than in the 24-HDRs. The FFQ overestimated the intakes of most food groups. Spearman's rank correlation coefficient ranged from 0.17 (cakes) to 0.71 (juice) for foods, and from 0.19 (iodine) to 0.69 (vitamin D) for nutrients. Agreement of quartile membership indicated that foods eaten frequently were ranked quite similarly by both methods, while foods eaten infrequently were misclassified to a greater extent.

Conclusion: The FFQ seemed to rank individuals well for foods consumed frequently, while ranking abilities were weaker for foods consumed less frequently. Ranking abilities of the FFQ varied within the category of macronutrients and micronutrients.

P15

Social inequality in prevalence and clustering of risk factors for non-communicable diseases – The seventh survey of the Tromsø Study 2015-2016

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Introduction: Levels of risk factors for non-communicable diseases (NCDs) vary with socioeconomic status (SES). There is a need for in-depth insights into the socioeconomic differences in the distribution and clustering of modifiable behavioral NCD risk factors (tobacco use, physical inactivity, unhealthy diet, and harmful use of alcohol) and underlying metabolic risk factors (overweight/obesity, and elevated blood pressure, blood cholesterol and blood glucose) to identify new target areas for prevention strategies.

Aim: We aim to study the association between SES and prevalence and clustering of NCD risk factors in a general Norwegian population.

Methods: We use data from women and men aged 40-49 years in the seventh survey of the population-based Tromsø Study (Tromsø municipality, Norway) (2015-2016). Information on indicators of smoking, physical inactivity (sedentary activity in leisure time), low fruit/vegetable intake (<5 portions/day), alcohol binge drinking (more than 6 units in one occasion, at least monthly), obesity (body mass index ≥ 30 kg/m^2), hypertension (blood pressure ≥140/90 mmHg and/or use of antihypertensives), hypercholesterolemia (serum total cholesterol ≥5.0 and/or use of lipid-lowering drugs) and pre-diabetes (HbA1c 39-46 mmol/mol and no self-reported diabetes) was obtained by questionnaires, biological sampling and clinical examinations. Educational level was self-reported (primary, secondary, short and long tertiary).

Results: Preliminary descriptive analysis shows that in women and men aged 40-49 years (N=6427, 53% women) there was an inverse educational gradient in all NCD risk factors. The prevalence of risk factors in the primary (n=625) compared to long tertiary (n=2629) educational groups was 32% vs. 6% for smoking, 27% vs. 11% for physical inactivity, 98% vs. 92% for low fruit/vegetable intake, 19% vs. 12% for alcohol binge drinking, 33% vs. 19% for obesity, 26% vs. 15% for hypertension, 70% vs. 57% for hypercholesterolemia and 26% vs. 17% for pre-diabetes.

Conclusions: In a general population of men and women aged 40-49 years, there was a clear educational gradient in prevalence of NCD behavioral risk factors and underlying metabolic risk factors, with higher prevalence of unfavorable risk in lower compared to higher educational groups.

P16

Maternal intake of sweetened carbonated beverages during pregnancy and association to ADHD symptoms in the offspring. A study from the Norwegian, Mother, Father and Child Cohort Study (MoBa)

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Introduction: The intrauterine period is of importance for later health and development of children. Neurodevelopmental disorders typically become apparent during childhood. They are an important cause of long-term disability. Attention-deficit/hyperactivity disorder (ADHD) is the most common of these conditions. A number of perinatal risk factors have been associated with later ADHD. We studied the association between maternal intake of sweetened carbonated beverages (SCB) during pregnancy and later ADHD symptoms in the offspring.

Methods: Our study was based on the Norwegian Mother, Father and Child Cohort Study (MoBa) and the Medical Birth Registry of Norway. Mothers' diet mid-pregnancy was assessed using a food frequency questionnaire (FFQ). We included 39 870 mothers who responded to the FFQ as wells as a questionnaire when their child was 8 years of age. Exposure was defined as maternal daily intake of SCB. Women with no daily intake of SCB served as reference. The study outcome was offspring ADHD symptoms. These symptoms were evaluated as a continuous standardized ADHD score and as a binary outcome of six or more ADHD symptoms vs. five symptoms or less. We analysed the associations using log-binomial regression and linear mixed regression models with adjustment for covariates.

Results: We found in this large, population-based pregnancy cohort study that maternal intake of SCB in pregnancy was associated with an increase in ADHD symptoms among offspring at 8 years of age. We attempted to control for unmeasured familiar factors in a sibling analysis, this strengthened the evidence for an association between the highest daily SCB intake and ADHD symptoms. However, the magnitude of associations we find in this study are weak, indicating SCB may only play a marginal role in the aetiology of ADHD.

Conclusions: Further research into causal agents of ADHD symptoms are warranted. SCB are common diet exposures, and even a small reduction of risk may still be of importance for children's ADHD symptoms at the population level.

P17

A mother with a complication in her last pregnancy, does she have similar excess risk as seen in 1st pregnancies? A register-based cohort study

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Introduction: Pregnancy complications in a woman's first pregnancy seem to increase risk of later cardiovascular disease (CVD) morbidity and mortality. However, less knowledge is found on the association between pregnancy complications in women's last pregnancy and CVD outcomes.

Aim: To examine pregnancy complications (preeclampsia, preterm delivery, and small for gestational age) in women's last pregnancy and their relation to later maternal CVD death, accounting for complete reproduction.

Methods: In this nationwide population-based cohort study, we have utilized registry-based data from the Medical Birth Registry of Norway (1967-2020) and the Cause of Death Registry. We followed mothers from date of their last childbirth to death or until December 31st 2020, whichever occurred first. Cox proportional hazards regression analyses were used to study maternal CVD death at the age of 40-69 years by pregnancy complications, adjusting for maternal age at first delivery and education.

Results: We found an elevated risk for premature CVD death for mothers who experienced any of the complications in their last pregnancy. Compared to mothers with two births without complications, the risk for CVD death was higher among mothers who had complications in the last pregnancy with two births (adjusted hazard ratio (aHR) 1.83; 95% confidence interval (CI): 2.60–2.09) and three births (aHR: 2.09; 95% CI: 1.72–2.54).

Conclusions: The risk for premature CVD death was higher among mothers who had complications in the last pregnancy and mothers who experienced complications in successive pregnancies.

P18

Causal effect of alternative treatment strategies on survival

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Introduction: In the clinical setting of patients on a waiting list for treatment, clinicians are faced with the decision of which patient(s) to treat once the treatment becomes available. Examples include waiting lists for organ transplantation, and ventilator availability at intensive care units. Given that we've observed data from such a decision process, we ask: Could the clinicians have done better? Would a different treatment strategy result in higher survival rates in the cohort?

Aims: To estimate the effect of different treatment strategies on survival outcomes.

Methods: We formulate causal models for survival data in the framework of counting processes. By specifying the observed treatment strategy, that is, the strategy followed by the clinicians, as an additive hazards model, we are able to express alternative hypothetical strategies that are proportional to this hazard model. In essence, the proportionality factor allows us to change the rate of treatment among patients and across follow-up time. Next, we impose the restriction that the marginal cumulative hazard for treatment is unchanged for any hypothetical treatment strategy compared to the observed strategy. This restriction keeps us from venturing into a world where treatment is more abundant than in the real world.

Results: A method for evaluating alternative treatment strategies occurring in continuous time, in the setting of limited resources, with respect to survival outcomes.

P19

A national initiative for a more inclusive working life in Norway and its effect on return-to-work after sickness absence – a multi-state longitudinal cohort study

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Introduction: Sickness absence (SA) from work is an important long-term health outcome for the individual, as well as a social and financial burden for society. To reduce SA and increase work participation, the tripartite Agreement for a More Inclusive Working Life (IA) was established in Norway in 2001. IA companies were given measures to prevent and reduce SA. However, systematic evaluations of this initiative are sparse.

Aims: Estimate the average individual effect of having IA at the time of entering SA, on later return-to-work and other work-related outcomes for the following 500 days. A secondary objective was to study how effects varied between women and men, and individuals with either musculoskeletal or psychological diagnoses.

Methods: Every individual born in Norway 1967-1976 who entered full-time SA during 2004-2011, with limited earlier SA, were included (n = 187 930). Individual characteristics and longitudinal records of SA, work and education were obtained from linked population-wide registries. The average individual effects of having access to IA, were assessed using differences in state probabilities over 500 days, estimated by hazard-based multi-state models, adjusting for confounding by inverse probability weighting.

Results: IA increased the probability of work after entering SA, with the largest effect after 29 days (3.4 percentage points higher (95% confidence interval: 2.5–4.3)). Difference in one-year expected length of stay was 8.4 more days (4.9–11.9) for work, 7.6 (4.8–10.3) fewer days in full-time SA and 1.6 (-0.2–3.4) fewer days in non-employment. Similar trends were found within subgroups of sex and musculoskeletal and psychological diagnoses.

Conclusions: Working in an IA company improved individuals' return-to-work after a first long-term SA episode.

P20

Mental health care utilization in pregnant women with depression and/or anxiety according to longitudinal antidepressant fill trajectories: an interrupted time-series analysis

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Objectives: To assess mental health care utilization patterns in pregnant women with depression and/or anxiety in Norway according to longitudinal antidepressant fill trajectories before, during, and after pregnancy.

Method: We conducted a registry-linkage cohort study of pregnancies within women having outpatient visit for depression and/or anxiety and antidepressant fills in the six months prior to pregnancy identified from the Medical Birth Registry of Norway (2009-2018), linked to other national registries. Mental health care utilization patterns were investigated using interrupted time-series analyses by modelling consultation rates for depression/anxiety with psychiatric specialists of outpatient clinics, contract psychologists and contract psychiatrists. We identified longitudinal antidepressant fill trajectories in the time window including six months prior to pregnancy, eight months into pregnancy, and one year after birth using longitudinal k-means trajectory modelling on antidepressant exposure by week.

Results: The cohort included 8 460 pregnancies within 8 062 women with depression/anxiety. Consultations for depression/anxiety with contract psychiatric specialists accounted for one third of total care with psychiatric specialists. We identified four trajectory groups: early discontinuers, late discontinuers, continuers, and interrupters. We observed reduced mental health care utilization when pregnant women entered the course of pregnancy (slope of trend during pregnancy: -1.18 (95% confidence interval: -1.53; 0.84); -0.30 (-0.36; -0.25); and -0.29 (-0.52; -0.06) consultations/100 pregnancies with psychiatric specialists at outpatient clinics, outpatient contract psychologists, and outpatient contract psychiatrists respectively). The declines were observed for all antidepressant fill trajectories. We found an increase in the consultation rates for depression/anxiety with psychologists in the postpartum year among those discontinuing their antidepressant treatment during pregnancy regardless of whether they resumed their treatment in postpartum period or not (slope of trend = 0.18 (0.10; 0.26)).

Conclusions: Pregnancy was associated with reduced mental health care utilization regardless of whether antidepressant treatment was maintained during pregnancy or not. An increase in mental health care utilization in the postpartum year was observed among those pregnancies where the antidepressant treatment was discontinued.

P21

Educational attainment, serum lipids and cardiovascular disease: a within-sibship Mendelian randomisation study

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Introduction: Previous Mendelian randomisation (MR) studies have reported beneficial effects of educational attainment on a number of health outcomes, including coronary heart disease. These studies used Genome-wide Association Study (GWAS) data from unrelated individuals, which can be biased due to uncontrolled confounding from population stratification, assortative mating and familial effects arising from non-inherited alleles (dynastic effects). Using related individuals may provide an approach to control for these sources of confounding.

Aims: To compare the effect estimates of educational attainment on serum lipid concentrations (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides) and cardiovascular disease (CVD) between population and within-sibship models.

Methods: We used population and within-sibship models to estimate the effects of educational attainment, both measured educational attainment and an educational attainment polygenic score (PGS), on serum lipid concentrations and CVD incidence. For these analyses, we used individual-level data on 19,843 siblings from the HUNT study and performed both linear regression (logistic for CVD) and 1-sample MR. We also performed two-sample MR analyses using summary data from a recent within-sibship GWAS and compared these estimates with those of the individual-level analyses.

Results: Effect estimates generally seemed consistent between within-sibship and population models, however with far less precision in within-sibship models as expected.

Conclusions: Our results suggest that the causal associations of education on serum lipids is robust to biases from population structure and familial effects.

P22

Detection of sensitive time windows of medication exposure during pregnancy and long-term follow up; a MoBa study on antidepressant use in pregnancy and school performance

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Background: Susceptibility to a teratogenic agent may vary with the developmental stage at which the exposure occurs. Despite this fundamental principle of teratology, few studies have investigated methods for detecting sensitive time windows for medication exposures in pregnancy.

Aim: To assess a method for detection of sensitive windows when the medication is taken multiple times across pregnancy. The motivating example used was timing of antidepressant exposure *in utero* and school performance in children 10 to 15 years later.

Methods: Data from the Norwegian Mother, Father and Child Cohort Study conducted in 1999-2008 was linked to national school performance data between 2009 and 2018. The exposure was antidepressant medication (ATC: N06A). The outcome was scores on the national exams given in 5th, 8th and 9th grade, in three different subjects (Reading, Mathematics, and English). By using a random walk model accounting for the exposure effect at each month of gestation, we can detect smooth changes in the effect of exposure on later outcomes. This was implemented using the Integrated Nested Laplace Approximation framework in R.

Results: Using monthly use data on 1341 mothers and up to eight exam results from the exposed children, both at different time points and in different school subjects, we showed a clear downward trend in exam performance with exposure later in pregnancy.

Conclusion: Antidepressant medication use during pregnancy is associated to reduced performance on national exams. Use later in pregnancy has a larger negative effect size for school performance than exposure early in pregnancy. Methods for detection of sensitive windows when the medication is taken multiple times across pregnancy may improve our understanding of medication safety in pregnancy.

P23

The Oslo-Study 1972/73: The first population based study in Norway and its follow-up study, the Oslo II-study

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Introduction: In the post World War 2 era there was a steady increase in cardiovascular disease incidence and mortality especially in men. This was becoming a large public health problem in Norway. Research to study effect of interventions and long term follow-up was needed to curb this trend.

Aims: To briefly present 40 years of research activity of the Oslo-study designed to study the effect of prevention and epidemiologic long-term follow-up of cardiovascular diseases.

Methods: The screening of men in Oslo started in 1972 until 1973. In all 30,025 men were invited to attend a health screening; all men aged 40-49 years and a 7% sample of men aged 20-39 years, 17,965 men in total. Two randomized controlled trials were carried out: 1) Coronary heart disease prevention and 2) Drug treatment of mild hypertension. Focuses in other doctoral dissertations were coronary risk factors as social status, ECG-findings, and long-term follow-up on incidence and mortality of myocardial infarction, stroke, and total mortality. A second health screening, the Oslo II-study was carried out in 2000 including 6,530 men.

Results: Until 1999 over 60 scientific publications as five doctoral dissertations, and several scientific papers had been published. The intervention by smoking and diet was positive in preventing coronary heart disease. Antihypertensive drugs reduced incidence of stroke but not myocardial infarction. Long-term follow-up of 12-, 18-, and 24-years showed the prediction of known coronary risk factors for stroke and myocardial infarction.

Epidemiologic analyses from the Oslo II-study have focussed on oral health, microbiology, osteoporosis, and mental health. Major parameters are included in CONOR, and The Oslo-study 1972/73 and Oslo-study 2000 are included in international cohort study co-operations.

Conclusions: The Oslo Study 1972/73 and its follow-up The Oslo II-study, randomized controlled trials, and long-term follow-up have yielded a lot of new information to our common knowledge base used to improve health.

P24

The Oslo II-study 2000: The blood microbiome and cardiovascular disease mortality

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Introduction: The infection hypothesis in cardiovascular disease epidemiology was first raised in 1823 by Rayer. Although research have been performed in this field internationally, little is known about the role of the blood microbiome in Norwegian men.

Aims: To study what role the blood microbiome has on cardiovascular disease mortality in men.

Methods: A case-cohort study design of the Oslo II-study from 2000 was performed. Full blood samples for 405 subjects were analysed in a 9 ½ years follow-up of the Oslo II study. The study subjects were men born in 1923 and 1926 to 1932; cases of men (n=227) who had died from CVD and randomly selected controls from the same cohort (n=178). The data were analysed by Cox-regression adapted to the case-cohort design. Bonferroni corrections for the many bacterial genera were used. This work is part of the Master Thesis by Graeme Lawrence at Faculty of Mathematics and Natural Sciences, University of Oslo.

Results: Bacterial DNA was found in 372 (82 %) of the blood samples and 78 main bacterial genera from six phyla were analysed. The results of the genera *Kocuria* was adjusted Hazard Ratio (HR) = 8.50 (95% confidence interval 4.05, 17.84) and *Enhydrobacter was* HR=3.30 (2.01, 5.57) and indicate an association with CVD mortality with increasing levels whilst *Paracoccus* was HR=0.29 (0.15, 0.57) inversely related. Feeling of bad health and coffee consumption of more than three cups per day increased the risk. History of heart failure, systolic blood pressure, and currently taking antihypertensive drugs versus previously were borderline significant.

Conclusions: Three bacterial genera were after Bonferroni correction significantly associated with cardiovascular disease mortality representing skin, oral, and soil microbiomes.

P25

The burden of colon cancer attributable to modifiable factors – The Norwegian Women and Cancer Study

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Introduction: Women in Norway have one of the highest incidences of colorectal cancer (CRC) in the world, as well as in the Nordic countries. Colon cancer is the second most frequently diagnosed cancer in women in Norway, with 1578 new cases of colon cancer diagnosed in 2018, and the age-standardized incidence rate of 52.4 per 100 000. The incidence rate of colon cancer has increased three-fold between 1955 and 2014. Only in the last five years, (between 2014 and 2018), colon cancer rates in women increased by 5.2% compared to the period 2009-2013. The reasons behind the increasing incidence of colon cancer in Norway remain unknown.

Aims: We aimed to assess the burden of colon cancer attributable to a large number of modifiable risk factors in Norwegian women using the data from the nationally representative Norwegian Women and Cancer (NOWAC) study.

Methods: The information on smoking status, alcohol consumption, body mass index (BMI), intake of calcium, fibers, and red and processed meat from 35 525 women were collected by self-report. Colon cancer cases were identified by linking the unique 11-digit personal number of every Norwegian citizen to the Cancer Registry of Norway. A flexible parametric piecewise constant hazards model were used to calculate multivariable adjusted risk ratios as the measure of association between the aforementioned risk factors and colon cancer. Population attributable fractions for CRC were calculated taking into account competing risk of death.

Results: During a maximum of 22 years of follow-up, 430 colon cancer cases were identified. We found that ever smoking explained 21.8% (95% CI 8.5%-33.1%), overweight/obesity 1.3% (95% CI -7.1%-9.0%), and alcohol consumption 11.8% (95% CI -4.9%-25.8%) of the colon cancer burden. No colon cancer cases were attributable to combined intake of red and processed meat over 500 grams per day and to low intake of fibers. Low intake of calcium contributed to 9.2% (95% CI -8.2%-23.6%) of all the colon cancer cases. Jointly, these modifiable risk factors explained 39.0% (95% CI 14.8%-56.2%) of the colon cancer burden in women in Norway.

Conclusions: We found that established, modifiable risk factors for colon cancer were responsible for a quarter of the colon cancer cases among Norwegian women. The reasons behind a substantial proportion of the colon cancer burden remain unexplained.

P26

Associations between postprandial triglyceride concentrations and sex, age, and body mass index: cross-sectional analyses from the Tromsø Study 2015-2016

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Introduction: Elevated serum triglyceride concentrations increase the risk of developing atherosclerosis, the leading cause of cardiovascular disease. Postprandial triglyceride concentrations have shown to be a stronger predictor of cardiovascular disease compared to fasting triglycerides. It is therefore clinically relevant to study patterns of postprandial triglyceride concentrations in a general adult population.

Aims: This cross-sectional analysis aimed to examine postprandial triglyceride concentrations in women and men, and the association with age, body mass index and menopausal status.

Methods: Data from the seventh survey of the Tromsø Study (2015-2016), including 21 083 women and men aged 40-99 years, was analyzed using descriptive statistics and linear regression models.

Non-fasting blood samples were drawn from an antecubital vein after a brief stasis, with the participant seated. Triglycerides were analyzed by enzymatic colorimetric methods with Cobas 8000 c702 (Roche Diagnostics, Mannheim, Germany) at the University Hospital of North Norway (NS-EN ISO 15189:2012. Time since last meal before blood sampling was self-reported and categorized in one-hour intervals with 7+ hours considered fasting.

Results: Men had higher triglyceride concentrations compared to women and a different pattern of postprandial triglyceride concentrations. In women, the highest triglyceride concentration (19 % higher compared to fasting level) was found among those with a blood sample taken 3-4 hours postprandially. In men, those with a blood sample taken 1-3 hours postprandially had the highest triglyceride concentration (30 % higher compared to fasting level). In normal- and overweight women, all age groups had higher triglyceride concentrations (13-21 %) than the reference group (40-49 years), but no linear trend was observed. In men, all age groups (except 50-59 years) had an inverse linear association with triglyceride concentration (11-21 % lower triglyceride concentration compared to 40-49 years). Body mass index was positively associated with triglyceride concentration in both women and men. In sub-analyses, postmenopausal women had higher triglyceride concentrations compared to premenopausal women.

Conclusions: Postprandial triglyceride concentrations differed in groups of sex, age, body mass index, and menopausal status. However, unknown meal compositions and sizes, as well as self-reported time since last meal should be taken into consideration when interpreting these results.

P27

Hazardous alcohol use and healthcare utilization in a Norwegian general population: Results from the Tromsø study

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Introduction: Hazardous alcohol use refers to a consumption pattern that increases the risk of negative events, such as a range of somatic and psychiatric health complaints. In addition, hazardous drinking is associated with an increased risk of accidents, which may increase the risk of needing medical help. Due to this, it is likely that having a hazardous alcohol use puts the individual at increased risk of utilizing the healthcare system, however, detecting hazardous alcohol use may be difficult, as it has no uniform profile. Previous studies have found contradicting evidence regarding whether individuals suffering from alcohol problems have fewer or more visits across the healthcare system.

Aims: The overall aim of this study was to investigate and describe the healthcare use of individuals with a hazardous or harmful alcohol use. We assessed what type of healthcare services are used, and what characterise frequent users of healthcare services who had a hazardous alcohol use. In addition, we estimated if a change in drinking pattern reflected a change in use of general practitioner or psychologist over time.

Methods: Data from the sixth and seventh Tromsø study was used, which allowed for measuring changes over time. In total 17 754 and 5994 were included in the cross-sectional and longitudinal analysis respectively. Hazardous or harmful alcohol use was measured by the Alcohol Use Identification Test (AUDIT). Participants self-reported use of GP, emergency room, psychologist/psychiatrist, outpatient care at hospital, seeing a medical specialist outside hospital, and admitted to a hospital.

Results and conclusions: For men, hazardous alcohol use was associated with higher odds for visiting all healthcare services measured, relative to men without a hazardous alcohol use. For women, this was only seen for psychiatric services and the emergency room, and fewer visits to hospital outpatient clinics. In addition, women with reduced hazardous alcohol use had less visits to a psychologist at follow up. Thus, individuals suffering from a hazardous alcohol use may interact with a variety of healthcare services, which may be relevant for screening, prevention and treatment.

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Prediagnostic serum 25-hydroxyvitamin D and leptin in relation to melanoma-specific and overall death

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Introduction: Twentyfive-hydroxyvitamin D (25(OH)D) has been inversely associated with Breslow thickness, the main prognostic factor in localized melanoma, while results on 25(OH)D in relation to melanoma death have been conflicting. Obesity has been associated with Breslow thickness, which is also associated with serum levels of the leptin hormone. Measured at diagnosis, leptin has been found to predict sentinel node metastasis in melanoma.

Aims: To examine 25(OH)D and leptin in relation to melanoma-specific and overall death and potential interaction between 25(OH)D, leptin and Breslow thickness.

Methods: We used stored, prediagnostic sera from 706 melanoma patients in the population-based Janus Serum Bank Cohort (Janus Cohort) followed from year of diagnosis (1976–2008) through December 31, 2018. Cox-regression was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) of 25(OH)D and leptin in relation to melanoma-specific and overall death. Missing values were imputed.

Results: During follow-up, 304 melanoma patients died; 141 were due to melanoma. We did not find an association between 25(OH)D and melanoma-specific or overall death, but we found significant interaction ($P_{interaction}$ <0.001) between tertiles of 25(OH)D and Breslow thickness categorized as T1 (<1 mm) vs. T2-4 (>1 mm). In T2-4 melanomas, we found a non-significant inverse association between 25(OH)D and melanoma death with a HR=0.75 (95% CI: 0.47, 1.18) for tertile 3 vs. tertile 1. Also for leptin, we did not find significant associations with melanoma death or overall death, but we found a significant interaction ($P_{interaction}$ <0.030) between tertiles of leptin and Breslow thickness categorized as T1-2 (≤2 mm) vs. T3-4 (>2 mm). For T3-4 melanomas, serum leptin tertile 3 vs. tertile 1 yielded HRs of 2.23 (95% CI: 1.15, 4.30) and 1.93 (95% CI: 1.14, 3.23) for melanoma and overall death, respectively. No association with leptin was found for T1-2 melanomas.

Conclusions: We did not find persuasive evidence overall for associations between prediagnostic serum 25(OH)D or leptin and risk of melanoma-specific and overall death. However, our findings in melanoma subgroups warrant future analyses with repeated measurements to clarify the role of 25(OH)D and leptin pertaining to prognosis in melanoma patients diagnosed at different stages.

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Injury Prevention and long-term Outcomes following Trauma—the IPOT project: a protocol for prospective nationwide registry-based studies in Norway

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Introduction: Traumatic injuries constitute a major cause of mortality and morbidity. Still, the public health burden of trauma in Norway has not been characterized by use of nationwide registry data. More knowledge is warranted on trauma risk factors and long-term outcomes following trauma. The IPOT project has established a comprehensive research database, where the Norwegian National Trauma Registry (NTR), has been merged with several data sources to pursue three main research topics the burden of trauma, trauma etiology, and trauma survivorship.

Aims:

- Public burden of trauma: To describe trauma incidence and mortality rates, to assess possible excess mortality of non-trauma deaths, to describe disability-adjusted life-years (DALY) rates among trauma survivors.
- Trauma etiology: What are the associations between trauma risk and demographic factors (i.e., age, sex, socioeconomic status, education, income, family situation, urban vs. rural), occupation, comorbidity, drug prescription?
- Trauma survivorship: Compared to healthy controls, are trauma survivors at increased risk of mental illness and other non-communicable diseases, reduced work ability, or death? To what extent is the quality of post-trauma rehabilitation associated with increased risk of these outcomes?

Methods: The NTR (n≈27,000 trauma patients, 2015–2018) has been coupled with data from Statistics Norway, the Norwegian Patient Registry, the Cause of Death Registry, the Registry of Primary Health Care, and the Norwegian Prescription Database. To quantify the public health burden, DALYs will be calculated from the NTR. To address trauma etiology, we will conduct nested case-control studies with 10 trauma-free controls (drawn from the National Population Register) matched to each trauma case on birth year, sex and index date. Conditional logistic regression models will be used to estimate trauma risk according to relevant exposures. To address trauma survivorship, we will use cohort and matched cohort designs and time-to-event analyses to examine various post-trauma outcomes.

Ethics and dissemination: The project is approved by the Regional Committee for Medical Research Ethics. The project's Data Protection Impact Assessment is approved by the Data Protection Officer, and the project is funded by the Oslo University Hospital. Results will be disseminated to patients, in peer-reviewed journals, at conferences and in the media.