Norsk Epidemiologi

Norwegian Journal of Epidemiology

Volum 30, supplement 1, oktober 2022

Utgitt av Norsk forening for epidemiologi

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Internettadresse for NOFE:
http://www.nofe.no

e-post: post@nofe.no

ISSN 0803-4206
Opplag: 170
Trykk: Grafiske tjenester UiT
Layout og typografi: Redaktøren

Tidsskriftet er åpent tilgjengelig online:
www.ntnu.no/ojs/index.php/norepid
Også via Directory of Open Access Journals (www.doaj.org)

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

DEN 28. NORSKE EPIDEMIOLOGIKONFERANSEN

TROMSØ,

26.–27. OKTOBER 2022

WELCOME 2
KEYNOTE SPEAKERS' BIOGRAPHIES 3
ABSTRACTS 4
LIST OF PARTICIPANTS 78

The 28th Norwegian Conference on Epidemiology Tromsø, 26th-27th October 2022

We wish you all a very warm welcome to Tromsø and the 28th conference of the Norwegian Epidemiological Association (NOFE).

The theme of this year's conference is *Translating epidemiological research into public health*. We have invited four keynote speakers who will address different aspects of translating the epidemiological research into public health: Professor Ann Ragnhild Broderstad (UiT The Arctic University of Norway), Associate professor Maarten van Smeden (UMC Utrecht), Professor Jo Røislien (The University of Stavanger), and Professor Nanna Lien (The University of Oslo).

During the conference, there will be 59 oral presentations in plenary and parallel sessions, and 15 posters, covering a wide range of epidemiological themes. 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!

Even though the funding for EPINOR, the national research school in population-based epidemiology has ended, we recognize the importance of training the next generation of epidemiologists. We are excited that we have been able to arrange a Young Investigator Day workshop as a substitute for what was previously the EPINOR-day, on the day before the conference. This workshop is fully supported by NOFE, and has attracted over 50 participants of all ages. We hope that NOFE will continue to serve as a venue for interaction and collaboration between senior and younger epidemiologists.

At the conference, NOFE will be awarding three prizes in two categories – 'Paper of the year' and 'NOFE Honorary membership' – and we look forward to celebrating these with you during the first day of the conference. We hope to see many of you at the NOFE annual meeting on Wednesday 26th October.

Finally, 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).

Welcome to Tromsø and NOFE 2022!

The NOFE Board
&
The organizing committee for the NOFE 2022 conference

Ilona Urbarova, Laila A. Hopstock, Jonas Johansson, Marko Lukic, Marie W. Lundblad, Bente E. Schøning, and Guri Skeie

Keynote speakers' biographies

Ann Ragnhild Broderstad

Dr Ann Ragnhild Broderstad is Research professor in epidemiology with Indigenous Health Research. She is Sami, living in the southern part of Troms County in Northern Norway. She is the Academic director at the Centre for Sami Health Research, at the UiT The Arctic University of Norway. Broderstad is a specialist in internal medicine and hematology, and works also as senior physician (MD) at the University Hospital of North Norway, Harstad. The main research interest is within chronic diseases and living conditions in the multiethnic Arctic, with special focus on the Sami society. Dialogues and knowledge exchange with local communities and the Sami society are prioritized issues in her research. Broderstad is the Head of two surveys, namely the SAMINOR Study and "From Rural to Urban Living". Through her research work, Broderstad has been a part in the work of develop the Proposal for Ethical Guidelines for Sámi Health Research and Research on Sámi Human Biological led by the Sami Parliament. She has been a member of the Arctic Human Health Research group at Sustainable Development Working Group, Arctic Council for several years, until 2017.

Maarten van Smeden

Maarten van Smeden: associate professor of epidemiologic methods and head of the research methods program at the Julius Center for Health Sciences and Primary Care, UMC Utrecht, the Netherlands. His research is focused on the development and evaluation of statistical methodology, with a particular interest in methodology related to the development and validation of prediction models, machine learning and artificial intelligence.

Jo Røislien

Jo Røislien is a professor of medical statistics with the Faculty of Health Science at the University of Stavanger, guest lecturer at King's College London, and Honorary professor at University of Aalborg. He has collaborated in numerous research project within the health sciences, contributing with statistical and methodological expertise in topics varying from public health, obesity and addiction to rehabilitation and prehospital critical care. Røislien is also an award winning science communicator. He has developed, written and hosted numerous science TV and video productions both nationally and internationally, for broadcasters like NRK, VGTV and Discovery Channel. He is a regular guest and contributor on radio and in the written press. Recently Røislien has been project manager and principial investigator for research project "Covid communication: Fighting a pandemic through translating science" (COVCOM) funded by the Trond Mohn Foundation. Merging academic know-how with practical experience from communication, the COVCOM project aims to develop evidence based mass communication of public health science to the general public and decision makers.

Nanna Lien

Professor Nanna Lien, Department of Nutrition, University of Oslo, Norway has more than 15 years of experience in school-based intervention research in nutrition and obesity prevention. The focus of her research has developed from effectiveness studies testing interventions in randomized controlled trials to the challenges of achieving population impact of these interventions considering the complex systems in which they will be implemented. Understanding and preventing social inequalities in dietary behaviours and obesity has been a subtheme of her research throughout.

Abstracts

Plenary talk

The use and expansion of results from the Global Burden of Disease Study in Norway

Ann Kristin Skrindo Knudsen[1], Benjamin Clarsen[1], Carl Baravelli[1]

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Introduction: The Global Burden of Disease Study (GBD) is a systematic, scientific effort to quantify and compare health loss from diseases, injuries and risk factors by age, sex and geography, and over time, at the most complete and updated way possible. In order to achieve this goal, the project aim to collect and use all available health data globally in their models. The Centre for Disease Burden at the Norwegian Institute of Public Health has had a close collaboration with the GBD study since 2013. The Centre aims for increasing the national collaboration around Norwegian input data to GBD and expand the use of GBD results.

Aims: Describe the GBD project and the GBD collaborator network, the importance of high quality input data, Norwegian GBD results, planned activities and future possibilities.

Methods: Norwegian data are identified and sent to GBD primarily by the Centre contacting the individual data-owners and organizing the data transfer. Analyses are done by GBD, and access to results are given to collaborators in the project, who can use these in collaborator-led papers. Examples of use and publication of the Norwegian results include online visualizations, scientific papers, policy reports, and oral presentations.

Results: GBD has published results on disease burden in Norway since 2014. In 2022, results on disease burden in the Norwegian counties were published. GBD results on forecasted disease burden in Norway has also been made available in national reports. Future plans include forecasted results on disease burden by county, and detailed analyses on the contribution from avoidable risk factors on the Norwegian disease burden.

Conclusions: Timely and updated burden of disease estimates are essential for health policy planning, and GBD results are met with great interest. The quality of the results are, however, strongly dependent on the quality of the underlying data. In order to improve the GBD results for Norway, an expansion of national collaboration around data production and use of results is desired. Increased production and use of Norwegian high quality health data into the analyses would increase the validity of national and county-wise disease burden results.

A1

Menopausal hormone therapy and breast cancer risk: a population-based cohort study in Norway

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3) Section for Colorectal Cancer Screening, Cancer Registry of Norway, Oslo, Norway

Introduction: The association between use of menopausal hormone therapy (HT) and breast cancer (BC) risk is established. It is, however, important to monitor this association as new products are introduced to the marked.

Aims: To provide updated and detailed estimates of the increased risk of BC in HT users.

Methods: The study is based on a linkage between the Cancer Registry of Norway, the Norwegian Prescription Database, the Norwegian Regional Health Studies, and Statistics Norway. We identified 1,275,783 women who were followed-up from June 2004 or the month they turned 45 years, whatever occurred latest, to December 2018. We used Cox-regression to estimate associations between use of HT and risk of breast cancer according to type of HT, route of administration and individual products overall, and stratified by molecular subtypes and body mass index (BMI).

Results: During a median follow-up of 12.7 years 30,310 BCs occurred and 370,847 women used HT. Use of oestrogen-progestin therapy (EPT) compared to no HT use was associated with the highest increased risk (HR: 2.34, 95% CI: 2.24-2.44), followed by tibolone (HR: 1.82, 95% CI 1.64-2.03) and oestrogen (HR: 1.05, 95% CI: 1.00-1.09). Use of transdermal (HR: 1.73, 95% CI: 1.47-2.03) and oral (HR: 1.38, 95% CI: 1.24-1.54) oestradiol was associated with increased BC risk compared to no use, while vaginal oestradiol use (HR: 0.96, 95% CI: 0.91-1.00) was not. Use of the newer oral EPT products Eviana (HR: 1.87, 95% CI: 1.45-2.41) and Cliovelle (HR:1.83, 95% CI 1.50-2.24) was associated with lower risk, than the other commonly used oral EPT products Activelle (HR: 2.44, 95% CI 2.28-2.61) and Kliogest (HR: 2.64, 95% CI: 2.35-2.97). Stratified by molecular subtypes, HT users compared to no-users had a higher risk of developing BC subtypes with more favourable outcomes (i.e. luminal BCs), than less favourable outcomes. Stratified by BMI, the risk of BC among HT users compared to non-users was highest for lean women and lowest for obese women.

Conclusions: Use of HT was associated with increased risk of BC, particularly luminal BC. The associations varied according to BMI and the type of product used.

A2

Parity and cumulative incidence of breast cancer in the Norwegian Woman and Cancer Study (NOWAC)

Sanda Krum-Hansen[1,2], Arne Bastian Wiik[1], Karina Standahl Olsen[1], Oxana Gavriluk[1], Eiliv Lund[1]

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Introduction: The reduced risk for breast cancer following increasing parity has been known for decades. Almost all studies have presented the percentage decrease for each child during follow-up. Since the risk reduction is less than ten percent for each child the overall lifelong risk could be under communicated.

Aim: Here we will use cumulative incidence to describe the lifelong risk.

Methods: NOWAC is a prospective cohort study that recruited 172,000 women between 1991 and 2007 with follow-up through national registers of cancer and death until end of 2018. Information on parity and selected covariates were based on questionnaires. For the present analyses, we included 165 238 postmenopausal women with start of follow-up from 01.01.2000 until the end of 2018. We used Poisson regression analyses based on Lexi diagrams to calculate cumulative incidence of breast cancer, stratified for parity and risk factors (mothers age at first birth, breastfeeding, BMI, smoking and alcohol consumptions).

Results: After 17.3 years of average follow-up, 8120 women aged 35-84 year developed breast cancer. Age-specific incidence rates increased up to age group 60-64 years, decreased till 75-79 years with another increase in the oldest. The cumulative incidence for all participants up to 84 years were 11.7%, similar to the national cumulative incidence of 11.3%. In stratified analyses the cumulative incidence rate was for nullipara 11.4%, for women who gave birth to one child 11.4%, 2 children 9.7%, 3 children 8.6%, 4 children 8.3% and 5-6 children 7.1%. The cumulative incidence rates presented the same pattern of decreasing risk in all sub strata.

Conclusion: The analyses clearly demonstrated the consistent decrease of the breast cancer risk for each additional child estimated by cumulative incidence rates throughout life.

A3

No impact of parity on global gene expression levels in breast cancer tissue and normal breast tissue – a nested case-control study in the NOWAC Postgenome biobank

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3) Norwegian Computing Center, Oslo, Norway

Introduction: No biological mechanisms can explain the established protective effect of increasing parity and early age at first birth on breast cancer incidence, as shown in many large cohort studies. Here, we explore for the first time the global gene expression profiles in breast cancer tissue and normal breast tissue in relation to parity using the population based Norwegian Women and Cancer (NOWAC) study.

Methods: NOWAC is a prospective cohort study (N=172 000) built 1991-2007. At ten Norwegian hospitals 2006-2010 NOWAC women attending for a diagnostic biopsy of breast cancer were asked for a second biopsy to be taken after the diagnostic one. Sampling of normal breast tissue from controls was done in 2010-2011 from NOWAC women participating in the national mammographic screening. The final study consisted of 278 age-matched case-control pairs. Differences in blood gene expression (Illumina microarray) between breast cancer cases and controls were identified using the Bioconductor R-package limma.

Results: A comparison between gene expression profiles found that almost all genes were significantly expressed between cases and controls; 10013 out of 11308. With a FDR5% 5768 were upregulated and 4245 downregulated. When parity (0, 1-3, 4-8) was included significant changes was found only in three genes in normal tissue and none in breast cancer tissue (FDR q-values 0.05). No gene set enrichment analyses could be done due to methodological problems with only significant genes.

Conclusions: Parity or number of children had no impact on gene expression in neither breast cancer tissue nor in normal tissue. We hypothesize that the protective effect on breast cancer incidence is not caused by changes in breast tissue during pregnancies.

A4

Low-dose aspirin and risk of breast cancer: a Norwegian nationwide population-based study

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Introduction: Several studies have evaluated the association between aspirin use and risk for breast cancer (BC), with inconsistent results.

Aims: To investigate the association between low-dose aspirin and BC risk in a nationwide population-based cohort, overall and by women's and tumours' characteristics.

Methods: We identified women aged ≥50 residing in Norway between 2004 and 2018 and we linked data on the women from the Cancer Registry of Norway, the Norwegian Prescription Database, and Statistics Norway. We used multivariable Cox regression models to estimate the association between low-dose aspirin (mainly 75mg/day) use and risk of BC, overall and by BC molecular subtype, women's age and body mass index (BMI).

Results: We included 1,083,629 women. During a median follow-up of 11.6 years, 257,442 (24%) women used aspirin, and 29,533 (3%) BCs were diagnosed. For current use, compared to never use, of aspirin we found a borderline association with a lower risk of estrogen receptor-positive (ER+) BC (hazard ratio [HR]=0.96, 95% confidence interval [CI]: 0.92–1.00), but not ER-negative BC (HR=1.01, 95% CI: 0.90–1.13). The association with ER+ BC was observed among women aged ≥65 years (HR=0.95, 95% CI: 0.90–0.99), but not in women aged 50-65 years. For ER+ BC, in women aged ≥65 years, HRs for past use and current use of <2, 2–3.9 and ≥4 years were 1.01 (95% CI: 0.93–1.08), 1.01 (95% CI 0.92–1.11), 0.93 (95% CI: 0.83–1.04) and 0.90 (95% CI: 0.84–0.97), respectively (p-value for trend=0.007). BMI was available for 340,953 (31%) women. We found an indication of an association between use of aspirin and reduced risk of ER+ BC in women with BMI≥25 (HR=0.92, 95% CI: 0.84–1.01), but not in women with BMI<25. For ER+ BC, in women with BMI≥25, HRs for past use and current use of <2, 2–3.9 and ≥4 years were 0.95 (95% CI: 0.84–1.08), 0.93 (95% CI 0.79–1.08), 0.97 (95% CI: 0.81–1.17) and 0.87 (95% CI: 0.76–0.98), respectively (p-value for trend=0.031).

Conclusions: Use of low-dose aspirin was associated with reduced risk of ER+ BC, particularly in older and overweight women.

A5

BMI, weight-changes, and blood gene-expression among cancer-free women: the Norwegian Women and Cancer (NOWAC) postgenome cohort

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Introduction: Obesity and weight-gain are major risk factors for diseases like diabetes, cardiovascular diseases, musculoskeletal disorders, and several cancers. Obesity has been linked to altered gene-expression in blood. Still, few studies have investigated blood gene-expression related to body mass index (BMI) in a large cancer-free population, and there has been no study to date that has assessed if past weight-changes are reflected in the blood gene-expression.

Aims: To assess gene-expression profiles in whole-blood in relation to current BMI and past weight-changes in cancer-free women.

Methods: We used data from 1,694 cancer-free women participating in the prospective, population-based Norwegian Women and Cancer (NOWAC) postgenome cohort. We analysed microarray-based gene-expression profiles of 7,713 unique genes, using a significance threshold of false discovery rate (FDR) ≤0.05, from whole-blood samples according to current BMI (both categories and continuous metric) and past weight-changes (weight-change categories; long-term (mean= 7 years) and short-term (mean= 1 year) weight-changes). Enriched pathways and gene ontology (GO) categories of genes associated with BMI and weight-changes were also assessed.

Results: Women with obesity had 2,394 and 769 differentially expressed genes (DEGs) when compared to women with normal-weight and overweight, respectively, and there were 768 DEGs when comparing women with overweight to women with normal-weight. The biological functions of the DEGs related to BMI were overall linked to general metabolism, blood, and immune processes. There were no DEGs associated with weight-change categories but there were nine and one DEGs associated with long- and short-term weight-changes, respectively, when an interaction with BMI categories at blood collection was included.

Conclusions: Blood gene-expression in Norwegian cancer-free women was strongly associated with current BMI but there was little association with past weight-changes. The biological functions of DEGs related to BMI agreed with known physiological effects of obesity. The evaluation of past weight-changes and gene-expression profiles in blood is novel but indicated few DEGs and thus related biological functions remain unexplained.

B1

A validation of register derived diagnoses of interstitial lung disease in patients with inflammatory arthritis. Data from NOR-DMARD

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Introduction: There is a lack of knowledge concerning the validity of International classification of diseases (ICD) diagnoses extracted from health registers but this information is often used in epidemiological studies.

Aims: To assess the validity of register derived diagnoses of interstitial lung disease (ILD) in patients with rheumatic diseases, using ILD identified on chest computed tomography (CT) as gold standard.

Methods: The Norwegian Anti-Rheumatic Drug Register (NOR-DMARD) is a multi-centre prospective observational study that includes patients with a diagnosis of inflammatory arthritides who start treatment with disease modifying anti-rheumatic drugs. NOR-DMARD was linked to the Norwegian Patient Registry (NPR) and Cause of Death Registry. We searched both registers for ILD ICD-10 codes (J70, J84 or J99) and also extracted chest CTs from participants at four hospitals. CTs taken three months before or within one year after the first ICD-10 diagnosis in the registries were considered relevant to the study, but images taken at a later date could confirm an ILD diagnoses. An expert thoracic radiologist (FA) scored all examinations according to presence of ILD and categorised the finding into; no ILD, possible ILD and confirmed ILD. Possible ILD CT images were re-examined by a second expert radiologist (TMA). Presence of confirmed ILD was assessed in patients with a registry ICD-code for ILD at ≥2 time points and across ILD diagnoses subgroups.

Results: We identified 80 cases with an ILD diagnosis (ICD10; J70 8(10), J84 56 (50) and J90 16 (20)). CT examinations were available in 72/80 (90%) patients, 60/72 (83%) within the pre-specified time-window. ILD was confirmed on CT in 31/72 (43%) of patients with available CT. The diagnosis was again confirmed on CT in 25 (56%) of 45 patients who had received an ILD code at ≥2 time points and had a CT within a relevant time-period. The diagnosis was confirmed in 19 (63%) of the 30 patients of this group who had received a J84 diagnoses. ILD diagnoses that were not confirmed on CT were most frequently given under investigations for respiratory symptoms 19/41 (46%).

Conclusions: The validity of registry-based diagnoses of ILD must be carefully considered in epidemiological studies.

B2

Comorbidity among elderly hospitalized patients assessed by different approaches − the IMMENSE study

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1) Department of Pharmacy, UiT The Arctic University of Norway

Introduction: Determining comorbidity in study populations may serve many purposes. In clinical research, comorbidity is used as an adjustment factor in analyses, and may be important for interpreting results.

Aims: To describe comorbidity for patients in the randomized controlled trial IMMENSE, and to compare comorbidity estimates by different approaches.

Methods: The IMMENSE trial included 480 patients ≥70 years, acutely admitted to either the geriatric or the general internal medicine ward at the University Hospital of North Norway (UNN) in 2016–2019. We assessed comorbidity at hospital admission by three approaches: 1) manual application of the Charlson Comorbidity Index (mCCI), 2) algorithm-based CCI (aCCI), and 3) medication-based Rx-Risk Index (RRI). Demographic data were extracted from electronic patient records; mCCI was based on diagnoses at admission (free-text) and ICD-10-codes from the discharge form; aCCI was based on ICD-10-codes from the discharge form and the Norwegian Patient Registry; RRI calculation was based on medication use recorded at hospital admission. Inter- and intra-rater reliability was excellent (all intra-class correlation coefficients >0.90).

Results: Overall, 88% of the population had at least one disease (mCCI), and all participants used at least one medication, 82% used ≥5. Comorbidity median score was 2 (range 0–13) for mCCI, 1.51 (range 0–10) for aCCI and 2 (range -3–16) for RRI. For all assessment methods, cardiovascular disease was the most prevalent disease group. Applying mCCI, dementia and chronic lung disease were the second and third most prevalent diagnoses. Applying aCCI, 79% had at least one disease and dementia and kidney disease was second and third most prevalent diagnoses. Applying Rx-Risk Index, gastrooesophageal reflux and chronic airways disease were the second and third most prevalent medications categories.

Conclusions: The IMMENSE study population had a high degree of comorbidity and polypharmacy at baseline. The comorbidity score and the most prevalent diagnosis varied depending on the scoring approach applied. Our results suggest that the choice of comorbidity assessment approach depends on the research question, data availability and the diseases or endpoints under investigation.

B3

Developing a 10-year survival prediction model based on the Norwegian drug prescription registry

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Introduction: The rise of multimorbidity and associated polypharmacy has not only contributed to a poorer quality of life among societies, but it also made validating epidemiological studies more difficult due to the confounding caused by coexisting medical conditions. To quantify the combined burden of these coexisting medical conditions, many numerical indices have been developed. The ever-expanding amount of health data collected from individuals in Norway can help develop a more accurate medication-based index to quantify the burden of multimorbidity.

Aims: To develop a robust medication-based comorbidity index using as few prescription drugs as possible.

Methods: Prescription data from more than 2 million individuals who are 40 years old or older on 1 Jan 2009 and living in Norway was obtained from The Norwegian Prescription Database (NorPD). Birth and death dates were obtained from Statistics Norway (SSB). Exposure to drugs classified by their therapeutic subgroup (ATC code level 2) will be monitored between 2004-2008 and the outcome (all-cause mortality) will be observed between the years 2009-2019. The data will be randomly split into three subsets, 80% for training, 10% for validation and 10% for testing. Two models, penalized Cox LASSO and Elastic net, will be used to pick the drug groups most significantly associated with mortality.

Results: The two models will be compared against each other. The model which gives the best prediction of mortality based on fewest drugs will be chosen as the final model.

Conclusions: The drug groups from the final model, together with their coefficients, can in the future be used to predict mortality of the patients even in settings when the entire history of prescription is not available. This predicted mortality can be used in epidemiological studies to adjust for confounding caused by coexisting medical conditions.

B4

A Lean Additive Frailty Model: With an Application to Clustering of Melanoma in Norwegian Families

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Introduction: Norwegian health registries enable detailed studies of clustering of cancers in families. Frailty models provide a framework for conducting such studies at a much higher level of detail than conventional studies. However, the complexity of these models grows with both family size and number of cancer diagnoses in each family. Consequently, these models have primarily been used in settings where cluster sizes are small, e.g. for twin pairs, or by considering only a few first-born children in a family. This poses a challenge for fully utilizing the detailed data available in the registries.

Aims: To modify the so-called additive genetic gamma frailty model so that the complexity growth in family size becomes more manageable and to use this modified model to analyze population-wide data on clustering of melanoma in Norwegian families.

Methods: By using a first-order approximation of the genetic structure in nuclear families of parents and children, we obtain a lean model that reduces the complexity with respect to family size. Although a large number of diagnoses within the same family still poses a challenge, this allows us to analyze a far greater class of datasets. The modified model is then applied to a dataset on melanoma in 2,391,125 Norwegian families.

Results: The lean model gives a significant speed-up in model fitting. This enables the analysis of a far greater class of datasets. Using the lean model, we are able to analyze the complete population-wide dataset on melanoma in all Norwegian families registered in 1960-2016. We find a substantial clustering of melanoma in Norwegian families and a large heterogeneity in melanoma risk across the population. We estimated a considerable frailty variance of 2.25, which is reflected in frailty relative risks (FRRs), where there is a 2-2.4-fold increase in one's risk if a sibling is affected by melanoma. Having two affected siblings increases the risk 4-5-fold.

Conclusions: Additive frailty models can be used to study relatively large clusters. Furthermore, there is a substantial clustering of melanoma in Norwegian families and a large heterogeneity in melanoma risk across the population.

B5

Development of a prognostic model for predicting quality of life decline in head and neck cancer survivors

Maurício Moreira-Soares[1,2], Erlend IF Fossen[1], Andrew R. Ness[3], Steve Thomas[3], Katrina Hurley[3], Susanne Singer[4], Kathy Taylor[4], Claudia Vener[5], Stefano Cavalieri[6], Lisa Licitra[5,6], Arnoldo Frigessi[1], Marissa LeBlanc[1,7], on behalf of the BD4QoL consortium

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Introduction: Head and neck squamous cells carcinoma overall-survival rate after 5 years or more from diagnosis can be as high as 66%, according to UK data in the period 2002-2006. Despite the relatively high survival rate, side effects from both the disease and its treatment can persist for years and impact quality of life (QoL), such as psychological distress and long-term disability.

Aims: The goal of this study is to develop a prognostic model to predict the probability of being alive and having a decline in QoL, given a set of covariates. In addition, we aim to identify variables that predict a clinically-relevant decline in self-reported QoL between end of treatment and two years after the end of treatment using the BD4QoL (Big Data for Quality of Life Consortium) historical cohort.

Methods: The BD4QoL cohort is composed of 4015 HNC survivors from different studies across Europe. We define survivors as patients that have survived their initial treatment with no detected cancer or recurrence. The data were split 50 times, stratified by outcome, age and sex into training and test data using a 70/30 split. We used penalized logistic regression, SVM, random forest and boosted tree models with 157 predictors. The predictors included demographic and clinical information at diagnosis, as well as psychometrics and quality of life scales obtained at 3 time points.

Results: We observed that logistic regression presented the least amount of optimism, generalising better in the test set with AUROC of 0.70. EORTC-QLQ-C30 global health score (GHS) and other QoL measurements at baseline show as the most important predictors of QoL decline in the models, taking into account several different explainability metrics across all methods implemented.

Conclusions: Logistic regression performed better due to low events per variable ratio and the high number of coefficients to be estimated in methods that introduce interactions agnostically. The GHS at baseline appearing as a strong predictor of QoL decline may be an artificial effect of the scale boundaries and the minimum clinically important difference (MCID) used in this study.

C1

Exploring the accessibility of Norwegian pharmacies before and after the liberalization of the pharmacy market

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Introduction: Accessibility of healthcare facilities and strategic planning of their locations are critical elements for any healthcare system. Distance and travel time are important indicators of healthcare facilities' accessibility. In 2002, the Norwegian pharmacy legislation was liberalized allowing for pharmacies to be opened wherever and for chains to own many pharmacies. This led to a sharp increase in the number of pharmacies in Norway.

Aims: In this study, we aimed to investigate if there was a change in the accessibility of Norwegian pharmacies between 2002 and 2022.

Methods: We utilized Geographical Information System (GIS) to study the traveling time between 12,000 randomly selected households to the registered pharmacies in 2002 and 2022. The sample of households' locations was obtained from the Norwegian Mapping Authority excluding the locations that are not for permanent stay purposes. Pharmacies' locations were obtained from the Norwegian Pharmacy Association. We calculated the distance from each household to the nearest three pharmacies, then we calculated the travel time to the nearest one using Open Route Services.

Results: The number of pharmacies increased from 420 in 2002 to 1037 in 2022. Most households in Norway have short travel time to the nearest pharmacy. 61,7 % of the households had no change in the traveling time between 2002 and 2022 versus 36,1% and 2,2% for shorter and longer traveling times respectively. 41,6% of the households had less than 5 minutes to the nearest pharmacy in 2002 versus 55,8% in 2022. 0,8% of the households has more than two hours to the nearest pharmacy in 2002, the percentage did not change in 2022.

Conclusion: Travel time to pharmacies in Norway is generally short. Most pharmacies opened after 2002 were in the central areas and did not increase accessibility, especially in the rural areas.

C2

Association between use of low-dose aspirin and detection of colorectal polyps and cancer in a screening setting

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Introduction: The possible protective effect of aspirin on the risk of colorectal cancer (CRC) is still highly debated.

Aims: To study the association between low-dose aspirin use and detection of different colorectal lesions in a screening population.

Methods: We used data from the Bowel Cancer Screening in Norway, a trial randomizing individual from the general population, aged 50-74 years, to flexible sigmoidoscopy or faecal immunochemical test (FIT). Prescriptions of low-dose aspirin during the four years before screening invitation were obtained from the Norwegian prescription database. Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between aspirin use and detection of CRC and two possible CRC precursors: adenomas and advanced serrated lesions (ASL; traditional serrated adenomas or any serrated polyp with diameter size ≥1 cm or any dysplasia).

Results: Among 64,889 screening attenders (24,159 sigmoidoscopy, 40,730 FIT), 314 (0.5%) had CRC, 6,208 (9.6%) adenoma and 659 (1.0%) ASL. Overall use and short-term use (<3 years) of low-dose aspirin versus no use, were not associated with any type of colorectal lesion. Long-term use (≥3 years) versus no use was associated with lower detection of CRC (OR 0.66, 95%CI 0.46-0.93; 0.56, 0.33-0.97 for sigmoidoscopy; 0.72, 0.45-1.15 for FIT), with no significant differences between CRC location (P=0.59), CRC stage (P=0.76), screening arm (P=0.49) and sex (P=0.67) strata. We found an association between long-term aspirin use versus no use and lower detection of adenomas only in sigmoidoscopy arm (OR 0.95, 95%CI 0.87-1.03 for attenders; 0.89, 0.80-0.99 for sigmoidoscopy; 1.03, 0.89-1.18 for FIT), but not ASLs (OR 1.02, 95%CI 0.80-1.31 for attenders; 0.97, 0.72-1.32 for sigmoidoscopy; 1.04, 0.68-1.60 for FIT).

Conclusions: Screening attenders who had used low-dose aspirin for three years or more had a lower detection of CRC. Low-dose aspirin use was associated with a lower detection of adenomas in the sigmoidoscopy arm, but not ASLs.

C3

Treatment of advanced non-small cell lung cancer patients with immunotherapy and targeted therapy in Norway

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Introduction: Non-small cell lung cancer (NSCLC) patients are often diagnosed at an advanced stage with a poor prognosis and until recently, had few available treatment options. Advances in immunotherapy and targeted therapy have introduced several new drugs into clinical practice, which have shown survival benefits in clinical trials. However, clinical trials are performed on a selected group of patients and less is known of whether these results are generalizable to patients treated in clinical practice in Norway.

Aims: We aimed to characterize advanced NSCLC patients treated with immune checkpoint inhibitors (immunotherapy) and tyrosine kinase inhibitors (targeted therapy) in an unselected, real-life population in Norway.

Methods: Our cohort study included all patients diagnosed with advanced (stage IIIB/C+IV) NSCLC between 2010–2018, as identified by the Cancer Registry of Norway. Treatment was identified using the Cancer Registry (including the quality registry and Increase Pharmaceutical Reporting, INSPIRE, project), the Norwegian Prescription Database and the Norwegian Patient Registry. We applied descriptive statistics to characterize advanced NSCLC patients receiving immunotherapy or targeted treatment (users) and compared them to non-users, with respect to clinical, socioeconomical, and geographical variables.

Results: Between 2010 and 2018, 9200 patients were diagnosed with advanced NSCLC. 1521 (17%) were identified as ever users of targeted (n=859) and immunotherapy (n=811) treatment. Users were younger than non-users (median age 66 vs 69 years), more likely to be female (54% vs 42%), and more likely to have completed post-secondary vocational or higher education (20% vs 11%). Users were also more likely to have a better clinical performance status. We did not observe any geographical differences in the application of these new treatment modalities.

Conclusions: About 20% of patients with advanced NSCLC received immunotherapy or targeted therapy as part of their treatment between 2010 and 2018; these patients were younger and appeared to be in better health at diagnosis compared to those that did not receive these new treatment options.

C4

Risk of antidepressant drug initiation among users of cardiovascular agents and metformin. Findings from the Trøndelag Health Study (HUNT) and Norwegian Prescription Database (NorPD), Norway

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Introduction: Evidence points to inflammation as linking mechanisms between cardiovascular diseases (CVDs), diabetes mellitus (DM) and depression, suggesting that cardiovascular and antidiabetic agents with inflammatory targets may be drug repurposed for depression. However, the relationships between CVDs and DM drug treatments and the risk of depression and subsequent depression treatment remain unclear.

Aims: To examine the risk of antidepressive agents initiation among users of angiotensin II receptor blockers (ARBs), angiotensin-converting enzyme inhibitors (ACE-I), acetylsalicylic acid (ASA), beta-blockers (BB), calcium channel blockers (CCB), diuretics and metformin.

Methods: A prospective population-based study with a 10-year follow-up. Data material included Trondelag Health Study (HUNT3), Norway, linked to the Norwegian Prescription Database (NorPD). Of the total sample of 50 815 participants aged 19 and up, 20 227 were aged 40-70 years and had not received any drug prescriptions in the last 6 months before baseline at HUNT3. Exposures, including ARBs, ACE-I, ASA, BB, CCB, diuretics or metformin were defined as mono- or polytherapy. The outcome was the initiation of antidepressant agent use based on the first antidepressant prescription. Cox proportional hazards models calculated hazard ratios (HRs) with 95% confidence intervals (CI) as risk estimates for antidepressant agent initiation.

Results: The risk of antidepressant initiation varied in users of cardiovascular agents and metformin, yet no drug was associated with increased risk. ARBs (HR 0.67; 95%CI 0.54-0.84) or CCB (HR 0.78; 95%CI 0.59-1.02) monotherapy was associated with a lower risk for the initiation of antidepressant use than no use of these drugs. Furthermore, a reduced risk of antidepressant initiation was found among ASA (HR 0.84; 95%CI 0.67-1.04) and statin (HR 0.63; 95%CI 0.63-0.98) polytherapy users.

Conclusions: Reduced risk of antidepressant initiation was found among users of ARBs or CCB, whereas there was no altered risk for ACE-I, BB, diuretics or metformin users. Our findings indicate that some cardiovascular have the potential to reduce antidepressant use, but findings remain mixed. As depression is common in CVDs, cardiovascular agents' potential mental health benefits require further attention.

C5

Time-varying exposure to anti-osteoporosis drugs and risk of first-time hip fracture – a population wide study within the Norwegian Epidemiologic Osteoporosis Studies (NOREPOS)

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Introduction: Norway has a high hip fracture incidence. Bisphosphonates and denosumab have been shown to prevent hip fractures in clinical trials, but there is a lack of population studies.

Aims: To investigate whether use of bisphosphonates and denosumab reduce the risk of first-time hip fracture in Norway when adjusting for morbidity by the medication-based Rx-Risk Comorbidity index.

Methods: The population was defined as inhabitants identified in the national census of 2001 who were still alive and resident by 1 January 2005. The Norwegian prescription database (NorPD) supplied data on exposures to bisphosphonates, denosumab, and other drugs for the calculation of the Rx-Risk score. Information on previous and incident hip fracture was available in the quality-assured NOREPOS hip fracture database. Persons 50 years or older were included starting from January 2005 and observed through December 2016. Sex-stratified Cox regression and flexible parametric survival analysis was used with age as time scale and with time-varying exposure to bisphosphonates and denosumab. Individuals were followed until hip fracture or censoring (death, emigration, age 90 years, or 31 December 2016, whichever occurred first). Rx-Risk score was included as a time-varying covariate, updated every two years. Other covariates were marital status, education, and time-varying use of bisphosphonates/denosumab with another indication than osteoporosis. Mean time to hip fracture within the observation period (restricted mean survival time) was estimated for the two different treatment exposures.

Results: Of 1,044,661 women and 1,040,782 men, 74,775 (7.2%) and 13,417 (1.3%), respectively, were ever-exposed to either drug. Women exposed to bisphosphonates had a hazard ratio (HR) of 1.09 (95% CI: 1.05–1.13) for hip fracture (age as time-scale), while women exposed to denosumab had an HR of 0.68 (95% CI: 0.53–0.87). The corresponding fully adjusted HRs were 0.95 (95% CI: 0.91–0.99) and 0.58 (95% CI: 0.46–0.74) respectively. Exposure to either of the two drugs gave a longer hip fracture free period in women. For men exposed to either drug, the HRs was well above 1 – also when adjusted.

Conclusions: In population-wide real-world data, women exposed to bisphosphonates had a hip fracture risk around the same level as the unexposed population after adjusting for comorbidity. Exposure to denosumab was associated with a lower risk of hip fracture in women.

D1

The association between educational attainment and premature mortality – A comprehensive burden of disease analysis

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Introduction: Substantial social inequalities in fatal health outcomes are one of the most consistent epidemiological findings and considered a key priority for researchers and policy makers. Traditional epidemiological metrics, however, such as mortality rate ratios (MRR), may not provide a complete picture. The Global Burden of Disease Study (GBD) is the most comprehensive worldwide observational epidemiological synthesis of data and uses metrics such as years of life lost (YLLs) and life expectancy, to provide a more detailed assessment of fatal health conditions. Currently, the GBD Study does not include socioeconomic factors, such as education or income level.

Aims: To use a panel of mortality metrics typically used in the GBD to provide a more complete description of the association between social inequality and premature mortality.

Methods: Several national compulsory registries were linked at the individual level and included the Norwegian Cause of Death Registry, and data regarding the population and education from Statistics Norway. We calculated age-standardised mortality rate differences (SMRDs), MRRs, age-standardised YLLs, and life expectancy across 100 GBD level-3 causes of death, in individuals aged 30 to 75 years, and between education groups (low=0-10y, middle=11-14y, high=14+y).

Results: The top ten differences between high and low education groups was observed for drug use disorders (HR=18.7, 95% confidence interval (CI)=15.1-23.2), alcohol use disorders (4.9, [4.5-5.4]), chronic obstructive pulmonary disease (COPD) (4.9 [4.6-5.3]), asthma (4.3 [3.6-5.0]), diabetes (3.4 [3.1-3.7]), lung cancer (2.9 [2.8-3.0]), upper digestive diseases (2.9, [2.5-3.4]), cirrhosis (2.9 [2.6-3.1]), cardiomyopathy (2.7 [2.3-3.1], and esophageal cancer (2.4 [2.1-2.7]). The greatest differences in SMR were observed for ischemic heart disease, lung cancer, COPD, diabetes, stroke, self-harm, stomach cancer, lower respiratory diseases, aortic aneurysm, and bladder cancer. Generally, a dose response was observed between education groups, with an overall risk of a premature death 2.0 and 1.5-times greater in individuals with low and middle education compared to high education, respectively. Analysis of SMRDs, age-standardised YLLs and life expectancy is ongoing.

Conclusions: We discuss the benefits of using a GBD approach to analyse individual-level registry data in regard to investigating the association between social inequalities and causes of death.

D2

Secular trends in body height according to educational level – A descriptive study from The Tromsø Study 1979-2016

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Introduction: Throughout the twentieth century, body height in the Norwegian population increased, mirroring the secular trend in height found in other Northern European countries. Height differences between socioeconomic status (SES) groups based on educational level have been reported in several European countries, pointing towards a social inequality in body height at population level. This phenomenon has previously been investigated in a cross-sectional study of Norwegians born between 1926 and 1940. However, data on body height according to educational level in Norwegian cohorts born after 1940 is currently missing from the literature.

Aims: The aim of our study was to describe time trends in body height according to educational level in women and men in Norway.

Methods: We used height measurements and self-reported educational levels from the population based Tromsø Study. Our study population consisted of 31 466 participants (50.9% women), aged 30-49 years, born between 1930 and 1977. Participants were stratified by 10-year birth cohorts and allocated into four groups based on attained levels of education. Descriptive statistics was used to calculate differences between groups and estimate mean body height.

Results: Mean body height increased by 3.4 cm (95% CI 3.0, 3.8) in women (162.5-165.9 cm) and men (175.9-179.3 cm) between 1930 and 1977. The height difference between groups with primary education compared to long tertiary education born in 1930-39 was 5.1 cm (95% CI 3.7, 6.5) in women (161.6-166.7 cm) and 4.3 cm (95% CI 3.3, 5.3) in men (175.0-179.3 cm). The height differences between educational levels were reduced to 3.0 cm (95% CI 1.9, 4.1) in women (163.6-166.6 cm) and 2.0 cm (95% CI 0.9, 3.1) in men (178.3-180.3 cm) born in 1970-77.

Conclusions: Body height increased in women and men in our population. Women and men with long tertiary education had the highest mean body height, which remained stable across all birth cohorts. Women and men in the three other groups had a gradual increase in height by birth cohort, reducing overall height differences between SES groups. Our study is limited by lack of data on the confounding variables of early year living conditions and parental SES.

D3

The relation between average level of education among all first-degree family members and risk of cardiovascular and all-cause mortality

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Introduction: Cardiovascular disease (CVD) mortality and all-cause mortality are associated with own educational attainment and parents' educational attainment. There is little evidence quantifying the relation between educational attainment of all first-degree relatives and mortality risk.

Aims: We investigated if there are associations between the average level of education in first-degree relatives and CVD and all-cause mortality. We also examined whether family educational attainment modified the relationship between own education and mortality risks.

Methods: Our sample included all Norwegians born between 1940 and 1959 who had at least one sibling participating in censuses from 1940 to 2001 (n = 972,832). A subsample consisted of individuals participating in any of three Norwegian Health Surveys (n= 363,918). We introduced education index as an average measure that is sum of education levels for all first-degree family members divided by the number of first-degree family members. We carried out both an effect modification analysis and a stratified analysis in Cox proportional hazards regression models.

Results: Lower individual and family education index were associated with higher hazard ratios for CVD mortality. The association of own education and CVD mortality was modified by family education index. We also found that the association of family education index with CVD mortality was modified by family size. These association patterns were similar in the all-cause mortality models. Parental education was more strongly associated with CVD mortality risk than sibling education. Adjusting the models for individual CVD risk factors or cognitive ability partially attenuated the associations. Our results also indicate that for a given family education index having a larger number of siblings was protective against CVD mortality.

Conclusions: Average educational attainment in first-degree family members was associated with CVD and all-cause mortality risk. In the shared genes and early-childhood environment, parent education index was stronger associated with decreased trend of the CVD mortality risk.

D4

Direct and indirect effects of socioeconomic status on sepsis risk and mortality: a mediation analysis of the HUNT Study

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Introduction: Socioeconomic status (SES) may influence risk of sepsis and sepsis-related mortality, but to what extent lifestyle and health-related factors mediate this effect is not known.

Aims: The main aim was to prospectively examine the effect of individually assessed SES on risk of a first sepsis episode and on sepsis-related mortality in the population-based HUNT study. Secondly, we examined to what extent the effect of SES on sepsis risk is mediated by known risk factors for sepsis.

Methods: The study included 65,227 participants of the population-based HUNT Study in Norway linked with hospital records to identify incident sepsis and sepsis-related deaths. Cox regression estimated hazard ratios of sepsis risk and mortality associated with different indicators of SES, whereas mediation analyses were based on an inverse odds weighting approach.

Results: During ~23 years follow-up (1.3 million person-years), 4200 sepsis cases and 1277 sepsis-related deaths occurred. Overall, participants with low SES had a consistently increased sepsis risk and sepsis-related mortality using education, occupational class, and financial difficulties as indicators of SES. Smoking and alcohol consumption explained 57% of the sepsis risk related to low education, whereas adding risk factors of cardiovascular disease and chronic diseases to the model increased the explained proportion to 78% and 82%, respectively.

Conclusions: This study shows that SES is inversely associated with sepsis risk and mortality. Approximately eighty percent of the effect of education on sepsis risk was explained by modifiable lifestyle and health-related factors that could be targets for prevention.

A6

Cancer epidemiology in practice: Working notes on cancer history-based selection and censoring.

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Introduction: Researchers conducting observational studies of exposure-cancer associations make decisions regarding the selection and censoring of study subjects with respect to their cancer history. Given available information, this may include cancers prior to start of follow-up (prevalent cancers), and multiple primary cancers (MPCs) at the same or different time-points during follow-up. The selection, definition and censoring of subjects constitutes an early part of the analysis in observational studies but may have implications for the statistical power and potential biases.

Aims: We discuss two approaches, each detailing a set of criteria aimed at subject selection and censoring, primarily for, but not limited to, cohort studies of exposure-cancer associations.

Methods: The two approaches are named the “all cancer approach” and “first primary cancer approach”. Both approaches exclude subjects with prevalent cancers to avoid information and selection bias. In the “all cancer approach”, subjects are censored on non-eligible cancer subtypes of the cancer under study, though subjects with MPCs are not censored on other incident cancers preceding or occurring simultaneously (at time of diagnosis) with the cancer under study. To limit the influence of prior treatment regimens, the “first primary cancer approach” censors subjects upon any first primary incident cancer not under study, including any “simultaneous” MPCs, as well as non-eligible subtypes of the cancer under study.

Conclusions: These alternative approaches may yield different estimates of the exposure-cancer association and are presented and discussed here as a potential resource and source of further discussion for peers in the field of cancer epidemiology.

A7

Establishment of a multi-source cohort of head and neck cancer patients with biomarkers and clinical outcomes – challenges, solutions and perspectives

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Introduction: Head and Neck Carcinomas (HNC) are aggressive and heterogenous tumors with a high fatality rate. Because of high tumor heterogeneity, establishing a large international cohort is needed to obtain good biomarkers for personalized treatment. However, heterogeneity in data collection is a major challenge.

Aims: We aim to describe and discuss the challenges faced when establishing a cohort of HNC patients with a variety of clinical outcomes and biomarkers by integrating prospectively collected data from multiple institutions across Europe (Germany, France and Italy).

Methods: A total of 1113 HNC patients were recruited over a span of 20 years and RNA was extracted from the primary tumor of each patient prior to treatment. Patients were followed for up to 20 years with clinical outcomes recorded during follow-ups. Recently, gene expression from each patient was measured to enable identification of biomarkers for clinical outcomes.

Results: Multiple sources of heterogeneity in data collection were identified and needed to be accounted for. Examples include data from multiple institutions, collected at different times using different recruitment procedures and inclusion criteria, different case report forms and different gene expression sampling and profiling protocols. Our approach for harmonisation of clinical variables included using common semantics and definitions, based on the already established BD2Decide HNC ontology. For gene expression, which was measured on different platforms, we followed community standards on data requirements using the MIAME and MINSEQE checklists. This focused on collecting annotations describing each data capture protocol and working with raw data files to ensure consistent gene annotation across platforms. Throughout this process, Findable, Accessible, Interoperable and Reusable (FAIR) principles were followed, with a semantics codebook being frequently updated during the establishment of the cohort. Understanding differences in inclusion criteria, procedures and recruitment time was critical when establishing an international cohort retrospectively and is key for subsequent research. Effective communication between partners from different disciplines (clinicians, bioinformaticians, biostatisticians) required cross-disciplinary communication, mutual respect and good effort.

Conclusions: We discuss challenges faced when establishing a large international cohort of HNC patients, how we solved key problems and important lessons from such collaborations.

A8

Age at menarche, age at natural menopause and risk of lung and colorectal cancers in Norwegian women: a Mendelian randomization analysis in the HUNT Study

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Introduction: The roles of age at menarche and at menopause in the aetiology of lung and colorectal cancers, among the most common cancers in women, are unclear.

Aim: We performed a one-sample Mendelian randomization (MR) study to investigate potential causal associations between age at menarche, age at natural menopause and risk of lung and colorectal cancers in Norwegian women. We also evaluated the direct effect of age at menarche after taking account of possible mediating effect of adult body mass index (BMI).

Methods: From the HUNT Study in Norway, we included 35,477 women with complete information on genetic variants, age at menarche and adult BMI, and 17,118 women with complete information on genetic variants and a natural menopause, respectively. We used polygenic scores as instruments for age at menarche and age at menopause. We run univariable MR to evaluate the potential causal associations. We also performed multivariable MR adjusting for genetic variants of adult BMI to evaluate the direct effect of age at menarche.

Results: Genetically predicted one-year increase in age at menarche was associated with a lower risk of lung cancer overall (HR 0.64, 95% CI 0.48-0.86), lung adenocarcinoma (HR 0.61, 95% CI 0.38-0.99) and lung non-adenocarcinoma (HR 0.66, 95% CI 0.45-0.95). After taking account of adult BMI using multivariable MR model, the direct effect estimates reduced to a HR 0.72 (95% CI 0.54-0.95) for lung cancer overall, HR 0.67 (95% CI 0.43-1.03) for lung adenocarcinoma and HR 0.77 (95% CI 0.54-1.09) for lung non-adenocarcinoma. Age at menarche was not associated with colorectal cancer. Moreover, genetically predicted age at natural menopause was not associated with lung or colorectal cancer.

Conclusion: Our MR study suggested that later age at menarche was causally associated with a decreased risk of lung cancer overall and its histologic types. These inverse associations might have been partially mediated by adult BMI, although age at menarche still had a direct effect on lung cancer overall. Age at menopause was not associated with the risk of lung or colorectal cancer.

A9

Epidemiology of gliomas in Norway: a 15-year registry-based study

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Introduction: Primary brain tumors are a heterogeneous group of tumors. Gliomas constitute about 75% of all malignant primary brain tumors in adults, of which glioblastoma (GBM) is the most frequent histologic subtype. GBMs cause substantial morbidity and mortality worldwide and show the highest age-standardized incidence rates in the Nordic countries.

Aims: To investigate changes in incidence rates of gliomas among adults in Norway.

Methods: We retrieved data from the National Population Register, the Cancer Registry of Norway and the Norwegian National Education Database. Incidence of glioma among adults (≥18 years old) over the study period (2004-18) was investigated in relation to sex and morphology. Incidence rates were age-standardized according to the World standard population.

Results: We identified 4329 glioma cases giving an overall age-standardized incidence rate of 6.7 per 100 000 person-years. The incidence rate fluctuated between 7.9 (2005) and 5.9 (2016) per 100 000 person-years, without any sharp turning point. During the study period, gliomas were diagnosed 1.4 times more often in males than in females. The median age at diagnosis was 59.3 years and the incidence increased with age. GBM was the most frequently reported subtype comprising 60.5 % of all gliomas, followed by diffuse astrocytoma (13.2 %). Compared to the other subtypes, GBMs were diagnosed at older ages. We found a higher proportion of oligodendroglioma among managers, professional and associate professionals and in patients with tertiary education (≥ 14 year) than in the glioma-free population.

Conclusion: In line with previous findings from different populations, our results did not show any noticeable trend in the age-standardized incidence rates of adult gliomas in Norway, however, the consistent male dominance pattern among glioma patients was clear.

A10

Profiles of mental health and its characteristics in childhood and young adult cancer survivors – the NOR-CAYACS study

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Introduction: Childhood, adolescent, and young adult cancer survivors (CAYACS) represent a growing population at risk of significant psychological distress. Survivors are twice as likely to experience anxiety and depression as the general population, especially in concurrence with fear of recurrence (FoR) and fatigue. These are largely studied separately, with little done to map the landscape of mental health profiles in CAYACS.

Aims: We aimed to identify and describe mental health profiles in adult CAYACS through latent profile analysis (LPA) and describe their characteristics.

Methods: The NOR-CAYACS study is a cross-sectional survey with survivors of childhood cancers (excluding central nervous system tumors), breast cancer, colorectal cancers, non-Hodgkin lymphoma, leukemias and malignant melanomas identified through the Cancer Registry of Norway. We included 1893 long-term survivors ≥5 years since last cancer diagnosis, and ≥18 years at the time of study. We used LPA to identify subgroups from six dimensions: self-reported physical and mental fatigue, depression, anxiety, post-traumatic stress disorder (PTSD), and FoR. Estimated marginal means and sample proportions are presented for each subgroup.

Results: We identified four profiles: 1)“low distress-moderate fatigue” (64%) with moderate fatigue but all other dimensions low, 2)“moderate distress-moderate fatigue” (18%) with moderate levels of fatigue and depression though slightly elevated PTSD and FoR, 3)“moderate distress-high fatigue” (13%) where physical and mental fatigue levels were high but moderate levels of depression, anxiety, PTSD, and FoR, and 4)“high distress-high fatigue” (5%) where all dimensions scored high.

The “high distress-high fatigue” group was characterized by lower age at study (39.5 years, standard deviation (SD) 11.7, vs. 42.2-43.5), shorter time since first diagnosis (15.1 years, SD: 6.9, vs. 16.0-17.1), and highest proportion compulsory education only (13% vs. 5-8%). Those “low-distress-moderate fatigue” had highest proportion with university education (61% vs 50-56%).

Conclusions: Our LPA suggests that a third of CAYACS struggle with moderate to poor mental health in all dimensions. Fatigue was moderate to high in all profiles. While anxiety, PTSD, and FoR presented in similar degrees of severity within each profile, fatigue manifested often nonconforming to the rest. Future interventions for survivors should target multiple dimensions simultaneously, beyond those used for individual conditions.

A11

Smoking and Pancreatic Cancer in the Multiethnic Cohort study

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Introduction: In the US, the incidence of pancreatic cancer (PC) ranks as number ten among men and eight among women. PC is number four of cancer deaths for both sexes. Smoking was established as a cause of PC in the 1980's.

Aims: To examine the risk of PC due to cigarette smoking and the benefits of smoking cessation by sex

Methods: We analyzed data from 192,035 participants aged 45-75 years, enrolled in the Multiethnic Cohort Study in 1993-1996. We identified PC cases via linkage to the Hawaii and California Surveillance, Epidemiology, and End Results Program cancer registries, through December 2017. We computed hazard ratios (HRs) with 95% confidence intervals (CIs) for the associations of PC with different measures of smoking exposure overall and by sex, using never smokers as the reference group. For former smokers, we computed HRs with 95% CIs for the association between years since quit smoking and PC, using current smokers as the reference group.

Results: During a mean follow-up of 19.2 years, we identified 1,936 incident PC cases. Compared with female current smokers, male current smokers had smoked for more years, smoked more cigarettes per day and, consequently, had smoked more pack-years. It was likewise for former smokers. In multivariate Cox regression models, as compared with sex-specific never smokers, current smokers had a similar elevated risk of PC for men, hazard ratio (HR) =1.48 (95% CI 1.22, 1.79) and women, HR=1.49 (95% CI 1.24, 1.79) *($P_{heterogeneity}$: 0.64).* Compared with their current smoking counterparts, former smokers showed within 10 years after quitting, a decrease in risk of PC for men (HR=0.66; 95% CI 0.50, 0.88) and women (HR=0.70; 95% CI 0.50, 0.96). Both sexes showed a consistent, positive dose-response association with PC for the three measures (duration, number of cigarettes per day, number of pack-years) of smoking exposure among current smokers and an inverse association for years of quitting among former smokers (all P_{trend} <0.001).

Conclusions: Our results show that although women smoke on average less than men, the overall smoking related increase in PC risk and the benefits of cessation, did not differ by sex.

B6

Benefit and risk assessment of fish in the Norwegian diet

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Introduction: Fish intake is an important source of both nutrients and environmental contaminants. The European Food Safety Authority has lowered the tolerable weekly intakes (TWIs) for dioxins, dioxin-like PCBs (dl-PCBs), and perfluorinated alkylated substances (PFASs). In 2022 VKM published a comprehensive benefit and risk assessment of fish intake commissioned by the Norwegian Food Safety Authority.

Aims: To estimate health consequences for the Norwegian population if fish intake 1) remains at current level, or 2) increases to meet recommendations by the Directorate of Health (300-450 g/week in adults).

Methods: Systematic literature reviews of fish and nutrient intake in relation to health outcomes (cardiovascular diseases/CVDs, neurodevelopment, cognition/mental health, birth outcomes, diabetes, bone health, body composition, immune health, and semen quality). Epidemiological evidence was graded by World Cancer Research Fund criteria. For associations graded "probable", published meta dose-response relationships were combined with registry data to estimate annual new cases or deaths for changes in fish intake in Norway. Current intake (based on national dietary surveys in ages 1-70 years) was compared to different scenarios (150, 300 and 450 g/week). Consequences for intake of nutrients (n-3 fatty acids, vit. D, vit. B_{12}, iodine, selenium) and contaminants (dioxins, dl-PCBs, PFASs, methyl mercury) were evaluated against average requirements and TWIs, respectively.

Results: There is "probable" evidence that fish intake reduces the relative risk of mortality (overall and for CVD outcomes), and incident coronary heart disease (CHD), stroke, dementia, Alzheimer's, preterm birth, and low birth weight. No "probable" evidence was found for adverse outcomes (children or adults). Current mean fish intake is 350 and 238 g/week in men and women, respectively. VKM estimates that intake of 450 g/week will mainly reduce annual cases of incident CHD (n=1600), dementia (n=780) and preterm birth (n=200), whereas intake of 150 g/week will increase cases. Most of the population currently exceeds TWIs for dioxins, dl-PCBs, and PFASs, but lower fish intake alone will probably not reduce exposures below TWIs. Assumptions, uncertainties, and data gaps are discussed in the report.

Conclusions: Current fish intake is beneficial compared with lower intakes. Higher intakes within recommendations are estimated to have a net benefit.

B7

Dietary magnesium intake among community-dwelling older adults in Oslo, Norway

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Introduction: Some studies have reported a relation between low magnesium levels and risk of cardiovascular disease, osteoporosis, depression, metabolic- and renal -disorders. Older adults over 65 years may be at higher risk of these diseases, but there is limited information on the dietary magnesium intake in this population.

Aim: The purpose of this study was to estimate the dietary magnesium intake in older community-dwelling adults in Oslo, Norway.

Methods: In this cross-sectional study, we included 102 participants aged ≥ 65 years from five selected senior centers in Oslo, Norway. Dietary intake, with and without supplements was collected through a standardized Food Frequency Questionnaire (FFQ), including the main food-items from the Norwegian diet. Magnesium intake was estimated through the nutrient calculation system (KBS) developed by the University of Oslo. Background characteristics (age, gender, education level, smoking status, prescription-based medicine use, family status, self-reported BMI and self-reported health status were collected through an additional questionnaire. Ninety-nine participants were included in the current analysis.

Results: The mean intake of dietary magnesium estimated through the FFQ was 352 mg/day for men and 380 mg/day for women from food only. Only 18 % reported the use of magnesium- containing supplements. For supplement users the total magnesium intake was 364 mg/day for men and 420 mg/day for women, respectively. Participants aged ≥75 years had a lower magnesium intake from diet compared with <75 years old. Men were found to have lower intake of magnesium in their diet (when including supplements) compared to women. No other background characteristics were found to be associated with intake.

Conclusion: In the current study, estimated dietary magnesium intake was above the Nordic Nutrition Recommendation (NNR) in women (618 mg/day) below the lower range of estimated magnesium intake in men (108 mg/day). However, the study was based on a selected population, and the FFQ commonly overestimates the nutrient intake. Still, the NNR is based on a younger adult population and the magnesium requirement of older adults may be different. Further research is required to estimate the level of dietary magnesium intake among a more broad older adults' population.

B8

Individualized nutrition plans and risk of death in older health care service users with chronic diseases

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Introduction: Nutritional risk is common in older health care service users. We recently showed an increased risk of earlier death in older health care service users at nutritional risk in a large register-based cohort study on persons receiving health care services from Norwegian municipalities.

Aims: We aimed to investigate whether individualized nutrition plans could reduce this risk of earlier death in older health care service users at nutritional risk in the same study cohort.

Methods: A register-based cohort study on 18,665 health care service users ≥65 years with chronic diseases (type 2 diabetes, COPD, osteoporosis, stroke, dementia, or heart failure) at nutritional risk. Data on nutritional risk, nutrition plan, sociodemographics and date of death was obtained from the Norwegian Registry for Primary Health Care (Kommunalt pasient- og brukerregister, KPR) and diagnoses from both KPR and the National Patient Registry (NPR) during the period 2017-2018. We performed Cox regression analysis to analyze possible associations of nutrition plans with risk of death within six months. Analyses were stratified by diagnosis, and adjusted for age, gender and living situation.

Results: Among older health care service users at nutritional risk(n=18,665), 82% had a nutrition plan, 31% were men, and 39% lived alone. Mean age ranged from 81 to 85 years for the different diagnostic groups and 18% died within six months. Having a nutrition plan was not associated with a reduced risk of death within six months in older health care service users at nutritional risk with COPD, stroke or dementia. Unexpectedly, nutrition plan was associated with a higher risk of death in older health care service users with type 2 diabetes, osteoporosis and heart failure (adjusted HRs 1.45(95% CI=1.11, 1.88), 1.71(1.25, 2.36) and 1.39(1.13, 1.72), respectively).

Conclusion: We found that nutrition plans did not reduce the risk of death within six months in older health care service users with chronic diseases at nutritional risk. Nutrition plans were associated with increased risk of death in some diagnostic groups. This may be due to insufficient control over illness severity and the indication for providing nutrition plans, or a low degree of implementation of the nutrition plans.

B9

The association of serum vitamin D with dental caries and periodontitis in Norwegian adults: The HUNT Study

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Introduction: Previous studies have shown inconsistent results for the associations of vitamin D with dental caries and periodontitis, partly due to selection bias of study population, confounding and different definitions of dental outcomes.

Aims: We used the 2017 AAP/EFP classification scheme for periodontitis diagnosis and considered a large panel of confounders to study the relationship between vitamin D and oral health in a general Norwegian adult population.

Methods: Study comprised participants with serum 25-hydroxyvitamin D [25(OH)D] measured in HUNT3 and oral health information collected at the HUNT4 Oral Health Study (n=1605) from the Trøndelag Health Study (HUNT) in Norway. Seasonal-standardized serum 25(OH)D was used as both categorical [<30.0, 30.0–49.9, 50.0–74.9 (reference) and ≥75.0 nmol/L] and continuous variables (per 25 nmol/L decrease). Oral health outcomes were dental caries using the decayed, missing and filled teeth (DMFT), periodontitis and the total number of permanent teeth. Periodontitis case was defined in participants with severity at stage 2 or above. Rate ratios (RRs) and 95% confidence intervals (CIs) were estimated using negative binomial regression models for DMFT and the total number of permanent teeth. Poison regression with robust error variance was used to estimate prevalence ratios (PRs) for the association between serum 25(OH)D and periodontitis.

Results: Serum 25(OH)D level was not associated with DMFT (<30 nmol/L: RR 1.05, 95% CI 0.99 to 1.11; 30–49.9 nmol/L: RR 1.00, 95% CI 0.97 to 1.03; and >75 nmol/L: RR 1.05, 95% CI 1.00 to 1.09). No association was observed for periodontitis (<30 nmol/L: PR 0.89, 95% CI 0.78 to 1.02; 30–49.9 nmol/L: PR 0.99, 95% CI 0.93 to 1.04; and >75 nmol/L: PR 0.98, 95% CI 0.91 to 1.06) and for total number of permanent teeth (<30 nmol/L: RR 0.98, 95% CI 0.93 to 1.02; 30–49.9 nmol/L: RR 0.99, 95% 0.97 to 1.02; and >75 nmol/L: RR 0.98, 95% CI 0.95 to 1.01). Serum 25(OH)D level as a continuous variable showed similar results for all oral health outcomes.

Conclusions: There was no clear evidence showing associations of serum 25(OH)D level with dental caries and periodontitis in this Norwegian adult population.

B10

The dose-response relationship of premenopausal alcohol consumption with age at menopause: a population study of 280,497 women in Norway

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Introduction: Although alcohol consumption has been associated with high age at natural menopause in several studies, knowledge about the dose-response relationship remains inconsistent. Menopause occurs when the number of ovarian follicles reaches a critical level. Thus, alcohol consumption has been assumed to delay the depletion of the ovarian follicles, and thereby, postpone menopause. If alcohol truly influences the ovarian reserve, the association of alcohol consumption with age at menopause would expectantly display a dose-response pattern.

Aim: To study the pattern of the association of premenopausal alcohol consumption with age at natural menopause.

Methods: We performed a retrospective population study among 280,497 women aged 50-69 years who had attended the Norwegian breast cancer screening program (BreastScreen Norway). Data were collected by two self-administered questionnaires during the years 2006-2015. Associations of weekly alcohol consumption (in grams) between the ages of 20-49 years with age at menopause were estimated as hazard ratios (HR) using Cox proportional hazard models with restricted cubic splines to allow for non-linear associations. We adjusted for year of birth, place of birth, number of childbirths, educational level, body mass index, and smoking habits.

Results: Mean age at natural menopause was 51.20 years (IQR: 49-54 years). The adjusted HR of reaching menopause was highest for women with no alcohol consume (reference), and the HR decreased by alcohol consumption up to 50 grams per week (adjusted HR 0.86; 95% CI: 0.85-0.88). Above 50 grams per week, there was no further decrease in the HR of reaching menopause (*P* for non-linearity < 0.001).

Conclusions: Women who did not consume alcohol, were youngest at menopause. Among alcohol consumers, however, there was no dose-repose association with age at menopause. Our findings may suggest that characteristics of the women who did not consume alcohol, not accounted for in the data analyses, explain their younger age at menopause.

B11

Potentially traumatic events and hazardous alcohol use in a large general population sample: The Tromsø Study 2015-2016.

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Introduction: Hazardous alcohol is an increasing threat to the public health, defined as a consumption pattern that increase the risk of adverse events. Due to the potential consequences of hazardous alcohol use it is crucial to identify factors that may be associated with hazardous alcohol to better enable prevention. PTEs may be one such factor, and it is found to be highly comorbid with alcohol related problems. However, past research has focused extensively on adverse childhood experiences, or on specific PTEs in relation to alcohol problems.

Aims: We aimed to examine which PTEs were most strongly associated with hazardous alcohol use. In addition, we looked at differences in PTEs experienced in childhood and in adulthood, in terms of associations with comorbid hazardous alcohol use.

Methods: Cross sectional data was drawn from the seventh survey of the Tomsø Study (N=21 083), a large population-based health survey in Northern Norway. Ten different types of self-reported potentially traumatic events were included, such as childhood neglect, sexual and physical abuse, bullying, loss of a loved one etc. Hazardous alcohol use was measured with the Alcohol Use Identification Test (AUDIT). The association of PTEs and hazardous alcohol use will be measured with logistic regression analyses.

Results and conclusion: Results will be presented in an oral presentation at the conference. The present study may provide insight into what types of potentially traumatic events are more strongly associated with hazardous alcohol use. It may also provide useful knowledge regarding age-period when the PTE occurred, where prevention may be important.

C6

Social anxiety and school absenteeism among adolesecents; from student behavioral engagement perspective; evidence from Young-HUNT3 and Statistics Norway

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Introduction: Adolescents spend much of their everyday life at school, which requires daily social interaction. Adolescents with social anxiety traits (SA) might therefore find it difficult to master and thrive in the school context. School absenteeism is, however, not only psychologically influenced, but also caused by multiple factors including the school setting. As such this study attempts to understand how student behavioral engagement (SBE) helps socially anxious adolescents attend school despite their avoidance behavior.

Objective: The focus is on how social anxiety traits among upper secondary school students is associated with absenteeism and how this is influenced by levels of SBE

Methods: Data sourced from the Young-HUNT3; and with participants' senior high school attendance records from national education registry. A preliminary sample size of 1,433 students was used for analysis. Student absenteeism was categorized into three sub-groups: Thus (0-5 days) were categorized as *"no school absenteeism,"*, (6-18days) as *"regular school absenteeism"* group, and 19 days and above as *"problematic school absenteeism*. A sub-dimension of the school functioning scale from Young-HUNT3 was used to evaluate SBE levels. Given that the outcome variable is ordinal an ordered logistic regression with interaction effect was estimated.

Results: Our hypothesis model was verified, with results indicating that social anxiety traits and student behavioral engagement together is associated with students' absenteeism. The marginal effect of SA on probability of problematic absenteeism when SBE is low is 0.3% more. For regular school absenteeism, the marginal effect of SA on probability of being at regular absenteeism increase by 2.5% points when SBE is low. For no absenteeism, the effect of SA on the probability of being at no absenteeism is 0.3% points lower when SE is low. Thus, for those in no and regular absenteeism group they are at risk of moving to problematic absenteeism group given a low SBE and an increase in social anxiety traits levels.

Conclusion: The results suggests that a high positive SBE is associated with a high probability of regular school attendance for adolescents associated with SA, particularly among students with no absenteeism and regular absenteeism.

C7

Upper secondary school completion in adolescents with social anxiety – A follow-up of the Young-HUNT3 Cohort, Norway

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Introduction: It is well established that social anxiety often emerge in late childhood or adolescence. This is a phase in life where school performance and social network building provide an important foundation for future health and socioeconomic prospects. Longitudinal population-based studies that explore and quantify school achievement and failure among adolescent with social anxiety are sparse.

Aims: We aim to investigate to what extent social anxiety in adolescence is associated with completion of upper secondary school.

Methods: This longitudinal study is based on 8,199 adolescents aged 13-19 years who participated in the Young-HUNT3 (Nord-Trøndelag Health Study, 2006-2008) population based study. The Young-HUNT3 data was linked to data from National Educational Data (2008-2019) enabling a follow-up of all participants to 25 years of age. Social anxiety was measured as 1) screening information from diagnostic interviews (Anxiety Disorder Interview Schedule for DSM IV: child version [ADIS-C]), and 2) mean scores of self-reported symptoms. Logistic regression analyses tested associations, and post estimation command “margins” estimated predicted probabilities for completion of upper secondary school.

Results: Our preliminary results show that adolescents screened positive for SAD (SP), were estimated to have about 15 percentage point lower predicted probability of upper secondary school completion within 21 years of age, compared to adolescents screened negative (SN). For completion within 25 years, the predictions were higher for both groups, but still lower for SP. Also, predicted probabilities for completion were decreasing by elevated mean levels of self-reported social anxiety symptoms.

Conclusion: Our results are in line with earlier findings of educational underachievement among social anxiety sufferers and contribute to new knowledge. Particularly the use of a longitudinal design on a population sample, registry-based educational data, as well as several measures of social anxiety represent considerable strengths. An increased effort should be put into finding ways to reduce this gap in school completion rates to reduce the risk for long-term burden on welfare and healthcare.

C8

Explaining variance in self-efficacy among adolescents: the association between quality of life, social support, and self-efficacy

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Introduction: Self-efficacy has been identified as an important health promoting factor both for physical and mental health. Previous studies have examined self-efficacy as a moderating factor between negative psychosocial factors and various outcomes, e.g., life satisfaction and stressors. There is however limited knowledge about factors that strengthen self-efficacy. Thus, from a public health perspective it is crucial to identify factors that strengthen self-efficacy.

Aims: The purpose of this study was to examine the association between quality of life, social support, and self-efficacy among adolescents.

Methods: This study was based on cross-sectional data from the Ungdata survey conducted in 2021. The sample comprised 9221 adolescents (aged 13–16 years). Sequential multivariate linear regression was conducted to explore the association between quality of life, social support, and self-efficacy. The independent variables were entered in three sequential steps. Sociodemographic variables were entered in the first model, whereas items about quality of life were added in the second model. In the final model (model 3), the independent variables about social support were entered in addition to the previously mentioned independent variables.

Preliminary results: The final model (Model 3) explained 25% of the total variance in self-efficacy. The 'quality of life'-related indicators explained more of the observed variance in self-efficacy than the other independent variables (change in R square = 15.2%). The items "master experiences" and "be useful", made the strongest and most significant contributions to the variance in self-efficacy in the final model ($\beta = 0.25$, $p < 0.001$ and $\beta = 0.16$, $p < 0.001$, respectively), followed by the variables "support from friends" and "support from teachers" ($\beta = 0.06$, $p < 0.001$ and $\beta = 0.06$, $p < 0.001$).

Preliminary conclusions: Master experiences and feeling useful are potential sources in creating and strengthening self-efficacy. Being aware the health promoting potential in (strengthening) self-efficacy among adolescents is important. Additional research is needed to further explore these associations.

C9

Educational attainment and mental health: analysing the impact of early-life family factors

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Introduction: Previous evidence has shown that higher educational attainment (EA) is protective against mental health conditions (MHC) including, mental disorders and psychosocial disabilities as well as damaging mental states. Early-life family factors can impact both EA and mental health, and partly explain an association between them.

Aims: To evaluate to what extend the association between EA and MHC is explained by early-life family factors using genetic instrumental variables.

Methods: The relationship between EA and MHC was analysed applying one-sample and two-sample Mendelian randomization (MR). One-sample MR analyses were performed using participant's data from the Nord-Trøndelag Health study (HUNT, Norway), while for two-sample MR we used summary statistics of publicly available Genome-Wide-Association-Studies (GWAS). Estimates from population and family-based analyses were compared to evaluate the impact of early-life family factors. Four MHC were analysed: anxiety and depressive symptomatology, neuroticism and consumption of prescribed medication to relieve MHC. In the case of one sample-MR, anxiety and depressive symptomatology as well as neuroticism were evaluated using Hospital Anxiety Depression Score and Eysenck Personality Questionnaire, respectively.

Results: We found evidence of a protective effect of EA on mental health. Individuals with higher EA were less likely to suffer symptoms of anxiety, depression, neuroticism or take prescribed medication. In contrast to population-based models, within-family models showed attenuation of the protective effect of EA. For anxiety symptoms, the estimate attenuated from -0.16 to -0.07 (95%CI: -0.31, 0.18); for depressed mood, from -0.08 to -0.01 (95%CI: -0.15, 0.18); and for neuroticism, from -0.19 to -0.12 (95%CI: -0.24, 0.00). For consumption of prescribed medication, EA even became risk factor (1.79; 95%CI: 0.62, 5.21).

Conclusions: Early-life family factors attenuate the protective effect of education on mental health conditions. Our findings suggest that some of the causal effect of education, as estimated using genetic instruments, is confounded.

C10

Preventative association of antidepressant treatment in pregnant women with eating disorders on antenatal mental outcomes – results from the Norwegian Mother, Father, and Child Cohort Study

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Introduction: The lack of evidence on the effectiveness of antidepressants in pregnant women with eating disorders (EDs) poses important challenges regarding clinical recommendations on pharmacological treatment.

Aims: To examine the effectiveness of antidepressant treatment in pregnant women with EDs on symptom severity of depression and anxiety in early and late pregnancy.

Methods: We used data from the Norwegian Mother, Father and Child Cohort Study (MoBa), linked to the Medical Birth Registry of Norway (MBRN). Based on MoBa questionnaires Q1 (at week 17) and Q3 (week 30), we identified the presence of ED (AN- anorexia nervosa, BN- bulimia nervosa, BED- binge eating disorder and EDNOS-P- recurrent self-induced purging in the absence of binge eating) and exposure to antidepressants, from six months before through late pregnancy. Our outcome was symptoms of depression and anxiety, as measured via the Symptom Checklist scale in Q1 and Q3. We estimated the association between antidepressant continuation in early or late pregnancy, on maternal mental outcomes in the corresponding time period. We adjusted for measured confounding via inverse probability of treatment weighting, and fit generalized linear models. Results are presented as outcome mean difference with 95% Confidence Intervals (CI).

Results: We identified 6739 pregnancies with ED before and/or during early pregnancy: 0.7% AN (n=50), 11.3% BN (n=763), 86.5% BED (n=5830) and 1.4% EDNOS-P (n=96). Of these, 95.3% (n=6424) did not use antidepressants six months before or during pregnancy, while 101 and 98 discontinued antidepressant respectively before and during early pregnancy; only 55 pregnancies were with continued antidepressant in pregnancy, and 54 initiated this treatment in pregnancy. Women who continued antidepressant during pregnancy had lower depressive/anxiety symptoms in early pregnancy than women who discontinued antidepressant treatment during pregnancy [β: -0.34, 95%CI (-0.60, -0.08)]. This association was only relevant in women with BED, but not for BN. There was no association between continued use of antidepressants and maternal outcomes relative to discontinuation before pregnancy.

Conclusions: Continuation of antidepressants during pregnancy in women with ED is associated with lower symptoms of depression and anxiety in early pregnancy relative to discontinuation of treatment during pregnancy, albeit with a small effect size.

C11

Veterans from early peacekeeping operations – how are they doing?

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Introduction: After the Second World War, Norway has contributed with troops to a number of foreign peacekeeping operations. Between 1947 and 1967 about 60,000 Norwegian soldiers served in the Allied occupation force stationed in Germany or in the United Nations peacekeeping operations in Gaza and Congo. Little is known about harmful exposures, injuries and illness among these soldiers; during deployment and later in life. Data about these operations and the participating veteran's health is stored on papers in The Armed Forces military archives, which has until now been unavailable for research. The Norwegian Armed Forces Joint Medical Services are exploring these archives in order to establish methods for identifying and transcribing data on military veterans into the Norwegian Armed Forces Health Register.

Aims: To provide information about the health and well-being of veterans who participated in peacekeeping operations between 1947 and 1967.

Methods: We identified a group of 122 veterans born 1922-1945 who served in peacekeeping operations in Germany, Congo and/or Gaza 1947-67. These veterans later re-deployed to the United Nations Interim Force in Lebanon, and participated in a survey on mental health conducted by the Institute of Military Psychiatry in 2016. We used their survey responses to investigate their psychological health and well-being in old age using descriptive statistics.

Results: Most of the veterans were content with their lives and said that they were in good health in 2016. Few had suffered from illness, unemployment or economic problems during their life, and most had lived with a spouse. However, about 20 % said that they had been exposed to alarming events during the peacekeeping operations, and about 10 % had symptoms of current mental health problems or harmful drinking.

Conclusions: This is the first results on health and well-being among veterans who participated in peacekeeping operations 1947-67. Further research should include complete cohorts and investigate whether mental health problems in old age could be linked to specific peacekeeping operations or combat events. Methods for collecting more comprehensive data from the military archives and the potential for conducting longitudinal population studies based on this promising data source will be discussed.

D5

Cesarean section, pregnancy complications and subsequent fertility

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Introduction: Studies have reported contradictory findings regarding the association between cesarean delivery (CD) and subsequent number of offspring. Furthermore, the ideal family size and obstetric procedures have evolved over time, so previous studies' findings may no longer be applicable today.

Aims: To assess the link between CD in first pregnancy and probability of having a second birth, in relation to pregnancy complications.

Methods: Using the Medical Birth Registry of Norway, we followed women who had their first singleton births (live or stillbirth) between 1999-2013 (N=320,895) until 2020. We compared the continuation rate to second pregnancy by mode of first delivery (vaginal delivery (VD) and CD) and infant's one year survival. Ten risk factors in first pregnancy (abruptio placenta, breech, congenital anomaly, diabetes mellitus, hypertension, preeclampsia, preterm, postdate, premature rupture of membrane and placenta previa) were used to define women as low- (no factors) and high-risk (one or more factors). The probability of having a second pregnancy was estimated by Cox regression models, expressed as hazard ratios (HR) with 95% confidence intervals (CI), adjusting for women's age, education and smoking.

Results: A total of 258,553 women (80.1%) had a second pregnancy during follow up. Among low-risk women whose infants survived the first year, 82.7% with VD and 81.1% with CD had a second pregnancy. Median time to next pregnancy was longest (26.5 months) in high-risk women with CD. Compared to low-risk women with VD, the probability of having second pregnancy was 19% (HR 0.81, 95% CI 0.80-0.82) and 2% (HR 0.98, 95% CI 0.97-0.99) lower in high- and low-risk women with CD, respectively. If the infant died within the first year, there was no difference in the probability of having a second pregnancy by mode of delivery.

Conclusion: A lower probability of having a second pregnancy following a first CD was found both in high- and low-risk women. However, this difference was only evident if the first infant survived the first year.

D6

Male-female genetic interactions influencing fertility

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Introduction: Subfertility is a heterogeneous phenotype, the etiology of which is not fully deciphered. One hypothesis is that interactions between maternal and paternal genes may influence the couple's fertility. Such interactions could potentially occur between any two genes in the maternal/paternal genotype, or between haplotypes. In our study, we have performed a genome-wide search for interactions between maternal and paternal alleles at the same locus.

Aims: To develop methodology for analyzing parental allelic interactions that may influence fertility.

Methods: We used genetic data from the Norwegian Mother, Father, and Child Cohort Study (MoBa). Our sample consisted of 15,789 pregnancies, of which 1304 were conceived using assisted reproductive technology (ART). We used ART as a proxy for subfertility and performed an initial genome-wide scan for allelic interaction effects using logistic regression and a multiplicative dose-response model, adjusting for maternal age, parity, and three principal components for each parent. We also accounted for multiple pregnancies by the same couple by adding a random effect term in a generalized linear mixed-effects model. In subsequent analyses performed on a subset of the top hits from the initial scan we also adjusted for maternal BMI and smoking, to investigate any potential mediating effects from these variables.

Results: We identified several interaction effects between parental alleles that were associated with ART. The top 30 SNPs were spread across the genome, with two (rs7595213 and rs7590554) located within the same gene, *SLC8A1*, which has been linked to endometrial maturation. Another gene featured among our most significant findings was *CPLX1*, one of several genes found to be hypomethylated in the placenta of patients with gestational diabetes.

Conclusions: Several of the genes identified in our analyses are relevant for the phenotype under study here. Validation in other similar cohorts is necessary to confirm these findings. More generally, the model we present here is applicable to genome-wide analyses of allelic interaction effects. In addition to the multiplicative dose-response model there are several other types of parameterizations that could be applied. Further plans include implementing the jointly dominant-dominant model for interaction and comparing the results.

D7

Environmental Exposure and Time to Pregnancy: The Norwegian Mother, Father, and Child Cohort Study

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Introduction: For many years birth rates in Norwegian and other industrialized countries have been below replacement level. Although extensively investigated, the reasons for these unsustainable fertility rates are not fully understood. Numerous environmental exposures are speculated to be associated with fecundability (time to pregnancy). This association is, however, complicated by fecundability being dependent on two individuals, in addition to the close link between behavioral changes in society and biological factors.

Aims: To study environmental exposures prior to conception and its association with fecundability in the Norwegian Mother, Father, and Child Cohort study (MoBa).

Methods: In this study, we examined the association between numerous environmental exposures (EE) prior to conception and fecundability in both women (N = 95.911) and men (N = 74.934) participating in MoBa. The women and men self-reported on a total of 16 and 18 EE, respectively. In addition, women self-reported, in months, on how long they had tried to conceive. We estimated fecundability ratios (FR) using log-binomial regression to evaluate the likelihood of conceiving during a given menstrual cycle among exposed versus unexposed participants. In the multivariate model we adjusted for previous live births, baseline- age, body mass index, smoking status, alcohol intake, education, and employment, in addition to partner traits.

Results: 74.4 % men and 50.2 % women reported EE to some extent prior to conception. Of these 15.9 % and 29.4 %, respectively, reported to a combination of multiple exposures. Mean age (years) at beginning of trying to conceive was 29 and 32 for exposed women and men, respectively, and 30 and 32 for those unexposed. A moderate correlation was detected between a selection of the EEs. So far, preliminary analyses have detected significant, but negligible effects on FR for a selection of EEs in both women and men.

Conclusions: Preliminary results are not indicating any convincing associations between various self-reported environmental exposures and fecundability in women and men. However, further analyses are necessary, and we are looking forward to presenting updated results at the NOFE conference in October.

D8

Reproductive outcomes in women and men conceived by assisted reproductive technologies

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Introduction: Pregnancies conceived using assisted reproductive technologies (ART) face increased risk of adverse perinatal outcomes, and there are some indications that children conceived by ART are at increased risk of later health problems. However, little is known of the reproductive health in adults who were themselves conceived by ART.

Aims: To determine whether perinatal outcomes differ in pregnancies to women or men conceived by ART compared to their naturally conceived peers.

Methods: The Medical Birth Registry of Norway was used to identify women and men born in Norway between 1984 and 2002 who were registered as the parent in a pregnancy before 2020. We compared the pregnancies of ART-conceived to naturally conceived women and men, and assessed mean birthweight, gestational age, and placental weight by linear regression, and the odds of low or high birthweight, congenital malformations, low 5-minute Apgar score, use of ART, hypertensive disorders of pregnancy and preeclampsia, preterm birth, and offspring sex, by logistic regression. The occurrence of any registered pregnancy in ART-conceived and naturally conceived persons from age 14 until end of follow-up was assessed using Cox proportional regression.

Results: Among 1,092,151 persons born in Norway from 1984 to 2002, 163,427 were registered at least once as mothers, and 121,883 as fathers. Of these, 317 men and 448 women were themselves conceived by ART. Those conceived by ART had little evidence of increased risk of adverse outcomes in their own pregnancies, use of ART, or any difference in mean birthweight, placental weight or gestational age. There was a slightly decreased risk of having a boy among mothers conceived by ART (odds ratio 0.79, 0.66 to 0.95). ART-conceived persons were slightly less likely to have a registered pregnancy within the follow-up period (women: adjusted hazard ratio 0.87; 95% confidence interval 0.79 to 0.95, men: 0.91, 0.82 to 1.02).

Conclusions: Persons conceived by ART were not at increased risk of obstetric or perinatal complications when becoming parents. The proportions of ART-conceived women and men with a registered pregnancy was lower than among naturally conceived, but longer follow-up time is required to fully assess their reproductive history.

D9

Association of parental subfertility with offspring cardiometabolic health trajectories from birth to 25 years: pooled analysis of three European pregnancy cohorts

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Introduction: Subfertility is a risk factor for parental future cardiovascular disease. It is unclear whether parental subfertility also associates with cardiometabolic health in the offspring.

Aims: To determine whether parental subfertility is associated with differences in cardiometabolic health trajectories from birth to 25 years.

Methods: We pooled data from 18,262 singletons from three pregnancy cohorts (the UK Avon Longitudinal Study of Parents and Children, the Portuguese Generation XXI, and the Amsterdam Born Children and their Development study) with follow-up information until adolescence or early adulthood. 28% of offspring were from subfertile parents (time-to-pregnancy ≥12 months). We used natural cubic spline mixed effects models to explore associations of parental subfertility with cardiometabolic health trajectories (body mass index [BMI], waist circumference, systolic and diastolic blood pressure [SBP, DBP], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], triglycerides, and glucose). We present graphs of trajectories and associations of parental subfertility with predicted levels of cardiometabolic traits at 5, 10, 15, 20 and 25 years adjusted for maternal age at pregnancy/birth, pre/early-pregnancy BMI, pre/early-pregnancy smoking, education, parity, and ethnicity.

Results: By age 25, offspring of subfertile couples had higher mean confounder-adjusted BMI (difference in mean predicted levels: +0.90 kg/m2, 95% confidence interval [CI] 0.76 to 1.03), waist circumference (+1.93 cm, 95% CI 1.33 to 2.53), SBP (+0.65 mmHg, 95% CI -0.04 to 1.34), and DBP (+0.84 mmHg, 95% CI 0.30 to 1.38), and lower HDL-C (-0.032 mmol/L, 95% CI -0.057 to -0.006). They also showed higher triglycerides at age 20 (+0.027 mmol/L, 95% CI 0.012 to 0.043). Despite offspring of subfertile couples had higher LDL-C levels at age 5 (+0.15 mmol/L, 95% CI 0.13 to 0.16), they showed lower LDL-C concentrations up to age 20 (-0.041 mmol/L, 95% CI -0.064 to -0.016). An inconsistent pattern of association with glucose levels was also observed.

Conclusions: Cardiometabolic health indicators could be poorer in offspring of subfertile couples.

D10

Long interpregnancy interval and increased risk of cardiovascular disease death after preterm preeclampsia: a population-based cohort study from the Medical Birth Registry of Norway

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Introduction: It has been well described in Norwegian data that preterm preeclampsia increases women's later risk of cardiovascular disease (CVD), with one-child mothers at especially high risk. Among those who have another pregnancy, having a long interpregnancy interval (IPI) increases risk of preeclampsia, but paradoxically it is short intervals that have been identified as having the strongest association with parental CVD. The purpose of this study is to examine the risk of heart disease by IPI, stratified by preeclampsia status.

Methods: This study was conducted using the Medical Birth Registry of Norway. Women who delivered singleton births from 1967-2013 were included. IPI was measured by number of complete years from the first birth to the conception of the second, categorized into short (≤ 1 year), medium (2 – 5 years) and long (≥ 6 years). Women who delivered non-preeclamptic pregnancies at term and had medium IPI were the reference group. We excluded women who had a new partner fathering the second pregnancy. Cox proportional hazard models estimated risk of CVD death from age 40 to 70.

Results: The mean IPI after a preeclamptic pregnancy was longer (2.62 years for term delivery and 2.75 for preterm delivery) than for the reference (2.56 years). We found no trend between IPI and CVD in women with term preeclampsia. Preterm preeclampsia was not associated with CVD mortality at short IPI but showed greater risk by longer time in both medium (HR 2.13, CI95% 1.10 – 4.10) and long (HR 4.08, CI95% 1.31 – 12.66) IPI. Increased CVD mortality by preterm preeclampsia with long IPI persisted after adjusting for maternal education, year of delivery, and preeclampsia in the next pregnancy (aHR 3.57, CI95% 1.14 – 11.16).

Conclusion: Long IPIs pose the greatest CVD risk and are most common for individuals with preterm preeclampsia, independent of recurrent preeclampsia, time period, and social status. IPI may have less of an impact on the long-term health of women with term preeclampsia. Some of the contributing factors to infertility, as observed in previous cohort of one-child mothers, may also be associated with long IPI, such body-mass index and underlying health conditions.

A12

Challenges in planning and conducting evidence based studies in a pandemic: are RCTs really the gold standard?

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Introduction: The Covid-19 pandemic has highlighted the need for high quality, evidence based studies, to base the implementation of decisions and policies on. In evidence-based medicine RCTs are often considered the gold standard, but while there have been several solid randomized trials for drug interventions and for testing vaccine effects, randomized trials for public health interventions bear many more challenges and difficulties.

Aims: We want to show that even seemingly simple trials on intervention effects can prove to be very difficult to conduct in the context of infectious disease pandemics, and lead to incorrect interpretations and conclusions. The methodological challenges of such RCTs arise from the fact that standard designs and methods for analyzing RCTs are not directly applicable in a pandemic setting with communicable diseases. Although some of the designs, as for example cluster-randomized designs, appear to be suitable for this setting, they may be difficult to implement and the results may not be causally interpretable on an individual level. In the same way, it is not trivial to define the population of interest, nor to identify appropriate endpoints to measure the intervention effect. In this work, we want to highlight such difficulties and show how most standard ways of performing and interpreting the results from RCTs do not apply to a pandemic setting, from the definition of the research question to the choice of design and methods of measuring and analyzing the outcomes, all the way to the final interpretation and generalizability of the results.

Methods: By following the CONSORT statement, we discuss each of the components of RCTs and explain how standard RCTs fail in estimating the intervention effect of interest when there is strong interference and contamination between participants as we have in pandemic settings.

Results and conclusions: We conclude that RCTs might not always be the optimal choice, and that resulting misleading conclusions on the effect of interest are particularly harmful given the status RCTs have in the evidence hierarchy. Therefore, in instances when suitable RCT design and methods are not available, other types of studies might prove to be a more appropriate and ethical choice.

A13

The impact of nosocomial bacterial co-infections on the mortality of COVID-19 patients

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Introduction: Since the early phase of the Covid-19 pandemic, it has been observed that mortality is highest among the elderly, immunocompromised individuals and patients with severe co-morbidities. In regions with high burden of endemic nosocomial pathogens there is an elevated risk of hospital transmission of virulent strains and it remains unclear how the risk posed by these organisms combines with SARS-COV2 infection for the vulnerable patients.

Aims: To investigate the role of bacterial co-infections on COVID-19 outcomes of the hospitalised patients.

Methods: A holistic approach was developed to simultaneously identify colonization, infection and transmission of all the major nosocomial bacterial pathogens and was applied to a cohort of 265 hospital in-patients from a large university hospital in Northern Italy which was first hit by the pandemic in Europe in early 2020. To enable capturing all the relevant pathogens present in the gut, upper airways or lungs of the patients, a targeted culturing of samples from nasal and rectal swabs was used, as well as sputum or bronchoalveolar wash. DNA extracted from plate sweeps of the detected growth for a sample was whole genome sequenced at high depth to identify pathogenic organisms present in the patients in a simultaneous fashion. Combining this wealth of detailed genomic information with the COVID-19 status of the patients and the relevant metadata from the hospital enabled investigating pan-pathogen hospital transmission and assessing the role of nosocomial pathogen load for patient mortality.

Results: The observed pathogen load was high in the hospital, and there were signs of intensive hospital transmission and several concurrent outbreaks of nosocomial pathogens. COVID-19 infection, any secondary infection, and even presence of any major pathogen in respiratory samples increased the mortality risk of the patients, but secondary infections were not found to have an additive contribution to the mortality risk of COVID-19, nor the survival time. Two bacterial species, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, known for their high rate of antibiotic resistance, were associated with the increased mortality risk.

Conclusions: The effect of secondary infections on mortality did not differ significantly between COVID-19 positive and negative patients.

A14

Long COVID after Omicron: Results from MoBa

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Introduction: Physical, psychological and cognitive symptoms have been reported as post-acute sequelae for early variants of SARS-CoV-2. Much is still unknown about how vaccination and reinfection with new SARS-CoV-2 variants affect the occurrence and duration of symptoms.

Aims: To estimate excess risk and identify patterns of 22 symptoms 3-5 months after SARS-CoV-2 Omicron infection using a large population-based cohort study.

Methods: We followed more than 60,000 participants in the Norwegian Mother, Father and Child Cohort study (MoBa) during the COVID-19 pandemic. Vaccine status was obtained from the Norwegian Immunisation Registry (SYSVAK) and lab-confirmed COVID-19 diagnoses were obtained by linkage to The Norwegian Surveillance System for Communicable Diseases (MSIS). Adult cohort participants were invited to answer short questionnaires every 14 days. The participants reported SARS-CoV-2 test results from either PCR or antigen tests (including self-testing). In June 2022, about 4 months after the first Omicron wave hit Norway, all participants registered presence or absence of 22 different symptoms (n=60993, response rate 61%). Participants who were infected with SARS-CoV-2 after March 2022 (n=8488) were excluded from the study sample (n=52505). We estimated the risks of long COVID symptoms after an Omicron infection, taking earlier COVID-19 infections and vaccination status into account.

Results: Preliminary analyses show that 3-5 months after Omicron infection, the symptom occurrences were relatively low among participants who were infected with SARS-CoV-2 for the first time in January or February 2022 (n=16623). For instance, 12% reported poor memory, 12% had fatigue, and 11% reported brain fog, which was similar to the prevalence among uninfected subjects (10-12%, unadjusted results). In comparison, participants who were reinfected with SARS-CoV-2 in the same period (i.e., with previously registered COVID-19 diagnosis, n=514) had increased risks of experiencing long COVID symptoms. For reinfections, the symptom occurrences 3-5 months later were 24% for poor memory, 22% for brain fog and fatigue, 17% for headache, 16% for dyspnea, and 13% for altered smell or taste.

Conclusion: Preliminary analyses suggest lower excess risks of long COVID symptoms 3-5 months after infection with the Omicron BA.1/BA.2 variant in the (largely vaccinated) Norwegian population, as compared to that of earlier variants.

B12

Geographical variation in cardiovascular disease mortality in Norway: the role of life course socioeconomic position and family factors

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Introduction: A substantial geographical variation in cardiovascular (CVD) mortality has been observed across regions within many countries.

Aims: To investigate geographical variation in CVD mortality in Norway, after taking individuals' life course socioeconomic position (SEP) and family factors into account.

Methods: All Norwegians (n=1,006,226), who were born between 1940 and 1959 and survived over 60 years, were linked to national registries and databases. To construct life course SEP, we used information on income and housing conditions from censuses in 1960–2011, and their educational attainment by age 60 from the National Educational Database. Family members were identified from a multigenerational database. Cox proportional hazards regression models with age as the time scale were performed to investigate the association between the county of residence at age 50s and CVD mortality. The study population were followed from the day when they turned the age of 60 to CVD death, emigration, or the end of the study period (31 December 2020), whichever occurred first.

Results: Of the 1,006,226 study population, 2.1% died due to CVD during the follow-up (the median follow-up years were 9.2 years). In the birth year and gender-adjusted model, those who lived in the northern part of Norway in their 50s were at increased risk of CVD mortality than those in Oslo (Troms HR: 1.03, 95% confidence interval: 1.00–1.17; Finnmark HR: 1.31, 95%CI: 1.18–1.44). Conversely, counties located in the western part of Norway and Akershus had relatively fewer CVD deaths. In Model 2 adjusting for the life course SEP and capturing familial dependences, the estimated CVD mortality risks in different counties changed slightly, ranging from -11% to 8% of Model 1. Despite these changes, we found two counties, Akershus and Vest-Adger, were constantly found to have lower mortality than Oslo.

Conclusions: Differences in CVD mortality persisted across Norwegian counties even after taking life course SEP and family factors into account. This indicates that there may be regional factors beyond individual characteristics that contribute to the geographical variation of CVD mortality in Norway.

B13

Cardiovascular risk factors and infertility

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Introduction: Fertility rates are decreasing in many European countries. Several cardiovascular risk factors are associated with increased risk of infertility in observational studies, but the causal nature of the relationship remains unclear.

Aims: To investigate the association between cardiovascular risk factors and infertility in both women and men.

Methods: We studied 12,983 women (mean age 36 years) and 6,639 men (mean age 37 years) participating in the Trøndelag Health Study (HUNT). We used data from the survey collections from 1995-1997 (HUNT2), 2006-2008 (HUNT3) and 2017-2019 (HUNT4). Infertility was self-reported as having tried to conceive for more than 12 months. Cardiovascular risk factors included body mass index (BMI), systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), non-HDL cholesterol (non-HDL-C), triglycerides, and lifelong smoking index. We studied the association between cardiovascular risk factors and infertility using multivariable logistic regression models adjusting for age, education, and lifelong smoking index. In two sample Mendelian randomization (MR) analyses we used the largest published genome-wide association studies (GWAS) to estimate genetically predetermined levels of cardiovascular risk factors as instruments (all F statistics > 10).

Results: Approximately 20% of women and men reported infertility. We found associations between more adverse levels of most cardiovascular risk factors and infertility in observational analyses in women even when adjusting for confounders. For example, adjusted OR per standard deviation (SD) increase in BMI was 1.20 (95% CI: 1.15-1.26). In men, only BMI was positively associated with infertility (adjusted OR per SD increase = 1.19, 95% CI: 1.08-1.30). In MR analyses, we found no strong evidence of linear associations between genetically predicted cardiovascular risk factors and infertility in women or men (e.g., adjusted OR per SD increase in genetically predicted BMI was 1.03 (95% CI: 0.99-1.08) in women and 1.01 (95% CI: 0.94-1.07) in men).

Conclusions: We found some associations between cardiovascular risk factors and infertility in observational analyses. However, these associations were not observed in MR analyses. This could be due to a lack of a true causal effect, unmeasured confounding in multivariable analyses, or due to weak genetic instruments in MR analyses.

B14

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

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Introduction: Atrial fibrillation (AF) is a large public health challenge with rapidly increasing prevalence and is associated with increased risk of stroke, myocardial infarction and death. AF is associated with lifestyle risk factors like obesity, physical activity, smoking, alcohol and hypertension, but specific primary prevention strategies are lacking. The population impact of lifestyle interventions on the risk of AF should ideally be estimated using randomized trials, but in practice answers need to be inferred from population-based cohort studies.

Aims: To use the parametric g-formula to estimate the 22-year risk of AF under hypothetical interventions on six modifiable risk factors.

Methods: We estimated the relative and absolute risk reduction under hypothetical risk reduction strategies for smoking, physical activity, alcohol drinking, body mass index, systolic and diastolic blood pressure in 14,923 men and women from the population based Tromsø Study with 22 years of follow-up (1994-2016).

Results: The estimated 22-year risk of AF under no intervention was 6.1% and 13.1% and baseline mean age was 46.8 and 49.5 years, in women and men, respectively. The risk was reduced by 42% in women and 13% in men under joint interventions on all five risk factors, 95% confidence interval (17%, 59%) and (29%, -7%) respectively. The most effective interventions were lowering body mass index to ≤ 25 kg/m2 and restricting alcohol intake to >1 ≤ 2 units per week (15% and 14%, and 14% and 7% lower AF risk in women and men, respectively).

Conclusions: Modification of population levels of lifestyle risk factors could have prevented two out of five cases of AF in women and almost one out of six cases of AF in men in the municipality of Tromsø during 22 years of follow-up.

B15

Age at onset and duration of adverse lipid levels before incident myocardial infarction. A study based on longitudinal data from the Tromsø Study 1974-2016

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Introduction: The atherosclerotic effect of an adverse lipid profile is assumed to accumulate throughout life, leading to increased risk of myocardial infarction (MI). However, little is known on duration of unfavorable lipid levels before MI, possibly due to a lack of longitudinal data.

Aims: We explored age at onset and duration of unfavorable lipid levels before MI by comparing mean lipid levels during adult lifetime in individuals of the same age and sex, with and without a subsequent incident MI.

Methods: The Tromsø Study (1974-2016) provided longitudinal data on serum lipid levels. The study population comprised 26,130 individuals (50.5% women) aged 20-89 years who participated in at least two of the seven health surveys before incident MI or end of follow-up in December 2019. The diagnoses of MI were obtained from local and national registers. A linear mixed model for repeated measurements was applied to estimate the adult lifetime lipid trajectories, compare mean lipid levels by MI status (MI vs. non-MI) and examine sex differences in this contrast.

Results: Compared to individuals of the same age and sex, individuals with a subsequent incident MI had on average unfavorable lipid levels 20-35 years before incident MI, though with a shorter or even longer duration for some subgroups. The adverse lipid levels were seen already from ages 20-30 years in individuals with incident MI <55 years and 55-74 years, whereas a delayed age at onset of adverse levels was seen in the subgroup with MI ≥75 years. There was also a clear trend towards more severe adverse levels the lower the age at the diagnosis of MI ($p<0.001$). This trend was particularly pronounced for the ratio between HDL-C and total cholesterol (both sexes) and the ratio between triglyceride level and HDL-C in proportion to total cholesterol (women). The difference by MI status was just as large in women as in men, but the age pattern differed ($p<0.05$, tests for 3-way interaction).

Conclusions: Both in men and women, adverse lipid levels were seen 20-35 years before incident MI, with a clear trend towards more severe lipid levels the lower the age at the MI.

C12

Device-measured and self-reported physical activity in adult offspring: The effect of physical active parents and genetic predisposition in the HUNT Study

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Introduction: Physical inactivity have been described as a global pandemic with great impact on morbidity, mortality, and public health. Initiatives that have been made to reduce the prevalence of physical inactivity have shown limited effect. The question “why some people are physical active and others not?” is still highly relevant, and physical activity and genetic predisposition within families could help inform future intervention and preventive strategies.

Aims: To explore device-measured and self-reported physical activity levels in adult offspring and the effect of having physical active parents independently and in combination with high or low genetic risk of being physical active.

Methods: Family trios of mothers, fathers and offspring was genetically identified from 86,147 genotyped participants in the HUNT Surveys. Physical activity was collected using questionnaires and accelerometers (in a subset of ~27,000 participants). These measurements were used to define both continuous and categorical phenotypes of physical activity such as MET hours/week, meeting physical activity recommendations and vigorous activity. Using summary statistics from physical activity phenotypes in UK biobank we calculated a genetic risk score to stratify offspring by genetic predisposition. Linear and logistic regression adjusting for dependence between observations (i.e., siblings) was used to estimate the independent and joint effect of parental physical activity and own genetic risk for being physically active.

Results: We identified 31,045 mother-offspring relations, 24,179 father-offspring relations and 19,469 complete trios with self-reported physical activity information. Offspring with parents that met physical activity recommendations had higher odds of meeting physical activity recommendations with similar estimates for mothers (1.31, CI 1.20-1.40) and fathers (1.37, 1.26-1.49). Phenotypes of increased intensity and duration and having two physical active parents increased the effects. Analyses of device measured physical activity are ongoing, and results will be presented at the conference.

Conclusions: Adult offspring reports more weekly physical activity with increasing parental physical activity, particularly if both parents report to be physically active, and the association were somewhat stronger with higher genetic risk score.

C13

Associations between accelerometer-measured physical activity and left atrial size in a general population: The Tromsø Study 2015-16

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Introduction: The influence of physical activity (PA) on cardiac structure and function is primarily studied in athletes, where exercise-induced cardiac remodeling is considered a benign physiological adaption. Paradoxically, left atrial (LA) enlargement associates with atrial fibrillation. Little is known about cardiac adaptations to PA in the general population.

Aims: We have previously shown that LA volume is larger among those in the highest quartile of accelerometer-measured total PA volume. We here assessed whether moderate intensity PA (minutes/day) in each quartile of total PA volume (counts/minute) complies with the World Health Organization (WHO) PA guidelines, and how this associate with LA volume and proportion with LA enlargement.

Methods: We used ANOVA to examine the association between PA and LA volume indexed to body surface area (LAVi) evaluated with 2D echocardiography in 1573 Tromsø Study participants 40-84 years. PA was measured with a triaxial ActiGraph wGT3X-BT accelerometer ≥10 hours/day ≥4 days. We quantified the amount of moderate PA (2690-6166 counts/min) in each total PA volume quartile (Q1=lowest, Q4=highest) to assess to what degree participants in each quartile reached moderate PA according to the recommendations of moderate PA (21.4-42.9 minutes/day). Amount of vigorous PA was neglectable.

Results: Average LAVi was 35.1 mL/m^2, 33.7 mL/m^2, 33.5 mL/m^2, and 34.9 mL/m^2, respectively, in Q1, Q2, Q3, and Q4 of total PA volume. The proportion with LAVi enlargement (>34.0 mL/m^2) was 41.5% (n=163), 38.8% (n=153), 38.3% (n=150), and 46.4% (n=183), respectively, in Q1, Q2, Q3, and Q4. We observed a U-shaped trend in the association between PA quartiles and LAVi (p=0.026). No significant group differences were found between PA quartiles for LAVi (p=0.167) or proportion with LAVi enlargement (p=0.067). Minutes/day of moderate PA was below the WHO recommended level in Q1 (11.1), within in Q2 (28.1), corresponded to the upper level in Q3 (41.3), and 1.6 times the upper recommended level in Q4 (70.1).

Conclusions: Our results indicate that those below and above the WHO recommended level of moderate intensity PA, have larger LA size than those fulfilling the recommendations, suggesting that PA intensity partly explains the U-shaped association between total PA volume and LA size.

C14

The relationship between physical activity and cuff-pressure algometry tolerance: The Tromsø Study 2015-2016

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Introduction: Physical activity (PA) has previously been demonstrated to have a dose-response relationship with pain tolerance assessed by the cold-pressor test in the general population. Other experimental pain modalities might relate differently to PA.

Aims: To assess the association between types of habitual PA and computerized cuff algometry-assessed pain tolerance thresholds (PTT) in the general population.

Methods: Data from 18,974 participants from the 7th survey of the Tromsø Study (2015-2016) with PTT and self-reported PA data, and 5,598 with accelerometry data, was used to model the relationship between PTT and PA measured as: self-reported leisure-time physical activity (LTPA), occupational physical activity (OPA), and estimated MET-hours spent in exercise, or accelerometer-measured moderate to very vigorous (MVV) counts and total counts. This was modelled using flexible parametric Royston-Parmar survival regression with time-dependent coefficients, yielding hazard rate ratios (HR). We also modelled sex and age interactions.

Results: Mean PTT was 61 kPa (standard deviation (SD) 20.1). There was an inverse dose-response association between LTPA and PTT (light: HR 0.87 (95% CI 0.83 – 0.92), moderate: HR 0.75 (CI 0.71 – 0.80), vigorous: HR 0.63 (CI 0.53 – 0.73)) with significant sex-interaction showing larger effect estimates for men. No higher categories of OPA had significantly different associations with PTT than sedentary OPA. Higher estimated MET-hours per week was associated with higher PTT (7.5-15: HR 0.92 (CI 0.88, 0.96), 15-22.5: HR 0.84 (CI 0.78, 0.89), >22.5: HR 0.86 (CI 0.82, 0.91)), with similar sex-interactions as for LTPA. One SD increase of both MVV minutes and total counts per minute per day was associated with higher PTT (MVV: HR 0.91 (CI 0.88, 0.95), counts: HR 0.93 (CI 0.90, 0.96)). Graphed hazard ratios demonstrated how LTPA-, MET-, and accelerometry groups gradually became more equal in hazard rates as the PTT increased. Graphing of standardized survival curves will be used to display absolute group differences.

Conclusions: Both higher self-reported and accelerometer-assessed estimates of physical activity were significantly associated with higher pain tolerance as assessed by cuff algometry in the general population.

C15

Physical activity and mortality: Effect modification by sedentary time. An individual participant data analysis of four cohorts with accelerometry measured physical activity

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Introduction: High sedentary time is associated with higher risk of non-communicable diseases and mortality. Physical activity influences this association but whether sedentary time modifies associations between physical activity and mortality is still uncertain.

Aims: Examine 1) whether sedentary time modifies the associations between physical activity and mortality, 2) whether meeting physical activity guidelines (150 minutes·week^{-1} moderate-and-vigorous physical activity (MVPA)) modifies associations between sedentary time and mortality and 3) joint associations of physical activity and sedentary time with mortality risk.

Methods: We used individual participant data from four prospective cohort studies (Tromsø Study 2015-16, HAI 2012-2019, NNPAS 2008-09 and NHANES 2003-06) with accelerometry-measured physical activity and sedentary time. Associations (HR, 95% CI) were examined using cubic spline Cox regressions adjusted for sex, age, education, body mass index, smoking, alcohol intake, history of cardiovascular disease, cancer and diabetes, stratified by median sedentary time (physical activity and mortality) and meeting physical activity guidelines (sedentary time and mortality). For joint associations, we used fractional polynomials in a Cox regression with similar adjustments.

Results: Of the included 11989 participants (50.5% women) ≥50 years, 805 (6.7%) died during follow-up (median: 5.2 years, interquartile-range: 4.2 years). 10 min·day^{-1} of MVPA (reference: 0 min·day^{-1}) was associated with 15% (HR:0.85, 0.74-0.96) and 35% (HR:0.65, 0.53-0.79) lower mortality risk among those accumulating <10.5 and ≥10.5 hours·day^{-1} of sedentary time, respectively. Over 12 hours·day^{-1} of sedentary time (reference:8 hours·day^{-1}) was associated with higher mortality risk among those not meeting physical activity guidelines (HR:1.38, 1.10-1.74) but not among those meeting guidelines (HR:1.08, 0.66-1.77). In joint associations (reference:8 hours·day^{-1} sedentary time, 0 min·day^{-1} MVPA), 10 min·day^{-1} of MVPA was associated with 28-55% lower mortality risk with the lowest mortality observed at 10 hours·day^{-1} of sedentary time (HR:0.45, 0.31-0.65), while at 0 minutes MVPA, even 13 hours·day^{-1} of sedentary time displayed overlapping CIs (HR:1.35, 0.81-2.24).

Conclusions: MVPA was associated with lower mortality risk irrespective of sedentary time. Sedentary time was associated with higher mortality risk only in individuals not meeting physical activity guidelines. Small amounts of MVPA may be an effective strategy to ameliorate negative consequences on mortality risk associated with high sedentary time.

D11

Status of knowledge and knowledge gaps in associations between occupational exposures and their health effects: inform priority setting

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Introduction: In industrialised countries, non-communicable diseases (NCDs) make up nearly all occupational diseases, including common disease groups such as cancers, cardiovascular, respiratory, neurodegenerative, and musculoskeletal disorders. Global burden of occupational disease has been estimated to 5-7% of global mortality, translating to 2.3 million deaths each year. However, these estimates are based on a limited set of single known risk factors and NCDs and likely represent the tip of the iceberg.

Aims: To provide an overview of the current status of knowledge on occupational exposures in relation to common NCDs, in order to identify main knowledge gaps and set priorities in occupational health research in general and guide the development of new research questions in the Exposome Project for Health and Occupational Research (EPHOR).

Methods: We conducted a narrative umbrella review of established and suspected occupational risk factors for six main disease groups: cancer, respiratory, cardiovascular/metabolic, and neurodegenerative diseases, and mental and musculoskeletal disorders, selecting the most relevant diseases and disorders within each group. The review was mainly based on systematic reviews and authoritative reports, supplemented with narrative reviews, reports, and original studies, as appropriate. For each disease group, we identified established associations (with sufficient evidence) and suspected associations (with limited or insufficient evidence) reported in the literature. The status of knowledge was summarized in tables and heatmaps.

Results: We identified over 200 occupational exposures with suspected or established associations to common NCDs. Several exposures were identified as possible risk factors for multiple disease groups, including diesel engine exhaust, silica, cadmium, particulate matter, and shift work. For each disease group and exposure–disease combination, we also identified knowledge gaps and areas for improvement, on which future research should focus. There is a need for more prospective cohort studies to establish causal relationships, including dose–response relations and effects of interactions.

Conclusions: By providing an overview of knowledge gaps in the associations between occupational exposures and their health effects, our narrative review informs priority setting in occupational health research and guides future research.

D12

Occupational differences in working life expectancy and working years lost in Nordic countries

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Introduction: Increasing work participation and extending working life is a key political objective in the Nordic countries. Although the Nordic countries are similar, differences in the occupational distributions as well as institutional differences in social security and pension systems may result in differences in time spent at work, unemployed and outside of the labour market.

Aims: To estimate the working life expectancy (WLE) and working years lost (WYL) for the general population of Denmark, Finland, Norway and Sweden and to explore occupational differences in WLE and WYL.

Methods: The study utilised registry-based general population cohorts in Denmark (N=2,162,390), Finland (N=2,617,963), Norway (N=3,898,166) and Sweden (N≈5.3 million). For individuals aged 30-64, we calculated age- and gender-specific proportion of time during 2015 spent in six states by applying the following hierarchy for overlapping states: retirement (early and old age retirement), disability retirement, sickness absence, unemployment, work and other. We then estimated WLE and WYL for a hypothetical cohort at age 30 until age 65 based on the age-specific period calculations of labour market participation and mortality rate (prevalence-based method). The results were stratified by major occupational group. To harmonise occupational groups between countries, we applied a Nordic crosswalk based on ISCO-88.

Results: WLE at age 30 was 24-30 years among men and 21-28 years among women. Total WYL was 8-10 years for men and 11-14 for women. Depending on country, most working years were lost due to unemployment, sickness absence, disability retirement and retirement. Highest WLE was found among legislators, senior officials and managers for both men (31-33 years) and women (30-33). Men with elementary occupations were expected to spend the least time at work (21-28) in all countries. Among women, WLE was relatively low for elementary occupations (24-27) in all countries, skilled agricultural and fishery workers in Finland and Sweden (21-24) and service and sales workers in Norway (26). The difference in WYL between occupational groups was largest in Finland (9 years difference).

Conclusions: Cross-country differences existed with regard to expected time spent at work and reason for not working. Occupational differences were found in all countries, but the degree varied.

D13

Gender-specific impact of a population-level agreement for a more inclusive working life on maintaining paid employment and reoccurring sickness absence: A Norwegian cohort study

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Introduction: The Norwegian Agreement for a More Inclusive Working Life (IA Agreement) aims to reduce sickness absence (SA), including recurrent SA. However, whether this is achieved remains uncertain.

Aims: To estimate the impact of the IA Agreement on reoccurring SA after returning to employment from an initial SA episode in young to middle-aged men and women, and to identify any modification by initial SA diagnosis (musculoskeletal/psychological).

Methods: Using register data, 79,268 men and 94,931 women born in Norway 1967-1976 were followed for one year after returning from their first SA episode >16 calendar days, occurring between 1.1.05 and 31.12.10. Cox regression models estimated the all-cause risk of re-exiting work, adjusted for IA status (yes/no) at baseline. Cause-specific cumulative incidence curves, accounting for competing risks, were calculated for the events of full SA, graded (<100%) SA, disability pension, non-employment, and death. Differences in cumulative incidence between IA/non-IA were graphed with 95% confidence intervals (CI) calculated using 1,000 bootstrap samples. Analyses were stratified by gender and diagnosis group (ICPC-2 codes L, musculoskeletal, and P, psychological). Stabilised inverse probability of treatment weights (IPTW) balanced the IA/non-IA groups according to age, civil status, education, length and grade of initial SA, industry, company size, and company region.

Results: The all-cause risk of re-exiting work in IA companies compared to non-IA companies was lower for women (hazard ratio (HR) 0.97, 95% CI 0.94-0.99) and men (HR 0.96, 95% CI 0.93-0.99). Only men with psychological diagnoses had a higher all-cause risk of exiting work (HR 1.03, 95% CI 0.97-1.10). In IA companies, the incidence of both full and graded SA was higher in both genders and diagnosis groups, but the incidence of non-employment was lower.

Conclusions: The IA Agreement was associated with a reduced risk of all-cause re-exit from work in both men and women overall, and in those with musculoskeletal diagnoses. However, this was mainly due to a reduction in non-employment rather than a reduction in recurrent SA. This indicates that the Agreement may be succeeding in keeping young to middle-aged people in work, but not through achieving its main goal of reducing SA.

D14

Utilization of a primary emergency clinic in Oslo by pregnant undocumented migrants compared to pregnant residents of Norway

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Introduction: Substandard antenatal care may have long-lasting effects on both mothers and their children. Pregnant undocumented migrants have since 2011 had the right to antenatal care in Norway, but are excluded from the general practitioner and reimbursement schemes. Restricted rights to antenatal primary care may alter the use of primary care emergency clinics and the severity of condition at encounter.

Aims: To explore pregnant undocumented migrants' utilization of a primary care emergency clinic compared to pregnant residents of Norway.

Methods: Consultations with female patients without a Norwegian national identity number seeking care at the Department of Emergency General Practice (DEGP) at the Oslo Accident and Emergency Outpatient Clinic were identified through manual search of attendance lists from 2009-2019. We included pregnant women categorized as "Uncertain migrant status" or "Probably undocumented migrants" (PUM) based on self-reported nationality and information in the medical record. We collected information on urgency level (Manchester Triage System code), use of professional translator, diagnosis, and discharge (to home or hospital). We extracted aggregated data on women with national identity number and an ICPC-2 category W diagnosis (pregnancy-relation conditions) by consultation year, age, Manchester Triage System code, and discharge.

Results: Among 3728 consultations with female patients categorized as PUM or with uncertain migrant status, we found 1012 (27.1%) consultations with pregnant patients. Of the consultations, 41.1% had a non-W ICPC-2 diagnosis. The consultations for PUM peaked in 2012 and for women with uncertain migrant status in 2016. Pregnant women that were PUM or with uncertain migrant status had an increased risk of being triaged Immediate or Very urgent compared to pregnant women with a Norwegian identity number (crude RR= 2.70, 95% CI:2.31, 3.16).

Conclusions: Pregnant women categorized as PUM or with uncertain migrant status use the DEGP for both pregnancy related and non-pregnancy related conditions. They have an increased risk of severe conditions at encounter compared to pregnant residents of Norway.

P1

Long-term cardiovascular mortality in women by pregnancy complications in sisters and brothers' partner: a population-based cohort study

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Introduction: Pregnancy complications cluster within families and they increase the risk of long-term cardiovascular disease (CVD) death in women who experienced the complications. However, knowledge is limited regarding the association between pregnancy complications experienced by sisters and brothers' partner and CVD death in women.

Aims: Explore the risk of CVD death in women by pregnancy complications (preeclampsia, preterm birth (PTB), placental abruption and small-for-gestational-age (SGA)) experienced by sisters and brothers' partner.

Methods: Using the Medical Birth Registry of Norway and the Population Registry, we identified women and siblings whose first pregnancies were registered in 1967-2013, with additional pregnancies registered until 2020. Information on CVD deaths until 2020 was obtained using the Cause of Death Registry. The first cohort consisted of 504,125 woman-sister(s) units. The second and third cohorts comprised of women with uncomplicated pregnancies including 230,752 women-sister(s) units and 231,194 women-brother(s) units, respectively. Uncomplicated pregnancies were defined as the absence of preeclampsia, PTB, placental abruption, SGA, large-for-gestational age, plural births, malformations, cesarean section, gestational hypertension, gestational diabetes and perinatal death in all pregnancies. Hazard ratios (HR) and 95% confidence intervals (CI) using Cox regression analyses were estimated to evaluate women's risk of CVD death before age 70 and adjusted for the highest-attained education, comorbidities (chronic hypertension, chronic kidney disease, epilepsy, asthma, thyroid disorder and pregestational diabetes), age at first pregnancy and year of first pregnancy.

Results: Compared to women and sisters without preeclamptic pregnancies, women with preeclampsia had an increased risk of CVD death (HR 2.25; 95% CI 1.30-3.91), doubling if both women and sisters had preeclampsia (HR 5.01; 95% CI 1.25-6.00). Women without preeclampsia also had an elevated risk if sisters had preeclamptic pregnancies (HR 1.58; 95% CI 1.09-2.28). A similar pattern was observed in pregnancies with SGA and PTB. Women with uncomplicated pregnancies had an increased risk of CVD death if sisters had preeclampsia (HR 1.95; 95% CI 1.12-3.40). This risk was not elevated by pregnancy complications experienced by the brothers' partner.

Conclusions: Women had an increased risk of CVD death if their sisters had preeclampsia or SGA. This association was not observed for complications experienced by the brothers' partner.

P2

Association between air pollution and fractures of the hip and forearm in Norway. A NOREPOS study

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Introduction: Norway has among the highest rates of osteoporotic fractures in the world, and the incidence is higher in urban compared to rural areas. Although emission intensity in Norway has declined over time, it still exceeds limits in several cities. We previously reported a higher risk of forearm fracture with high air pollution exposure in men from Oslo. No study has investigated the association between air pollution and osteoporotic fractures at a national level.

Aims: To determine the association between two important indicators of air pollution (NO_2 and $PM_{2.5}$) and the incidence of forearm- and hip-fracture in Norway.

Methods: Register data on forearm-and hip-fracture from the entire Norwegian population >40 years were combined with data on the background population (Statistics Norway) 2008-2018. Monthly levels of air pollution indicators were modelled (with 1x1 km^2 resolution) by the NordicWelfAir project, in collaboration with the Norwegian Institute for Air Research (NILU). The data were combined in Geographic Information systems. Age-adjusted Incidence Rate Ratios (IRRs) with 95% Confidence Intervals (95% CIs) were estimated in men and women separately using Poisson regression.

Results: Median levels of air pollution were lower in 2016-2018 compared to 2008-2010 (NO_2: 4.1 vs. 5.0 µg/m^3, $PM_{2.5}$: 3.5 vs. 4.4 µg/m^3). They were higher in the urban areas and in the South of Norway. Categorizing into tertiles, the age-adjusted incidence of *forearm* fracture in women was 13% higher in areas with the highest NO_2 levels (12.5-71.8 vs. 0.22-6.08 µg/m^3: IRR=1.13, 95% CI: 1,11, 1.14), and 30% higher at the highest $PM_{2.5}$ levels (6.7-66.2 vs. 0.9-4.1 µg/m^3: IRR=1.30 ,95% CI:1.28, 1.32). The corresponding associations in men were: NO_2- IRR=1.18, 95% CI:1.14, 1.22 and $PM_{2.5}$- IRR=1.18, 95% CI:1.15, 1.21. There was also a higher risk of *hip* fracture at high levels of $PM_{2.5}$ in both women (IRR=1.12, 95% CI: 1.10. 1.14) and men (IRR=1.13, 95% CI: 1.10. 1.15). At high NO_2, the risk-increase in hip fracture was only seen in women: IRR=1.05, 95% CI: 1.03, 1.06.

Conclusions: Preliminary analyses found age and gender-adjusted associations between air pollution and osteoporotic fractures in nationwide data. We will present results also according to other variables.

P3

Are there still differences between Norwegian hospitals? Ten years reporting of 30-day survival as a quality indicator

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Introduction: Since 2011, 30-day mortality for all Norwegian hospitals has been calculated. As mortality is perceived as a negative framing the results are reported as total survival and survival following hospitalization for first time acute myocardial infarction (AMI), stroke and hip fracture. This was the beginning of the Norwegian quality indicator system for hospitals. Annual reports are made for hospital level, hospital trust level, and regional health authority level.

Aims: To study if there is less variation between Norwegian hospitals after ten years of public reporting of 30-day survival.

Methods: Hospital administrative data from the Norwegian Patient Registry are merged with alive/dead status from the National Population Registry. We use a logistic regression model to calculate the probability of death within 30 days as the response depending on case-mix and dummy variables for all hospitals, and back calculate to survival probabilities. Then, each hospital is compared to an average over all hospitals and is a low/high mortality outlier if deviating from this reference value. When comparing a small number of hospitals where some hospitals have very low or very high mortality, these outlier hospitals may highly influence the average. Thus, we use a trimmed mean as reference. The report in 2011 was based on data from 2005-2009 for the condition specific 30-mortality and data from 2009 for total mortality; data from about 60 hospitals. Later, we modified and used 3-year data for the condition specific 30-day mortality, and the report based on data for 2019 included 50 hospitals

Results: Number of outlier hospitals were as follows:

	Number of hospitals, lower/higher 30-day survival 2009	Number of hospitals, lower / higher 30-day survival 2019
Total	5 / 7	10 / 6
AMI	1 / 6	4 / 8
Stroke	5 / 0	3 / 2
Hip fracture	2 / 0	0 / 1

Conclusions: In 2011, hospitals identified to have low survival were triggered to initiate quality improvements. However, ten years later there is still variation between hospitals, and the hospitals still need to be reminded of the importance of quality and patient outcome.

P4

Primary care diagnoses in patients developing Post COVID Condition

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Introduction: Defining Long-COVID is a challenge, and it has been questioned if the symptoms of the condition varies between children and adults.

Aims: To identify diagnose codes from primary care in persons with a diagnosis of Post COVID Condition (PCC) between the time for a positive COVID-19 test or diagnosis and the diagnosis of PCC, and compare the prevalence of these diagnosis codes between children and adults.

Methods: Using the Norwegian Surveillance System for Communicable Diseases and the Norwegian Patient Registry we identified persons with positive tests and/or diagnoses (ICD-10 code U07.1) and PCC (ICD-10 code U09.9), the time of the test or diagnosis and the persons' ages at this time (<18 years or ≥18 years). We then explored which ICPC-2 codes these persons were diagnosed with in the Norwegian Control and Payment of Health Reimbursements Database between the time of the first positive COVID-19 test or diagnose and the first time of the PCC diagnose.

Results: 381 022 persons had a positive test or diagnosis in 2020-2021. Of these, 1140 developed PCC, whereof 46 were younger than 18 years at the time of the positive COVID-19 test or diagnose. Apart from diagnoses for COVID-19 and administrative diagnose codes, the most common ICPC-2 diagnoses were A04 (Weakness/tiredness general), R02 (Shortness of breath/dyspnea), A99 (Disease/condition unspecified nature/site) and A29 (General symptom/complaint other). Among the adult population, 25% were diagnosed with weakness/tiredness, 19% with shortness of breath/dyspnea, 16% with disease/condition unspecified and 12% with general symptom/complaint. The results were similar for children, where 20% were diagnosed with weakness/tiredness and disease/condition unspecified. Very few children had any other diagnose codes in this time window.

Conclusions: Two of the most common diagnoses from primary care in the time window between a positive test or diagnosis of COVID-19 and a diagnosis of PCC in both adults and children were weakness/tiredness and disease/condition unspecified. In adults shortness of breath and general symptom/complain were also among the most prevalent. However, as only one fourth or less of these patients had these diagnose codes registered, it might be difficult to identify these patients from Norwegian primary care data.

P5

Emergency preparedness, ambulance response time and patient outcome

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Introduction: The parliament in Norway has committed to regulation of emergency ambulance response time. Response time for life-threatening emergencies is the time from the alarm central answers an emergency call until an ambulance is present at scene of the incidence. Ensuring a rapid response can limit potentially harmful consequences of the emergency incidence for patients. For society, providing timely and high-quality care can be an effective strategy to save lives, reduce later burden of disease, and costs. A central challenge however is the dimensioning of services to ensure sufficient capacity to help people whenever needed.

Aims: To study response time for ambulance cars and patient outcome as measured by 30-day survival for persons experiencing a life-threatening incidence outside hospital.

Methods: Response time data and hospital administrative data from the Norwegian Patient Registry were merged with alive/dead status from the National Population Registry for the period 2017-2021. In line with national guidelines, response time was categorized in three groups: ≤12 minutes, >12–25 minutes and >25 minutes. 30-day survival was calculated for all emergency incidences and compared for the three groups. Descriptive analysis assessed changes in activity, patient population and response time over time.

Results: Number of emergency responses increased from slightly more than 111 000 in 2017 to almost 154 000 in 2021. Overall, 55.5% of the responses were within 12 minutes or less, 33.5% were between 12 and 25 minutes and 8.3% were longer than 25 minutes. The corresponding 30-day survivals were 93.9%, 95.1%, and 94.8%, respectively.

Conclusions: Assessing how patient outcomes are associated with response times provide a better understanding of how time matters. There remains however a range of factors not included in this analysis that potentially impact response time and/or patient outcome, such as prioritization of the patients with the most life-threatening conditions, or differences in access to ambulances based on geographical location.

P6

The validity of the Rx-risk comorbidity index among adults in the Outcomes & Multimorbidity In Type 2 diabetes cohort (OMIT)

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Introduction: The Rx-risk comorbidity index define disease categories according to WHO's Anatomical Therapeutic Chemical (ATC) Classification System based on filled prescriptions and has been found to be a valid tool to measure an individual's current comorbidities. However, the validity of the index to predict mortality among persons with Type 2 diabetes (T2D) is not known.

Aims: To evaluate the validity of the Rx-risk index in prediction of 5-year mortality among adults with T2D.

Methods: A calibration sample of 42290 adults diagnosed with T2D before 2014 and a validation sample of 7085 adults diagnosed 2014-2016 was identified within the "Outcomes & Multimorbidity In Type 2 diabetes" (OMIT) cohort, which is constructed via linkages between the Norwegian Diabetes Register for Adults, the Rogaland-Oslo-Salten-Akershus-Hordaland (ROSA4) study, the Norwegian Prescription Database, Statistics Norway and the Population Registry. For the calibration sample, filled medication prescriptions in 2013 were mapped to 46 comorbidity categories. Weights for each category were estimated using regression coefficients from a Cox regression model with 5-year mortality as the outcome and all comorbidity categories included as covariates in addition to age and sex. The Rx-risk index was calculated for as a weighted sum of comorbidities. The ability of the index to predict mortality was evaluated both in the calibration sample and in the validation sample using C-statistic from Cox regression and plots of observed and predicted mortality for each level of the comorbidity index.

Results: Mean (SD) age at start of follow-up and duration of T2D was 63.8 (12.4) and 10.1 (7.0) years in the calibration sample. The overall C-statistic was 0.82 and varied from 0.74 to 0.85 when stratifying on age groups, gender, level of education and country of origin. In the validation sample, mean (SD) age and duration of T2D was 59.7 (13.0) and 2.0 (0.8) years respectively. Despite younger age, shorter duration of diabetes and later time period the C-index was high both in the total sample (0.84) and separately for men (0.83) and women (0.85).

Conclusions: The Rx-risk index showed good validity in predicting mortality and may be a useful tool to study multimorbidity among persons with T2D.

P7

Maternal birthplace and risk of postpartum hemorrhage by length of residence: a registry-based study

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Introduction: Postpartum hemorrhage (PPH) is a major cause of maternal morbidity and mortality worldwide. During the past two decades, an increasing trend of PPH in high-income countries have been reported.

Aims: To explore the association between maternal birthplace and postpartum hemorrhage differ by mode of delivery and length of residence.

Methods: We used a nationwide registry-based cohort study including all women with a live birth of a singleton fetus weighing ≥500g after 21 gestational weeks registered in the Medical Birth Registry of Norway between 2008 and 2017 (n=574 583). Linkage to the National Population Registry was also provided. The exposure was maternal birthplace, defined as the country where the woman was born, and categorized into regions based on the Global Burden of Disease framework. The outcomes were moderate and severe PPH, defined as estimated blood loss of 500-1500mL and >1500mL with or without blood transfusion, respectively. Multinomial regression models simultaneously estimated adjusted relative risk ratios (RRR) for moderate and severe PPH, with 95% confidence intervals (CI) stratified by mode of delivery and length of residence.

Results: The overall prevalences of moderate and severe PPH were 18.5% and 2.4%, with great variations by maternal birthplace. Women from Southeast Asia/East Asia/Pacific had more than twice the risk of moderate and severe PPH compared to Norwegian-born women, across modes of delivery. Among newly arrived women (<5 years), those from Southeast Asia/East Asia/Pacific had the highest risk of moderate and severe PPH (RRR 1.83, 95% CI 1.70-1.97; RRR 2.32, 95% CI 1.96-2.75). Women from the same region with length of residence ≥5 years, were also at high risk of moderate and severe PPH (RRR 1.75, 95% CI 1.62-1.89; RRR 1.99 (1.67-2.38)). Similarly, sub-Saharan African women were at increased risk of moderate and severe PPH in both strata of length of residence.

Conclusions: Women from Asia & the Pacific were at particular high risk of moderate and severe Postpartum hemorrhage compared to Norwegian-born women. The associations between maternal birthplace and moderate and severe Postpartum hemorrhage did not seem to change with different lengths of residence.

P8

Risk of atrial fibrillation and stroke among older men exposed to prolonged endurance sport practice – a 10-year follow-up. The Birkebeiner Ageing Study and the Tromsø Study

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Introduction: Endurance sport practice is associated with a high prevalence of atrial fibrillation (AF) which increases the risk of stroke in the general population. However, stroke risk in endurance athletes with AF is sparsely investigated. Most studies have been limited by design and are largely restricted to younger and middle-aged populations.

Aims: To investigate AF and stroke risk in older athletes exposed to prolonged endurance training.

Methods: During a 10-year period, 505 male athletes aged ≥65 years frequently participating in a long-distance ski race was compared with 1867 men of the same age from the general population. The main exposure was endurance sport practice with self-reported AF and stroke as outcomes. Stroke risk was further examined by joint modeling of AF and endurance practice. Statistical analysis was conducted with a modified Poisson model.

Results: Athletes (median age: 68, range: 65-90) participated in a long-distance ski race over a median of 14 years (range: 1-53). Prevalence (28.5% vs. 17.8%) and adjusted risk of AF (risk ratio (RR): 1.88, 95% confidence interval (CI): 1.49-2.37) were higher in athletes compared to non-athletes, whereas the prevalence (5.4% vs. 9.7%) and risk of stroke were lower (RR: 0.60, 95% CI: 0.37-0.95). Compared with athletes without AF, risk of stroke was two-fold in athletes (RR: 2.38, 95% CI: 1.08-5.24) and nearly four-fold in non-athletes (RR: 3.87, 95% CI: 1.98-7.57) with AF.

Conclusions: Although older male endurance athletes experienced an increased risk of AF, the long-term risk of stroke was substantially reduced compared to non-athletes.

P9

How is your health compared to others of your age? Self-rated health in women and men aged 40-99 years: The Tromsø Study 2007-2016

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Introduction: According to the World Health Organization, health is a personal, social, and physical capacity resource, defined by well-being and lack of disease. Self-rated health (SRH) is considered a holistic reflection of a person's disease burden as well as mental and social condition. Although a subjective measure, SRH is a strong predictor of morbidity and mortality. A dimension less studied is SRH compared to others of the same age.

Aims: To study how SRH compared to others of the same age is associated with sex and age in a Norwegian general population.

Methods: We used prevalences and regression models to study the relationship between age and SRH in 12,100 participants aged 40-87 years from the sixth (Tromsø6 2007-2008, attendance 66%) and 20,825 participants aged 40-99 years from the seventh (Tromsø7 2015-2016, attendance 65%) survey of the Tromsø Study, adjusted for prevalent non-communicable disease (NCD) (cardiovascular disease, cancer, COPD, diabetes), NCD risk factors (smoking, harmful use of alcohol, physical inactivity, unhealthy diet), and NCD conditions (overweight, hypertension, hyperlipidemia). SRH was categorized as worse, same, or better with the questionnaire question *"How is your health compared to others of your age?"*.

Results: At both time-points, better SRH was more prevalent in men than in women in all age-groups, and better SRH was more prevalent in older compared to younger age-groups in both sexes. In Tromsø7, better SRH was reported by 23.9% of the women 40-49 years versus 49.4% of the women 80+ years, and by 33.2% of the men 40-49 years versus 56.7% of the men 80+ years. In Tromsø 7, the odds of high SRH increased by 4% (95% CI 1.04-1.05) in women and 3% (95% CI 1.03-1.04) in men by each 10-year age-group, adjusted for NCD risk factors, -conditions, and -disease. Results were similar in Tromsø6.

Conclusions: In this population-based study, better SRH compared to others of the same age was more common in men than women at any age, and in older compared to younger age-groups in both sexes. This could be explained by survival of healthy individuals in older age-groups in the general population and study participant selection.

P10

Is military service in desert areas associated with increased risk of cancer? Cancer incidence in Norwegian veterans deployed to Afghanistan between 2001 and 2019

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Introduction: Afghanistan is situated at low latitude and is characterized by high mountains and arid lowlands with sandy deserts. Possible exposure to high doses of UV-radiation to the troops might cause increased risk of skin cancer, and service in desert areas might cause exposure to particulate matter through inhalation, especially during sand storms. A link between lung disease and service in Iraq and Afghanistan has been reported (Iraq/Afghanistan War-Lung Injury). Inhalation of airborne dust is associated with increased risk of developing lung cancer.

Aims: We aimed to investigate the incidence of skin cancer, lung cancer and other cancers in a cohort of 8504 male Norwegian veterans deployed to Afghanistan between 2001 and 2019.

Methods: We followed cohort members from their first day of service in Afghanistan through 2020. We computed standardized incidence ratios of cancer (SIRs) with 95% confidence intervals (CIs) by comparing the observed number of cancers in our cohort with the expected number in the general male population. SIRs were computed for the overall cohort, and for two groups according to service length with a cut-off at average service duration (258 days). Poisson regression was used to assess the effect of length of service (≥258 days vs. <258 days) on cancer risk. Rate ratios (RRs) were calculated for the long-term service group, using the shorter-term service group as the reference.

Results: We observed 192 cancer cases. Observed cancer incidence did not deviate from the national rates, but the incidence of lung cancer was somewhat beneath the rates in the short-time service group (SIR=0.29, 95% CI 0.04–1.05). The Poisson regression showed no effect of service duration on all-site cancer incidence (RR=0.92, 95% CI 0.68–1.24), while the 71% higher risk of melanoma skin cancer in the long-term service group did not reach statistical significance (RR=1.71, 95% CI 0.75–3.89).

Conclusions: Military service in Afghanistan was not associated with increased risk of cancer. However, extended follow-up is necessary to be able to provide more robust estimates.

P11

Risk factors for the increase in adolescent anxiety and depression symptoms 1995-2019. (Decennial trends from) the young-HUNT study, Norway

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Introduction: In the last decades, a striking increase in mental health problems in adolescents has repeatedly been reported from several large western population-based surveys. This decennial trend towards increasing mental health problems in children and adolescents raises questions about changes in risk and protective factors, that can inform intervention targets going forward. Here we use three decades of individual, relational and contextual data from Young HUNT to explore a broad range of potential risk factors associated with increasing rates of mental health problems in young populations.

Aims: The aim of this study is to present risk factors potentially driving the increasing levels of anxiety and depression symptoms in Norwegian adolescents over the last three decades

Methods: Data was obtained from three waves of the Young HUNT, in the county of Trøndelag, Norway. The study include data from over 24.000 unique children and adolescents. Descriptive statistics were used to present the development of mental health problems (measured with HSCL-5) and potential risk factors for mental health problems in Norwegian adolescents aged 13-19 years, between 1995 and 2019. Using generalized linear model we calculated changes in relative and absolute differences between risk factors and mental health problems in the same time period.

Results: We found high and increasing prevalences for several of the risk factors for anxiety and depression symptoms in adolescence between 1995 and 2019, especially among girls. The most prominent trends were found for loneliness, musculoskeletal pain, fatigue, bullying and overweight. Stronger associations between several determinants and mental health problems were observed over the same time span, in poor self-perceived health, loneliness, fatigue, musculoskeletal pain and sleep problems evening in girls. Lesser changes over time were seen in boys.

Conclusions: Our findings suggest that several modifiable risk factors for poor mental health in adolescence are on the rise and should be further studied and then targeted in schools and in clinical populations.

P12

A picture is worth a thousand words: the construction of a large histopathology image dataset for the Norwegian Women and Cancer (NOWAC) study

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Introduction: One of the greatest challenges in scientific investigation is the availability of data. In the field of cancer epidemiology, this holds true particularly for image data. Currently, based on a systematic search, there are only 11 available datasets of breast histopathology images with a total of 3791 whole slide images (WSI) in Norway. These images form the basis of tumour classification, giving the differing microscopic characteristics of breast cancers.

The Norwegian Women and Cancer study (NOWAC) is a prospective cohort study made up of women randomly selected from the Norwegian Central Population Register. NOWAC studies female cancers with focus on breast cancer, however, NOWAC study lacks histopathology images data.

Aims: The aim of this work is to create a dataset of breast WSIs from samples collected in NOWAC study that can be used as epidemiological data in ongoing research.

Methods: This work was done on a pre-existing subset of the NOWAC study known as The Clinical and Multi-Omic (CAMO) cohort, which is made up of 388 breast cancer patients with about 31 biopsy samples per patient. Anonymized glass slides were retrieved from the archive and scanned, using a whole-slide scanner; The digitized whole-slide images were stored and then segmented manually using the QuPath software.

Results: 1273 breast histopathology tissue samples were digitized and can be compared with the Breast WSI dataset of The Cancer Genome Atlas with 1133 WSIs. In addition to tissue segmentations, 682 tumours were segmented of slides which have been previously marked manually by pathologists, demarcating tumour areas. The average area of the tumours was 0.78 cm^2 and the average largest diameter of tumours was 0.49 cm.

Conclusion: We were able to create the largest available WSI dataset in Norway through digitization of the NOWAC breast tissue samples. We hope it will enable greater progress and further research in cancer epidemiology in Norway.

P13

Establishment of the Norwegian Offshore Heliport Cohort and prospective studies of exposure-related disease risk: a study protocol

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Introduction: Work histories and exposure information in Norwegian offshore workers the past 20 year are lacking. The establishment of the Norwegian Offshore Heliport Cohort will provide updated data, and will facilitate evaluation of exposure-related risks of disease among Norwegian offshore petroleum workers who have been active in recent years.

Aims: 1) To establish a complete cohort of Norwegian offshore petroleum workers based on helicopter transport records between 2000 and 2021; 2) to undertake a questionnaire survey among these workers for work histories and lifestyle data; and 3) to conduct studies of mortality, morbidity and injury according to occupation, exposures and lifestyle factors.

Methods: The present project will combine the new Heliport cohort (n≈72 000 with ≥2 days offshore) with the existing Norwegian Offshore Petroleum Worker cohort (NOPW cohort, n≈28 000 ≥ 20 days offshore) with employments during 1965–1998. The combined cohort (n≈93 000) will cover the period 1967-2021, and will be linked to national registries for prospective studies of cancer, cardiovascular, respiratory, neurological diseases, injuries, and mental disorders. Complete work histories and lifestyle factors will be collected by questionnaire. External comparisons with the general Norwegian population will examine deviations in mortality or incidence by standardized mortality and incidence ratios. Disease risk within the combined cohort according to work and exposure, will be assessed in a time-to-event analytic framework, using a cohort or case-cohort design (Cox regression).

Discussion: Up until now, the main research focus has been cancer risk. Exploitation of other health outcome registries is warranted for a better understanding of the total disease burden. Norway is in a unique position to conduct registry-based studies of health outcomes in offshore petroleum workers. Results may add important new evidence related to petroleum-related exposures and risk of multiple diseases.

P14

Association between cognitive function and pain sensitivity – preliminary findings from the Tromsø Study

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Introduction: Pain is processed by an extensive network of brain areas, which overlap with areas important for cognitive function. Previous studies have suggested that experimental pain sensitivity is associated with cognitive function.

Aims: To assess the association between cognitive function and pain sensitivity in a general population.

Methods: We included 5561 participants from the 7th wave of the population-based Tromsø Study who had been examined with cognitive tests and experimental pain sensitivity, and for whom information on covariates were available. Cox regression models were fitted using standardized score on cognitive tests (12-word immediate recall test and Digit Symbol Coding test) as the independent variable, cold pressor endurance time as the time variable and hand withdrawal as the event. Statistical adjustment was made for putative confounders, namely age, sex, education, smoking, exercise, systolic blood pressure, BMI, anxiety or depression assessed by HSCL10, sleep problems, analgesic use and chronic pain.

Results: Mean age was 61.4 years (range 40-84), 52.2% were women. In multivariable adjusted analysis, higher score on cognitive test was associated with decreased risk of hand withdrawal, both for the 12-word immediate recall test (HR 0.93, 95% CI 0.89 – 0.96, p<0.001) and Digit Symbol Coding test (HR 0.93, 95% CI 0.89 – 0.98, p=0.003).

Conclusions: Higher test scores of cognitive function, assessed by 12-word immediate recall test and Digit Symbol Coding test, were associated with increased cold pain tolerance time, suggesting lower pain sensitivity.

P15

Cesarean delivery in Norwegian nulliparous women with singleton cephalic term births, 1967-2020: A population-based study

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Introduction: Nulliparous women contribute to increasing cesarean delivery in the Nordic countries and advanced maternal age has been suggested as responsible for rise in cesarean delivery rates in many developed countries. The aim was to describe changes in cesarean delivery rates among nulliparous women with singleton, cephalic, term births by change in sociodemographic factors across 50 years in Norway.

Methods: We used data from the Medical Birth Registry of Norway and included 1 067 356 women delivering their first, singleton, cephalic, term birth between 1967 and 2020. Cesarean delivery was described by maternal age (5-year groups), onset of labor (spontaneous, induced and pre-labor CD), and time periods: 1967-1982, 1983-1998 and 1999-2020. We combined women's age, onset of labor and time period into a compound variable, using women of 20-24 years, with spontaneous labor onset during 1967-1982 as reference. Multivariable regression models were used to estimate adjusted relative risk (ARR) of cesarean delivery with 95% confidence interval (CI).

Results: Overall cesarean delivery increased both in women with and without spontaneous onset of labor, with a slight decline in recent years. The increase was mainly found among women < 35 years while it was stable or decreased in women >= 35 years. In women with spontaneous onset of labor, the ARR of CD in women >= 40 years decreased from 14.2 (95% CI 12.4-16.3) in 1967-82 to 6.7 (95% CI 6.2-7.4) in 1999-2020 and from 7.0 (95% CI 6.4-7.8) to 5.0 (95% CI 4.7-5.2) in women aged 35-39 years, compared to the reference population. Despite the rise in induced onset of labor over time, the ARR of CD declined in induced women >= 40 years from 17.6 (95% CI 14.4-21.4) to 13.4 (95% CI 12.5-14.3) while it was stable in women 35-39 years.

Conclusion: Despite growing number of Norwegian women having their first birth at a higher age, the increase in cesarean delivery was found among women <35 years, while it was stable or decreased in older women. The increase in cesarean delivery cannot be solely explained by the shift to an older population of first-time mothers.