Norsk Epidemiologi

Norwegian Journal of Epidemiology

Volum 32, supplement 1, oktober 2024

Utgitt av Norsk forening for epidemiologi

Redaktør:
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ISSN 0803-4206

Tidsskriftet er åpent tilgjengelig online:
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Utgis vanligvis med to regulære temanummer pr. år. I tillegg kommer supplement med sammendrag fra Norsk forening for epidemiologis årlige konferanse, som fra 2023 ikke publiseres i papirutgave, bare online.

DEN 30. NORSKE EPIDEMIOLOGIKONFERANSEN

OSLO (QUALITY HOTEL EXPO, FORNEBU), 15.-16. OKTOBER 2024

The 30th Norwegian Conference on Epidemiology

Intersecting Frontiers in Epidemiology: Environment, Climate and Genetics in a Public Health Perspective

Oslo, 15th-16th October 2024

The Norwegian Epidemiological Association (NOFE), and the local organizing committee for the NOFE 2024 conference warmly welcomes you to Fornebu and the 30th NOFE conference.

Over two days, this conference will cover the topics of environmental epidemiology, climate, and genetics in a public health perspective. A big thank you to our keynote speakers Joan Ballester Claramunt (ISGlobal, Barcelona), Virissa Lenters (Vrije Universiteit, Amsterdam), and Therese Nøst (UiT The Arctic University of Norway).

In addition, nearly 70 participants will present abstracts of the most recent research in a variety of epidemiological fields in parallel and poster presentations. Dear presenters, thank you for completing the conference program by updating us on modern research, and to moderators, for facilitating fruitful discussions.

Our aim is that all participants at the conference gain a greater understanding of epidemiology, find new tools and inspirations for future projects, and gain insight into new research and find cooperative opportunities.

Enjoy the conference!

The NOFE Board

Cecilie Dahl, Ida Henriette Caspersen, Sairah Lai Fa Chen, Trond Peder Flaten, Ingeborg Forthun, Thea Karoline Walstad Grindstad, Kristin Hestmann Vinjerui, Paz Lopez-Doriga Ruiz, and Anne Lovise Nordstoga

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Keynote speakers

Joan Ballester Claramunt is an Associate Research Professor at the ISGlobal Barcelona Institute of Global Health. As a researcher in climate and health, he aims to describe the major sources of vulnerability in societies and whether we have started to adapt to climate change. He predicts weather and climate effects at a range of time-scales, from days to seasons, aiming at generating early warning systems of disease risk. His ultimate goal is to improve the well-being of societies by increasing human resilience and adaptation to climate variability and change.

Title of presentation: Integrating climate techniques and models to explore new avenues in environmental epidemiology

Summary: The growing availability of climate data and models, as well as the increasing body of transdisciplinary work at the interplay between environmental epidemiology and atmospheric sciences, open the door to new research avenues in both fields. The presentation will review several research lines in ISGlobal's Adaptation Group (https://www.joanballester.eu/group.html), including impact-based early warning systems from weather and air pollution forecasts, air pollution estimates from machine learning, climate change detection and attribution of climate-related health impacts, or air transport models estimating imported transboundary air pollution related mortality.

Virissa Lenters is an Assistant Professor and environmental epidemiologist from the Vrije Universiteit Amsterdam and the Julius Center for Health Sciences and Primary Care at the University Medical Center Utrecht. She researches how plastic and chemical pollution impact reproductive and child health, with a particular focus on the health effects of plastic waste exceeding planetary boundaries and the challenge of risk assessment for complex pollutants like microplastics.

Title of presentation: Plastic and chemical pollution – a challenging road to risk assessment

Summary: Pollution is a complex exposure. This talk will introduce how plastic and chemical pollution are planetary health problems and highlight challenges in human health risk assessment. Recent evidence for exposure and health effects of micro- and nanoplastics will be presented. The broader context of public perceptions of risk related to pollution, susceptibility and exposure disparities, and possible mitigation strategies will be addressed.

Therese Haugdahl Nøst is an Associate Professor in molecular genetics and environmental epidemiology at the UiT Arctic University of Norway. She focuses on markers in blood: 'omics markers' (for example genetics, gene expression, and DNA methylation) in the understanding of how environmental exposures can influence health and systemic reactions leading to diseases like cancer.

Title of presentation: Investigating environmental contaminants and health – Insights from population-based studies in Northern Norway

Summary: Our research team at UiT has, for several years, focused on environmental contaminant exposures and their potential health effects. Repeated measurements in the population-based Tromsø Study and the Norwegian Women and Cancer Study have enabled longitudinal studies and unique research designs. Investigations of time trends for both legacy and newer environmental contaminants in northern Norway have emphasized the importance of international conventions regulating these contaminants. Accompanying modeling efforts have provided conceptual representations of blood concentrations of PCBs throughout life. Using repeated samples also revealed that the time-trends of legacy POPs differed between T2DM cases and controls, thereby questioning POPs as risk factors for T2DM. Investigations of dietary habits and profiles of environmental contaminants confirmed fish as a dietary source of POPs although other factors such as birth year and reproductive history also have substantial impact on the body burden of these contaminants.

Abstracts

A: Cancer Epidemiology

A1

The counterintuitive association of sun exposure and melanoma-specific mortality in a cohort of Norwegian women

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Introduction: Counterintuitively, some studies have found that sun exposure, a well-known melanoma risk factor, may be associated with improved survival among melanoma patients. Using the Norwegian Women and Cancer cohort (NOWAC), we investigated the association between pre-diagnostic sunburns and melanoma-specific death, and potential impact of unmeasured confounding and selection bias (common causes of counter-intuitive associations in observational studies).

Methods: We ascertained all first primary cutaneous melanoma in NOWAC via the Cancer Registry of Norway. The association between pre-diagnostic sunburns and melanoma-specific death was estimated with Cox regression. Observed covariate E-values were used to investigate the potential impact of unmeasured confounding based on the observed covariates: histopathological variables (tumor thickness, melanoma subtype, clinical stage and body site of the tumor), age at diagnosis, hair color, body mass index, education, residential ambient UVR exposure and sunbathing vacations. Frailty analysis quantified the potential magnitude of selection bias.

Results: Among 2234 melanoma patients, 168 died from melanoma after mean follow-up of 8.0 years. We found reduced risk of melanoma-specific death for ever- versus never-sunburn (hazard ratio: 0.43, 95% confidence interval: 0.26–0.73) and significant negative trend for cumulative number of sunburns (p_{trend}=0.004). Unmeasured covariates altering the association is unlikely as they needed to be more strongly associated with both sunburn and melanoma-specific death than all the variables in our analysis. Frailty analysis suggested the observed relative risk between sunburn and melanoma-specific death may reflect selection bias.

Conclusion: The observed reduced risk of melanoma-specific death in women with pre-diagnostic sunburn is probably not explained by unmeasured confounding but could be explained by selection bias, i.e., including only patients.

A2

Ionizing radiation and childhood cancer in Norway: a national register-based case-control study from 1990-2020

Agnes Rutherford[1], **Geir Aamodt**[1], Ingvild Finne[3], Anne Liv Rudjord[3], Ying Wang[4], Suleman Atique[1], Deborah Oughton[2]

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Introduction: High doses of ionizing radiation are known to cause cancer, but the effect of low doses is less certain. Children are more susceptible to radiation than adults and given the same doses of radiation children are more likely to develop cancer than adults. The association between low doses of ionization radiation (gamma and radon) and childhood cancer (leukaemia and CNS) has been studied in several countries; however, studies show weak or no associations between ionization radiation and childhood cancer and the results vary between leukaemia and CNS.

Aims: The aim of this study is to investigate the association between ionizing radiation and childhood cancer in Norway.

Methods: The study is case-control study including 1436 cases of childhood cancer diagnosed between 1990 and 2020, identified in the Norwegian Cancer Registry, and 3094 age and gender matched controls from the National Population Registry. We included information on potential confounding variables from the Norwegian Birth Registry and Statistics Norway. The exposure variables, indoor radon concentration and gamma radiation, were produced by DSA and NGU respectively, and machine learning technique is used for both variables where knowledge of geology and ground conditions are included. We fitted conditional logistic regression models to assess the relationship between exposure variables and disease outcome and their subtypes.

Results: We found no main significant associations between indoor radon concentration and gamma radiation and childhood cancer. However, we found a significant trend between indoor radon concentration and all cancer types ($p = 0.024$). We also found a significant association between acute lymphoblastic leukaemia (ALL) ($p = 0.044$) for children aged 1 to 5 years. We did not find any associations between gamma radiation and childhood cancer.

Conclusions: The study suggests weak associations between indoor radon concentration and childhood cancer. The study shows the importance of systematic monitoring and supervision in Norwegian schools and kindergartens to reduce the concentration of indoor radon in Norway as well as the implementation of appropriate measures to reduce radon concentration in Norwegian homes. These results will be included in a meta-study with participants in the RADONORM project.

A3

Proximity to agriculture and livestock and childhood cancer in Norway: a national register-based case-control study from 2004-2020

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Introduction: Childhood cancer remains one of the main causes of death among children in Norway, despite its relatively low incidence and considerable increase in survival rates. Leukaemia and tumours in the central nervous system (CNS) are the most frequently occurring entities, accounting for 25.0 % and 28.3 %, respectively, of all diagnosed childhood cancer cases in Norway in the period 1993-2023. The causes of childhood cancer are largely unknown, but it has been suggested that environmental factors may play a role in the aetiology of these cancer types. Exposure to pesticides has been identified as a possible risk factor for childhood leukaemia and CNS tumours, but the available evidence remains inconclusive.

Aims: The aim of this study is to investigate the association between proximity to agriculture and livestock and childhood cancer in Norway.

Methods: The study is a case-control study including 641 cases of childhood cancer diagnosed between 2004 and 2020, identified in the Norwegian Cancer Registry, and 1547 age and gender matched controls drawn from the National Population Registry. Information on potential confounding variables were obtained from the Norwegian Birth Registry and Statistics Norway. Information regarding proximity to agriculture and livestock exposure was obtained from Norwegian Institute of Bioeconomy Research (NIBIO) and The Norwegian Agricultural Agency. Conditional logistic regression was used to assess the relationship between exposure variables and disease outcome.

Results: We found no significant associations between proximity to agriculture and risk of childhood leukaemia or CNS tumours. We observed increased odds of leukaemia in association with exposure to hogs and sheep: an increase of 50 animals corresponded to 4% 95 % CI: 1 % - 8 %) and 7% (4 % – 9 %) increase of odds ratios, respectively.

Conclusions: The findings in this study show no significant association between proximity to agricultural which is a proxy for pesticide exposure and risk of childhood cancer in Norway. However, the results suggest that exposure to livestock might be associated with increased risk of childhood cancer. The results might be interpreted in light of the structure of Norwegian agriculture, with less widespread use of pesticides compared to several other countries.

A4

Physical activity and longitudinal change in fatigue in young childhood cancer survivors. A Physical Activity in Childhood Cancer Survivors (PACCS) study

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Introduction: Cancer-related fatigue is a common late effect in childhood cancer survivors (CCS). We aimed to describe longitudinal change in fatigue, and how device-measured physical activity (PA) predict change in fatigue in young CCS.

Methods: We included CCS (≥1-year post-treatment) aged 9-16 years at inclusion from the multicenter PACCS study, who self-reported fatigue (PedsQL–Multidimensional Fatigue Scale) at two time points (T1, T2; median time interval of 2.0 years). Total fatigue score (range 0-100, where higher scores corresponds to less fatigue) was categorized into low (≥67.16), moderate (≥53.83<67.16) or severe fatigue (<53.83). PA was measured by accelerometers (Actigraph GT3X+) for 7 days at T1. A Sankey plot and weighted Kappa statistics were used to describe longitudinal change in fatigue. We performed multivariable linear mixed effects models to assess associations between PA level (steps/day) and intensities (minutes of light (LPA), moderate (MPA), and vigorous (VPA)) at T1 with change in fatigue score from T1 to T2, with interaction of baseline fatigue level (low vs. moderate or severe).

Results: We included 101 CCS of mixed cancers (51% leukemia), aged on average 12.1±2.0 years at T1. Mean age at diagnosis was 5.3±3.3 years. Mean total fatigue scores were 76.60±14.12 at T1 and 70.72±15.85 at T2 (p=0.006). About one in four (26%) had a deterioration in their fatigue level from T1 to T2, 7% improved, whereas the majority (67%) maintained their level of fatigue ($Kappa_w$=0.80, 95% CI: 0.74, 0.86). In those with low fatigue at baseline, higher levels of daily steps or LPA/MPA/VPA were not associated with fatigue development from T1 to T2 (all p>0.05). In those with moderate or severe fatigue at baseline, higher LPA was associated with a steeper improvement in total fatigue (p=<0.001), whereas higher VPA was associated with a steeper deterioration in total fatigue (p=0.027) from T1 to T2.

Conclusions: Mean total fatigue score worsened over time (~2 years) in young CCS. For those struggling with fatigue, higher LPA was associated with improved fatigue, whereas VPA seemed to increase the fatigue symptoms. These important findings suggest focusing on increasing LPA, rather than VPA, to improve fatigue in these young CCS.

A5

Association between prostate cancer and myocardial infarction management and post-infarction outcomes: A Norwegian registry study

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Introduction: Prostate cancer (PCa) is the most frequently diagnosed cancer in men in Norway and as survival rates improve, cardiovascular disease (CVD) has emerged as a primary cause of morbidity and mortality, including acute myocardial infarction (AMI). Cancer and CVD share some important risk factors and PCa treatment may increase the risk of CVD. The aim of this study was to compare rates of invasive management, in-hospital complications including severe bleeding, major adverse cardiovascular events (MACE), re-infarction and death, as well as rates of guideline recommended secondary prevention after an AMI between PCa patients and the general male AMI population.

Methods: Data included nation-wide longitudinal registry data to identify all males over 40 years in Norway who had their first AMI during 2013-2019. We compared outcomes between those diagnosed with localized PCa between 2014-2019 and the general AMI population using logistic and cause-specific Cox regression.

Results: We included 34,362 AMI patients, of whom 1405 (4.1%) had PCa. We observed no differences in invasive management or secondary medical treatment post-AMI between PCa patients and non-cancer patients. While PCa patients had a lower risk of overall complications (OR 0.77; 0.64-0.92), they experienced an increased risk of serious bleeding (OR 1.66; 1.08-2.44). PCa patients had better 1-year survival (HR 0.82; 0.69-0.98) but there was no difference in MACE or re-infarction events.

Conclusions: There was no evidence of reduced quality of AMI care for PCa patients in Norway. These findings support treatment of AMI as usual for PCa patients with localized disease, but with attention to increased bleeding risk.

A6

Educational disparities in cancer incidence, stage, and survival in Norway

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Introduction: Social inequality in health is a persistent issue, both in Norway and the rest of the world. The correlation between life expectancy and socioeconomic status is well documented, also in Norway. Regarding social inequality and cancer, previous research indicates that both socioeconomic status and place of residence are significant factors in how early cancer is diagnosed, as well as in survival rates in Norway. A recent study from Oslo, found regional and social variations in incidence, stage, and survival. Having a diagnosis in late stages is more common among patients with low socioeconomic status, and survival rates are highest among patients with high socioeconomic status.

Aims: This study will replicate the design of a study of cancer incidence, stage at diagnosis, and survival rates in Oslo to study whether the patterns are the same in the country as a whole.

Methods: We will use aggregated data from the Cancer Registry of Norway in the period 2013-2021. The data will be used to describe the distribution of cancer incidence and survival across different municipalities that belong to Norway's 20 health trusts. The trusts provide hospital services. Further, we will categorize the health trusts into low, medium, and high education levels based on the population's average level of education. Subsequently, we will use the data to calculate age-standardized incidence rates, the stage at the time of diagnosis, and five-war relative survival for colon, rectal, lung, melanoma, breast, and prostate cancer. Based on this, the study we will delve further into the most prevalent forms of cancer and describe how treatment pathways and survival rates vary between regions and educational groups in Norway.

Results: This is ongoing research and the results from the study will be presented at the NOFE conference in October.

B: Reproductive and Genetic Epidemiology

B1

Change in BMI from adolescence to adulthood among men and risk of infertility: The Norwegian Mother, Father and Child Cohort Study

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Introduction: Higher body-mass-index (kg/m^2 [BMI]) in adulthood is associated with reduced semen quality among men, and some studies also indicate a greater risk of infertility. However, the relationship between the change in BMI from adolescence to adulthood with subsequent infertility is unclear.

Aims: To study whether change in BMI from adolescence to adulthood among men is associated with infertility.

Methods: We conducted a retrospective cohort study including 62,596 men and their pregnant partners participating in the Norwegian Mother, Father and Child Cohort Study. Self-reported height and weight and time to pregnancy was available through questionnaires. We obtained measurements of the men's height and weight at conscription (age 17) from the Norwegian Armed Forces Health Registry. We calculated the odds ratios (OR) with 95% confidence intervals (CI) of having used assisted reproductive technologies (ART) or spent ≥12 months to conceive in the current pregnancy according to the change in BMI between conscription and time of pregnancy. We present unadjusted analyses, and analyses adjusted for paternal age, first-time pregnancy or not, paternal educational attainment at time of pregnancy, and maternal BMI at time of pregnancy.

Results: 1815 (3%) men had used ART in the current pregnancy, and their mean change in BMI from conscription until time of pregnancy was 4.3 kg/m^2 compared to 3.7 kg/m^2 among those who conceived without ART. Among 49,480 men with a partner who reported that the pregnancy was planned, 5612 (11%) spent ≥12 months to conceive, with a mean change in BMI of 4.1 kg/m^2 compared to 3.7 kg/m^2 among those who spent <12 months. Compared to those who remained normalweight, those who went from underweight to overweight (OR 1.79; 95% CI: 1.12-2.86), normalweight to overweight (OR 1.25, 95% CI: 1.13-1.40), normalweight to obese (OR 1.53, 95% CI: 1.25-1.87) or overweight to obese (OR 1.51, 95% CI: 1.22-1.88) had an increased likelihood of having used ART. Similar patterns were observed for taking ≥12 months to conceive.

Conclusions: Increasing BMI was associated with infertility among men. There is a need to replicate these findings in larger studies where couples who are unable to achieve a pregnancy are included.

B2

Does male infertility matter? Use of assisted reproductive technologies for male and female infertility and perinatal outcomes

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Introduction: An increased risk of adverse perinatal outcomes is observed in pregnancies conceived by assisted reproductive technologies (ART). Whether this risk varies according to use of ART for male versus female infertility remains unclear.

Aim: To compare the risk of adverse perinatal outcomes in ART and naturally conceived pregnancies according to whether the underlying cause was male infertility, female infertility or a combination of both.

Methods: We used information on all live births in Norway between 2000 and 2021 from the birth registry to compare the perinatal outcomes in ART (n=30,453) and spontaneously conceived pregnancies (n=1,210,709) according to whether the underlying cause was male infertility (n=9,957), female infertility (n=10,031), a combination of both (n=3,287), or unexplained (n=7,178). We compared the birthweight and gestational age using linear regression, and the risk of pre-eclampsia, caesarean section, stillbirth, preterm birth, low birthweight, small-for-gestational age and transfer to neonatal unit using logistic regression, adjusting for parental age, maternal parity, maternal country of birth and year of birth.

Results: Gestational age and birthweight were decreased in all ART groups. However, the decrease in gestational age was less pronounced in ART deliveries resulting from male infertility (adjusted difference -2.14 days; 95% CI: -2.47 to -1.80), compared to ART deliveries resulting from female infertility (-3.20 days; 95% CI: -3.55 to -2.84). Similarly, there was a smaller decrease in birthweight in ART deliveries resulting from male infertility (-48 grams; 95% CI: -61 to -35), compared to ART deliveries resulting from female infertility (-76 grams; 95% CI: -89 to -62). We also observed an increased risk of adverse birth outcomes in all ART groups, except for small-for-gestational age, although a more modest increased risk was observed for ART deliveries which were the result of male infertility, compared to what was observed for ART deliveries which were the result of female infertility.

Conclusions: We observed an increased risk of most adverse birth outcomes in pregnancies conceived by ART due to male infertility, although less pronounced than in ART pregnancies with female infertility. Whether this may reflect an influence of male characteristics through germ cells should be further explored.

B3

Parental history and risk of celiac disease in the Norwegian Mother, Father and Child Cohort Study (MoBa)

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Introduction: In type 1 diabetes (T1D), the relative risk conferred by maternal disease is lower than that by paternal disease, possibly explained by parent-of-origin effects including genomic imprinting, genotype-dependent fetal loss in affected mothers, or other environmental effects. Celiac disease (CD) and T1D cluster in families and share genetic susceptibility loci. Familial aggregation of CD is established, but the relative risk conferred by maternal vs paternal CD is not well studied.

Aims: In analogy with T1D, we hypothesized that the relative risk of CD is lower for those with an affected mother compared those with a father affected by CD.

Methods: Using over 87,000 triads in the Norwegian Mother, Father and Child Cohort study, diagnosed CD was ascertained by the Norwegian Patient Register (n=1388 children, 485 fathers, and 958 mothers). Over 75,000 children were genotyped for the tag SNPs rs2187668 (HLA-DQ2.5) and rs7454108 (DQ8 haplotype).

Results: The relative risk of CD in children conferred by maternal CD was 11.5 (95%CI: 9.7-13.7) and for paternal CD 18.5, 95%CI:14.7-23.4), robust towards alterative case-definitions. Adjusting for DQ2- and DQ8 reduced the RRs by maternal- and paternal CD to 6.2 (5.0-7.8) and 10.5 (7.7-14.3).

Conclusions: The relative risk conferred by maternal CD was lower than that for paternal CD, also after adjustment of child's HLA-genotype. Because of the well-known female bias in risk of CD, we believe this association has gone unnoticed in clinical practice. If replicated, potential mechanisms explaining this phenomenon is warranted.

B4

Statistical methods to explore genetic effects influencing fertility and early fetal viability with a genome-wide application

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Introduction: Infertility is a global issue affecting millions of couples, with genetic factors potentially contributing in various ways. For example, genetic selection may occur prior to fertilization, driven by parental genotypes individually or through interactions. Post-fertilization, the embryo's genotype becomes a key determinant of fetal survival. By analyzing parental interaction effects and fetal effects jointly in the same model within mother-father-child triads, we aim to distinguish between these effects. Furthermore, focusing on families who conceived using assisted reproductive technology (ART) may help clarify whether these genetic effects are more pronounced in couples requiring reproductive assistance and in ART-conceived children.

Aims: 1) To develop statistical models capable of disentangling parental interaction effects influencing fertilization success from fetal effects associated with fetal survival, and 2) to evaluate these models using simulated data and real genome-wide data from ART families.

Methods: We extended the models available in the R package Haplin to include parental interaction effects, testing several implementation strategies. These models were applied to genome-wide scans of 1,336 parent-child triads and dyads from the Norwegian Mother, Father, and Child Cohort Study, where the child was conceived by ART. Additionally, we extensively tested these models using simulated data, discussing the genetic results in this context.

Results: Several of the models tested identified the same genome-wide significant parental interaction effects in the ART sample. Notably, some associated genes, such as *ACTB*, *FSCN1*, and *RNF216*, have established links to fertility. We also identified fetal effects in variants residing in for example *MTMR14*, a gene with associations to both the male and female reproductive system. A key limitation of these analyses was the low minor allele frequencies, as also highlighted by the simulations.

Conclusions: The models we developed are applicable in genome-wide scans of family triads and dyads. Our analyses revealed significant parental interaction effects as well as fetal effects in fertility-related genes. However, challenges remain in analyzing rare variants, underscoring the need for replication of our analyses in other cohorts.

B5

Telomere length and fecundability in the Norwegian Mother, Father and Child Cohort Study

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Introduction: In women, shorter telomeres have been reported to be associated with conditions such as endometriosis and polycystic ovary syndrome, whereas other studies have reported the opposite. In men, studies mostly report associations between shorter telomeres and sperm quality. To our knowledge, no studies have thus far investigated the associations between telomere length (TL) and fecundability or the use of ART.

Aims: To investigate if TL is associated with fecundability, infertility, or use of assisted reproductive technologies (ART).

Methods: This study is based on the Norwegian Mother, Father, and Child Cohort (MoBa) Study and uses data from the Medical Birth Registry of Norway (MBRN). We included women (24,645 with genotype data and 1,054 with TL measurements) and men (18,339 with genotype data and 965 with TL measurements) participating between 1998 and 2008. We investigated the associations between leukocyte TL and fecundability, infertility, and the use of ART. We also repeated the analyses using instrumental variables for TL, including genetic risk scores for TL and genetically predicted TL.

Results: Approximately 11% of couples had experienced infertility and 4% had used ART. TL was not associated with fecundability among women (fecundability ratio [FR], 0.98; 95% confidence interval [CI], 0.92-1.04) or men (FR, 0.99; CI, 0.93-1.06), nor with infertility among women (odds ratio [OR], 1.03; CI, 0.85-1.24) or men (OR, 1.05; CI, 0.87-1.28). We observed an increased likelihood of using ART with increasing TL among men (OR, 1.22; CI, 1.03-1.46), but not among women (OR, 1.10; CI, 0.92-1.31). No significant associations were observed using the instrumental variables.

Conclusions: We found no indication that TL can act as a biomarker for fecundability, infertility and use of ART in MoBa. Additional studies are required to replicate the association observed between TL and ART in men.

B6

Can assisted reproductive technologies (ART) impact the association between DNA methylation and genotypes?

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Introduction: Assisted reproductive technologies (ART) may interfere with processes involved in zygote formation, particularly with mechanisms responsible for the re-establishment of DNA methylation (DNAm) profiles in early embryogenesis. Many single-nucleotide polymorphisms (SNPs) passed from parents to offspring serve as blueprints for establishing important DNAm marks, called methylation quantitative trait loci (mQTLs). mQTLs are associated with a wide range of phenotypes and diseases. Additionally, cytosine-phosphate-guanine dinucleotide motifs (CpGs) with higher heritability are more likely to be within mQTLs. However, in the context of ART, it remains unclear whether these procedures directly influence mQTL formation and whether there is a difference in mQTL formation based on the parental origin of the inherited SNP alleles.

Aims: To examine whether ART procedures alter mQTL patterns in children and whether these changes are parent-of-origin (PoO) specific.

Methods: We leveraged whole-genome genotype and DNAm data from the Study of Assisted Reproductive Technology (START), a substudy within the Norwegian Mother, Father and Child Cohort Study (MoBa). The dataset comprised samples from triads in categories of ART and non-ART conceptions (totaling 4948 samples). After quality control, 6,972,864 SNPs and 770,586 CpGs were available for analysis. An agnostic search for cis-mQTLs (where the distance between SNP and CpG is <1 Mbp) was initially conducted on the parents. Significant mQTL pairs identified in the parents were then assessed in children using following models: (a) additive: DNAm ~ SNP + ART-status, (b) with interaction: DNAm ~ SNP + ART-status + SNPxART-status, and (c) stratified by ART-status. Analyses were performed using PLINK, R, and JuliaLang.

Results: A preliminary search for cis-mQTLs on chromosome 20 revealed that several of the mQTLs identified in parents were confirmed in children using the additive model. Some of them also showed significant interaction and stratified effects. We are currently working on implementing the model to test for PoO effects among the significant results in the offspring, which could indicate the impact of ART procedures is before fertilization.

Conclusions: We showcase the use of statistical models with interaction and stratification to pinpoint genomic regions where ART procedures could potentially impact the association between genotypes and DNA methylation.

C: Bone Health

C1

Acquisition of peak bone mass in a Norwegian youth cohort: Longitudinal findings from The Fit Futures Study 2010-2022

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Introduction: Although osteoporotic fractures mainly occur in older age, peak bone mass acquisition during adolescence is an important predictor of future fracture risk.

Aim: To examine longitudinal trends in bone mineral density (BMD) levels in Norwegian adolescents into young adulthood.

Method: In a prospective cohort design, we followed 980 adolescents (473 (48%) females) aged 16-19 years into adulthood (age of 26-29) on three occasions: 2010-11 (Fit Futures 1(FF1)), 2012-13 (FF2) and 2021-22 (FF3), measuring BMD (g/cm^2) at the femoral neck, total hip, and total body with dual x-ray absorptiometry (DXA). We used linear mixed models to examine longitudinal BMD changes from FF1 through FF3.

Results: From median age 16 years (FF1), femoral neck BMD (mean g/cm^2 (95%CI)) slightly increased in females from 1.070 (1.059-1.082) to 1.076 (1.065-1.088, p=0.015) at median age 18 years (FF2) but declined to 1.041 (1.029-1.053, p<0.001) at median age 27 years (FF3). Similar patterns were observed in males, 16 years: 1.104 (1.091-1.116), 27 years: 1.063 (1.050-1.077, p<0.001), and for total hip in both sexes (both p<0.001). Total body BMD increased from age 16 years through 27 years in both sexes (females, 16 years: 1.141 (1.133-1.148); 27 years: 1.204 (1.196-1.212), p<0.001; males, 16 years: 1.179 (1.170-1.188; 27 years: 1.310 (1.296-1.315), p<0.001).

Conclusion: BMD levels increased from 16 to 18 years at the femoral and total hip sites in young Norwegian females and males, and a small decline was observed at the femoral sites when the participants were followed up to 27 years. Total body BMD continued to increase from adolescence through young adulthood.

C2

Associations between accelerometer-measured physical activity and bone mineral density from adolescence to young adulthood. Fit Futures.

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Introduction: Physical activity (PA) is positively associated with areal bone mineral density (aBMD) during adolescence, a critical period for bone mass accrual. However, there are limited longitudinal studies investigating this association into the third decade of life using accelerometer-measured PA.

Aims: To investigate the longitudinal association between accelerometer-measured moderate-to-vigorous physical activity (MVPA) and aBMD from adolescence to young adulthood.

Methods: We used data from the Fit Futures study, with surveys at ~16, ~18, and ~27 years of age, to assess the relationship between MVPA and aBMD at the femoral neck (FN), total hip (TH), and total body (TB). MVPA and aBMD was measured with triaxial accelerometry and dual-energy x-ray absorptiometry, respectively. Sex-stratified analyses were done using mixed-effects models fitted with random intercepts and random slopes at the subject level. The models were adjusted for relevant time-varying covariates with data from all three surveys. The analyses included 442 females and 381 males, providing a total number of 828 and 657 observations, respectively.

Results: MVPA was positively associated with aBMD at all sites for both sexes. For females, each additional minute of MVPA per day was associated with a 0.0002 g/cm² (95% CI: 0.00003 to 0.0004, $p = 0.019$) higher aBMD at the FN, 0.00021 g/cm² (95% CI: 0.00007 to 0.0004, $p = 0.005$) at the TH, and 0.00014 g/cm² (95% CI: 0.00006 to 0.0002, $p = 0.001$) at the TB. For males, each one-minute-increment of MVPA per day was associated with a 0.00044 g/cm² (95% CI: 0.0002 to 0.0007, $p < 0.001$) higher aBMD at the FN, 0.00038 g/cm² (95% CI: 0.0002 to 0.0006, $p < 0.001$) at the TH, and 0.00016 g/cm² (95% CI: 0.00002 to 0.0003, $p = 0.022$) at the TB.

Conclusions: The positive association between MVPA and aBMD into young adulthood suggests advantages that endure past adolescence. As a modifiable lifestyle factor, MVPA represents a viable option for bone health promotion and should be encouraged. For inactive young persons, 30 minutes MVPA increase per day may have profound benefits for bone health.

C3

Air pollution and fracture risk in Norwegian children, a nationwide cohort study

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Introduction: Forearm fractures are common among children and adolescents, with high incidence rates in Norwegian youth. Recent research suggests air pollution may negatively affect childhood bone health through increased inflammatory markers, reduced vitamin D uptake and increased bone turnover.

Aims: To estimate the association between outdoor air pollutants and forearm fracture risk in Norwegian children and determine the influence of demographic, environmental and geographic variables.

Methods: We used nationwide cohort data of Norwegian children and adolescents aged 5-18, with forearm fractures from 2008 to 2018, identified by the Norwegian Patient Registry (NPR), with background data from Statistics Norway. Air pollution data were obtained from the NordicWelfAir project using the Urban Background Model (uEMEP), climate data from the Norwegian Meteorological Institute (MET Norway), and geography was estimated in Geographic Information Systems (GIS).

We calculated age-standardized Incidence Rates (IRs) per 10,000 person years. Negative binomial models gave Incidence Rate Ratios (IRRs) with 95% Confidence Intervals (95% CIs), adjusting for demographic, geographic, and environmental factors and stratified by region, temperature, and urbanization.

Results: We identified 87,643 forearm fractures, with higher incidence rates per 10,000 person-years in boys (104) than girls (75). Higher pollutant levels (tertiles) were associated with increased fracture risk (IRR $PM_{2.5}$: 1.09, IRR NO_2: 1.07). This association was attenuated after adjusting for geography and environment. Individuals in areas with lower annual mean temperatures had a 9% higher fracture incidence with high $PM_{2.5}$ and NO_2 levels. In cities, high pollutant levels were associated with higher fracture incidence (IRR $PM_{2.5}$: 1.12, IRR NO_2: 1.11).

Conclusions: $PM_{2.5}$ and NO_2 are associated with an increased risk of forearm fractures in Norwegian children and adolescents, particularly in colder climates and in cities. This is the first study on air pollution and fracture risk in children in Norway, highlighting the need for continued action to reduce air pollution levels.

C4

Trends in hip fracture rates in Oslo across sociodemographic characteristics and the role of the COVID-19 pandemic

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Introduction: Oslo has historically experienced the world's highest hip fracture incidence. Within Norway, Oslo distinguishes itself in terms of population size and density as well as demographic and ethnic composition. Along with demographic changes, several fall- and fracture preventive initiatives have been implemented in recent years. Furthermore, unanticipated changes have affected society: Oslo underwent the country's strictest COVID-19 restrictions in 2020-21, involving abrupt changes to daily life activities, with the potential to affect fracture rates.

Aims: To describe trends in incidence rates of hip fractures in older adults (70+ years) in Oslo during 2012-2022 and to examine the role of individual characteristics including sex, age, educational level, marital status, and ethnic background.

Methods: Annually updated information for the population aged 70+ years in Oslo from Statistics Norway was linked with information on hospital-treated hip fractures from the Norwegian Patient Registry. Incidence rates by demographic characteristics were estimated using Poisson regression.

Results: A total of 7,905 individuals suffered a hip fracture in the 11-year period. The incidence declined steeply in both men and women. The lowest rates were observed in 2020, the year characterized by reduced activity level due to COVID-19 restrictions. By then, age- and sex-adjusted incidence rates had declined by 37% (95% CI: 31% to 44%) since 2012. Additional adjustment for changes in ethnic composition and marital status yielded similar results. The rate of decline was generally consistent across sex, age, marital status, and education level. However, the decline tended to be steeper in women who were younger (70-79 years) and who had attained college- and university education, and the drop in 2020 was particularly apparent in those subgroups. There were insufficient fracture numbers among people with non-Norwegian background to appraise any variation in time trends by ethnic background. By 2022, the fracture rates had rebounded to pre-pandemic levels.

Conclusions: There was a dramatic decline in hip fracture incidence in Oslo during the last decade, which was clearly more pronounced than the national decline in this period. The decline was consistent across sociodemographic subgroups. The COVID-19 restrictions appeared preventive for hip fractures particularly among younger-old women with higher education.

C5

Forecasting the burden of hip fracture in Norway towards 2050 by educational level. The Norwegian Epidemiologic Osteoporosis Studies (NOREPOS)

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Introduction: Despite declining incidence rates of hip fracture, the future fracture burden will likely increase due to the aging of the population. Global hip fracture burden has been projected to double by year 2050. There is a clear educational gradient in hip fracture incidence in Norway. Furthermore, a shift toward higher educational attainment has occurred in later birth cohorts, which will manifest itself in older age groups in the coming decades.

Aims: We aimed to assess future hip fracture burden in Norway and whether the trends will vary by attained educational level.

Methods: We estimated annual numbers of hip fractures during 2020-2050 in the population aged 50+ years based on information from the NOREPOS hip fracture database and the main alternative for population projections from Statistics Norway. Projected educational attainment 2020-2050 for Norway by sex and five-year age groups was available from the Wittgenstein Centre for Demography and Global Human Capital. Two scenarios were explored; one assuming that the sex- and age-specific incidence rates observed in 2019 will remain constant until 2050, and a second scenario assuming a continued decline at an average annual rate of 1.0% in men and 1.3% in women, corresponding to the observed rate of decline during 1999-2019.

Results: By year 2050 the annual numbers of hip fractures were projected to increase by 91% in women and 131% in men if assuming constant rates. If assuming continuously declining rates, they were projected to increase by 27% in women and 66% in men. While most hip fractures will keep occurring in people with attained secondary education who comprise the largest group, fracture burden will increase steeply in people with tertiary education, and by 2050, the number of hip fractures among women with tertiary education will surpass that of women with primary education.

Conclusions: Despite declining individual fracture risk, the number of hip fractures in Norway may approximately double by 2050, placing high demands on the healthcare services. As much of the preventive potential from secular changes in population risk factors may have been realised, it is vital to identify the high-risk population and intensify targeted preventive efforts.

D: Pharmacoepidemiology

D1

Quantification of vaccine waning as a challenge effect

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Knowing whether vaccine protection wanes over time is important for health policy and drug development. However, quantifying waning effects is difficult. A simple contrast of vaccine efficacy at two different times compares different populations of individuals: those who were uninfected at the first time versus those who remain uninfected until the second time. Thus, the contrast of vaccine efficacy at early and late times can not be interpreted as a causal effect. We propose to quantify vaccine waning using the challenge effect, which is a contrast of outcomes under controlled exposures to the infectious agent following vaccination. We identify sharp bounds on the challenge effect under non-parametric assumptions that are broadly applicable in vaccine trials using routinely collected data. We demonstrate that the challenge effect can differ substantially from the conventional vaccine efficacy due to depletion of susceptible individuals from the risk set over time. Finally, we apply the methods to derive bounds on the waning of the BNT162b2 COVID-19 vaccine using data from a placebo-controlled randomized trial. Our estimates of the challenge effect suggest waning protection after 2 months beyond administration of the second vaccine dose.

D2

Time-dependent effect of prenatal antidepressant exposure on symptoms of eating, depressive, and anxiety disorders in children at 14 years of age

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Introduction: The long-term reproductive safety of antidepressants on psychiatric disorders in offspring up to adolescence remains unresolved.

Aims: To quantify the association between time-dependent prenatal antidepressant exposure and symptoms of eating, depressive, and anxiety disorders in offspring at age 14.

Methods: Data stem from the Norwegian Mother, Father, and Child Cohort Study (MoBa), linked to the Medical Birth Registry of Norway and MoBa genetics. We included 2,144 children born to women with pre-pregnancy mental illnesses. Children of women exposed to antidepressants both during and in the six months before pregnancy (n=144 *continuers*) were compared to those born to women unexposed before and during pregnancy (n=1,899 *unexposed*), and who used antidepressants only before pregnancy (n=104 *discontinuers*). Antidepressant continuation was further examined by timing of exposure (early, mid- and/or late pregnancy). Our primary outcomes were symptoms of depression and eating disorder, reported by adolescents, and anxiety reported by their mothers. We controlled for time-varying and time-fixed confounding via inverse probability of treatment weights, using marginal structural models and weighted generalized models.

Results: In the weighted analysis, children born to antidepressant *continuers* had greater depressive symptoms at age 14 than *unexposed* (adjusted z-score: 0.37, 95% CI: 0.08, 0.66), but not when compared to *discontinuers*. No difference in eating disorder symptom severity emerged across comparisons. Children born to *antidepressant continuers* had greater risk of having clinically relevant anxiety symptoms (weighted Risk Ratio (wRR): 1.85, 95% CI: 0.89, 3.82) and perception of being too thin (wRR: 1.48, 95% CI: 0.88, 2.47) than *unexposed*, although the 95% CI crossed the null. These associations were weaker when *discontinuers* acted as comparator (wRR: 1.51, 95% CI: 0.43, 5.35; wRR: 1.36, 95% CI: 0.72, 2.58, respectively). Generally, these risks emerged only among female adolescents. Adjustment for maternal psychiatric symptoms and adolescents' sedentary behaviour did not change our association measures.

Conclusions: In this population of adolescents born to women with pre-pregnancy mental illnesses, prenatal antidepressant exposure did not confer any substantial risk of eating, depressive, and anxiety disorders at age 14 beyond that posed by the underlying maternal mental illnesses.

D3

Timing of antidepressant initiation postpartum and maternal mental health outcomes up to 18 months after childbirth

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Introduction: Evidence about the effectiveness of antidepressants for treatment of postpartum mental illness in real-world setting is very limited, despite this being a common intervention. Whether timing of antidepressant initiation within the first 6 months postpartum poses different clinical benefit to maternal mental health outcomes is not elucidated.

Aims: In a population of women with psychiatric history, we aimed to evaluate the effectiveness of timing of antidepressant initiation within the 0-6-months postpartum on a broad set of maternal mental health outcomes at 6- and 18-months following childbirth. Our secondary aim was to assess whether this association varied by type and course of maternal psychiatric history.

Methods: Using data from the Norwegian Mother, Father and Child Cohort Study (MoBa) linked to MoBa genetics, we included 1,146 women: 154 (13.4%) antidepressant initiators in the 0-6 months postpartum (37.0% in early and 63.0% in mid-postpartum), and 992 (86.6%) with unmedicated new mental illness episode within same period. Self-reported outcomes at 6 and 18 months postpartum included depression/anxiety symptoms using validated psychometric scales. To control for measured confounding, we fit linear and modified Poisson models using overlap weighting, stratified by polygenic propensity for antidepressant response.

Results: Early antidepressant initiators had reduced severity of depression/anxiety symptoms at 6, but not at 18 months postpartum, compared with unmedicated (weighted mean difference (MD): -0.23, 95% CI = -0.39, -0.06). No association emerged with mid-postpartum initiation. Upon outcome dichotomization, there was 44% reduced risk of having active, clinically relevant depressive/anxiety symptoms at 6 months since childbirth (weighted RR= 0.56, 95% CI = 0.35, 0.91) with early antidepressant initiation. In stratified analyses, lower severity of depressive/anxiety symptoms with early antidepressant initiation was evident only among those women with higher polygenic propensity for antidepressant response (weighted MD: -0.50, 95% CI: -0.84, -0.16), and the effect persisted at 18 months.

Conclusions: Our findings suggest that initiation of antidepressant in the early, but not in mid postpartum, is associated with reduced severity of depression/anxiety symptoms at 6 months after childbirth. This association was long-lasting and prominent in those women having high polygenic propensity towards antidepressant response, highlighting the importance of personalized pharmacotherapy in perinatal psychiatry.

D4

Substantially different trends in the use of drugs with weight loss effect in Scandinavia from 2017 to 2023

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Introduction: The number and demand of drugs with weight loss effect increased substantially after 2020.

Aims: To compare current user trends of drugs with weight loss effect and corresponding reimbursement policies in Scandinavia.

Methods: A cohort study including all residents of all ages in Denmark, Norway, and Sweden. Annual prevalence of users per 1000 from 2017 to 2023 were investigated by sex and country, based on aggregated data from three nationwide prescribed drug registers, and corresponding reimbursement policies and changes were described.

Results: In 2022, the prevalence of bupropion-naltrexone users in Norway had increased to a peak of 7.9 users per 1000 inhabitants (11.6 in women), compared to only 0.2 (0.3 in women) in Denmark and 0.2 (0.4 in women) in Sweden. After 2020, liraglutide use accelerated quickly in Norway with a peak in 2022 of 8.3 users per 1000 compared with 5.2 in Denmark, while Sweden had a later and lower peak at 3.9 in 2023. Notably, Norway reimbursed bupropion-naltrexone and liraglutide with weight loss indication with some restrictions, while Denmark and Sweden had no similar reimbursement for these drugs for weight loss. The use of semaglutide increased dramatically in all countries, with a nearly three-fold higher use in Denmark (34.6) than Sweden (11.9) by 2023. Only Sweden continued prescribing more semaglutide to men than women by 2023.

Conclusions: Bupropion-naltrexone use increased substantially only in Norway until 2022 and decreased afterwards. The use of liraglutide and semaglutide increased dramatically during the last 3 years primarily in Norway and Denmark, whereas Sweden showed a much more cautious increase in using all drugs. The notably differing trends are probably affected by specific national reimbursement policies.

D5

Mortality among individuals with long-term prescription opioid use in Norway: A nationwide registry-based cohort study

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Introduction: Opioid analgesics are essential medications for managing acute and cancer-related moderate-to-severe pain conditions. Their long-term use, however, may be associated with elevated mortality due to multiple factors like impaired cognition, sedation, physical dependence, immunosuppression, cardiovascular events, and respiratory depression.

Aims: This study aimed to estimate sex-specific age-standardized all-cause and cause-specific mortality ratios (SMR) comparing long-term prescription opioid users to the general population.

Methods: This cohort study utilized data from linked nationwide health registers of non-cancer patients aged 15-69 years with long-term opioid analgesics use (n=116,006) in Norway between 2011 and 2019. The primary outcomes were natural (ICD-10 group A00-R99) and unnatural causes of death (V01–Y98), including death due to poisoning (X40–X49), suicide (X60–X84 and Y87.0), and accidents (V01–V89; X59; Y85-Y86).

Results: The SMRs for all-cause mortality were nearly 4-fold higher in long-term opioid analgesics users compared with the general population (SMR = 3.8 [95% CI = 3.6–3.9] in men and 3.7 [3.5–3.9] in women). For natural causes, the SMRs were 3.8 (3.7–4.0) in men and 3.8 (3.6–4.0) in women. The SMRs were highest for unnatural causes of death (5.0, 4.6–5.5 versus 5.5, 4.8–6.3), especially for death due to poisoning (9.1, 7.9–10.5 versus 8.7, 7.8–10.7) and accidents (5.6, 5.0–6.2 versus 5.7, 4.8–6.8). For suicides, the SMRs were 4.3 (3.7–5.1) versus 5.5 (4.5–6.6).

SMRs decreased with age across all categories, with the youngest age group (15–34 years) having the highest mortality compared with the general population. There were also variations in SMRs between the sexes, with men aged 15–34 years having higher SMRs than women in most causes of death. The SMR for accident deaths in men aged 15–34 years was (12.1, 9.3–15.9) and in women (7.3, 3.9–13.5).

Conclusions: Our findings indicated an increase in excess mortality associated with long-term treatment with prescription opioids in non-cancer patients. The observed higher mortality indicated by the SMR highlights the need to carefully consider the benefit-risk profile of opioid pharmacotherapy for each patient.

E: Health Inequality

E1

The changing social gradient in age at menarche across cohorts and generations in Norway

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Introduction: Age at menarche (AAM) is important for women's health across the life course, and has been declining over time. Simultaneously, while children growing up in wealthier families used to experience menarche relatively early, the pattern now appears to have reversed. The reasons behind this uneven decline are not well understood.

Aims: First, to investigate whether the secular decline in AAM is a shared experience across socio-economic strata. Second, to determine whether the emerging social gradient is caused by selection of women with early menarche into low-income childbearing, or low socio-economic position (SEP) during childhood affecting AAM.

Methods: We used data on AAM from CONOR, MoBa and HUNT linked to register data with information on SEP defined as ranked family income per consumption unit at age 7 within each birth cohort, for 99,921 women born 1960-2007. Data on girls yet to reach menarche were imputed using multiple imputation. Second, we used a balanced panel of 10,896 mother-daughter dyads in MoBa with information on childhood SEP and AAM in both generations, and decomposed the decline in each SEP quintile into a within-family between-generations component and a between-family within-generation component.

Results: AAM for the lowest income quintile (Q1) declined from 13.14 years for females born 1960 (CI: 13.10-13.17) to 12.63 for those born in 2007 (CI: 12.58-12.69). For the highest quintile (Q5), AAM was at the similar level as Q1 in 1960 (13.12 years, CI: 13.09-13.15) but declined less to 12.79 for those born in 2007 (CI: 12.75-12.84). In the balanced panel, AAM declined 0.44 years in Q1 (CI: 0.33-0.55) and only 0.24 years in Q5 (CI: 0.16-0.30). Nevertheless, there was no difference between the quintiles in the within-family component.

Conclusions: A social gradient in AAM has emerged in Norway. This is driven by earlier AAM among mothers whose children grow up in low-SEP than for mothers who themselves had low SEP during childhood, suggesting health selection rather than social causation.

E2

Geographical and socioeconomic inequalities in years of life lost across Norwegian municipalities: A pre-pandemic 2019 Burden of Disease Study

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Introduction: Despite longstanding policies to reduce health inequalities, Norway, with 5.5 million inhabitants spread across 356 municipalities, still faces significant socioeconomic and spatial disparities.

Aims: This study assesses the association between socioeconomic factors, centrality, and premature mortality – measured in years of life lost (YLLs) – across Norwegian municipalities.

Methods: This ecological registry-based study included all Norwegian municipalities with populations of 1,000 or more as of 1 January 2019 (n=393). Data on all-cause mortality, demographics, socioeconomic indicators, and centrality were sourced from the National Population Register and Statistics Norway. All-cause YLLs were calculated by multiplying age group-based mortality counts by aspirational life expectancy obtained from the GBD 2019 lifetables. Municipalities were categorised into quartiles based on educational attainment and income separately, and divided into three groups based on centrality classes. Negative binomial regression models, both crude and adjusted for age categories, sex, centrality, and socioeconomic factors, evaluated relative associations, while absolute inequalities were assessed by calculating marginal mean differences in YLLs across socioeconomic quartiles and centrality groups, adjusting for age and sex.

Results: High-deprivation municipalities exhibited significantly higher YLL rates compared to the least deprived ones: 9% higher for education (IRR = 1.09, 95% CI = 1.01-1.17) and 15% higher for income (IRR = 1.15, 95% CI = 1.07-1.24), translating to absolute differences of 1,391 and 2,165 YLLs per 100,000 population, respectively. Adjusting for centrality had minimal impact on these estimates. In a separate model for centrality, the least central municipalities had a 15% higher YLL rate compared to the most central ones (IRR = 1.15, 95% CI = 1.05-1.26), equating to an absolute difference of 2,096 YLLs per 100,000 population. Age emerged as a strong confounder, impacting the association between centrality and premature mortality more strongly than the relationship with socioeconomic factors.

Conclusions: Significant relative and absolute inequalities in premature mortality exist across Norwegian municipalities. Educational attainment and income are particularly powerful predictors of these disparities. Our study demonstrates the feasibility of using burden of disease methods to assess geographical and socioeconomic inequalities in premature mortality at the municipal level, providing valuable insights for public health policy and interventions.

E3

Educational attainment and risk of sepsis: A Mendelian randomization study and mediation analysis

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Introduction: Traditional observational studies have found an inverse association between socioeconomic status and risk of sepsis. However, these studies often suffer from residual confounding and the literature on potential mediators of this association is limited.

Aims: The main aim was to investigate the association between genetically predicted educational attainment and risk of sepsis using a Mendelian randomization (MR) analytical approach. Secondly, we aimed to assess potential mediators of this association.

Methods: We performed a two-sample MR study to estimate the effect of genetically predicted educational attainment on risk of sepsis. Inverse variance-weighted MR was used as the main analysis, in addition to several sensitivity analyses to assess robustness of the results, including weighted median, weighted mode, and MR Egger. To account for potential population stratification, dynastic effects, and assortative mating, a secondary analysis was performed using a within-sibship GWAS of educational attainment. A multivariable MR was conducted to evaluate potential mediation by alcohol use, smoking, body mass index, HDL cholesterol, systolic blood pressure and diabetes mellitus type 2. The mediators were assessed individually and combined.

Results: For each standard deviation increase in genetically predicted educational attainment (3.4 years), the odds ratio (OR) for risk of sepsis was 0.73 (95% confidence interval (CI) 0.64-0.83, P=1.41 x 10^{-6}). The MR sensitivity analyses supported the findings from the main analysis and did not indicate bias due to pleiotropy. Analyses with genetically predicted educational attainment within-sibship also supported a protective effect of increased educational attainment. Almost sixty percent of the association was mediated by lifestyle and health related risk factors for sepsis (proportion mediated (PM) 56%, 95% CI 0-130%). The majority of the effect was mediated by body mass index (PM 44%, 95% CI 14-87%), smoking (PM 19%, 95% CI -27-65%) and diabetes mellitus type 2 (PM 16%, 95% CI %).

Conclusions: Our study indicates that increased genetically predicted educational attainment has a protective effect on risk of sepsis. Lifestyle and health related factors mediated almost sixty percent of this effect. Public health interventions towards the identified mediators may contribute to reduce socioeconomic disparities in health and reduce the burden of sepsis.

E4

Health literacy and oral health-related habits among conscripts in the Norwegian Armed Forces – a cross-sectional survey

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Introduction: Health information is widely available to the Norwegian population. Still, a lack of health literacy is common, and remains a challenge to public health.

Aim: The study aims to assess health literacy and self-reported oral health habits among soldiers undergoing basic military training. Furthermore, we aimed to investigate health habits related to oral health, sugary diet and tobacco use that may characterize soldiers with inadequate health literacy.

Methods: An electronic questionnaire was sent out to conscripts who completed first time military service in 2022 and was answered by 2225 conscripts. Descriptive statistics were performed using cross-tabulations, correlations, and Chi-squared tests. The survey is part of an internal quality study of the Norwegian Armed Forces routines.

Results: In the study population 43% scored inadequate health literacy on the HLS-Q12, and 57% scored adequate health literacy. We found a significant difference between those having inadequate and adequate HLS-Q12 scores in categories of self-rated health habits of oral health and diet. With lower health habits scores in the inadequate health literacy group. While the reported use of tobacco was higher in the group of conscripts with adequate health literacy scores. The conscripts generally reported a lower standard of health habits during field exercises with significantly less brushing and flossing, higher use of tobacco products and higher consumption of sugary drinks and snacks compared to reported habits in camp and at home.

Conclusion: The results from our study suggest that the conscripts in the Norwegian armed forces have a lower health literacy compared to the general population, and this is reflected in reported higher frequency of unhealth habits in service settings than at home. The Armed Forces have an opportunity to take responsibility to optimize the health skills of their soldiers and to encourage them to make informed decisions about their own health. Improved adaptation to the national recommendations regarding nutrition, tobacco use, and oral health are areas with potential to greatly improve the overall health habits of conscripts.

E5

Internalizing and externalizing symptoms before and into the Covid-19 pandemic: Exploring gender and resilience differences among Norwegian adolescents. The HUNT Study

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Introduction: When investigating the possible impacts the Covid-19 pandemic may have had on adolescents, it is also important to investigate individual differences as this could identify subgroups that coped particularly well or that were particularly harmed by the pandemic.

Aims: To study whether the change in internalizing and externalizing symptoms prior to and during the Covid-19 pandemic depended on the adolescents' gender or resilience level.

Methods: We included data from adolescents (n = 1565, 61% girls) who participated in the Young-HUNT4 (2017-2019, T1) and the Young-HUNT COVID (2021, T2) surveys. The Strength and Difficulties Questionnaire (SDQ) was used to assess internalizing and externalizing symptoms, and the Resilience Scale for Adolescents (READ) was used to assess resilience (i.e., family cohesion, social competence, and personal competence). Each resilience factor was dichotomized by using the median as the cut-off point. We fitted separate linear mixed models to investigate whether change depended on the adolescents' gender and resilience level by specifying an interaction term between time (T1 vs. T2) and the main predictor of interest. Gender and age were included as covariates in all models.

Results: Although the change in internalizing symptoms (β = -.27, p = .165) did not significantly differ between girls and boys over time, there was a significant gender difference in the change in externalizing symptoms (β = -.47, p = .007). A similar pattern emerged for all resilience factors as the change in both internalizing and externalizing symptoms was found to differ between high and low levels of family cohesion (β = -.70, p <.001; β = -.35, p = .047), personal competence (β = -.77, p <.001; β = -.52, p = .003), and social competence (β = -.86, p <.001, β = -.45, p = .010). Plots depicting the change in internalizing and externalizing symptoms will be presented at the conference.

Conclusions: Our study showed, for the most part, that the change in internalizing and externalizing symptoms before and into the Covid-19 pandemic varied between girls and boys as well as between high and low levels of resilience.

F: Environmental and Occupational Health

F1

Benzene exposure and risk of colorectal cancer by anatomical subsite in the Norwegian Offshore Petroleum Workers cohort

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Introduction: The association between benzene and colorectal cancer (CRC) is unclear. Although positive associations have been observed, existing studies lack high-quality exposure assessment and adjustment for potential confounding factors.

Aims: To investigate the association between low levels of benzene exposure (average intensity<0.05 parts per million [ppm]) and risk of CRC including its anatomical subsites.

Methods: Among 25,347 male workers in the Norwegian Offshore Petroleum Workers (NOPW) cohort with offshore work history between 1965 and 1998, 455 CRC cases were diagnosed from 1999–2021. We compared these with a subcohort (n=2,031) drawn from the full cohort. Work histories were linked to a previously developed industry-specific benzene job-exposure matrix (JEM). Weighted Cox regression for case-cohort analyses was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for overall CRC and by anatomical subtypes, adjusted for age, body mass index, smoking, alcohol intake, red/processed meat intake, and physical activity.

Results: Risks of CRC increased with increasing benzene exposure. For all CRC, the HRs (95% CI) for the most exposed [quartile 4] vs. the unexposed were 1.32 (0.96 to 1.81, [0.177 to 0.879 ppm-years]; p-trend=0.085) for cumulative, 1.52 (1.11 to 2.07, [17 to 34 years]; p-trend=0.032) for duration, and 1.56 (1.15 to 2.12, [0.015 to 0.046 ppm]; p-trend=0.005) for average intensity of benzene exposure. For right-sided colon cancer, the association was most evident for exposure duration (HR=2.25, 1.33 to 3.80, quartile 4 [17 to 34 years] vs. unexposed; p-trend=0.007). Sensitivity analyses showed consistent associations.

Conclusions: This study found positive exposure-response associations between low-level benzene exposure and CRC risk in offshore petroleum workers. These findings add to emerging evidence of benzene's association with other solid tumours including lung and bladder, and have important occupational and public health implications.

F2

Exposure to dust and fibres and risk of lung cancer in 25,000 offshore oil industry workers

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Introduction: Crystalline silica dust (CSD) and asbestos are known to cause lung cancer, and refractory ceramic fibres (RCF) is a possible lung cancer carcinogen. In the offshore working environment, exposure to these dust and fibres may occur when mixing drilling mud, during cementation or during sandblasting. Yet, no assessment of lung cancer risk according to job exposure matrices (JEMs) of CSD, asbestos, and RCF have been performed in offshore petroleum workers. Furthermore, there is an ongoing debate about banning engineered stone products due to the high CSD content.

Aims: We aimed to investigate associations between exposure to CSD, asbestos, and RCF, and lung cancer risk among offshore petroleum workers.

Methods: We conducted a case-cohort study on 475 lung cancer cases and 2015 randomly drawn non-cases in the Norwegian Offshore Petroleum Workers cohort followed up for cancer in the Cancer Registry of Norway 1999–2021. CSD, asbestos, and RCF exposure were assessed with expert-made JEMs. Weighted Cox regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for lung cancer, adjusted for age, tobacco smoking, CSD, asbestos, RCF, and welding fumes. Analyses with 10–30-year exposure lag periods, and a histological subtype analysis were also conducted.

Results: An increased risk of overall lung cancer was indicated for workers with the highest cumulative CSD exposure (HR=1.46, 95% CI: 0.92–2.34; P-trend=0.230), compared to unlikely exposure. This effect increased with up to 30 years of exposure lag (HR=2.49, 95% CI: 1.05–5.94; P-trend=0.129). Compared to unlikely CSD exposure, an increased risk of squamous cell carcinoma (HR=2.82, 95% CI: 1.37–5.83; P-trend=0.035) and small cell carcinoma (HR=2.92, 95% CI: 1.23–6.91; P-trend=0.018) was also found for workers with the highest cumulative CSD exposure. No significant associations were found for asbestos or RCF.

Conclusions: High cumulative exposure to CSD may increase the risk of lung cancer, overall and by histological subtypes, in offshore petroleum workers.

F3

Exposure to perfluoroalkyl substances and immuno-dysfunctional biomarker patterns in a cross-sectional study of healthy adolescent population: The Fit Futures Study

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Introduction: Perfluoroalkyl substances (PFAS) are stable, synthetic, large group of chemicals extensively used in the manufacturing of consumer products. They have high heat tolerance, water- and oil- repellent properties, and are recalcitrant to environmental and biological degradation. PFAS exposure is global and has been associated with undesirable health outcomes such as immune dysregulation, cardiometabolic diseases, and endocrine disruption. However, the mechanism underlying the adverse health effects of PFAS exposure is not adequately understood.

Aim: This study was to investigate the relationship between PFAS exposure and proteomic biomarkers in a cross-sectional cohort of healthy adolescents aged 15-19 years in northern Norway.

Methods: The first-year students in the eight high schools in the municipalities of northern Norway were invited to the Fit Future Study in 2010-2011, and 839 of the 1117 invited were included in this study. Eight PFAS - perfluorooctanesulfonate (PFOS), perfluorooctanate (PFOA), perfluorohexane-sulfonate (PFHxS), perfluorononanoate (PFNA), perfluorodecanoate (PFDA), perfluoroheptane-sulfonate (PFHpS), perfluoroundecanoate (PFUnDA) and perfluoroheptanoate (PFHpA) - were detected in >70% of the sample population, while 75 proteomic biomarkers were detected in >70% of the sample population. This study investigated these detected PFAS and biomarkers. Factor analysis (FA) was used to reduce the dimensionality of the 75 biomarkers into five factors. We applied a multivariate regression modelling with the five factors as dependent variables and each of the PFAS as independent variables in separate models, while adjusting for age, sex and body mass index.

Findings: FA extracted five *factors* with explanatory variance of 73%. *Factor 2* loaded 10 proteomic biomarkers which are important in innate and adaptive immunity. *Factor 3* loaded five biomarkers which are important in mitogenic, cell-proliferation, and inflammation processes. PFOS, PFUnDA, and PFHpS were inversely associated with *factor 2*: PFOS -0.26 [-0.42, -0.11], PFUnDA -0.20 [-0.30, -0.10], and PFHpS -0.17 [-0.28, -0.05]; while PFOA was positively associated with *factor 3*: PFOA, 0.28 [0.12, 0.44].

Conclusion: Exposure to PFOS, PFUnDA, and PFHpS may be linked to immunosuppression, while exposure to PFOA linked to carcinogenesis.

F4

Associations between prenatal per- and polyfluoroalkyl substances (PFAS) and antibody response to childhood vaccines in Norwegian children: Effect modification by sex and age

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Introduction: Per- and polyfluoroalkyl Substances (PFAS) are shown to have immunosuppressive effects seen as reduced vaccination responses to childhood vaccines and increased risk of common infectious diseases. Some studies find sex-differences in the exposure-health associations.

Aims: To assess potential effect modification by sex and age on immunotoxic effects of PFAS on responses to childhood vaccines in Norwegian school-aged children.

Methods: We combined two sub-populations of the Norwegian Mother, Father and Child Birth Cohort Study (MoBa, 1999-2009): HELIX (n=268, aged 7-10 years) and the Norwegian Environmental Biobank II (NEB II, n=642, 7-14 years). PFAS were measured in maternal samples. Ten persistent organic pollutants (POPs) were also measured. Antibody response (IgG) to tetanus, diphtheria and rubella was measured in childhood samples using in-house multiplex immunoassays. We assessed single-pollutant associations between PFAS and IgG, adjusted for covariates, and stratifying analyses by age (<12 yrs/ ≥12 years) and sex. To assess multiple-pollutants we used Bayesian Kernel Machine Regression (BKMR). Analyses were restricted to those following the Norwegian Vaccination Programme (4 doses DTP, 2 doses MMR).

Results: Regarding diphtheria antibodies, prenatal perfluorononanoic acid (PFNA) was associated with higher diphtheria antibodies in boys under 12 years (β=0.19, 95% CI: 0.02–0.36; per interquartile range (IQR) increase in exposure). Whereas for children 12 years or older, perfluorooctanoic acid (PFOA) was associated with lower diphtheria antibodies (β=-0.39, 95% CI: -0.75– -0.02) in girls and perfluorooctane sulfonic acid (PFOS) in boys (β=-0.42, 95% CI: -0.84– -0.01). Additional adjustment for POPs did not affect results. Similar trends were found for tetanus and rubella antibodies. BKMR showed similar results for diphtheria antibodies with the joint mixture effect trending negatively in the adolescents.

Conclusions: Prenatal PFAS exposure may have differing effects on the immune response based on both the child's age and sex. We will further investigate current exposure.

Grant number: NFR 275903

F5

Low levels of long-term residential particulate matter components and mortality in the NordicWelfAir project – A cohort study from Norway

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Introduction: Several studies have shown that particulate matter (PM) exposure increases the risk of mortality. However, it is unclear which components and sources are most relevant, and low PM levels need more focus.

Aims: To investigate the association between long-term exposure to low level PM components and mortality in Norway.

Methods: We used the Cohort of Norway (CONOR), including 170,740 adult participants. The participants were followed up from enrollment 1994-2003 through 2018, by linkage to the National Cause of Death Registry. The Danish Eulerian Hemispheric Model (DEHM) combined with the Urban Background Model (UBM) were used to calculate daily concentrations of total $PM_{2.5}$ and the components Elemental Carbon (EC), Primary Organic Aerosols (POA), dust, Secondary Inorganic Aerosols (SIA) and Secondary Organic Aerosols (SOA) on 1 km × 1 km grid. Residential annual PM exposures were assigned by linking residential address history from 1991 onwards. Pearson correlations between the pollutants were assessed. Cox regression with age as underlying time scale was used to estimate hazard ratios for natural mortality, adjusting for socio-demography, lifestyle, traffic noise, green surroundings and temperature.

Results: Preliminary results found that the median (interquartile range) exposures of $PM_{2.5}$, EC, POA, dust, SIA and SOA were 5.5 (5.2) µg/m3, 0.3 (0.4) µg/m3, 0.3 (0. 2) µg/m3, 2.2 (3.4) µg/m3, 1.9 (1.4) µg/m3 and 0.2 (0.1) µg/m3, respectively. The correlation coefficient was high (> 0.7) between $PM_{2.5}$ and the components, between EC and POA, dust, and SOA, and between POA and SIA and SOA, and moderate (0.5-0.7) between the others. Associations between the PM components and natural mortality will be presented at the conference.

Conclusions: High correlations between most PM components will reduce the possibility of distinguishing associations of single components. Still, due to large variation in exposure, the study allows to estimate associations of low-level components with high precision.

G: Plenary Presentation

G1

The fifth Trøndelag health survey, HUNT5

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The Trøndelag health study (HUNT) is a population-based cohort study established in 1984 (HUNT1) in former Nord-Trøndelag County, Norway. All inhabitants of the county from 20 years of age have been invited to repeated surveys with approximately 11-year intervals. From 1995 (HUNT2), adolescents from 13 to 19 years of age have also been included in the Young-HUNT Study. From 2017 (HUNT4), former Sør-Trøndelag County was also included in the survey.

In total, about 250,000 individuals have participated in HUNT, which is administered by HUNT Research Centre. HUNT Databank contains variables from self-reported questionnaires, interviews, clinical examinations and analyses of biological samples, including genotyping. HUNT Biobank includes a state-of-the-art biobank facility with biological samples from the participants, including serum, plasma, DNA, urine, stool and saliva since 1995. Data from HUNT can be linked to national registries and health care records using the national identity number assigned to each Norwegian inhabitant.

The next wave of the study, HUNT5, is scheduled to run from September 2027 to June 2029. In HUNT5, all residents from 13 years of age in former Nord-Trøndelag County will be invited to participate in the survey with questionnaires, interviews, selected clinical examinations and sampling of biological material. Additionally, a representative sample of the adult Trondheim city population will be invited to a similar survey. Moreover, all inhabitants from 13 years of age in former Sør-Trøndelag County will be invited to complete an online questionnaire.

The HUNT study has a comprehensive approach to ensure that a wide range of data is collected to support various health research objectives, with the main goal to improve public health by an understanding of health and lifestyle, identifying disease risk factors and informing healthcare policies.

A call is now open for all to bring forward topics of interest for the coming HUNT5 survey. More information about the plans for HUNT5, the call and contact information can be found at ntnu.no/hunt5.

H: Noncommunicable Diseases – NCDNOR

H1

NCD multimorbidity in Norway 2010-2020 – a NCDNOR study

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Introduction: The prevalence of multimorbidity (≥2 co-occurring chronic conditions) is increasing. Multimorbidity increases the risk of premature death and disproportionally affects groups with lower socioeconomic position. This challenges United Nations' Sustainable Development Goal 3.4 of reducing premature mortality from noncommunicable diseases (NCDs) by one third by 2030.

Aims: We explored the association between socioeconomic position and risk of NCD multimorbidity including mental disorders in Norway.

Methods: A population-wide cohort study was conducted using registries on primary and specialist healthcare, deaths, dispensed drugs, and demographic factors. The study population was all people resident in Norway on 1 January 2008, 2009 and 2010 (all three years) and turning at least 30 years in 2010. We estimated the risk of attaining ≥2 NCDs from the start of 2008 to the end of 2020. The outcomes were somatic NCDs (cancer, diabetes, cardiovascular and chronic obstructive pulmonary diseases) without and with mental disorders (minor mental disorder, major mental disorder, and drug-related disorder). Results were stratified by sex, age (30-39, 40-49, 50-59, 60-69, 70+ years), income (quartiles) and individual and parental educational attainment (low/medium/high).

Results: Among 2,963,734 residents, the multimorbidity risk, i.e., the proportion of the study population attaining at least two NCDs by end of follow-up, was 22.4% for somatic NCDs and 31.6% when including mental disorders. The multimorbidity risk was inversely associated with education level and income within each age group of females and males. Including mental disorders had a larger impact on the multimorbidity risk in those with low educational level or income than those with high, especially in those <60 years. For example, among males who were 30-39 years in 2010 the absolute difference between those with low and high educational level in risk of multimorbidity at the end of follow-up was 3.5% without and 15.1% with mental disorders included.

Conclusions: NCD multimorbidity risk was inversely associated with socioeconomic position. Including mental disorders in the measurement exacerbated the social gradient in the risk. Preventive strategies should take this into consideration.

H2

Patterns, prevalence, and risk of noncommunicable disease comorbidities and death in cancer patients: A comprehensive nationwide Norwegian registry study – the NCDNOR Project

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Introduction: Increased life expectancy and improved survival after cancer increases the susceptibility to noncommunicable disease (NCD) comorbidities, representing substantial challenges to individuals and healthcare systems. While studies have investigated prevalence of specific comorbidities in selected cancers, no comprehensive mapping of the patterns of NCD comorbidity before and after cancer diagnosis exists.

Aims: This study examines patterns of NCD comorbidity at first diagnosis of 19 cancers and estimates the five-year post-cancer probabilities of NCD comorbidities (second cancers, cardiovascular diseases (CVD), chronic obstructive pulmonary disease (COPD), diabetes, mental disorders (MD)) and death.

Methods: We included 269,956 individuals aged ≥18 years registered with a first cancer in the Cancer Registry of Norway between 2009 and 2019. NCD comorbidities were defined using primary and secondary healthcare data from mandatory national health registries included in the NCDNOR project. Patterns of comorbidity prevalence at cancer diagnosis were analyzed using intersection diagrams, and post-diagnosis probabilities estimated through a multistate framework. We focused on major cancers (colorectal, lung, skin, female breast, and prostate). Results for other cancers are also included.

Results: Comorbidity prevalence at diagnosis ranged from 35% in skin cancer patients to 83% in lung cancer patients. CVD was the most prevalent comorbidity, usually co-occurring alongside MD, diabetes, or COPD. Comorbidity patterns differed by cancer site, age, and sex, with reduced prevalence in younger patients and in women. Five years post-diagnosis, probability of death ranged from 6% to 88%. Conditioning on being alive five years post-diagnosis, the probability of having no comorbidities ranged from 6% (lung cancer, men) to 50% (skin cancer, women). The probability of having one, two, or three or more comorbidities ranged from 26% to 47%, from 12% to 43%, and from 3% to 26%, respectively, and the most likely NCD comorbidity was CVD, followed by MD and diabetes.

Conclusion: In this study, we showed a high variation in NCD comorbidity burden by cancer site, age, and sex. Knowledge of these patterns could improve NCD prevention, effectiveness of care and treatment, ultimately leading to better patient outcomes.

H3

Socioeconomic inequalities in allostatic load in a large Norwegian cohort study, the NCDNOR project

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Introduction: Socioeconomic gradients in mortality and morbidity are well documented, but less is known about the mechanism of how socioeconomic position leads to inequalities in health and mortality. Allostatic Load (AL) is designed to capture the physiological burden of chronic stress. The aim of this article was to study trends in AL over three decades, comparing sex and socioeconomic groups.

Methods: Harmonized data from the Trøndelag Health Study 2-4 (1995-2019), Tromsø 4-7 (1994-2016), the Age 40 Program (1985-99) and CONOR (1994-2003) was used. In total 264,824 participants aged 30-79 years contributed with 346,312 participations (range 1-4). A combined score of Allostatic Load (AL) was calculated based on eight variables: systolic blood pressure, diastolic blood pressure, heart rate, triglycerides, total cholesterol, high-density lipoprotein cholesterol, body mass index, and waist-hip ratio. High-sensitive c-reactive protein (CRP) and glycated haemoglobin (HbA1c) were only available for a subset of the participants and were included in sensitivity analyses. Life course trajectories were analyzed by using a linear mixed model. Potential survivor bias was evaluated in a shared-parameter model.

Results: Men had higher AL score than women, and primary educated had higher AL compared to secondary and tertiary educated groups. For both women and men AL increased with age but levelled off at higher ages among women and decreased at higher ages among men.

Conclusion: We found significant sex and socioeconomic differences AL throughout the life course. This highlights the potential of effective treatment and preventive measures reducing risk factors contributing to disease through the pathway of chronic stress.

H4

Noncommunicable disease risk factor groups, socioeconomic position and longevity in Norway: a prospective cohort study of 576 299 men and women – the NCDNOR project

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Introduction: Several modifiable risk factors are associated with noncommunicable diseases (NCDs). However, the majority of studies on NCD risk factors employ a 'one risk factor and one disease' approach, often adjusting for other risk factors. This may distance analyses from real-world applications, where such 'all-else-equal' scenarios are rare and risk factors impact several NCDs simultaneously. The combined exposure to risk factors form underlying groups of individuals in the population, but associations between risk factor clustering and NCD mortality remains largely unknown.

Aims: To identify NCD risk factors clustering groups and compare NCD survival time differences between them.

Methods: We used data on NCD risk factors (smoking, physical activity, body mass index, blood pressure, total cholesterol, and triglyceride) collected in Norwegian health examination surveys from 576 299 individuals (52% women) aged 20-65 years that were followed for a mean (SD) of 25·8 (8·3) years. We used Latent Profile Analysis (LPA) to identify risk factor clusters, and flexible parametric survival models to estimate survival time differences.

Results: We identified four distinct clusters containing 44% (Group 1, 'Healthy'), 45% (Group 2, 'Sub-optimal'), 4% (Group 3, 'Dyslipidemics), and 7% (Group 4, 'Hypertensives') of the full sample, respectively, with significant between-cluster differences in exposure to the risk factors considered. Comparing with the 'Healthy' Group 1, we observed significantly shorter survival times for all the other groups: in men and women born in 1930, 1945, and 1960. Overall, differences were largest in both sexes when predicted for birth year 1930, with the largest differences observed between Group 3 and Group 1 (~9 years). When predicted for those born in 1960, survival time differences were smaller, and largest between Group 1 and Group 4. In both sexes, the differences between Group 3 and Group 1 were reduced by almost seven years for the 1960 prediction compared to the 1930 predication. Both education and income significantly modified associations.

Conclusions: We provide important new insights into how NCD risk factors cluster in a population, and how the risk of NCD mortality differs significantly between risk factor clustering groups.

I: Ageing

I1

Adolescent to midlife exercise trajectories and age at menopause: a population study of 246 147 women in Norway

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Introduction: Menopause represents the end of a woman's reproductive period, and age at menopause is a marker of health and fecundity. Exercise is associated with health and longevity, but its role in the timing of menopause remains uncertain. To our knowledge, no previous research has studied whether exercise trajectories across the life course is associated with age at menopause.

Aim: To study the associations of adolescent to midlife exercise trajectories with age at natural menopause.

Methods: We performed a retrospective population-based cohort study of 246 147 women aged 50-69 years attending the Norwegian breast cancer screening programme (BreastScreen Norway). During the years 2006 to 2015, all participants were invited to fill in two self-administered questionnaires. Adolescent to midlife exercise trajectories were identified by using latent class mixed models. The associations of exercise trajectories menopause between the ages 15-49 and age at menopause were estimated as hazard ratios (HR) using Cox proportional hazard models. We adjusted for year of birth, country of birth, educational level, number of childbirths, smoking habits, and body mass index.

Results: We identified four exercise trajectories: high (reference), increasing, decreasing, and low exercise levels from adolescence to midlife. Median age at menopause was 52 years (IQR 49-54 years). The adjusted HR of reaching menopause was 1.06 (95% CI: 1.05-1.07) for women with low exercise levels, compared to women with high exercise levels. The corresponding adjusted HRs were 1.02 (95% CI: 1.00-1.03) for women with increasing exercise levels, and 1.02 (95% CI: 1.01-1.04) for women with decreasing exercise levels.

Conclusions: Women with low exercise levels reached menopause earlier than those with high exercise levels. Women with an increasing or decreasing exercise level reached menopause slightly earlier than those with high exercise levels. However, the associations were weak, suggesting little influence of exercise on age at menopause.

I2

The burden of mental and somatic health among people experiencing incarceration later in life. A 13-year cohort study

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Background: The prison populations worldwide are aging, and the number of older people incarcerated is increasing, challenging the prison systems that are primarily designed for a younger and healthier population. This is the first study of the burden of mental and somatic health among people incarcerated later in life in Norway using national register data over 13 years.

Aims: The specific aims are to describe people incarcerated later in life with regard to a) type of crime, characteristics of the imprisonments, and sociodemographic information (sex, age, educational level); b) prevalence of mental and somatic disorders, and comorbidity, compared to the general population in Norway using Global Burden of Disease-data, and; c) all cause and cause-specific mortality.

Method: The study population include all individuals incarcerated at age 50 or older in Norwegian prisons during the years 2010-2022. We utilized data from the Norwegian Prison Release Study (nPRIS) cohort linked with The Norwegian patient register (NPR), sociodemographic variables from Statistics Norway (SSB), and the Norwegian cause of death registry (NCoDR). Study prevalences were calculated as ICD 10 diagnoses registered in NPR up until release-date of the persons last incarceration.

Preliminary results: A total of 10 787 individuals were eligible for the study, 1120 (10%) women and 9667 (90%) men. Most (81%) were registered with one incarceration in the study period, and median age at imprisonment was 55 years. At date of their last release 60% of the women and 48% of the men had at least one mental health diagnosis, with substance use disorders being the most prevalent (42% of women and 34% of men). 78% of women and 71% of men had a least one somatic diagnosis.

Preliminary conclusions: This study presents the first comprehensive description of the mental and somatic health burdens faced by older individuals incarcerated in Norway. Our findings illustrate high prevalence of both mental and physical health problems among both men and women imprisoned. Given the growing proportion of older people in prison, these results underscore the urgent need for correctional services to implement tailored interventions that address the unique healthcare requirements of this aging population.

I3

Risk factors for dementia in the HUNT4 cohort study among the 70 year and older population

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Background: The Lancet Commission paper from 2024 reported 14 risk factors for Alzheimer's disease and related dementias (ADRD). LDL-cholesterol and vision impairment were added to the risk factors of the 2020-report. We wanted to add to this literature by investigating the Lancet Commission's risk factors in the large cohort study in Trøndelag (HUNT4 70+), in Norway.

Methods: We included 9 745 participants aged 70+ (HUNT4 70+). The outcome, an ADRD diagnosis, was assessed by clinical experts (applying a consensus-based process using all relevant information). Information on ADRD risk factors were collected from three previous HUNT waves (HUNT1, HUNT2, HUNT3) and divided into mid- (45-65 years old) and late-life (>65 years old). The predictors from the Lancet commission were low education (≤ 9 years, obesity (≥30 kg/m^2), ever smoking, high alcohol intake (>168g/week) moderate and high hearing impairment, moderate and high vision impairment, social isolation (no friends), hypertension (diastolic ≥ 90 mm Hg/systolic ≥ 140) , diabetes (≥ 11.1 mmol/L), high LDL-cholesterol (>130mg/DL), physical inactivity (MVPA-score <2.5), traumatic brain injury and depression (HADs-score ≥8). Logistic regression models were run in the cohort, for each age group and by sex adjusted for year of birth, sex and education. We weighted the analyses to the population in Norway and for non-response using registry data for all invited participants. We present the results in Odds ratios and 95% confidence intervals and population attributable fraction (PAF) for each risk factor and for all combined, by age group and by sex.

Results: For midlife risk factors, the percentage of ADRD cases that could have been avoided were in descending order (highest for low education) (PAF=18.7%), high alcohol intake (10.6%), physical inactivity (9.5%), hearing (4.7%) or vision impairment (5.8%) and depression (4.5%). For late life; low education (16.2%), physical inactivity (10.7%), hypertension (9.8%), high alcohol intake (5.8%), vision (4.1%) or hearing impairment, (3.9%), ever smoking (3.9%) and depression (3.6%). For all the factors combined the percentage of late life ADRD cases that could be avoided by reducing midlife and late life exposures were summed up to 56% and 55%, respectively.

Conclusion: Based on the most recent update on risk factors for ADRD and under the assumption that these risk factors are causal, we found that around 55% of ADRD cases in HUNT4 70+ could have been prevented if the risk factors were eliminated.

I4

Sex differences in loss in expectation of life after a diagnosis of dementia, mild cognitive impairment, or subjective cognitive impairment – a study from the Norwegian register of persons assessed for cognitive symptoms (NorCog)

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Introduction: A consistent finding is the male survival disadvantage following a dementia diagnosis, but the male survival disadvantage in the general population is often not considered. More knowledge about sex differences in survival is needed to be able to evaluate the potential differences in impact of risk factors symptomatology and response to treatment in Alzheimer's disease (AD), other subtypes of dementia, and in the preclinical stages; mild cognitive impairment (MCI) and subjective cognitive impairment (SCI).

Aims: In this registry-based study, we aimed to study sex differences in life expectancy and loss in expectation of life after a diagnosis of dementia, MCI, or SCI.

Methods: The study population comprised incident cases (N=16,358; 7,805 men and 8,556 women), aged 50-90 years at time of diagnosis in the Norwegian register of persons assessed for cognitive symptoms (NorCog) and mortality (5650 deaths) during 2009-2022. Sex differences in survival were predicted using flexible parametric survival models, and age-adjusted Kaplan-Meyer survival curves were fitted to the data. Mortality rates from Statistics Norway by age, sex for year 2017 were used as reference population.

Results: Women had the largest loss in life expectancy compared to life expectancy in the general population; A typical women turning 60 in 2017 could expect to live another 25.7 years, while a woman diagnosed with dementia at age 60 could expect to live only another 8.7 years. The corresponding numbers for men were 22.7 years 9.0 years. Thus, dementia cuts 17.0 years of life expectancy in women and 13.7 years in men. Thus, an excess of 3.3 years in females compared to men. This female survival disadvantage narrowed with age but was evident across the whole age range. Similar female survival disadvantages were observed for dementia sub types and for MCI, while for SCI the sex differences in life years lost were negligible.

Conclusions: The female survival disadvantage related to dementia and MCI has likely multifactorial causes, but we lack solid knowledge on this, and further research should investigate and try to pinpoint these causes.

P: Poster presentations

P1

Prevalence of mental and neurodevelopmental disorders in families of women taking psychotropics during pregnancy – a study of familial confounding by indication

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Introduction: The aetiology of neurodevelopmental disorders (NDDs) involves a complex interplay of environmental and genetic factors, including shared familial dispositions. Prenatal exposure to certain medications, including psychotropics, has been associated with increased risk of NDDs in offspring. Given the heritability of NDDs, it is crucial to understand the influence of familial confounding when investigating the safety of medications during pregnancy.

Aim: The study aims to assess the prevalence of NDDs in mothers, fathers, and previous offspring, among women with mental disorders stratified by psychotropic medication use in pregnancy.

Methods: We included data from the most recent pregnancy of Norwegian women with mental disorders who gave birth between 2010–2018, facilitated by linking Norwegian registry databases. Maternal psychotropic use included antidepressants, antipsychotics, anxiolytics, or hypnotics and sedatives during pregnancy, as recorded in the Norwegian Prescription Database. The presence of NDDs was defined as having at least one diagnostic code for intellectual disabilities, language or scholastic disorders, pervasive developmental disorders, or attention-deficit hyperactivity disorders (ADHD) among women, their partners, and previous offspring. Multivariable logistic regression estimated crude and adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for the associations between prenatal psychotropic use and a family history of NDDs.

Results: The study included 27,638 women. The prevalence of any NDD was 4.0% in mothers, 3.0% in partners, and 2.9% in previous offspring. ADHD was most prevalent (3.4% in mothers, 2.5% in partners, and 1.4% in offspring). Maternal anxiolytic use during pregnancy was associated with a history of any NDD in both mothers (aOR: 2.33 [95% CI: 1.83 – 2.96]) and partners (aOR: 2.16 [95% CI: 1.62 – 2.90]) but not in siblings (aOR: 1.36 [95% CI: 0.66 – 2.81]).

Conclusion: The association between maternal anxiolytic use and history of NDDs in parents underscores the importance of considering both maternal and paternal NDD histories when exploring the effects of psychotropic use during pregnancy on neurodevelopmental outcomes in children. While maternal use of other psychotropics was associated with NDD history in mothers, these did not correlate with paternal NDD history or the history of NDDs in offspring.

P2

Validity of methods to infer data on maternal characteristics using data from a medical birth registry: Longitudinal methods versus multiple imputation

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Introduction: In birth registries, incomplete recording of information often leads to missing values. Multiple Imputation by Chained Equations (MICE) is a widely used method for analyzing datasets with missing data. It is not known whether using registry records from multiple pregnancies contributed by the same woman could potentially give more accurate values when resolving missing data.

Aims: To investigate the performance of five methods for inferring maternal characteristics in a medical birth registry, comparing longitudinal methods and MICE, using data from previous and future pregnancies.

Methods: We used data from the Medical Birth Registry of Norway (MBRN), selecting records among mothers with more than one pregnancy between 2004 and 2018. We created missing values for 19 variables in the index pregnancy. Longitudinal methods used reference pregnancies in three time-directions: past, future, and closest pregnancy record. MICEs were conducted with only index pregnancy records (cross-sectional MICE) and with both index and closest reference pregnancy records (longitudinal MICE). The actual value of the variable in the index pregnancy was the reference standard. For continuous variables, we calculated the proportion of inferred values within predefined increments. For binary variables, we calculated agreement rate, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results: We included 578,670 pregnancies among 256,658 women. For maternal age at delivery, over 99% values were within 1 year in all longitudinal methods, compared to 22% in cross-sectional MICE, and 49% in longitudinal MICE. For maternal weight before pregnancy, 78−80% of the inferred values were within 10% of the correct value in longitudinal methods, compared to 40% in cross-sectional MICE and 65% in longitudinal MICE. For the longitudinal methods, agreement ranged between 62% (multivitamin use) and >99% (hypertension, rheumatoid arthritis), with the closest pregnancy reference having the most inferable records Cross-sectional MICE had substantially lower agreement while longitudinal MICE was similar to longitudinal methods.

Conclusions: The longitudinal method, though less sophisticated, outperformed MICE in inferring missing data on maternal characteristics in a medical birth registry.

P3

BNT162b2 mRNA COVID-19 vaccine effectiveness in pregnancy: Emulating trial NCT 04754594 using observational data from Norwegian health registries

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Introduction: Prior studies on mRNA COVID-19 vaccine effectiveness in pregnancy deviate from the NCT 04754594 trial, limiting our appraisal of causal inference from observational research in a pregnancy context.

Aims: To evaluate the real-world effectiveness of the BNT162b2 mRNA vaccine in pregnant individuals using a target trial emulation design, thereby examining the reliability of causal inference on vaccine effectiveness in pregnant individuals.

Methods: We emulated trial NCT 04754594 using Norwegian health registries data, applying comparable inclusion and exclusion criteria. In an intention-to-treat (ITT) approach, we identified pregnancies recorded in 2021-2022 with the first dose of the BNT162b2 vaccine administered between weeks 24-34 of gestation, assuming the second dose was administered within 21 days. We additionally conducted a per-protocol analysis, requiring uptake of the second vaccine dose. Outcomes included COVID-19 infection and severe COVID-19 (i.e., leading to hospitalization) within 1 and 6 months post-delivery. We analysed outcomes in vaccinated pregnant individuals and propensity-score matched unvaccinated individuals based on the calendar time of the last menstrual period and delivery. Pooled incidence rate ratios (IRR) and corresponding 95% CIs were estimated using Poisson regression with robust variance.

Results: For a total of 6,770 eligible pregnancies (3,385 vaccinated with first dose, matched to 3,385 unvaccinated), the median baseline age was 31 years (IQR 7), and the median preconception BMI was 23.8 (IQR 5.7). ITT analysis showed a 9% and 14% reduced risk of COVID-19 infection at 1 and 6 months post-delivery, respectively (IRR: 0.91, 95% CI 0.89-0.94; IRR: 0.86, 95% CI 0.85-0.97). The IRR for severe COVID-19 was 0.25 (95% CI 0.17-0.36) at both time points. Per-protocol analysis indicated greater risk reductions for infection (IRR: 0.76, 95% CI: 0.74-0.78; IRR: 0.78, 95% CI: 0.77-0.80) and severe COVID-19 (IRR: 0.19, 95% CI 0.13-0.28) at both time points.

Conclusions: Using Norwegian health registry data, we demonstrated real-world effectiveness of the BNT162b2 vaccine in pregnancy. Our results align with the RCT, showing a 40% reduction in infection risk at 1 month postpartum. This study illustrates the feasibility of using real-world data to assess vaccine effectiveness during pregnancy.

P4

Dietary vitamin D and risk of multiple sclerosis in the Norwegian Mother, Father and Child cohort

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Introduction: Higher vitamin D has been consistently associated with a lower MS risk, but some controversy remains around whether it is vitamin d itself or sunlight that modifies the disease risk, and whether vitamin D is merely a marker of sunlight exposure. Investigating dietary vitamin D intake, especially in regions with low sun-induced vitamin D production most of the year, can shed light on this question.

Aims: To investigate the association between dietary vitamin D and risk of MS.

Methods: We conducted a prospective study among women in the Norwegian Mother, Father and Child Cohort Study (MoBa) followed form enrollment in 1999-2008 to 2002. We identified incident cases of MS through data-linkage with the Norwegian MS registry. Dietary vitamin D (food and supplements) was calculated from a food frequency questionnaire administered in pregnancy week 22. Information about pre-pregnancy body mass index (BMI), smoking, age at pregnancy and other possible confounders was obtained from MoBa Questionnaire 1 in week 15. We used Cox regression to estimate hazard ratios (HR) for MS risk with 95% confidence intervals (CI).

Results: Among 84,307 women in the cohort, 387 developed MS during follow-up. Higher intake of total dietary vitamin D was associated with 41% lower risk of MS (HR for top vs bottom quintile: 0.59; 95% CI: 0.38-0.90, p for trend<0.01). Results remained similar after adjusting for total energy intake, pre-pregnancy BMI, Age at pregnancy and smoking. We found similar associations for vitamin D intake from food only (HR for top vs bottom quintile: 0.66; 95% CI: 0.44-0.99, p for trend=0.01), and supplements only (HR for >600IU/day vs <200IU/day: 0.67; 95% CI: 0.42-1.08, p for trend=0.02).

Conclusion: In this prospective study conducted in a Nordic country with insufficient sun-induced vitamin production during most of the year, the association of higher dietary vitamin D with lower MS risk supports the hypothesis that vitamin D itself modifies MS risk.

P5

Gestational weight gain and postpartum weight retention: What is the role of perinatal antidepressant use in the Norwegian Mother, Father and Child Cohort Study?

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Introduction: Excessive gestational weight gain (GWG) and postpartum weight retention (PPWR) are associated with adverse health outcomes in mothers. We aimed to determine whether various trajectories of perinatal antidepressant use were associated with GWG or PPWR.

Methods: For this study, we used data from the Norwegian Mother, Father and Child Cohort Study and the Medical Birth Registry of Norway. We included singleton, live birth pregnancies with pre-pregnancy maternal depression and/or anxiety. Through linkage with the Norwegian Prescribed Drug Registry, we obtained information on antidepressant exposure in the perinatal period per one-week intervals. Trajectories of antidepressant use for prenatal and perinatal timeframes were constructed using longitudinal k-means clustering. GWG and PPWR at 6 and 18 months postpartum were calculated using self-reported data. We estimated weighted relative risks (RR) and 95% confidence intervals (CI) using modified Poisson regression with robust variance estimators and overlap weights.

Findings: Among 3,365 pregnancies included, we observed five prenatal antidepressant use trajectories: non-users (n = 2,789, 82.9%), pre-pregnancy discontinuers (n = 123, 3.7%), early pregnancy discontinuers (n = 154, 4.6%), late pregnancy discontinuers (n = 167, 4.9%), and continuers (n = 132, 3.9%). For the perinatal period we identified five trajectories: non-users (n = 2,809, 83.5%), early pregnancy discontinuers (n = 201, 6.0%), late pregnancy discontinuers (n = 196, 5.8%), continuers (n = 101, 3.0%), and post-pregnancy initiators (n = 58, 1.7%). In the present study, pre-pregnancy discontinuers had increased risk of inadequate GWG compared to non-users (weighted RR 1.32, 95% CI 1.02 – 1.71). Early pregnancy discontinuers (weighted RR 0.89, 95% CI 0.76 – 1.01) and late pregnancy discontinuers (weighted RR 0.88, 95% CI 0.76 – 1.0) had a borderline decreased risk of excessive PPWR at 6 months postpartum compared to non-users. We observed no other associations between antidepressant use trajectories and GWG or PPWR.

Interpretation: Results from this study enhance knowledge on safety of perinatal antidepressant use, specifically regarding weight changes. While this study did not indicate increased risk of excessive GWG or PPWR, pregnant women should make careful considerations about risks and benefits when deciding on perinatal antidepressant continuation.

P6

ADHD medication use in pregnancy and risk of miscarriage

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Introduction: An increasing number of women of childbearing age are being treated for attention-deficit/hyperactivity disorder (ADHD). There is limited evidence on the risk of pregnancy loss associated with ADHD medication use in early pregnancy.

Aims: To assess whether the use of ADHD medication during pregnancy is associated with an increased risk of miscarriage.

Methods: We conducted a case-control study among pregnant women diagnosed with ADHD identified from Norwegian health and population registers. Cases were miscarriages (2009-2019), identified from diagnoses in primary and specialist care (gestational age assumed to be 10 weeks) or defined as fetal death before 20 gestational weeks, registered in the Medical Birth Registry. For each case, up to four live-birth controls were matched by year of conception and age at conception. Exposure to ADHD medication was defined as having filled a prescription during pregnancy for cases, with the same exposure period for matched controls (10 weeks from last menstrual period). We used conditional logistic regression to estimate odds ratios (ORs) with 95% confidence intervals (CIs) for the association between ADHD medication use and risk of miscarriage, adjusting for potential confounders including other psychiatric disorders and psychotropic medication use.

Results: There were 2,986 cases and 10,291 controls included in the analysis. Overall, 1,434 (11%) were exposed to any ADHD medication. We observed an 83% increase in crude odds of miscarriage among those exposed to ADHD medication during pregnancy compared to unexposed (OR 1.83, 95% CI 1.62-2.06). After adjusting for potential confounders, the increased risk remained (aOR 1.73, 95% CI 1.52-1.96). For specific ADHD medications, the odds of miscarriage were statistically significantly elevated for methylphenidate (n=1,162, aOR 1.70, 95% CI 1.48-1.96), lisdexamfetamine (n=74, aOR 1.85, 95% CI 1.11-3.09), and atomoxetine (n=75, aOR 2.36, 95% CI 1.44-3.86), but not amphetamine (n=15, aOR 1.05, 0.31-3.53) or dexamphetamine (n=131, aOR 1.33, 0.89-2.00).

Conclusions: This study suggests that the use of ADHD medication during pregnancy is associated with an increased risk of miscarriage. The overall increased risk mainly reflects methylphenidate use, the most commonly used ADHD medication in Norway, but increased risks were also seen for other medications.

P7

Association of antidepressant exposure during pregnancy with birth weight to placenta weight ratio

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Background: Depression and anxiety during pregnancy are common and often managed with antidepressant medications. However, the impact of continued antidepressant exposure throughout pregnancy on placental outcomes remains unclear.

Objectives: To assess the association of antidepressant continuation during pregnancy on the birthweight-to-placenta weight ratio.

Methods: We used data from the nationwide, prospective Norwegian Mother, Father, and Child Cohort Study (MoBa), linked to MoBa Genetics and Medical Birth Registry of Norway (MBRN). We included 6537 pregnancy-child dyads of mothers with pre-pregnancy depression/anxiety, who were either medicated with antidepressants before and during pregnancy (n=709 *continuers*) or only before pregnancy (n=442 *discontinuers*) or did not use antidepressants either before nor during pregnancy (n=5386, *unexposed*). We calculated the birthweight to placental weight ratio by dividing the birth weight by the placenta-weight, then computed gestational age-adjusted percentiles using GAMLSS, stratified by infant sex. A low birthweight to placental weight ratio was defined as below the 10th percentile. Stabilized Inverse Probability of Treatment Weighting (SIPTW) was used to adjust for potential confounding factors. We used unadjusted and adjusted modified Poisson regression models with robust standard errors.

Results: Among the 6,537 pregnancy-child dyads involving women with pre-pregnancy depression or anxiety, 12.8% (n = 742) of infants were born with a low birth weight relative to placental weight. In the adjusted analysis, infants born to women with *continued antidepressant* during pregnancy had a higher risk (Relative Risk [RR]: 1.86; 95% Confidence Interval [CI]: 1.04 to 3.32) of low birthweight to placental weight ratio compared to *unexposed*. Conversely, women who *continued antidepressant* use during pregnancy had a lower risk (RR: 0.07; 95% CI: 0.01 to 0.65) of giving birth to an infant with a low birth weight to placental weight ratio compared to discontinuers.

Conclusion: These results suggest that a moderate association between *antidepressant continuation* during pregnancy and greater risk of giving birth to an infant with a low birthweight to placental weight ratio, compared to *unexposed*. However, this risk was substantially lower when compared to *antidepressant discontinuers* before pregnancy, suggesting a possible key role played by unmedicated mental illness in pregnancy on placental weight outcomes. These findings underscore the importance of carefully weighing the risks and benefits of continued antidepressant use during pregnancy.

P8

Prenatal exposure to the Chernobyl fallout in Norway and cognitive abilities among conscripts

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Introduction: Exposure to low-dose ionizing radiation during pregnancy may affect the developing brain, with long-term consequences. We previously reported an association of Chernobyl fallout in Norway with reduced mathematics school grades, an association also described in a Swedish study.

Aims: We use cognitive tests among conscripts in Norway to further investigate the association with mathematical skills.

Methods: The medical birth registry was linked with data from The Norwegian Armed Forces Health Registry on conscript cognitive scores. Radiation doses were estimated for each municipality and calendar month from May 1986 to April 1989. Dose in the mother's residential municipality in the 5th calendar month of the pregnancy was used as exposure. Total cognitive score among boys was analyzed using a natural-experiment design with pregnancy cohorts from years prior to the fallout as reference. For each calendar month and municipality in the exposure period, pregnancies in the same municipality in the calendar month three years earlier were used as reference. Our analyses estimated a change in scores from before exposure to exposure that was specific to areas with higher doses. Sub-scores for numerical, general, and verbal reasoning were available only for cohorts after 1986. Younger brothers born after the exposure period were used as comparison in analyses of sub-scores.

Results: We found no evidence of reduced total cognitive score in areas with relatively higher radiation exposure. Similarly, there was no evidence that numerical reasoning was reduced with radiation exposure in our analyses among brothers. The test for trend in brother difference by dose yielded a p-value of 0.17. Finally, we found no associations for the two other sub-scores.

Conclusions: Our analyses did not identify any associations between the Chernobyl radioactive fallout in Norway and cognitive abilities among conscripts exposed in utero. We found no support for the earlier association with mathematics abilities. Not all Norwegians participate in the conscript testing and the possibility of selection bias is a limitation, although this selection was not associated with level of exposure.

P9

Childbirth with maternal myasthenia gravis, a nationwide registry-based cohort study

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Introduction: Myasthenia Gravis (MG) is an autoimmune neuromuscular disease that can impact childbirth. MG is rare, with a prevalence of 120 per million women under the age of 50, but incidence peaks during the childbearing years. MG weakens striated muscles, which can complicate the late second phase of vaginal labor, leading to an increased risk for operative vaginal delivery and emergency Caesarean section (C-section). High-quality real-world data on maternal MG and childbirth for guiding clinical decision-making is sparse and largely outdated.

Aims: To describe childbirth and assess risks for adverse outcomes in mothers with MG compared to the general population, in a contemporary unselected birth cohort.

Methods: All singleton births in the Medical Birth Registry of Norway during 1999–2022 were included. Maternal MG was identified from the birth notifications by the specific MG diagnosis (ICD-10: G70.0) or pyridostigmine-use during pregnancy, in the current or a prior pregnancy. Births prior to a diagnosis of maternal MG were excluded. MG-exposed births were compared to all unexposed births, comprising all other singleton births in the nationwide cohort. Group differences as odds ratios (OR) with 95% confidence intervals (CI) were calculated using logistic regression with robust standard errors, to account for sibling dependency. The following confounders were adjusted for: year of birth, maternal age, parity, co-habitation status, and autoimmune comorbidity-score.

Results: The cohort comprised 134 MG-births and 1 349 430 unexposed births. Maternal MG was associated with a higher rate of elective C-section (aOR 1.8, 95% CI: 1.1–3.1). On the other hand, emergency C-section (0.9, 0.5–1.7) and operative vaginal delivery (1.3, 0.7-2.2) were not more common with MG. Induction of labor (1.6, 1.1–2.4), epidural anesthesia (1.8, 1.3–2.7), episiotomy (1.8, 1.1–3.0), and preterm pre-labor rupture of membranes (2.7, 1.1–6.6) were more common in MG.

Conclusions: Most delivery interventions associated with maternal MG were planned, not emergencies. Major complications were uncommon, and most deliveries were spontaneous vaginal deliveries. Despite the higher rate of elective C-section for MG-births, this rate was still low. Our findings support that for most women with MG, vaginal delivery can be the aim.

P10

Women's pregnancy history and partners' cardiovascular mortality

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Introduction: A woman's full pregnancy history is associated with her risk of dying from atherosclerotic cardiovascular disease (CVD).

Aims: To assess whether a woman's total pregnancy history is associated with her spouse's risk of dying from CVD.

Methods: In this population-based, prospective study we used data from Norwegian registries in the period 1967-2020. We identified 566 187 men registered as partner to women with a pregnancy in 1967 or later, and surviving to age 40. Main outcome was CVD mortality up through age 69 across their partners reproductive history by categories of parity and number of complicated pregnancies. Men whose partners had three pregnancies and no complications had lowest CVD risk and served as the reference group. Estimates were adjusted for women's birth year.

Results: For fathers contributing with up to two pregnancies, the risk of premature CVD increased with increasing number of complicated pregnancies. For men contributing to 3-4 pregnancies, the shape of the association was less clear, peaking at two complications [HR=1.8; 95% confidence interval 1.2-2.8).

Conclusions: While the number of pregnancy complications seem to increase CVD mortality for women in a linear pattern, this seem not to be the case for their partners. Pregnancy history seems to be less useful in prediction of men's risk of dying from CVD. CVD risk factors are known to increase risk of pregnancy complications. However, the correlations between partners of diet, SES, and other CVD risk factors are apparently not strong enough to produce a strong pregnancy-related CVD risk in male partners.

P11

Risk of hypertension and cardiovascular disease according to number of cycles with assisted reproductive technologies

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Introduction: The use of assisted reproductive technologies (ART) is increasing. The potential impact on women's risk of hypertension and cardiovascular disease (CVD) remains unclear.

Aims: To estimate the risk of hypertension and CVD according to the number of ART cycles a woman has undergone.

Methods: We studied number of ART cycles in relation to risk of chronic hypertension (23,084 women) and CVD (23,351 women) among all women in Norway registered with their first ART cycle between 2009 and 2020 without a registered pregnancy or pre-existing history of the conditions of interest prior to their first ART cycle. Fresh and frozen ART cycles were identified by sequences of dispensed prescriptions relating for fertility treatments. We evaluated the risk of the two outcomes using Cox-proportional hazards regression, with number of ART cycles as a time-varying exposure, adjusting for age at start of follow-up, education level, diabetes, PCOS, endometriosis and parity during follow-up time.

Results: There was modest increased risk of hypertension (HR 1.04; 95% CI: 1.00-1.09) and CVD (HR 1.11; 95% CI: 1.04 -1.19) per additional ART cycle. The increased risk of CVD appeared to reflect an increased risk of deep vein thrombosis (HR 1.16; 95% CI: 1.04-1.29) and pulmonary embolism (HR 1.18; 95% CI: 1.00 -1.39). For frozen programmed cycles, we observed no notable increased risk of hypertension (HR 1.04; 95% CI: 0.91-1.19) but an increased risk of CVD (HR 1.27; 95% CI: 1.05-1.54).

Conclusions: We observed an increased risk of hypertension and CVD with increased number of ART cycles women had been exposed to. Our findings should be replicated in separate samples, preferably with longer follow-up time.

P12

Early-life environmental factors and genetic risk in juvenile idiopathic arthritis: Insights from Norwegian and Danish pregnancy cohorts

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Introduction: As one of the most common autoimmune diseases in childhood, Juvenile idiopathic arthritis (JIA) presents a significant health challenge, marked by chronicity, high costs, and disability, yet lacking a cure. The aetiology of JIA remains elusive, but it is believed to arise from a complex interplay involving multiple genes and environmental factors.

Aims: We aim to identify risk factors that may explain the high incidence of JIA in Northern European countries by exploring the interplay between genetics and environmental exposures early in life.

Methods: Leveraging data from two prominent prospective pregnancy cohorts – the Norwegian Mother, Father and Child Cohort study (MoBa) and the Danish National Birth Cohort (DNBC) – and population registry databases, we are investigating potential associations between various environmental factors and JIA risk and severity. Specifically, we will scrutinize individual exposures such as maternal dietary patterns during pregnancy, breastfeeding patterns, and occurrences of prenatal and early-life infections. Furthermore, by employing advanced machine learning methods, we will explore combinations of different risk factors and potential interactions between them. Finally, we will apply both case-control and offspring-parent triad designs to explore genetic risk, calculate polygenic risk scores, and investigate gene-environment interactions.

Conclusions: In conclusion, our study aims to unravel the factors contributing to JIA risk by focusing on the intricate interplay between genetics and environmental exposures early in life. Through this comprehensive approach, we will shed light on the elusive aetiology of JIA and pave the way for targeted interventions and improved outcomes for affected individuals.

P13

Is the relative protective effect of maternal vs paternal type 1 diabetes on risk of type 1 diabetes explained by differences in predisposing genes potentially induced by selective foetal loss?

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Introduction: The phenomenon that children of mothers with type 1 diabetes have lower risk of type 1 diabetes compared to children of fathers with type 1 diabetes is well known but the explanation remains elusive. Risk genotype-dependent fetal loss inducing differences in frequencies of predisposing genes in children is one proposed mechanism, which has not been investigated for non-HLA genes.

Aims: To investigated whether the frequency of established type 1 diabetes susceptibility genes differed in offspring of mothers versus fathers with type 1 diabetes.

Methods: The Norwegian Mother, Father and Child Cohort study has genotyped over 76 000 children born 2000-2009 and followed to 2021. Type 1 diabetes diagnosis was ascertained by linkage to nation-wide registries (n=461 children, 939 fathers, and 709 mothers).

Results: The odds ratio of type 1 diabetes conferred by maternal type 1 diabetes was confirmed to be lower than that for paternal diabetes (OR=6.5,95%CI:4.10-10.25 vs. OR=8.3,95%CI:6.98-11.41). The risk allele frequencies of the HLA DQ8 tag SNP rs7454108 and of the DQ2 tag SNP rs2187668 was similar in offspring of mothers with type 1 diabetes versus fathers with type 1 diabetes (26.2% vs 26.0%, and 20.0% vs 19.6%, respectively). Furthermore, the frequencies of the risk alleles of the INS (rs689: 77.9% vs 76.5%), PTPN22 (rs2476601, 84.7% vs 85.6%), and CTLA4 (rs3087243: 62.3% vs 62.1%) were similar in offspring of mothers compared to fathers with type 1 diabetes.

Conclusion: We found no support for a difference in frequencies of the most important type 1 diabetes susceptibility genes in offspring of mothers with type 1 diabetes compared to offspring of fathers with type 1 diabetes. Selective fetal loss depending on fetal genes predisposing to type 1 diabetes is therefore not a likely explanation for the differential association of maternal versus paternal type 1 diabetes.

P14

Sociocultural factors influencing care among immigrant women with endometriosis/adenomyosis in Norway

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Introduction: Female-specific conditions like endometriosis/adenomyosis have long been overlooked. While awareness is growing, women with these conditions often face isolation and frustration as their symptoms are regularly dismissed by family, friends, and even doctors. Immigrant women living in Norway with endometriosis/adenomyosis face additional unique challenges of navigating unfamiliar foreign healthcare systems and adapting to new sociocultural norms. Identifying these factors in depth can help healthcare professionals better understand their needs, leading to improved medical practices and stronger doctor-patient relationships.

Aims: This study aims to explore the sociocultural factors that contribute to the challenges faced by immigrant women in Norway living with endometriosis/adenomyosis.

Methods: The study design uses semi-structured in-person interviews. Interview topics will include the participant's journey living with endometriosis/adenomyosis, cultural background and associated practices for pain management, experiences with the Norwegian healthcare system, past and current doctor-patient relationships, interpersonal relationships with family and friends, perceptions of pain, and understanding of reproductive health.

Participants will be recruited by a gynecologist at the Ullevål Hospital. Participants must have been born outside of Norway, be older than 18 years of age, have lived in Norway for at least one year, previously received treatment for endometriosis/adenomyosis, not have mental disabilities, and not currently undergoing any treatment for other serious illnesses.

Thematic analysis will be the main qualitative data analysis method used to identify patterns within the participants' experiences, views, and opinions. As this is an exploratory process, it is understood that the research question can develop or even change as the study progresses.

Results: While the results are yet to be determined, the resulting data has the potential to help bridge gaps in doctor-patient relationships in the Norwegian healthcare system. A deeper understanding of patients' needs could improve patient care services and management.

P15

Hypertensive disorders of pregnancy: Examining the paternal contribution across generations

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Introduction: Hypertensive disorders of pregnancy (HDP) tend to reoccur intergenerationally through the maternal line, but the paternal contribution remains understudied.

Aims: To investigate the association between paternal HDP exposure in-utero and HDP in first pregnancy and to explore whether paternal HDP exposure in-utero modifies the association between maternal HDP exposure in-utero and HDP in first pregnancy.

Methods: Using the Medical Birth Registry of Norway (1967-2020), we identified 416,231 men-offspring units and 296,114 men-women-offspring units. The primary outcome was HDP in first pregnancy and secondary outcomes were preeclampsia, gestational hypertension, placental abruption, stillbirth and preterm delivery. Relative risks (RR) with 95% confidence intervals (CI) were calculated using log-binomial regression models.

Results: Compared to men born to mothers without HDP, those exposed to preeclampsia in-utero had a higher risk of fathering pregnancies complicated by both preeclampsia (RR 1.4; 95%CI 1.3-1.5) and gestational hypertension (RR 1.2; 95%CI 1.1-1.4). Men exposed to gestational hypertension in-utero had an elevated risk of fathering pregnancies complicated by preeclampsia only (RR 1.2; 95%CI 1.1-1.3). No increased risks were observed for other pregnancy complications.

Men born from normotensive pregnancies to mothers with HDP in other pregnancies did not show increased risks for any pregnancy complication.

Among women, those exposed to HDP in-utero had the highest risk for HDP in their first pregnancy (pooled RR 2.2), followed by women born from normotensive pregnancies to mothers with HDP in other pregnancies (pooled RR 1.7), compared to the reference group of women and men born to mothers without HDP.

The elevated risk in women exposed to HDP in-utero was not influenced by men's HDP exposure status. However, women born from normotensive pregnancies to mothers with HDP in other pregnancies had a risk similar to those exposed to HDP in-utero if men were also exposed to HDP in-utero (RR 2.4; 95% CI 2.0-2.8 versus pooled RR 2.2).

Conclusions: Paternal HDP exposure in-utero independently contributes to the risk of HDP in women born from normotensive pregnancies. Familial susceptibility alone does not explain the heightened risk. Paternal HDP exposure does not significantly modify the already heightened risk of HDP among women exposed to HDP in-utero.

P16

The association of adolescent to midlife weight change with age at natural menopause: A population study of 263 586 women in Norway

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Introduction: A high body mass index (BMI) has been associated with later menopause, whereas a low BMI has been associated with earlier menopause in previous studies. Also changes in body weight across the life course may influence age at menopause, although the evidence remains inconclusive.

Aim: To study the association of adolescent to midlife weight change with age at natural menopause.

Methods: We performed a retrospective population-based cohort study of 263 586 women aged 50-69 years attending the Norwegian breast cancer screening program (BreastScreen Norway). During the years 2006 to 2015, all participants were invited to fill in two self-administered questionnaires. The associations of adolescent to midlife weight change with age at menopause were estimated as hazard ratios (HR) using Cox proportional hazard models. We included nine categories of weight change based on recalls of adolescent weight, compared to peers, and quartiles of midlife weight in kilograms. The nine weight change categories were: stable low, stable average (reference), stable high, average to low, high to average, high to low, average to high, low to average, and low to high weight. We adjusted for year and country of birth, education, number of childbirths, height, smoking, and exercise.

Results: Median age at menopause was 52 years (IQR 49-54 years). Women with the largest weight loss had the highest HR of reaching menopause (adjusted HR 1.11, 95% CI: 1.06-1.17), compared to women with a stable average weight. Conversely, women with the largest weight gain had a lower hazard (adjusted HR 0.96, 95% CI: 0.93-0.99). Women who remained at a stable high weight from adolescence to midlife had the lowest HR of reaching menopause (adjusted HR 0.93, 95% CI: 0.90-0.95).

Conclusions: Women with the largest weight loss had the earliest menopause, and women who remained at a high weight from adolescence to midlife had the latest menopause. Our findings suggest that weight change from adolescence to midlife may influence the timing of menopause.

P17

Associations between prenatal and childhood PFAS exposure and thyroid hormone levels in children from the Norwegian Environmental Biobank

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Introduction: Per- and polyfluoroalkyl substances (PFAS) are persistent environmental pollutants known to disrupt endocrine function. Studies suggest potential links between PFAS exposure and thyroid function, especially in vulnerable populations such as pregnant βwomen and children.

Aim: This project investigates the association between maternal PFAS levels during pregnancy and thyroid-stimulating hormone (TSH) levels in newborns, as well as the relationship between PFAS exposure and thyroid function in children aged 7-14.

Method: This study is based on data from the Norwegian Environmental Biobank, a subset of the Norwegian Mother, Father and Child Cohort Study (MoBa). Two analyses are conducted: (1) A longitudinal cohort study exploring associations between PFAS levels in maternal blood samples collected during pregnancy (week 17) and newborn TSH levels measured from neonatal serum; (2) A cross-sectional study assessing the relationship between current PFAS levels and TSH, free triiodothyronine (FT3), and free thyroxine (FT4) in children aged 7-14. Biological samples were collected in 1999-2009 (cohort study) and 2016-2017 (cross-sectional study), with PFAS levels quantified using validated laboratory methods.

Descriptive analyses, including density plots and scatter plots, will be used to visualize the distribution of PFAS levels and thyroid hormone levels. Spearman's rank correlation will be applied to assess associations between PFAS levels and thyroid hormone outcomes. Simple regression analyses will be performed to explore the relationships between PFAS exposure and thyroid hormone outcomes, adjusting for relevant covariates such as maternal BMI, fish intake, and smoking habits.

Conclusion: The study may contribute to the growing evidence on the endocrine-disrupting potential of PFAS, particularly in early development. The findings will potentially underline the importance of stricter regulations and policies to limit PFAS exposure in vulnerable populations. Future research should focus on longitudinal effects of PFAS exposure and its broader implications for child health.

P18

Polygenic risk score of physical activity related to long-term trends in physical activity and body mass index: the population-based HUNT study, Norway

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Introduction: Physical inactivity is associated with higher risk and mortality of non-communicable diseases, and may contribute to an increasing obesogenic environment over the past few decades. Although obesity related genetics have been associated with temporal shifts in body mass index (BMI), thus indicating gen-environment interactions, it is not known if physical activity related genes play a similar role.

Aims: Explore temporal trends in physical activity and BMI by genetic predisposition to being physically active. We will also explore if genetic variants of physical activity interact with observed physical activity level on temporal shifts in BMI.

Methods: The HUNT Study, Norway assessed physical activity and BMI at consecutive surveys over the past four decades (HUNT1, 1984-86; HUNT2, 1995-97; HUNT3, 2006-08; and HUNT4, 2017-19). From HUNT2 onwards, participants also provided a blood sample for genotyping. Genetic variation associated with moderate-to-vigorous physical activity was used to calculate a polygenic risk score (PRS) using LDpred2. We used linear mixed models to estimate mean difference in reported physical activity (min/week) and BMI (kg/m^2) between low (1st fifth), intermediate (2nd-4th fifth) and high (5th fifth) PRS at each HUNT survey.

Results: Participants with high PRS reported 61 min/week (95% CI 59 to 63) of physical activity while those with low PRS reported 50 min/week (49 to 52) at HUNT1. According to the same groups in HUNT4, we observed 90 min/week (88 to 91) and 111 min/week (109 to 112), respectively. Participants with high PRS had a mean BMI of 24.3 kg/m^2 (24.2 to 24.3) in HUNT1, with a mean difference of -0.3 kg/m^2 (-0.4 to -0.2) compared to those with low PRS. The corresponding estimates at HUNT4 were 27.5 kg/m^2 (27.4 to 27.6), with a mean difference of -0.8 kg/m^2 (-0.9 to -0.7). Estimates were attenuated regardless of PRS if participants reported to be physically active ≥150 min/week. We found evidence of interaction between PRS and calendar time for both physical activity and BMI ($p_{interaction}$<0.001).

Conclusions: Participants with high genetic predisposition to being physically active are more robust against the obesogenic environment, and being physically active decelerates the genetic impact on temporal trends in BMI.

P19

Short-term effects of temperature and air pollution on mortality in Norway: A nationwide cohort-based study

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Background: This time-stratified case-crossover study examined short-term associations of air temperature with cause-specific mortality and morbidity and potential effect modification by daily mean air pollution concentrations and individual characteristics in the Cohort of Norway (CONOR) cohort.

Methods: The CONOR cohort recruited ~173,000 participants from 1994 to 2003. Participants' vital status and cause of death were collected from the Cause of Death Registry of Norway until 2018. Daily mean air temperatures and concentrations of fine particulate matter (PM2.5) and ozone (O3) estimated by spatial-temporal models were assigned to participants' residences. We applied conditional logistic regression models with the distributed lag non-linear model approach to assess cold and heat effects on cause-specific mortality. The potential effect modification was analyzed by incorporating an interaction term between air temperature and the modifier in the regression model. The cold and heat effects were estimated for different subgroups of participants and at the low (5th percentile), medium (50th percentile), and high (95th percentile) levels of air pollution.

Results: During the follow-up period, we identified 40,040 cases of natural-cause deaths, including 14,457 and 3,699 cases of deaths from cardiovascular and respiratory diseases, respectively. This was accompanied by a trend for increased risks of cardiopulmonary, cardiovascular, ischemic heart disease, and cerebrovascular mortality associated with decreasing air temperature. The cold effect on natural-cause mortality was more pronounced among participants who were female, had lower socioeconomic status, lived in sparsely populated areas, and had no history of CVD. We did not find adverse heat effects on mortality.

Conclusion: Our findings provide evidence for adverse short-term cold effects on mortality at the individual level in a Nordic country. Besides, we identified sub-populations who were likely to be more at risk of cold-related mortality. These findings could be important in developing integrated strategies for adaptation.

P20

The mediating role of physical activity in the association between adolescent sports and exercise participation and adult adiposity: Longitudinal data from the Norwegian HUNT Study

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Introduction: Behaviour established during adolescence tend to continue into adulthood and can therefore have long-term effects on health and risk of non-communicable diseases later in life. For instance, sports and exercise participation during adolescence has been associated with adiposity in adulthood. However, whether this effect is mediated by physical activity remains unexplored.

Aims: To examine the mediating role of physical activity on the association between sports and exercise participation in adolescence and adiposity composition in adulthood.

Methods: Prospective study based on data from the Norwegian HUNT Study, including 1150 adolescents (60% female) with a mean age at baseline of 16.2 years (SD 1.8). At baseline, the participants answered three questions indicating sports and exercise participation during adolescence. Self-reported physical activity was assessed by three questions on frequency, intensity and duration when participants were ~27 years old. Adiposity was measured with bioimpedance when participants were ~38 years old. We assessed the mediating effect of self-reported physical activity at age ~27 years on the association between adolescent sports and exercise participation and adiposity at age ~38 years. Baseline age, sex and parental education was included as covariates.

Results: Compared with those who participated in sports and exercise less than once per week, participants who participated once per week, 2-3 times per week, and ≥4 times per week, had -0.8% (95% CI, -2.4 to 0.8), -1.2% (95% CI, -2.6 to 0.2), and -3.0% (95% CI, -4.5 to -1.6) lower body fat, respectively. The corresponding proportion of the association mediated by self-reported physical activity was 38.8%, 16.3% and 25.7%.

Conclusion: We found a strong association between sports and exercise participation during adolescence and adiposity during adulthood. The association was mediated by self-reported physical activity.

P21

The disease burden in Norway – Findings from the Global Burden of Disease Study 2021

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Introduction: The Global Burden of Disease (GBD) study provides a comprehensive overview of both fatal and non-fatal health losses in a population. It identifies important differences in disease burden between men and women and by age groups.

Aims: To describe the disease burden in Norway in 2021, with a focus on differences across sex and age groups.

Methods: We used data from the GBD2021 study for Norway, examining life expectancy (LE), healthy life expectancy (HALE), years of life lost (YLL) as a measure of mortality, and years lived with disability (YLD) as a measure of morbidity. Data were analyzed by sex and age groups, across 175 diseases and injuries classified at level 3 in the GBD cause hierarchy.

Results: Between 1990 and 2021, both LE and HALE increased for men and women in Norway, with men experiencing a slightly greater increase. In 2021, HALE was nearly identical for men and women (71.1 years for men vs. 70.9 years for women). These gains coincided with a significant decrease in mortality from cardiovascular diseases, which remains the leading cause of YLL for both sexes. In 2021, Norway was estimated to have a total of 687 685 YLLs and 724 928 YLDs, with men accounting for 54% of YLLs and women 56% of YLDs. These sex differences were more pronounced in the working-age group (20-54 years). Musculoskeletal, anxiety, depression, and headache disorders, as well as a high disease burden from gynecological diseases, were major contributors to the higher morbidity observed in women.

Conclusions: Since 1990, there have been significant gains in life expectancy for both men and women in Norway, with men seeing a slightly larger increase. Women, however, carry a greater burden of morbidity due to a higher prevalence of years lived with disability, while men experience higher premature mortality.

P22

Mediators of educational differences in dementia risk later in life: Evidence from the HUNT Study

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Background: Despite a well-known inverse association between education and dementia risk, the mediating mechanisms are not well understood. We explored how lifestyle and health risk factors across the life course mediate the relationship between education and dementia among adults aged 70+ years.

Methods: We included N=7,655 participants with education data and prospectively registered data on exposure to mediators across the life course using a historical cohort design, linking data from the HUNT4 70+ Study in 2017-2019 with registry data from Statistics Norway and previous HUNT surveys starting in the 1980s. Data on clinical dementia diagnoses were derived from HUNT4 70+. Causal mediation analysis was conducted to assess the mediating role of occupational characteristics (routine task intensity score, except for late adulthood); lifestyle factors (daily smoking and physical inactivity); and health risk factors (obesity, hypertension, diabetes, hearing impairment, cardiovascular diseases, low-density lipoprotein cholesterol level, and depression and anxiety symptoms) assessed during early, middle, and late adulthood in the association between education and dementia.

Results: Participants with lower secondary education were more likely to have dementia compared to those with at least upper secondary education. This was consistent across models accounting for exposure to risk factors in early (OR: 2.0, 95% CI: 1.6, 2.5), middle adulthood (OR: 1.9, 95% CI: 1.7, 2.2), and late adulthood (OR: 1.8, 95% CI: 1.6, 2.1). This associations were partially mediated by the joint effect of health and lifestyle risk factors from middle and late adulthood, mediating 11.1-19.8% of the educational differences in dementia risk. Moreover, up to 12% and nearly 3.7% of the association between education and dementia was mediated by the joint effect of health risk and lifestyle factors, respectively, from middle adulthood onwards.

Conclusions: Educational differences in dementia risk can be partly explained by modifiable lifestyle and health risk factors across the life course. If truly causal, the findings could indicate highlight potential targets to address the varying risks of dementia associated with different levels of education.

P23

Differences in psychological job demand among male and female farmers in Norway: The HUNT Study

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Introduction: Farming is a physically and psychologically demanding occupation. There has been a steady increase in number of female farmers in the occupation, and it is well established that there are differences in how males and females perceive aspects of work environment. The work environment and working conditions of female farmers have, therefore, been highlighted as an area needing more research.

Aim: To estimate differences in self-reported psychological job demand between male and female farmers in Norway, and the possible role of health status on perceived job demand.

Methods: We used data from the fourth main wave of The Trøndelag Health Study (HUNT4, 2017-2019). The study sample consisted of occupationally active participants registered with a main occupation in ISCO group 61 (n = 1,559). Three questions from the Swedish Demand Control Support Questionnaire were used to measure psychological job demand. Each question was scored on a Likert scale (1 to 4). The scale was reversed, before the scores were added to create a scale ranging from 3 (low) to 12 (high). High job demand was defined as values above the sample median score. We used logistic regression analyses to estimate associations between sex and high job demand, adjusting for age and self-reported health status.

Results: The final sample consisted of 987 farmers (743 (75%) males and 244 (25%) females). Of these, 37% male and 27% female farmers reported high psychological job demand. Female farmers had significantly lower odds than male farmers of high job demand (OR 0.56, 95% CI 0.41-0.78), adjusting for age. Adjusting for health status in addition to age, did not substantially alter the findings (OR 0.54, 95% CI 0.39-0.76). Female and male farmers with poor self-reported health had higher predicted probabilities of high psychological job demand than those with good self-reported health, in all age groups.

Conclusions: Male farmers are more likely to report of high psychological job demand than female farmers. Similar trends in the effect of poor self-reported health on high demands were seen in both sexes. The results contribute to increased knowledge on the work environment of both male and female farmers.

P24

Mortality among Norwegian military women veterans from international peacekeeping missions during 1978-2023

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Background and aim: Previous mortality studies among Norwegian military veterans from international peacekeeping missions have been restricted to men, as the number of women participants in each mission have been too small to give statistically robust results. Hence, we established a cohort comprising all military women who participated in such service back to 1978 to gain increased statistical strength.

Methods: The cohort was established by the Norwegian Armed Forces Health Registry and include 2365 women eligible for follow-up from their first day of peacekeeping service through 2023. We calculated standardized mortality ratios (SMRs) with 95% confidence intervals (CIs) by comparing the observed numbers of deaths with the expected numbers calculated from national population rates in Norway.

Results: The accumulated person-years for the cohort over the study period was 47 919. Average follow-up time was 20.3 years. A total of 65 deaths were observed, which gave a lower-than-expected all-cause SMR of 0.79 which was bordering on statistical significance (95% CI 0.61-1.01). Mortality from all external causes combined and of suicide, as well as overall disease-related mortality did not differ from that of the national rates, the same was true for breast cancer and lung cancer mortality. Mortality from (non-malignant) respiratory diseases was lower than expected (SMR=0.18, 98% CI 0.00–0.99), on the other hand, the risk of dying from cerebrovascular diseases was elevated (SMR=2.63, 95% CI 1.21–5.01).

Conclusion: Generally, participating in peacekeeping missions was not associated with increased risk of mortality, while the risk of death from cerebrovascular diseases was increased in the cohort. Cerebrovascular accident is the fourth leading cause of death in women (in the US), and common behavioural risk factors such as smoking, high alcohol consumption, physical inactivity and poor diet probably do not apply to our cohort members. As few deaths in our cohort limit the possibility to look more closely at specific causes of death, we are planning a joint study that will include deaths among Swedish and Danish women veterans.