ABSTRACT BOOK

EPPEC2024

European Perinatal and Paediatric Epidemiology Conference

University of Copenhagen

August 2024

The association between maternal migraine in pregnancy and ADHD symptoms in their offspring: triangulate the evidence

Yaxin Luo[1,2], Christina Dardani[1,2], Rachel Blakey[1,2], Gemma Sharp[3], Evie Stergiakouli[1,2]

[1]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK, [2]MRC Integrative Epidemiology Unit, Bristol Medical School, University of Bristol, Bristol, UK, [3]School of Psychology, Faculty of Health and Life Sciences, University of Exeter, Exeter, UK

Background: The association between maternal migraine and offspring's ADHD can be explained by transmitted genetic effect or nurture effect. Distinguishing the association is important because they have different prevention and treatment implications.

Method: Logistic regression and negative control were utilized to test the observational association between maternal migraine during pregnancy and ADHD symptoms in their offspring in Avon Longitudinal Study of Parents and Children (ALSPAC). Polygenic score regression and Linkage disequilibrium score regression were implemented to estimate the genetic correlation. Mendelian randomization (MR) was conducted to infer the causal relationship.

Result: Compared with participants whose mother never had migraine before 12 weeks' gestation, participants whose mother reported migraine at 12 weeks' gestation were more likely to experience ADHD symptoms at age 7 (OR = 1.55 [1.2, 1.99]), little difference was found if mother had experienced migraine before 12 weeks' gestation (OR = 1.09 [0.87, 1.37]). Participants whose mother had higher genetic liability to migraine were more likely to experience ADHD symptoms (OR = 1.21 [1.11, 1.32]). Shared genetic liability was found between migraine and ADHD (r = 0.2 [0.14, 0.26]). MR found little evidence of causal effect of migraine on ADHD (ORIVW = 1.01 [0.94, 1.09]), and ADHD on migraine neither (ORIVW = 1.08 [1,1.16]).

Conclusion: The association between maternal migraine and ADHD symptoms in their offspring is more likely due to shared genetic risk factors. There is little evidence to suggest a causal relationship.

Crowding in the delivery ward and the relationship with postpartum hemorrhage

Linnea Viktoria Ladfors[1], Natalie Holowko[1], Can Liu[1,3], Louise Lundborg[1], Mia Ahlberg[1,2], Fredrik Granath[1], Olof Stephansson[1,2]

[1]Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, [2]Department of Women's Health, Division of Obstetrics, Karolinska University Hospital, [3]Department of Public Health Sciences, Stockholm University

Background: Crowding in delivery wards can limit the possibility to offer high-quality care, potentially affecting labor management and risk of postpartum hemorrhage (PPH). In this study, we investigated the impact of delivery ward crowding on PPH risk and explored whether giving birth during a summer month, typically an indicator of lower staffing, or weekend further increases this risk.

Method: A case-control study, including 1,027,510 births in Sweden (2004-2019) using data from the Medical Birth Register. PPH cases were matched (1:10) with controls by delivery ward, year and time of birth (night/day). After standardization for delivery ward, year and time of birth (day vs night), high crowding was defined as the number of births in a ±2-hour interval around the birth exceeding the 75th percentile. Conditional logistic regression was used to study the association between crowding and PPH, and to examine whether giving birth during a weekend or summer vacation month (June-August) modified this association.

Result: High crowding was not associated with increased risk of PPH, the odds ratio for PPH for with high crowding was 0.97 (95% confidence interval: 0.95-0.99. This association did not vary between the summer and the rest of the year or between weekends and weekdays.

Conclusion: We did not find a significant association between high delivery ward crowding and risk of PPH. Instead, our estimates suggest a small reduction in PPH risk with high crowding. Future studies should investigate how staffing in relation to crowding influences the risk of PPH and other adverse birth outcomes.

The Association between In-Vitro Fertilization, Twin Pregnancy and HELLP Syndrome: A Population-Based Study

Jenna Victory[1], Sofia Nicolls[1], Johanna Koegl[1], Sid John[1], Li Qing Wang[1], Hamideh Bayrampour[1], KS Joseph[1], Sarka Lisonkova[1]

[1]*University of British Columbia*

Background: HELLP syndrome is a rare severe complication of pregnancy characterised by haemolysis, elevated liver enzymes, and low platelets. In-vitro-fertilization (IVF) is associated with adverse pregnancy outcomes like HELLP syndrome and multifetal pregnancy. The association between IVF, twin pregnancy and HELLP syndrome is understudied.

Objective: To compare the rates of HELLP syndrome in singleton and twin pregnancies in women with spontaneous vs IVF conception.

Method: We included all women with singleton or twin live birth or stillbirth in British Columbia, 2008/09-2020/21 with data obtained from the BC Perinatal Database registry. We used logistic regression to adjust for potential confounders (e.g. body-mass index, smoking, etc.) and to assess potential modification of the association between mode of conception and singleton/twin pregnancy.

Result: Among 523,867 women, 16,707 (3.2%) women had conceived after using IVF. The proportion of twin deliveries was 14.7% (2,455) among women who conceived by IVF, and 1.2% (5,882) among women with spontaneous conception. The adjusted odds ratio (AOR) for HELLP syndrome among twins vs singletons for women who conceived by IVF was 3.83 (95% confidence interval [CI] 2.76 – 5.30) while the AOR among women who conceived spontaneously was 8.34 (95% CI 6.98 – 9.97; Table 1).

Conclusion: IVF modifies the association between twin pregnancy (vs singleton pregnancy) and HELLP syndrome. Women who conceived a twin pregnancy spontaneously have a significantly greater risk of HELLP syndrome relative to women who conceived a twin pregnancy by IVF. Our results can inform preconception counselling and prenatal care for women who plan IVF.

Seafood consumption and dietary pollutant exposure during pregnancy and JIA risk: a population-based nationwide cohort study

Vilde Øverlien Dåstøl[1,2], Ida Henriette Caspersen[1,3], Anne Lise Brantsæter[4], Helga Sanner[1,5]

[1]Oslo New University College, [2]University of Oslo, [3]Norwegian Institute of Public Health, Centre for Fertility and Health, [4]Norwegian Institute of Public Health, Depart. Food Safety, [5]Oslo New University College

Background: Juvenile idiopathic arthritis (JIA), one of the most common pediatric autoimmune diseases, has unknown etiology and higher prevalence in girls. A Swedish study found that weekly fish consumption in pregnancy and infancy increased JIA risk up to five-fold.

Method: In the Norwegian Mother, Father, and Child Cohort Study we used a validated semi-quantitative food frequency questionnaire to investigate associations between maternal seafood consumption and dietary pollutant exposure and JIA risk. Associations were examined according to high consumption (≥90th percentile) vs low (<P90), and across quintiles, using 1st quintile as reference. We used multivariable logistic regression analyses adjusted for relevant factors.

Result: Among 72,110 mother-child pairs, we identified 217 JIA cases. High maternal consumption of lean/semioily fish was positively, but weakly associated with JIA (aOR 1.50, 95% CI 0.99-2.18). High maternal lean/semioily fish and shellfish intake was positively associated with JIA in boys (aOR 2.02, 95% CI 1.13-3.83, and aOR 1.87, 95% CI 1.03-3.40). Among girls, we found inverse associations for dioxins (total TEQ) and PCB-153 intakes (5th vs 1st quintile) with JIA (aOR 0.40, 95% CI 0.20-0.79 and aOR 0.44, 95% CI 0.23-0.82).

Conclusion: High intake of lean/semioily fish during pregnancy was weakly associated with JIA. Sex-specific analyses suggested positive associations between seafood consumption, PCB-153 and JIA in boys, while in girls these were mainly inverse.

Characterising effects of autoimmune disease liability and targets of their treatment on adverse pregnancy outcomes using Mendelian randomization

Elisabeth Aiton[1], Deborah Lawlor[1], Carolina Borges[1]

[1]*University of Bristol*

Background: Autoimmune diseases are often more common in women than men, diagnosed in early adulthood, and associated with adverse pregnancy outcomes. However, whether these diseases or medications used to manage them cause adverse pregnancy outcomes is unknown.

Methods: We used two-sample Mendelian randomization (MR) to explore the effect of liability to seven autoimmune diseases on nine pre-selected adverse pregnancy outcomes. Genetic instruments were selected from published GWAS and outcome genetic association data included up to 400,000 women within the MR-PREG collaboration. Main analyses used the inverse variance weighted (IVW) method, and sensitivity analyses included MR-Egger and weighted-median.

Results: We found evidence that liability to rheumatoid arthritis increased risks of low birthweight (OR=1.12, 95% CI:1.06-1.18), neonatal intensive care unit admission (OR=1.08, 95% CI:1.03-1.12), and gestational diabetes (OR=1.06, 95% CI:1.03-1.09), while systemic lupus erythematosus increased risks of low birthweight (OR=1.04, 95% CI:1.01-1.08) and preeclampsia (OR=1.03, 95% CI:1.00-1.05). Multiple sclerosis decreased risks of several outcomes, including preeclampsia (OR=0.95, 95% CI:0.93-0.98) and low birthweight (OR=0.94, 95% CI=0.90-0.98). Sensitivity analyses supported these IVW results. For psoriasis vulgaris, psoriatic arthritis, axial spondyloarthritis and inflammatory bowel disease there was limited evidence supporting any effects, though several estimates were imprecise.

Conclusion: Our preliminary findings suggest an effect of some autoimmune diseases on fetal growth and preeclampsia. In ongoing analyses, we are exploring the role of the HLA locus in these effects, and using drug target MR to investigate the effects of perturbing targets of monoclonal antibody drugs used to manage these autoimmune conditions on the same pregnancy outcomes.

Assessing the benefits and risks to mothers and offspring of continuing treatment for maternal hypertension and hypothyroidism: an observational cohort study in the UK Clinical Practice Research Datalink

Ciarrah-Jane Shannon Barry[1,2], Venexia Walker[1,2,3], Christy Burden[4], George Davey Smith[1,2], Neil Davies[5,6,7]

[1]Medical Research Council Integrative Epidemiology Unit, University of Bristol, [2]Population Health Sciences, Bristol Medical School, University of Bristol, [3]Department of Surgery, University of Pennsylvania Perelman School of Medicine, [4]Translational Health Sciences, Bristol Medical School, University of Bristol, [5]K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, Norwegian University of Science and Technology, [6]Division of Psychiatry, University College London, [7]Department of Statistical Science, University College London

Background: Exclusion of pregnant women from clinical trials, due to ethical concerns, has limited evidence on medication safety during pregnancy, resulting in conservative guidance. Yet, rising prevalence of chronic conditions in reproductive-age women has increased medication use. This study evaluates risks and benefits of discontinuing drug prescriptions for chronic hypertension and hypothyroidism during pregnancy, using linked primary care records in a longitudinal intergenerational cohort.

Methods: Utilizing UK Clinical Practice Research Datalink GOLD, we conducted multivariate regression models, adjusted for covariates, to assess maternal treatment discontinuation on various outcomes.

Results: Samples included 3,232, and 3,334 pregnancies with chronic hypertension or hypothyroidism respectively. Within the hypertension cohort, vasodilator antihypertensive drugs were the only subclass for which discontinuation of prescription was associated with an increase in gestational age, with estimated mean difference 3.98 weeks (95%CI: 1.61, 6.35). There was little evidence of association between discontinuation of a prescription for diuretics, renin-angiotensin system drugs or calcium-channels blockers with any study outcomes. There was no evidence of an association between discontinuation of prescription for thyroid hormones and any method of delivery outcome, e.g., mothers who discontinued treatment had estimated OR for breech birth of 1.00 (95% CI: 0.474, 2.11). There was some evidence discontinuation of thyroid hormones may increase gestational age, with estimated increase 1.84 weeks (95%CI: 0.120, 3.57).

Conclusion: This study reports a reassuring lack of association between many drug subclasses and adverse offspring outcomes. The evidence may guide clinical decision-making for treating chronic hypertension and hypothyroidism during pregnancy in similar populations.

Assessing neonatal outcomes across prenatal exposure trajectories to antidepressant

Anastasia Giorcelli[1,2], Nhung TH Trinh[3], Giovanni Corrao[2], Angela Lupattelli[3], Anna Cantarutti[1,2]

[1]Unit of Biostatistics, Epidemiology and Public Health, Department of Statistics and Quantitative Methods, University of Milano-Bicocca, [2]National Centre for Healthcare Research and Pharmacoepidemiology, [3] PharmacoEpidemiology and Drug Safety Research Group, Department of Pharmacy, Faculty of Mathematics and Natural Sciences, University of Oslo

Background: The understanding of prenatal antidepressant (AD) exposure and newborn outcomes at birth is currently limited.

Methods: We conducted a population-based cohort study encompassing all deliveries between 2007-2022 in Lombardy, Italy, using administrative databases. We evaluated the risk of preterm birth (PTB<37 gestational weeks), low Apgar score (LAS<7 at 5 min), and neonatal abstinence syndrome (NAS ICD-9-CM 779.5) among infants born to mothers with pre-pregnancy mental illnesses and/or exposed to ADs in pregnancy using modified Poisson regression analysis. Weight-overlapped on the propensity score accounted for all potential confounders. AD exposure was modeled using k-means trajectory model over a period from one year before the last menstrual period and gestation week 32.

Results: Among 31,788 mother-child pairs, we identified five antidepressant exposure group: (i) discontinuers before pregnancy (n=652), (ii) late discontinuers (2,331), (iii) very low exposure (1,457), (iv) continuers (255), and (v) non-exposed (27,094). Compared to unexposed deliveries, those exposed to ADs during pregnancy had an increased risk of PTB (adjusted RR ranging 1.28-1.45); (ii) and (iv) had an increased risk of LAS (aRR 2.35 and 5.77, respectively), and an increased risk of NAS (aRR 1.91 and 3.44, from (ii) and (iv) respectively). When (i) was chosen as a reference, we found weaker associations crossing the null.

Conclusion: Children born to AD continuers during pregnancy had a moderately increased risk of PTB, LAS, and NAS compared to unexposed. However, no evidence of such risks was found when comparing with antidepressant discontinuers, emphasizing the influence of confounding by maternal psychiatric illness severity.

Lower breastfeeding rates in mothers treated with chronically used anti-inflammatory medications

Essi Whaites Heinonen[1,2], Alec Todd[1], Diana L Johnson[1], Christina D Chambers[1]

[1]University Of California San Diego, [2]Karolinska Institutet

Background: Breastmilk is the recommended nutrition for the first 6 months. Mothers requiring chronic medications may be advised or choose not to breastfeed due to lack of safety data. We aimed to determine whether mothers treated with chronically used medications are less likely to follow breastfeeding recommendations than untreated mothers.

Methods: Pregnant women from the US and Canada were enrolled in a prospective cohort study conducted by MotherToBaby between 2010 and 2022. Those with medications with potential to harm were excluded. Exposures were defined as use of 1) antidepressants; 2) anti-inflammatory drugs; 3) asthma drugs and 4) no chronic medications at delivery. Outcomes were not breastfeeding, supplementing with formula, and stopping breastfeeding before 6 months. Risks were calculated with modified Poisson regression and Cox regression, adjusted for year of delivery, parity, socioeconomic status, body mass index, race and ethnicity.

Results: The sample consisted of 293 antidepressant exposed, 799 anti-inflammatory drug exposed, 217 asthma drug exposed and 4,439 unexposed. Mothers taking anti-inflammatory drugs were more likely to not breastfeed (adjusted risk ratio [aRR] 4.05; 95% confidence interval [CI] 3.12-5.26), supplement with formula (aRR 1.13; CI 1.02-1.26) and to stop before 6 months (adjusted hazard ratio 1.75; CI 1.30-2.35). Mothers taking antidepressants were also more likely to supplement (aRR 1.27; CI 1.10-1.48).

Conclusion: Women treated with anti-inflammatory drugs were less likely to breastfeed than unexposed. Therapeutics for chronic inflammatory diseases have been approved without adequate safety data in lactation. Timely development of safety data is needed to support clinical decision-making on breastfeeding.

Severe maternal morbidity and the impact on subsequent birth; a nationwide population-based cohort study and a sibling control analysis 1999-2021

Eleni Tsamantioti[1], Anna Sandström[1], Charlotte Lindblad Wollmann[1], Jonathan Snowden[2], Neda Razaz[1]

[1]Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, [2]School of Public Health and Department of Obstetrics and Gynecology, Oregon Health and Science University - Portland State University, Portland, Oregon, USA

Background: To examine the association between severe maternal morbidity (SMM) and the probability of a subsequent birth.

Methods: Population-based cohort study in Sweden, including women who delivered their first birth between 1999 and 2021. Overall SMM and SMM subtypes were identified among all deliveries at ≥22 weeks of gestation from the Medical birth and National Patient Register.
Women with recorded first delivery were followed up from 43 days postpartum until the conception date of the second birth, death, emigration or the end of follow up (31st December 2021). Using a Cox model, we estimated the association between SMM and subsequent birth, with adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs). Sibling analysis was performed to evaluate potential genetic and familial confounding.

Results: A total of 36,797 (3.5%) women experienced an SMM condition in their first pregnancy. Women with any SMM had a lower incidence rate of subsequent birth compared with those without SMM in their first delivery (136.5 vs 182.3 per 1,000 person-years, respectively, aHR 0.88, 95% CI 0.87-0.89). The probability of subsequent birth was significantly lower among women with severe uterine rupture (aHR 0.48, 95% CI 0.27-0.85), cardiac complications (aHR 0.49, 95% CI 0.41-0.58), cerebrovascular accidents (aHR 0.60, 95% CI 0.50-0.73) and severe mental health conditions (aHR 0.48, 95% CI 0.44-0.53) in first birth. Sister analyses showed that the associations were not influenced by familial confounding.

Conclusion: Our findings suggest that women who experience SMM in their first birth are less likely to have a subsequent birth.

Predicting caesarean delivery in nulliparous women with a prolonged, low-risk pregnancy - Machine-learning approaches using Swedish population-based Health Registers

Stefanie Schmauder[1], Anna Sandström[1,2], Magnus Boman[1,3], Christian Martin[4], Olof Stephansson[1,2]

[1]Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, [2]Department of Obstetrics, Karolinska University Hospital, [3]MedTechLabs, BioClinicum, Karolinska University Hospital, [4]Center for Scalable Data Analytics and Artificial Intelligence (ScaDS.AI) Dresden/Leipzig

Background: Induction of labour (IOL) around 41+0 gestational weeks (GW) and not "expectant management" (EM), i.e. waiting for a later onset of birth, is often recommended to prevent adverse perinatal outcomes. To individualize these recommendations, the present study used a novel, data-driven approach to predict caesarean delivery (CD) in first-time mothers at or beyond 41+0 GW.

Methods: Low-risk primiparous women (≥ 41+0 GW) were derived from the nationwide Swedish Medical Birth Register between 1998-2019. A two-day-wise prediction in four subgroups with increasing gestational age was conducted (SG1: IOL 41+0-41+1 vs. EM > 41+1; SG2; IOL 41+2-41+3 vs. EM > 41+3; SG3: IOL 41+4-41+5 vs. EM > 41+5; SG4: IOL 41+6-42+0 vs. EM > 42+0). Sixty-four diagnoses and clinical characteristics available at the usual time for decision-making regarding IOL in each subgroup, were used as predictors ("features"). IOL was included as a binary feature (IOL vs. EM) respectively.

Results: The subgroups contained 178,932 (SG1), 129,449 (SG2), 90,448 (SG3) and 61,301 (SG4) pregnancies (CD = 20% (SG1) - 27% (SG4)). Random Forest and Naïve Bayes models outperformed the analyses with other classifiers (logistic regression, support vector machine, neural network). However, CD was predicted with a low sensitivity (15-21%).

Conclusion: Although the considered features lacked predictive power for CD, the study provides valuable methodological information for predicting the timing of IOL beyond 40+6 GW. The application of larger feature sets aims to enhance model performance and to predict further perinatal outcomes which could form the basis for an IOL decision-making tool to support an informed choice.

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

Huong Nguyen Thu[1], Hans Ivar Hanevik[1,2], Abigail Fraser[3,4], Deborah A. Lawlor[3,4], Kari Furu[1,5], Jacqueline M. Cohen[1,5], Maria C. Magnus[1]

[1]Norwegian Institute of Public Health, [2]Fertility department Sor, Telemark Hospital Trust, [3]MRC Integrative Epidemiology Unit at the University of Bristol, Oakfield House, Oakfield Grove, [4]Population Health Science, Bristol Medical School, University of Bristol, [5]Department of Chronic Diseases, Norwegian Institute of Public Health

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

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 were 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.

Defining neighborhood walkability for children in the ELFE cohort study

Devin Parker[1], Eloi Chazelas[1], Maria Melchior[1]

[1]*INSERM, Sorbonne University*

Background: Although walkability is known to be associated with obesity in adults, there is a paucity of data evaluating the association of walkability and health outcomes in children. In particular, little is known regarding the possible association with children's mental health.

Methods: We used data from the Etude Longitudinale Française depuis l'Enfance (ELFE) cohort study. Participating mothers gave birth in 2011 in a representative sample of 320 maternity hospitals in mainland France. This pilot study is limited to participants in Paris and children at 5.5 years old. Walkability is defined by three parameters: population density (defined by census data), street connectivity (defined by intersection density), and land-use mix (entropy index). To approximate walkable areas, 500-meter street-network buffer zones were created around each participants address using a geographic information system. Children's mental health was assessed using parent-reported Strengths and Difficulties Questionnaire at age 5.5 years.

Results: There was a total of 280 children in this pilot study. On measures of land-use mix, we found a mean of 0.79 (SD: 0.12), representing high accessibility. Residential and intersection density were highly correlated ($p<0.01$). The walkability index demonstrated high variability among participants (mean: 10.6; SD: 10.44; range: -1.67 – 30.59).

Conclusion: Developing a walkability index is a multifactorial measure to describe a children's neighborhood environment. Future work includes determining the association with children's mental health disorders, while accounting for individual and neighborhood variables. This ecological model can inform social epidemiology and contextual disparities in children's health.

Perinatal Medication Exposure and Mother-Infant Outcomes: Insights from the BELpREG registry in Belgium

Laure Sillis[1,2], Veerle Foulon[1], Karel Allegaert[1,3], Annick Bogaerts[3], Maarten De Vos[4], Titia Hompes[5], Anne Smits[3], Kristel Van Calsteren[3], Jan Y Verbakel[6], Michael Ceulemans[1]

[1]Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, [2]Research Foundation Flanders (FWO), [3]Department of Development and Regeneration, KU Leuven, [4]Department of Electrical Engineering (ESAT), KU Leuven, [5]Department of Neurosciences, KU Leuven, [6]Department of Public Health and Primary Care, KU Leuven

Background: The Belgian pregnancy registry, BELpREG, collects real-world data on perinatal medication exposure and mother-infant outcomes through online self-reported questionnaires. After enrollment, women receive follow-up questionnaires every four weeks until eight weeks postpartum, with additional questionnaires on child development at 6 and 12 months post-birth. This study assessed the first year's cohort characteristics, including prevalence estimates and type of medication used as well as longitudinal follow-up rates.

Methods: Data collection started in November 2022. Pregnant women aged ≥18 and receiving care from any Belgian healthcare service, were eligible for enrollment. Data for this descriptive analysis were extracted on December 7th, 2023.

Results: In total, 656 women participated, with 549 fully completing the enrolment questionnaire (83.7%). Most participants were aged 25-34 (84.8%) and recruited through social media (53.8%). Median gestational age at enrolment was 18 weeks. Completion rates for the 1st, 2nd and 3rd follow-up questionnaires during pregnancy and the two postpartum questionnaires were 81.1%, 74.4%, 73.1%, 88.1% and 81.0%, respectively. Most participants were highly educated (85.2%) and employed (97.0%). 18.6% of pregnancies occurred after fertility treatment. 36.4% reported pre-pregnancy chronic conditions. 87.1% reported medication use since pregnancy onset, mainly analgesics and systemic antihistamines, with paracetamol (43.1%) and doxylamine/pyridoxine (26.1%) being the most reported compounds. BELpREG also includes pregnancy cases using less studied and teratogenic medications.

Conclusions: Perinatal medication exposure and outcome data are collected in the BELpREG registry. Its ability to gather information on poorly studied medications, coupled with increasing participant engagement, highlights its potential as a valuable research instrument.

Early-life environmental factors and genetic risk in Juvenile Idiopathic Arthritis: Insights from Norwegian and Danish pregnancy cohorts

Kristine Løkås Haftorn[1], Hamid Rudsari[1], Sigrid Hestetun[1], Vilde Dåstøl[1], Anne Lise Brantsæter[2], Piotr Jaholkowski[3], Ida Caspersen[1,4], Siri Håberg[4], Ketil Størdal[5], Sjurdur Olsen[6], Helga Sanner[1]

[1]Department of Rheumatology, Oslo University Hospital, [2]Department of Food Safety, Norwegian Institute of Public Health, [3]Institute of Clinical Medicine, NORMENT Centre, University of Oslo, [4]Centre for Fertility amd Health, Norwegian Institute of Public Health, [5]Division of Pediatric and Adolescent Medicine, Oslo University Hospital, [6]Statens Serum Institut

Background: 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.

Objective: 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.

Conclusion: 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.

Sociodemographic and perinatal characteristics related to suboptimal body mass index among five-year-old children born very preterm: results from a European cohort

Soodabeh Behboodi[1], Adrien Aubert[1], Jennifer Zeitlin[1]

[1]1 Université Paris Cité, Inserm, INRAE, Centre for Research in Epidemiology and StatisticS (CRESS), Obstetrical Perinatal and Pediatric Epidemiology Research Team, EPOPé, F-75004

Objective: Very preterm (VPT) birth may be associated with increased risks of metabolic disease in later life. We described the prevalence and sociodemographic and perinatal characteristics associated with underweight and overweight-obesity (OWOB) among five-year old children born VPT, a key baseline point, for which data are sparse.

Methods: Data come from the population-based EPICE-SHIPS cohort of VPT births (<32 weeks' gestation) in 11 European countries in 2011-2012, with follow-up at five years of age by parental questionnaire (N=3310). We used multinomial logistic regression to estimate associations of underweight and OWOB, defined using IOTF cut-offs, with sociodemographic and perinatal characteristics, applying inverse probability weights to correct for attrition.

Results: Thirty percent (n=915) of children were underweight and 9.4% (n=288) were OWOB. Young maternal age was associated with underweight, whereas low maternal education, household unemployment and non-European maternal country of birth were associated with OWOB. Children with birthweight <3rd percentile were more often underweight and less often OWOB. Other characteristics were associated with a lower likelihood of OWOB only (male sex, multiple birth and postnatal growth restriction) or a higher likelihood of underweight only (late onset infections, bronchopulmonary dysplasia). Gestational age and non-respiratory neonatal morbidity were not related to either outcome.

Conclusions: At five years of age, 40% of children born VPT had a suboptimal BMI status, principally due to being underweight. Sociodemographic and perinatal characteristics associated with underweight and OWOB were distinct. These may independently determine future growth patterns and metabolic risks and should be considered in future investigations.

Statistical methods to detect genetic effects associated with infertility and assisted reproductive technology

Siri Nærland Skodvin[1,2], Miriam Gjerdevik[1,3], Astanand Jugessur[1,2], Julia Romanowska[1,2], Christian Magnus Page[4], Alexandra Havdahl[5,6], Elizabeth Corfield[5,6], Yunsung Lee[1], Siri Eldevik Håberg[1,2], Hans Ivar Hanevik[1,7], Robert Lyle[1,8], Rolv Terje Lie[1,2], Håkon Kristian Gjessing[1,2]

[1]Centre for Fertility and Health, Norwegian Institute of Public Health, [2]Department of Global Public Health and Primary Care, University of Bergen, [3]Department of Computer Science, Electrical Engineering and Mathematical Sciences, Western Norway University of Applied Sciences, [4]Department of Physical Health and Ageing, Division of Mental and Physical Health, Norwegian Institute of Public Health, [5]PsychGen Centre for Genetic Epidemiology and Mental Health, Norwegian Institute of Public Health, [6]Nic Waals Institute, Lovisenberg Diaconal Hospital, [7]Department of Fertility, Telemark Hospital Trust, [8]Department of Medical Genetics, Oslo University Hospital and University of Oslo

Background: Several stages of genetic selection are at play prior to a birth. Genetic factors may influence one or both parents' ability to conceive, as well as the likelihood of fetal survival. For couples struggling to conceive, assisted reproductive technology (ART) may provide help. Analyzing parents and children within the context of ART usage, we explored the timing of these genetic selection events. Our study introduces innovative statistical models that enable the separate and joint estimation of genetic impacts from parents and their offspring.

Methods: We analyzed genetic data from family triads and dyads in the Norwegian Mother, Father, and Child Cohort Study, which included approximately 1,300 children conceived by ART. We studied interaction effects of parental alleles with their use of ART as the study outcome. We also investigated differences in allele distributions between ART- and non-ART-conceived children. Finally, we analyzed parental and fetal effects simultaneously in a combined model.

Results: Parental interaction effects were identified in genes such as DNAH17. Additionally, we identified fetal effects in ART-conceived offspring in CXXC4 and DYNLRB2. Our combined model further identified significant parental interaction effects in MOV10L1.

Conclusion: Some genes identified in our analyses have previously been linked to fertility-related traits. It is plausible that these genetic effects manifest at different stages of genetic selection, before or after fertilization. Interpretations of these gene findings must be contextualized within the framework of our model specifications. In conclusion, our findings comprise a significant foundation for further exploration into genetic selection processes prior to birth.

Trends in adverse pregnancy outcomes and treatment in pregnancy with systemic lupus over two decades in Sweden

Ngoc V. Nguyen[1], Julia Simard[1,2], Annica Dominicus[1], Anna Sandström[1,3], Karin Hellgren[1], Elisabet Svenungsson[4], Elizabeth Arkema[1]

[1]Clinical Epidemiology Division, Department of Medicine Solna, Karolinska Institutet, [2]Division of Immunology and Rheumatology, Department of Medicine, Stanford School of Medicine, and Department of Epidemiology and Population Health, Stanford School of Medicine, [3]Division of Obstetrics, Department of Women's Health, Karolinska University Hospital, [4]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Karolinska University Hospital

Background: Pregnancies with systemic lupus erythematosus (SLE) have a high risk of adverse pregnancy outcomes (APOs). We examined nationwide temporal trends in APOs and treatments in SLE pregnancies in Sweden.

Methods: This register-based cohort study included 1,417 SLE pregnancies matched 1:10 to 14,169 pregnancies from the non-SLE general population on maternal age, delivery year, and parity during 2003-2022. We assessed calendar trends of the following APOs: preeclampsia, preterm delivery, and small for gestational age (SGA) using linear regression. We compared trends in SLE and non-SLE pregnancies using an SLE*year interaction in logistic models. Among SLE pregnancies, hydroxychloroquine, glucocorticoid, and low-dose aspirin use within six months before and during pregnancy were examined (2007-2022).

Results: Among SLE pregnancies, the mean (min-max) of annual risk of preeclampsia, preterm delivery, and SGA was 9.4% (4.6-18.2%), 16.0% (9.0-34.0%), and 7.5% (2.6-14.9%), respectively. Overall, APOs in SLE pregnancies decreased during 2003-2022, more noticeably in nulliparous vs. parous pregnancies. The mean annual reductions (p-values for trends) in preeclampsia, preterm delivery, and SGA risks were 0.2% (p=0.17), 0.7% (p=0.001), and 0.3% (p=0.004), respectively. APO risks in non-SLE pregnancies were relatively stable during the same period. During 2007-2022 in SLE pregnancies, hydroxychloroquine and aspirin use increased substantially (hydroxychloroquine before pregnancy: 23.4% to 70.0%; hydroxychloroquine during pregnancy: 17.0% to 75.6%; aspirin during pregnancy: 34.0% to 87.8%; all p<0.001). Glucocorticoid use decreased over time both before (p=0.04) and during pregnancy (p=0.07).

Conclusion: APOs in SLE pregnancies in Sweden have improved, which could be partially attributable to enhanced medication treatment and prevention.

Temporal trends and regional variation in severe neonatal morbidity: A nationwide cohort study

Hillary Lynn Graham[1], Martina Persson[1], Kari Johansson[1], Mikael Norman[1], Neda Razaz[1]

[1]*Karolinska Institutet*

Background: Despite reductions in neonatal mortality, defining severe neonatal morbidity (SNM) uniformly remains challenging. The Neonatal Adverse Outcome Indicator (NAOI) offers a comprehensive approach, yet its global adoption varies.

Methods: We conducted a retrospective cohort study in Sweden (2000-2021) using data from the Swedish Medical Birth Register (MBR), linked with the Swedish Neonatal Quality Register (SNQ) and National Patient Register. SNM definitions were derived from NAOI criteria and refined through expert consultation. Patient characteristics and regional variations were examined.

Results: Our cohort included 2.37 million live births. We identified 118,066 SNM cases, with a rate of 505 per 10,000 births (95% CI: 461.2-549.3). Common SNM conditions included infections, resuscitation, ventilation, and intravenous fluids. Composite SNM rates varied regionally, notably higher in Jämtland Härjedalen (RR 1.36, 95% CI 1.34-1.38) and Västerbotten (RR 1.44, 95%CI 1.42-1.47) regions. Temporal trends indicate an increase of SNM in recent years.

Conclusion: Implementing a standardized SNM definition using NAOI criteria in Sweden resulted in comparable SNM rates to peer European countries. This study emphasizes the importance of consistent SNM surveillance for global comparability and may aide in a greater understanding of health monitoring among vulnerable neonates in Sweden.

Global trends in analgesic opioid use in pregnancy

Jonathan Brett[1], Carolyn E Cesta[2], Malcolm B Gillies[1], Brian T Bateman[3], Adrienne YL Chan[4,5,6], Michael Chun-Yuan Cheng[7], Yongtai Cho[8], Eun-Young Choi[8], Jacqueline M Cohen[9], Sarah Donald[10], Kari Furu[9], Mika Gissler[11,12,13], Tara Gomes[14,15,16], Alys Havard[1,17], Sonia Hernandez-Diaz[18], Miyuki Hsing-Chun Hsieh[7], Krista Huybrechts[19], Pär Karlsson[2], Erin Kelty[20], Edward Chia-Cheng Lai[7], Shaleesa Ledlie[14,15,16], T Wang[16], Maarit K Leinonen[11,21], Lianne Parkin[10], Johan Reutfors[2], Ju-Young Shin[8], Chris Tzu-Ting Su[7], Bianca Varney[1], Ian Chi Kei Wong[4,5,22], Kenneth KC Man[4,5,6], Helga Zoega[1,23]

[1]School of Population Health, Faculty of Medicine and Health, University of New South Wales, [2]Centre for Pharmacoepidemiology, Department of Medicine Solna, Karolinska Institutet, [3]Department of Anesthesiology, Perioperative and Pain Medicine, Stanford University, [4]Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, University of Hong Kong, [5]Laboratory of Data Discovery for Health (D24H), Hong Kong Science Park, [6]Research Department of Practice and Policy, UCL School of Pharmacy, [7]School of Pharmacy, Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, [8]School of Pharmacy, Sungkyunkwan University, [9]Department of Chronic Diseases & Centre for Fertility and Health, Norwegian Institute of Public Health, [10]Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, [11]Knowledge Brokers, Finnish Institute for Health and Welfare, [12]Academic Primary Health Care Centre, [13]Karolinska Institutet, Department of Molecular Medicine and Surgery, [14]Li Ka Shing Knowledge Institute, St Michael's Hospital, [15]Leslie Dan Faculty of Pharmacy, University of Toronto, [16]ICES (Institute for Clinical Evaluative Sciences), [17]National Drug and Alcohol Research Centre, Faculty of Medicine and Health, University of New South Wales, [18]Harvard T.H. Chan School of Public Health, Harvard University, [19]Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, [20]School of Population and Global Health, University of Western Australia, [21]Teratology Information Service, Emergency Medicine and Services, University of Helsinki and Helsinki University Hospital, [22]Aston School of Pharmacy, Aston University, [23]Centre of Public Health Sciences, Faculty of Medicine, University of Iceland

Background: Pain is common during pregnancy yet few studies of opioid utilisation in pregnancy exist. We aimed to describe prescription analgesic opioid use during pregnancy across four regions: Oceania [New South Wales (Australia), New Zealand], N-America [Ontario (Canada), United States (US)], Northern Europe [Denmark, Finland, Iceland, Norway, Sweden, United Kingdom (UK)], and East Asia (Hong Kong, South Korea, Taiwan).

Methods: We leveraged linked population-based data and applied a common protocol to measure analgesic opioid use during pregnancy in 2000-2020. We examined prevalence of use and estimated trends over time using prevalence ratios (PR) and 95% confidence intervals (CIs). We quantified use by sociodemographic- and pregnancy characteristics.

Results: Among a total of 20,306,228 pregnancies, 1,115,853 (55 per 1000 pregnancies) had at least one analgesic opioid dispensing or prescription, ranging from 4 per 1000 in the UK to 191 per 1000 in the US publicly insured population. From first to latest years available, we observed the greatest relative decrease in prevalence in Hong Kong (PR 0.2; 95%CI 0.1-0.2) and greatest increase in Iceland (PR 4.4; 95%CI 3.7-5.2). Prevalence tended to be higher among pregnancies of women with lower socioeconomic status, with obesity and those not cohabiting with a partner. Use was more common in late pregnancy than early pregnancy across all populations.

Conclusions: We observed wide global variation in prevalence of analgesic opioid use in pregnancy, yet patterns of use by sociodemographic- and pregnancy characteristics were relatively consistent. Analgesic opioid use remained stable or downward trending over time in most countries.

Intergeneration recurrence of hypertensive disorders of pregnancy through fathers

Aditi Singh[1], Sage Wyatt[1], Liv Grimstvedt Kvalvik[1], Rolv Skjærven[1]

[1]University Of Bergen

Background: Hypertensive disorders of pregnancy (HDP), including preeclampsia (PE) and gestational (GH) hypertension, demonstrate strong intergenerational recurrences through the maternal line. However, the paternal contribution has been relatively unstudied.

Methods: Using the Medical Birth Registry of Norway (1967-2020), we identified 451501 men who fathered their partners' first singleton pregnancies. Relative risks (RR) with 95% confidence intervals (CI) were calculated using log-binomial regression models, adjusted for year of pregnancy, men's age at pregnancy, men's educational status, and partners' age at pregnancy and pre-pregnancy comorbidities. The outcomes were complications in the first pregnancy: preeclampsia, gestational hypertension , placental abruption, small-for-gestational-age 2.5 and stillbirth.

Results: Men exposed to PE in-utero had higher risks of fathering PE (RR 1.4; 95%CI 1.3-1.5) and GH (RR 1.2; 95%CI 1.1-1.4); while men exposed to GH in-utero had increased risks for PE only (RR 1.2; 95%CI 1.1-1.3). Increased risks were not observed for the other pregnancy complications. Partners with in-utero exposure to HDP had higher risks for HDPs in their own pregnancies, but this was not influenced by the men's in-utero exposure to HDP. Men unexposed to HDP in-utero, born before or after HDPs, had no increased risks of fathering pregnancies with complications.

Conclusion: Our findings suggest that men exposed to HDP in-utero independently contribute to the occurrence of HDP in their partners' pregnancies. Familial susceptibility alone doesn't account for the heightened risk of fathering HDP following in-utero exposure. Furthermore, the increased risk among partners exposed to HDP in-utero was not modified by the men's in-utero HDP status.

Preterm birth, being born small for gestational age and the risk of multimorbidity in childhood: a whole-population cohort study

Katriina Heikkilä[1], Johanna Metsälä[1], Anna Pulakka[4], Sara Marie Nilsen[5], Kari Risnes[7], Suvi Alenius[1], Eveliina Ronkainen[8], Eero Kajantie[8]

[1]Finnish Institute for Health and Welfare, [2]Department of Public Health, University of Turku, [3]Centre for Population Health Research, University of Turku and Turku University Hospital, [4]Research Unit of Population Health, University of Oulu, [5]Centre for Health Care Improvement, St Olavs Hospital, [6]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, [7]Children's Clinic, St. Olavs Hospital, [8]Clinical Medicine Research Unit, Oulu University Hospital and University of Oulu

Background: Multimorbidity affects people of all ages but the risk factors of multimorbidity in childhood are unclear. We examined the associations of preterm birth and birth weight with the risk of multimorbidity in childhood.

Methods: We used whole-population multi-register data from Finland (1,035,190 children born in 1998-2015). Gestational age was categorised as 23-36 weeks (preterm), 37-38 weeks (early term), 39-41 weeks (full-term) and 42-44 weeks (post-term). Birth weight in relation to gestational age was categorised into small for gestational age (SGA: weight <10th percentile of weights expected for the gestational age) and appropriate for gestational age (AGA: weight ≥10th percentile). Multimorbidity at age 1-10 years was ascertained from specialised healthcare, cancer and mortality registers. We calculated hazard ratios (HRs) and population attributable fractions (PAFSs) with 95% confidence intervals (CIs) for multimorbidity (two, three or four health outcomes) during childhood.

Results: During the 5,569,817 person-years of follow-up from age 1 to 10 years (mean: 6 years; standard deviation: 3 years), 334,699 health outcomes and 1,693 deaths occurrred. Confounder-adjusted HRs comparing children born preterm and SGA to those born full-term and AGA were 2·04 (95% CI: 1.95 to 2·15) for two health outcomes (PAF: 8·0%, 95% CI: 7·5 to 8·5), 3.2 (95% CI: 2.97 to 3.43) for three health outcomes (PAF: 15.1%, 95% CI: 14.2 to 16.1) and 5·15 (95% CI: 4·62 to 5·73) for four health outcomes (PAF: 23·6%, 95% CI: 21·9 to 25·2).

Conclusion: Our findings indicate that children born preterm and SGA have increased risks of diverse multimorbidity patterns

Evaluating perinatal health in Europe: a comparison of routine population birth data sources

Marianne Philibert[1], Mika Gissler[2,3], Oscar Zurriaga[4,5], Serena Donati[6], Zeljka Drausnik[7], Günther Heller[8], Ashna Mohangoo[9,10], Alison Marcfarlane[11], Luule Sakkeus[12], Vlad Tica[13], Petr Velebil[14], Jennifer Zeitlin[1]

[1]EPOPé, Université Paris Cité, Inserm, [2]THL Finnish Institute for Health and Welfare, [3]Karolinska Institute, [4]Preventive Medicine and Public Health Departement, University of Valencia, [5]FISABIO, Rare Diseases Research Area and Mixed Unit FISABIO-UVEG, [6]National Center for Disease Prevention and Health promotion - Istituto Superiore di Sanità, Italian (ISS), [7]Division of Public Health, Croatian Institute of Public Health, [8]Institute for quality assurance and transparency in healthcare IQTIG, [9]Foundation for Perinatal Interventions and Research in Suriname (PeriSur), [10]Tulane University School of Public Health and Tropical Medicine, [11]Maternal and Child Health and Care Research Centre, City University London, [12]Estonian Institute for Population Studies, Tallinn University, [13]East European Institute for Reproductive Health, Faculty of Medicine, University "Ovidius" Constanţa, [14]Institute for the Care of Mother and Child, Prague and 3rd Medical School of Charles University

Background: International comparisons of national data provide essential benchmarks for evaluating perinatal health. This study described population birth data sources in Europe and their ability to provide core perinatal indicators.

Methods: The Euro-Peristat Network collected routine national data on a recommended set of core indicators from 2015 to 2021 using a federated protocol based on a common data model with 17 data items. Data providers filled in a questionnaire about the sources used. We classified countries by the number of data items they provided (all 17, 16-15, <15).

Results: 27 countries responded to the survey. Routine data sources included birth certificates (N=14), electronic medical records (EMR) from delivery hospitalizations (N=12), direct entry by health providers (N=8), EMR from other care providers (N=6) and Hospital Discharge Summaries (N=6). Completeness of population coverage was over 97%, with 15 countries reporting 100%. Databases most often included births on the national territory, regardless of nationality or residency (N=18). Most databases linked sources (N=21), including births with death certificates (N=14). Countries providing 17 items (N=7) were more likely to use delivery hospitalization EMRs, 86%, compared to 55% and 38% in countries with 16-15 items (N=11) and <15 items (N=8). Linkage was more common in these countries (86%), versus 64% and 50%, respectively. Other data source characteristics did not differ by data items provided.

Conclusions: There is high diversity in the data sources used to construct perinatal health indicators in Europe. Countries using EMR with linkage to other sources had the best data availability.

Integrating human genetics and proteomics to accelerate the development of new therapies for adverse pregnancy outcomes

Maria Carolina Borges[1,2], Marwa Al Arab[1,2], Nancy McBride[1,2], Qian Yang[1,2], Maria Magnus[3], Deborah Lawlor[1,2]

[1]MRC Integrative Epidemiology Unit at the University of Bristol, [2]Population Health Science, Bristol Medical School, University of Bristol, [3]Centre for Fertility and Health, Norwegian Institute of Public Health

Background: Pregnant women are underrepresented in clinical research. There is a pressing need to discover new drug targets for managing adverse pregnancy and perinatal outcomes (APPOs). Using Mendelian randomization (MR), we examined the effect of 1,615 circulating proteins on the risk of 20 APPOs.

Methods: We used data from the deCODE plasma proteomics genome-wide association study (GWAS) with 35,559 participants to identify 4,650 genetic instruments strongly associated with protein levels and located within/nearby the respective protein-coding gene. Maternal GWAS data for APPOs were obtained from the MR-PREG collaboration (N up to 623,808). We estimated MR effects using the generalised inverse variance weighted method.

Results: MR results suggest potential causal effects of 173 proteins on one or more APPOs (false discovery rate (FDR) p-value < 0.05). These include new targets for treating APPOs with limited therapeutic options; e.g. 19 proteins identified as potentially causal for spontaneous preterm birth. Additionally, we identified proteins currently targeted by existing drugs approved for other indications, which may have causal effects on APPOs — e.g. renin, targeted by antihypertensives, is related to preeclampsia risk.

Conclusion: Our preliminary findings illustrate the potential of human genetics and high throughput proteomics to identify new drug targets, as well as repurposing opportunities, to improve management of APPOs. We are currently incorporating data from additional studies to increase statistical power and assess replication, as well as conducting sensitivity analyses to validate our genetic instruments in pregnancy and assess key sources of bias (e.g. due to linkage disequilibrium or fetal genetic effects).

Pilot study of a model for a national health profile among pregnant women

Tina Harmer Lassen[1], Mette Rasmussen[1], Heidi Rosendahl[1], Lotte Broberg[2], Peter Elsborg[2], Peter Bentsen[2,3], Trine Pagh Pedersen[1], Christina Bjørk Petersen[1,2]

[1]National Institute of Public Health, University of Southern Denmark, [2]Center for Clinical Research and Prevention, Copenhagen University Hospital – Bispebjerg and Frederiksberg, the Capital Region of Denmark, [3]Department of Geosciences and Natural Resource Management, University of Copenhagen, [4]Centre for Childhood Health

Background: Maternal health surveillance is an essential part of public health as it can identify important risk factors and thereby point towards relevant areas of interventions to promote health and well-being among the women and their children. The aim of this pilot study is to develop a model for using existing, nationally representative data to establish a health profile with information on maternal health, well-being, and health behavior before and during pregnancy.

Methods: The health profile will be based on self-reported data routinely collected through the electronic patient-reported (PRO) questionnaires, which are filled out by the pregnant women before their first antenatal visit. The PRO-questionnaires provide information about e.g., maternal mental health, health behavior and social relations. Currently, eight maternity units from three of five regions in Denmark have implemented the PRO-questionnaires as part of routine clinical practice. In addition, the self-reported data will be linked to register-based information, e.g. from the Danish Medical Birth Register.

Results: The prevalence of relevant indicators of health, well-being, and health behavior among Danish pregnant women will be presented. In addition, the quality and representativeness of the PRO-questionnaire data will be described.

Conclusion: The routinely collected PRO-questionnaire data combined with clinical register-based information constitute a valuable source of information on health, well-being and health behavior among pregnant women in Denmark, which will be presented through this pilot study and the applicability of the data for a future national health profile among pregnant women will be evaluated.

A population-based cohort to assess drug safety in pregnancy using real-world data. Characterization of the PregVal cohort.

Francisco Sánchez-Sáez[1], Gabriel Sanfélix-Gimeno[1], Isabel Hurtado[1], Aníbal García-Sempere[1], Celia Robles-Cabaniñas[1], Salvador Peiró[1], Clara Liliana Rodríguez-Bernal[1]

[1]Health Services Research and Pharmacoepidemiology Unit. FISABIO.
Background: Electronic health- and associated records offer an important opportunity to assess real-world safety of medications during pregnancy.

Methods: Design: Retrospective population-based cohort, comprised by all pregnancies (Jan-2009-Dec-2021), followed from 1y pre-conception until end of study. Data source: Valencia Integrated database (VID), Spain, covering a 5 million population; Statistical analyses: 1) Descriptive analysis of the characteristics of the cohort 2) Rates of pregnancy outcomes; 3) Frequency of drug use by therapeutic group.

Results: We identified 620107 pregnancies during the study period. Mean age of the cohort was 31.4y, 26.2% were foreigners, 17.8% were at risk of social exclusion. Regarding clinical variables, 2.1% had chronic hypertension,1.7 % diabetes, 7.1% depression and 6.4% obesity at baseline; 6% had diagnosis of gestational diabetes, 0.9% gestational hypertension and 1.1% preeclampsia. Rates of pregnancy outcomes were: 1.38% congenital anomalies (1.8% for LB, 4.1 for SB); 18.6% spontaneous abortion; 2.5% elective termination; 0.37% stillbirth; 73.9% live birth (LB), 9.1% preterm birth and 8.8% LBW. Lost to follow was 0.07%. Drug use: 56.4% of the cohort had at least 1 medicine dispensed (62.2% for LB). The most used ATC's were: B03 antianemics 30%, J01 antibacterials 20% and N02 analgesics 18%.

Conclusion: The population-based nature of PregVal, the ability to detect livebirths and pregnancy losses, and to link mothers-offspring with long-term follow up, the availability of a large number of covariates and outcomes, and the possibility to estimate drug exposure and its timing accurately, are key features to generate reliable evidence on drug safety in pregnancy.

Women’s pregnancy history and partners' cardiovascular mortality

Liv Grimstvedt Kvalvik[1], Rolv Skjærven[1], Gerhard Sulo[1], Aditi Singh[1], Quaker Harmon[2], Allen Wilcox[2]

[1]Universitetet i Bergen, [2]The National Institute of Environmental Health Sciences

Background: A woman’s full pregnancy history is associated with her risk of dying from atherosclerotic cardiovascular disease (CVD). We assessed 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.

Prematurity and risk of suicidal behavior in adulthood: emulating a target trial using national cohort data

Ophélie Collet[1], Sylvana M Côté[1], Massimiliano Orri[2], Annette Erlangsen[3]

[1]University of Montreal, [2]McGill University, [3]Danish Research Institute for Suicide Prevention

Background: Suicide is a leading cause of premature mortality among youths. At the same time, prematurity, i.e. preterm birth, affects around one in ten births and has been linked to an increased risk of suicide. Yet, it is unclear to what extent this association reflects a causal mechanism, since multiple residual biological and socioeconomic factors can confound this association. Given that randomised trials to test causality are unfeasible in this context, the aim of this study is to examine whether prematurity is associated with suicide using a causal inference design.

Methods: Using data from Danish administrative registers (N 4,400,000) we investigate the putative effect of prematurity on suicide. Using Poisson regressions, we estimated intention-to-treat effect of prematurity while adjusting for baseline risk factors via inverse-probability-weighting. Sex differences and a possible dose-response effect of prematurity (late, severe, extreme) were examined.

Results: Preliminary findings showed that severe prematurity (<32 weeks of amenorrhoea) was linked to an excess risk of suicide (OR:1.15, CI-95%: 1.06-1.24) for both male and female offspring, while no association was associated for moderate prematurity (≥32-37 weeks of amenorrhoea; OR:0.99, CI-95%: 0.93-1.06). In the next step, we will investigate whether these associations hold using the planned causal inference analyses, and whether they are moderated by sex.

Conclusion: A better understanding of the role of prematurity in suicide aetiology is important to inform early population-based actions for suicide prevention. These results can inform health care policies and enhance support systems for individuals born preterm with the goal of early life suicide prevention.

Melatonin use in pregnancy: a Scandinavian drug utilization study

Silvia Segovia Chacón[1], Mette Bliddal[2], Phillip Brenner[1,2], Jacqueline M Cohen[4], Julia Eriksson[1], Kari Furu[4], Natalie Holowko[5], Anne Örtqvist Rosin[5], Johan Reutfors[1], Carolyn E Cesta[1]

[1]Centre for Pharmacoepidemiology, Karolinska Institutet, [2]Research Unit OPEN, University of Southern Denmark, [3]Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, & Stockholm Health Care Services, [4]Dept of Chronic Diseases & Centre for Fertility and Health, Norwegian Institute of Public Health, [5]Division of Clinical Epidemiology, Karolinska Institutet

Background: Melatonin is commonly used for sleep disturbances, and its use has greatly increased over the last decades in the general population. Whether use has also increased among pregnant women is unknown.

Methods: Data sources included publicly available national statistics in Denmark (2006-2022) and individually linked data from nationwide health registers in Sweden (2006-2019) and Norway (2005-2020). Prevalence of melatonin use was calculated as the proportion of pregnancies in which women filled ≥1 prescription of melatonin from the last menstrual period (LMP) to delivery. Characteristics of melatonin users were described.

Results: Melatonin use occurred in 580 (0.06%) pregnancies in Denmark, 1210 (0.08%) in Sweden, and 1416 (0.16%) in Norway, of which the majority had a prescription filled only in the first trimester. Over the study period, use increased from 0% to 0.20% in Denmark, to 0.34% in Sweden, and to 0.37% in Norway. In all three countries, the highest use was among pregnant women ≤19 years of age followed by those aged ≥40 years. In the Swedish and Norwegian cohorts, melatonin users more often smoked in early pregnancy, had higher BMI, and used antiepileptics, antipsychotics, anxiolytics, antidepressants, and central stimulants in the year before LMP to the end of pregnancy, compared to non-users.

Conclusion: In the last two decades, use of melatonin in pregnant women in Scandinavia has increased substantially. Concurrent psychotropic co-medication reflects a higher psychiatric burden among melatonin users. Planned future research on the safety of melatonin use in pregnancy will include robust confounding adjustment for psychiatric-related covariates.

Patterns of antihypertensive medication use in the first two years postpartum - Influence of antenatal antihypertensive medication use and hypertensive disorders of pregnancy

Frederikke Lihme[1], Saima Basit[1], Baskaran Thilaganathan[2], Heather Boyd[1]

[1]Statens Serum Institut, [2]Fetal Medicine Unit, St. George's Hospital, University of London

Background: Women who had a hypertensive disorder of pregnancy (HDP) have increased risks of later chronic hypertension, but management of postpartum hypertension remains poorly informed, inconsistent, and fragmented.

Methods: In a register-based cohort study, we estimated cumulative incidences and hazard ratios for initiation of antihypertensive medication use in the two years following a woman's first pregnancy in the period 1995-2018, by HDP status and antenatal antihypertensive medication use.

Results: The cohort included 784,782 women. Two-year cumulative incidences of initiating antihypertensive treatment were influenced by the severity of HDP and antenatal antihypertensive use and ranged from 1.8% in women who had not had HDPs to 44% in women with severe preeclampsia who required antihypertensive medication during pregnancy. Most women who required postpartum antihypertensive medication after an HDP initiated use within three months of delivery (severe preeclampsia, 87%; preeclampsia, 75%; gestational hypertension, 75%). In contrast, 13% of women with severe preeclampsia, 25% of women with preeclampsia, 25% of women with gestational hypertension, and 77% of those without an HDP in pregnancy first filled a prescription for antihypertensive medication more than three months after delivery.

Conclusion: Postnatal antihypertensive use is influenced by HDP status, HDP severity, and antenatal antihypertensive medication use. Up to a quarter of women initiated antihypertensive medication more than three months after an HDP, with up to 12% initiating treatment after one year. Routine and systematic postpartum blood pressure monitoring might prevent diagnostic delays and improve cardiovascular disease prevention in women.

Rationale and design of proteogenomics in a Danish population-based birth cohort

Roelof Adriaan Johan Smit[1], Inger Meder[2], Nis Brix[3], Mette Nyegaard[2], Katrine Strandberg-Larsen[1], Cecilia Ramlau-Hansen[3], Sjurdur Olsen[2], Bjarke Feenstra[2], Ruth Loos[1]

[1]University of Copenhagen, [2]Statens Serum Institut, [3]Aarhus University

Background: The global prevalence of child and adolescent obesity has quadrupled in recent decades, coinciding with earlier pubertal timing, a rise in eating disorders, and reduced fertility. Biomarkers associated with rapid infancy and childhood weight change, measured at birth or shortly after, could be early predictors of these outcomes and future obesity. Moreover, changes in maternal health, encompassing pregnancy, and the pre-/postnatal environment play crucial roles in determining growth and maturation of the child. We aim to identify proteogenomic drivers and predictors of early life development and maternal health in mother-child pairs.

Methods: We will genotype the DNA of 15,819 'children' (born 2000-2003) and their mothers from the Danish National Birth Cohort (DNBC) Puberty Cohort, using a modified version of the Illumina Global Screening Array. In addition, we will perform proteomic measurements of neonatal dried blood spots (PKU cards) of 2,000 children and corresponding maternal plasma samples at two pregnancy stages using mass spectrometry and the Olink Explore-HT platform (5,400+ proteins). Sample selection will balance representativeness with phenotype availability.

Results: ----The data generation is expected to begin by summer 2024. The proteogenomic datasets will be made available via application to the DNBC management (https://www.dnbc.dk).

Conclusion: Enriching the DNBC with proteogenomic data will enable the identification of genetic variants and proteins that play a role in the intricate relationship between pregnancy, growth and maturation during childhood and adolescence, eating disorders, and fertility. These biomarkers may facilitate early identification of individuals at risk during or after pregnancy, allowing timely prevention or intervention.

School performance of children born to mothers with hyperemesis gravidarum

Martha Veber Fogh[1], Rikke Wiingreen[2,6], Anne Ostenfeld[7], Tine Dalsgaard Clausen[2,3], Lone Krebs[2,4], Olav Bjørn Petersen[2,3], Gorm Greisen[2,5], Christina Engel Hoei-Hansen[1,2], Mads Langager Larsen[1,3]

[1]Center for Cerebral Palsy, Department of Pediatrics and Adolescent Medicine, Copenhagen University Hospital – Rigshospitalet, [2]Department of Clinical Medicine, University of Copenhagen, [3]Department of Fertility, Gynecology and Obstetrics, Copenhagen University Hospital – Rigshospitalet, [4]Department of Obstetrics and Gynecology, Copenhagen University Hospital – Amager-Hvidovre Hospital, [5]Department of Neonatology, Copenhagen University Hospital – Rigshospitalet, [6]Department of Paediatrics, Copenhagen University Hospital – Nordsjaelland Hospital, [7]Department of Gynecology and Obstetrics, Copenhagen University Hospital – Nordsjaelland Hospital

Background: Hyperemesis gravidarum (HG) is characterized by severe nausea, vomiting, and potentially undernutrition during pregnancy. Despite affecting up to 3% of pregnancies, little is known about the impact of HG on the cognitive development of the child. We aimed to compare school performance in children exposed to HG during pregnancy compared with non-exposed children.

Methods: A population-based cohort study including all liveborn children in Denmark between 1986–2005. School performance was evaluated using overall grade point averages (GPAs) and a composite outcome of low academic performance, defined as a low (<4) or no registered GPA. Furthermore, where possible, exposed siblings were compared with their unexposed siblings. Groups were compared using mixed-effects models, adjusting for sex, birth year, parity, multiple pregnancy, and maternal age, smoking and education.

Results: Among 1,229,234 included children, 12,720 (1.1%) had a maternal diagnosis of HG during pregnancy. In total, 29.3% of exposed children had low academic performance compared to 25.7% of non-exposed children, yielding an adjusted odds ratio (aOR) of 1.19 (1.14–1.24). Furthermore, exposed children had a lower mean GPA of 6.55 compared with 6.78 in non-exposed children, with an adjusted mean difference of -0.18 (-0.22– -0.14). However, the within-sibling analyses revealed no difference in low academic performance (aOR 0.98 (0.92–1.04) or adjusted mean difference (-0.02 (-0.8–0.05)) between exposed and unexposed siblings.

Conclusion: We found a small association between exposure to HG during pregnancy and lower school performance. However, the differences seem without clinical relevance and the within-sibling analyses indicate it being attributable to unmeasured confounders.

Is Placental Weight associated with Placental Pathology?

Genevieve Monaghan[1], Gemma Clayton[1], Carolina Borges[1], Deborah Lawlor[1], Rachel M. Freathy[2], W. Tony Parks[3], Janet Catov[4], Abigal Fraser[1]

[1]University of Bristol, [2]University of Exeter, [3]University of Toronto, [4]University of Pittsburgh

Background: Placental weight (PW) is an accessible placental measurement, available in large birth registries. PW is thought to be a marker of placental function, although PW to birthweight ratio (PW/BW) has been suggested as a more accurate measure of placental function. Associations of PW and PW/BW with maternal mortality, preeclampsia, and cardiovascular disease have been previously reported. Here we investigated whether PW and PW/BW are associated with placental pathology, classified as maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM), chronic inflammation (CI), or acute inflammation (AI).

Methods: We used data on N=22,716 women with singleton pregnancies and available placental pathology data, who delivered at Pittsburgh's Magee-Women's Hospital from January 2008 to October 2012. We used logistic regression to estimate odds ratios (OR) of placental pathology traits per 1 standard deviation (SD) difference in PW or PW/BW, adjusted for gestational age and fetal sex.

Results: Mean PW and PW/BW were 444.1g (SD=119.4) and 0.14 (SD=0.04) respectively. Higher PW was associated with lower odds of MVM (OR=0.94; 95% confidence intervals: 0.91, 0.97) and CI (0.97; 0.94, 1.00), but not with FVM or AI. Higher PW/BW was associated with higher odds of MVM (1.07; 1.04, 1.11), FVM (1.14; 1.10, 1.18), AI (1.20; 1.16, 1.24), and CI (1.13; 1.09, 1.17).

Conclusion: Our results show that both PW and PW/BW are indicators of multiple types of placental pathology.

Infant environmental phenol exposure and ovarian function during minipuberty

Helen Chin[1], Jenna Krall[1], Danielle Stevens[2], Mandy Goldberg[2], Margaret Adgent[3], Donna Baird[2], Walter Rogan[2], David Umbach[4]

[1]Department of Global and Community Health, College of Public Health, George Mason University, [2]Epidemiology Branch, National Institute of Environmental Health Sciences, [3]Department of Health Policy, Vanderbilt University Medical Center, [4]Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences

Background: Phenols are endocrine-disrupting chemicals that can dysregulate estrogen signaling. Infancy represents a period of increased vulnerability to phenols because of hormonal changes known as minipuberty. Previously in the Infant Feeding and Early Development (IFED) study, we measured anti-Mullerian hormone (AMH) in 153 infant girls from serum collected up to 11 times between 2 to 36 weeks of age and classified girls into four groups based on their AMH trajectories. Here we investigate the association between urinary phenol concentrations and AMH group: decreasing, early peak (at 12 weeks), middle peak (at 20 weeks), and low.

Methods: IFED is a longitudinal cohort of healthy term infants recruited from hospitals in Philadelphia (2010-2013). We quantified phenol concentrations from urine samples collected at 6 or 8 and at 12 weeks in 94 of the 153 girls. We considered average concentrations as representing infant exposure and estimated the association between an interquartile range increase in individual phenol concentrations and AMH group using multinomial logistic regression.

Results: Compared to the early peak group, higher methylparaben was positively associated with the low AMH group (relative risk ratio (RRR) 2.45, 95%CI: 0.89, 6.73). Bisphenol A and 2,4 dichlorophenol were positively associated with the decreasing AMH group (RRR 1.51, 95%CI: 0.78, 2.92 and RRR 1.59, 95%CI: 0.87, 2.90).

Conclusion: In this exploratory analysis, urinary phenols were associated with an increased likelihood of being in the low and the decreasing AMH groups. Both groups were first described in IFED and represent hormone patterns outside of the expected minipubertal response.

Attention-deficit/hyperactivity disorder medication use and cardiometabolic conditions in pregnancy: A population-based cohort study

Claudia Mary Bruno[1], Andrea Sit[2], Malcolm Gillies[1], Masako Araki[1], Hegla Zoega[1,3]

[1]Medicines Intelligence Research Program, School of Population Health, University of New South Wales, [2]Postgraduate Program in Public Health, School of Population Health, University of New South Wales, [3]Centre of Public Health Sciences, University of Iceland

Background: Use of medications to treat attention-deficit/hyperactivity disorder (ADHD) is becoming increasingly prevalent among women of reproductive age, but little is understood about their cardiometabolic effects in pregnancy. We aimed to examine potential associations between ADHD medication use and cardiometabolic conditions during pregnancy (gestational hypertension, preeclampsia and gestational diabetes) and the pharmacological treatment thereof.

Methods: Linking statewide hospital and dispensing data, we conducted a population-based matched cohort study of women who gave birth between January 2014 and June 2021 in New South Wales, Australia. We compared the prevalence of cardiometabolic conditions and new cardiometabolic medication use during pregnancy among women who used ADHD medications during pregnancy (n=366) with a 1:10 matched cohort of unexposed women, and also with women who had used ADHD medications in the 12 months before pregnancy (n=252). We used Poisson regression models adjusted for various sociodemographic and pregnancy-related factors.

Results: Compared with unexposed women, women who used ADHD medications during pregnancy had an increased risk of gestational hypertension (RR: 1.76, 95% CI: 1.20-2.57) and gestational diabetes (RR: 1.41, 95% CI: 1.09-1.82), with slightly elevated risk estimates for preeclampsia (RR: 1.30, 95% CI: 0.82-2.05) and new cardiometabolic medication use (RR: 1.40, 95% CI: 0.97-2.01). Compared with women who used ADHD medications before pregnancy, they had a greater risk of gestational diabetes (RR: 1.76, 95% CI: 1.06-2.93).

Conclusions: Women using ADHD medications have higher incidence of cardiometabolic conditions during pregnancy, but it remains unclear to what extent this is attributable to the medication rather than the underlying ADHD.

How do we make population-based, observational research more community-engaged? Experiences from a team studying severe maternal morbidity

Suzan Carmichael[1], Ifeyinwa Asiodu[2], Rachel Berkowitz[3], Patricia Rodriguez Espinosa[1], Audrey Lyndon[4]

[1]Stanford University School of Medicine, [2]University of California, San Francisco, [3]San Jose State University, [4]Rory Meyers School of Nursing, New York University

Background. In recent years, acknowledgement of the importance of community-engaged research practices has increased. Here, we describe our team's journey toward our goal of making our population-based observational research more community-engaged, which is especially important for teams committed to health equity.

Methods. To support our goal, we sought funding; identified ways to enhance our team's community-engaged research expertise; and implemented activities to enhance our team's actual community engagement: e.g., development of a Community Advisory Board (CAB) and a qualitative study of lived experience of severe maternal morbidity (SMM) among Black and Latine women.

Results. We obtained internal pilot funding to support new activities related to community engagement, and later we incorporated support of these activities into broader external grants. We developed further expertise within our team through working with experienced collaborators and seeking supportive immersive experiences (e.g., fellowships). We developed a CAB to inform our research on SMM; the 10-member CAB began meeting quarterly in June 2022. We used the Research Prioritization by Affected Communities protocol to obtain CAB input on priority research questions related to SMM. We have conducted a qualitative study to understand the lived experience of SMM among Black and Latine individuals. We are developing ways to improve dissemination of our work.

Conclusion. As stakeholders rightly increase expectations of research to be more community-engaged, we believe it is important for teams to share their journeys, and that approaches for developing and evaluating a research team's community engagement are needed to bring rigor and accountability to the process.

Preconceptional exposure to metformin and hyperemesis gravidarum in the MotherToBaby cohort

Laure Sillis[1,2,3], Essi Whaites Heinonen[1,4], Michael Ceulemans[2], Diana Johnson[1], Yunjun Luo[1], Christina D Chambers[1]

[1]Department of Pediatrics, University of California San Diego, [2]Department of Pharmaceutical and Pharmacological Sciences, [3]Research Foundation Flanders (FWO), [4]Department of Clinical Science, Intervention and Technology, Karolinska Institutet

Background: Hyperemesis gravidarum (HG), the most severe form of nausea and vomiting of pregnancy (NVP), is reported in 0.3-2.0% of pregnancies, and around 70% of pregnant women experience some level of NVP. The risk of HG has been connected to high levels of fetal growth development factor (GDF) 15 in maternal blood, but higher pre-pregnancy levels of GDF15 seem protective for HG. Treatment with metformin has been shown to increase the levels of GDF15. This study aimed to determine whether pregnant women treated with metformin before pregnancy were less likely to experience HG and NVP than non-exposed.

Methods: This prospective cohort study included pregnant women who participated in the MotherToBaby pregnancy studies between July 29, 2010, and April 9, 2021. Information on HG, NVP and preconceptional metformin treatment was collected through telephone interviews during pregnancy and when available, medical records. Frequencies of HG and NVP were compared between women exposed to metformin before conception and unexposed women.

Results: Information on HG was available for 75 exposed and 1917 unexposed women, and on first-trimester NVP symptoms for 43 exposed and 2640 unexposed women. None of the exposed women experienced HG (0.0%), compared to 28 (1.46%) of unexposed women. The rates of NVP did not significantly differ between the 35 exposed (81.40%) and 2072 unexposed women (78.48%).

Conclusions: In this cohort, women treated with metformin before pregnancy were experiencing similar rates of NVP as the unexposed, but a protective effect on HG cannot be ruled out.

Pregnancy outcomes in mothers with type 1 diabetes in Denmark – Development over 25 years

Tina Wullum Gundersen[1], Sine Knorr Johnsen[2], Lene Ringholm[3,4], Dorte Møller Jensen[5], Peter Damm[3,6], Karoline Kragelund Nielsen[7], Helena Backman Fadl[8], Jeannet Kepp Bruun Lauenborg[9], Elisabeth Reinhardt Mathiesen[3,4], Anne Helby Petersen[10], Niels Skipper[11], Allan Kofoed-Enevoldsen[1], Tine Dalsgaard Clausen[3,6]

[1]Steno Diabetes Center Zealand, Zealand University Hospital Nykøbing F/Denmark, [2]Department of Endocrinology, Aarhus University Hospital, [3]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, [4]Department of Endocrinology, Rigshospitalet, [5]Steno Diabetes Center Odense, Odense University Hospital, [6]Department of Gynecology, Fertility and Obstetrics, Rigshospitalet, [7]Department of Prevention, Health Promotion and Community Care, Steno Diabetes Center Copenhagen, [8]Department of Obstetrics and Gynecology, Faculty of Medicine and Health, Örebro University, [9]Department of Obstetrics and Gynecology, Herlev Hospital, [10]Department of Public Health, Section of Biostatistics, University of Copenhagen, [11]Department of Economics and Business Economics, Aarhus University and CIRRAU, Aarhus Universitet

Background: Maternal type 1 diabetes (T1D) is associated with adverse pregnancy outcomes, widely due to intrauterine hyperglycemia, however, genetics may play a role. We compared pregnancy outcomes of three groups: mothers with T1D (mT1D), fathers with T1D (fT1D), and no parental T1D (noT1D) over 25 years.

Methods: Using Danish, nationwide registers, we included all births and stillbirths after 22 weeks from 1997-2021, divided into 5-year periods. Outcomes: large for gestational age (LGA), preterm delivery (PD) (< 37 weeks), very PD (< 34 weeks), hypertensive disorders in pregnancy (HDP), and cesarean section (CS). We fitted a logistic regression model with an interaction term between time and diabetes. ARs and ORs were calculated.

Results: 1,464,926 deliveries were included, hereof 5,176 mT1D and 7,780 fT1D. ARs for all outcomes remained significantly increased for mT1D compared to both fT1D and noT1D, whereas fT1D were similar to noT1D. ORs showed a significant ($p<0.01$) decrease in LGA, PD, vPD, and CS in mT1D over time as well as an increase in HDP for all three groups. For fT1D and noT1D, we found an increase in CS. Effect modification between diabetes and time showed a significant decrease in PD, vPD, and CS for mT1D relative to noT1D.

Conclusion: Adverse outcomes remain increased in pregnancies of mT1D but not in pregnancies of fT1D. All outcomes, except HDP, decreased over time for mT1D. The development of PD, vPD, and CS showed a relative improvement for deliveries in mT1D. Findings support adverse effects of intrauterine hyperglycemia rather than genetic factors.

The Association of Autism Spectrum Disorder in the Offspring of Mothers and Fathers Diagnosed with Postpartum Depression.

Weiyao Yin[1], Sven Sandin[1], Abraham Reichenberg[2], Michael Silverman[2]

[1]Karolinska Institutet, [2]Icahn School of Medicine at Mount Sinai

Background: Postpartum depression (PPD) affects 7-20% of all parents. While parental psychiatric history is associated with an increased likelihood of autism spectrum disorder (ASD) in the offspring, few studies of PPD exist exploring ASD outcomes, and no study has investigated the association with paternal PPD or the combined influence.

Methods: We explored all live births from 1997 through 2021 using the Swedish National Registers. Depression diagnoses in mothers and fathers within the first postpartum year were obtained from the National Patient Register. Offspring were followed from age one until the first ASD diagnosis, emigration, death, or December 31, 2022, whichever came first. Associations between parental PPD and ASD outcomes were quantified by relative risk (RR) and two-sided 95% confidence intervals (CIs) from Cox regressions.

Results: Among 1,753,195 infant observations, 27,208 were born to parents with PPD (20,502 in mothers, 6,303 in fathers, and 403 in both). For mothers with PPD, the RR of an ASD outcome was 2.63[CI: 2.46-2.80], for fathers 2.56[CI: 2.30-2.85], and both 5.54[CI:4.00-7.68]. When parental age, socioeconomic status, and depression history were controlled for, the RR of ASD outcome when mothers had PPD was 1.71[CI:1.60-1.83], for fathers 1.53[CI:1.37-1.71], and both 2.18[CI:1.57-3.02]. Adjustment for SSRI use or any mental illness before childbirth provided similar results.

Conclusion: ASD outcomes increased comparably when either parent was diagnosed with PPD and increased further when both parents were diagnosed. After adjusting for depression history, SSRI history, or psychiatric history before delivery, this association was reduced, but remained independently associated with increased risk.

Analgesic opioid exposure in pregnancy and the risk of ischemic placental disease

Claudia Mary Bruno[1], Jonathan Brett[1], Bianca Varney[1], Alys Havard[1,2], Malcolm Gillies[1], Hegla Zoega[1,3]

[1]Medicines Intelligence Research Program, School of Population Health, University of New South Wales, [2]National Drug and Alcohol Research Centre, University of New South Wales, [3]Centre of Public Health Sciences, University of Iceland

Background: Studies suggest analgesic opioid use in pregnancy modestly increases the risk of placental disease outcomes, but this relationship is incompletely characterised. We aim to evaluate the association between analgesic opioid use in pregnancy and perinatal outcomes associated with ischemic placental disease.

Methods: We conducted a population-based cohort study, including all pregnancies resulting in birth between July 2012 and 2019, among women residing in New South Wales, Australia. We used linked data on pregnancy and birth outcomes, medication dispensing and health service utilisation. We defined opioid exposure as at least one dispensing between conception until birth, stratifying by different exposure periods during pregnancy (early, late only, both early and late) and individual opioid medication (oxycodone, codeine). We estimated risks for placental abruption, preterm birth, small for gestational age (SGA) and preeclampsia, using time-varying Cox proportional hazard models adjusting for demographics, comorbidities, and medication use.

Results: Of 670,981 pregnancies 41,855 (6.2%) were dispensed an opioid; 22,388 (3.3%) in early, 19,467 (2.9%) in late only and 4,693 (0.7%) in early and late pregnancy. We observed increased risks for placental abruption (aHR 1.20,95% CI 1.06-1.36) and for preterm birth (aHR 1.24,95% CI 1.20-1.29) with opioid use anytime during pregnancy, estimates were higher for oxycodone and in both early and late pregnancy exposure strata. Opioid use did not appear to increase risk for SGA, or preeclampsia.

Conclusions: Our findings are largely consistent with prior studies, with novel findings on the use of individual opioid medications during pregnancy and the risk of ischemic placental disease.

Prenatal Exposure to Acrylamide and Metabolic Status at 20 Years of Age: A Biomarker-Based Cohort Study from Denmark

Marie Pedersen[1], Stéphane Tuffier[1], Efstathios Vryonidis[2], Thorhallur Ingi Halldorsson[3,4], Anne Ahrendt Bjerregaard[3,5], Charlotta Granström[3], Dorte Rytter[6], Bodil Hammer Bech[6], Tine Brink Henriksen[7], Sjurdur Frodi Olsen[3,8], Margareta Törnqvist[2]

[1]University Of Copenhagen, Department Of Public Health, [2]Department of Environmental Science, Stockholm University, [3]Department of Epidemiology Research, Statens Serum Institut, [4]Faculty of Food Science and Nutrition, University of Iceland, [5]Centre for Clinical Research and Prevention, Copenhagen University Hospital - Bispebjerg and Frederiksberg Hospital, [6]Department of Public Health, University of Aarhus, [7]Department of Paediatrics, Aarhus University Hospital, [8]Department of Nutrition, Harvard School of Public Health

Background: Acrylamide (AA) forms in a wide range of commonly consumed foods and drinks during high temperature cooking. Prenatal exposure to AA is of concern as AA crosses the human placenta and maternal dietary intake of AA in pregnancy has been associated with low birthweight and childhood overweight/obesity. It is unknown if prenatal exposure to AA increases the risk of poor metabolic health in adult humans. Our aim was to examine associations between prenatal exposure to AA and metabolic health of adult offspring in a birth cohort from Aarhus, Denmark.

Methods: Hemoglobin (Hb) adducts were measured as internal dose of AA in blood from pregnant women. Waist circumference, weight, height, blood pressure, insulin, leptin, adiponectin and lipid levels were measured in the offspring at 20 years of age (n=359).

Results: AA was detected in all women with a medium level of 84 (range: 27-650) pmol/g Hb. Higher prenatal exposure to AA was associated with higher levels of low-density lipoprotein (LDL) cholesterol in the offspring, where concentrations increased by 0.013 mmol/l (95% confidence interval [95% CI]: 0; 0.03) for every 10 pmol/g Hb increase in AA adduct levels. Also, waist circumference increased with 0.13 cm (95% CI: 0.01; 0.25) per 10 pmol/g Hb increase in AA adduct levels. Associations were attenuated when restricting analyses to offspring of non-smoking mothers (n=222). Other associations evaluated were null.

Conclusions: Our study provides some evidence that prenatal exposure to AA may slightly increase the levels of LDL cholesterol and waist circumference in adult offspring.

Hearing problems and their association with autism spectrum disorder

Nicole Talge[1], Sarah Keim[2], Samrawit Yisahak[2], Ursula Findlen[2], Lindsey Kovacs[2], Brooke Ingersoll[1]

[1]Michigan State University, [2]Nationwide Children's Hospital

Background: Auditory processing difficulties are observed with autism spectrum disorder (ASD). Contributions of hearing problems to this phenomenon are unclear because its association with ASD is not well-characterized. This has implications for diagnosis and intervention for ASD and co-occurring conditions.

Methods: We analyzed cross-sectional, caregiver-reported data from the National Survey of Children's Health (2016-2020). Our United States-based sample included children with data on the presence or absence of hearing problems and ASD (ages 2-18; n=150,327). We used weighted logistic regression to evaluate the association between hearing problems and: 1) ASD diagnostic status (no, yes), 2) ASD symptom severity (none, mild, moderate/severe), and 3) the co-occurrence of ASD with intellectual disability (ID) (neither, ASD only, ID only, both). The "no diagnosis" group served as the referent for each outcome.

Results: Approximately 1% and 3% of children had hearing problems and ASD, respectively. Hearing problems were associated with ASD (OR=2.7, 95%CI 1.8, 3.9). This association was stronger for moderate/severe ASD symptoms (OR=3.5, 95%CI 2.1, 5.7) relative to mild symptoms (OR=1.8, 95%CI 1.1, 3.1) and among children with co-occurring ID (OR=5.0, 95%CI 2.8, 9.0) or ID only (OR=8.6, 95%CI 6.0, 12.4) relative to ASD only (OR=2.4, 95%CI 1.5, 3.8). Findings persisted after adjusting for socio-demographics and were not modified by preterm birth.

Conclusion: Hearing problems are associated with ASD, particularly-though not exclusively-among children with more severe symptoms and co-occurring ID. Future research is needed to determine whether hearing problems in ASD are driven by sensory and/or attentional processing or explained by residual confounding (e.g., congenital anomalies).

Parental psychiatric disorders, preterm birth, and offspring autism risk

Weiyao Yin[1], Jonas Ludvigsson[1], Ulrika Åden[1], Kari Risnes[2], Martina Persson[1], Abraham Reichenberg[3], Michael Silverman[3], Alexander Kolevzon[3], Eero Kajantie[4], Anna Pulakka[4], Marius Lahti-Pulkkinen[4], Matilda Morin[1], Caroline Fyfe[1], Sven Sandin[1,3]

[1]Karolinska Institutet, [2]NTNU, [3]Icahn School of Medicine at Mount Sinai, [4]Finnish Institute for Health and Welfare

Background: Over one in six adults worldwide suffer from psychiatric disorders. Sporadic studies have associated parental psychiatric disorders with preterm birth (PTB) and offspring autism spectrum disorder (ASD). Comprehensively examining association between parental psychiatric disorders, PTB and ASD risk is needed to guide health policy, and inform etiologic studies.

Methods: We included all children born in Sweden and Finland between 1997 and 2016. Diagnoses were obtained from national registers until 2017. We calculated relative risk (RR) and 95% confidence intervals (CIs) for PTB in offspring of fathers and mothers with psychiatric disorders and in both parents jointly using log-binomial regression, and for ASD using Cox regression.

Results: Among 2,505,842 children, 33,612 had ASD, and 145,098 were PTB, with 20% of ASD and 18% of PTB children having parents with psychiatric disorders. We observed a shift towards earlier gestational age in offspring of parents with psychiatric disorders. The PTB and ASD risks were increased across all psychiatric disorders in fathers(PTB: RR=1.12, 95%CI=1.08-1.15; ASD: RR=1.90, 95%CI=1.82-1.99), mothers (PTB: RR=1.31, 95%CI=1.28-1.34; ASD: RR=2.29, 95%CI=2.21-2.37), and both (PTB: RR=1.52, 95%CI=1.46-1.59; ASD: RR=3.72, 95%CI=3.48-3.97), compared to neither parent, and increased with number of co-occurring disorders. The ASD risk was partially mediated by preterm/early-term birth.

Conclusions: Psychiatric disorders in both parents conveyed the highest risk for PTB and ASD, followed by mothers and then fathers. Co-occurring disorders further increased the risk.
To reliably assess ASD risk in children, consider the full range of psychiatric disorders in both parents and number of disorders, not just familial ASD.

Combined effects of perinatal exposures on the risk of hospitalised childhood infections

Isobel Todd[1,2], Maria Magnus[4], Lars Henning Pedersen[3], Natasha Nassar[5], Jessica Miller[1,2], David Burgner[1,2]

[1]Murdoch Children's Research Institute, [2]The University of Melbourne, [3]Aarhus University, [4]Norwegian Institute of Public Health, [5]The University of Sydney

Background: Infections cause significant health burden in early childhood. Despite their interrelatedness, few studies have assessed the effects of multiple adverse perinatal exposures on childhood infection risk. We investigated the combined effects of perinatal exposures on the risk of hospitalised infections using different analytic approaches.

Methods: We studied all live births in Norway between 2008-2018 (n=471340) through national registry linkage. Seven exposures were considered: prenatal antibiotics, smoking during pregnancy, maternal diabetes, hypertensive disorders of pregnancy, birth mode, small for gestational age (SGA) and preterm birth. Using Cox proportional-hazards models, we estimated the risk of hospitalised infection from birth to 5 years for: (1) each exposure independently; (2) number of exposures; (3) each unique combination of the seven exposures; (4) pairwise interactions between exposures.

Results: Each exposure was independently associated with greater hospitalised infection risk with hazard ratio estimates ranging from 1.07 (95% CI 1.05-1.09) for SGA through to 1.55 (95% CI 1.52-1.59) for preterm birth. Cumulative risk was observed for increasing number of exposures from 1.19 (95% CI 1.17-1.20) for one exposure to 2.36 (95% CI 2.06-2.70) for five or more exposures. Analyses of unique exposure combinations showed a particular increased risk among preterm children who were also exposed to one or more other exposures.

Conclusions: Our findings show the cumulative risk of childhood hospitalised infections associated with multiple interrelated perinatal exposures. Our approach highlights a simple and intuitive method for visualising combined effects of co-occurring exposures on a single outcome. We plan to replicate the analyses in other populations.

Parental epigenetic aging and risk of adverse birth outcomes: the Norwegian Mother, Father and Child Cohort Study

Maria Christine Magnus[1], Yunsung Lee[1], Ellen Øen Carlsen[1], Lise Andrea Arge[1], Astanand Jugessur[1,2], Cecilia Ramlau-Hansen[3], Miko Myrskyla[4,5,6], Per Magnus[1], Siri Eldevik Håberg[1,2]

[1]Norwegian Institute of Public Health, [2]University of Bergen , [3]Aarhus University, [4]Max Planck Institute for Demographic Research, [5]Max Planck-University of Helsinki Center for Social Inequalities in Population Health, [6]University of Helsinki

Background: Few studies examined associations between maternal epigenetic age and adverse birth outcomes, while no studies have yet examined associations with paternal epigenetic age.

Methods: We evaluated associations between parental epigenetic age and adverse birth outcomes among 2,198 mothers and 2,193 fathers in the Norwegian Mother, Father and Child Cohort Study (MoBa). Parental epigenetic age was estimated using seven established epigenetic clocks. Linear regression was used for continuous outcomes such as gestational length and standardized birthweight, while logistic regression was used for binary outcomes such as preterm birth, post-term birth, small-for-gestational age (SGA), large-for-gestational age (LGA), and pre-eclampsia. These analyses were adjusted for chronological age, parity, educational level, smoking, and body-mass index.

Results: Increasing maternal epigenetic age acceleration was associated with shorter gestational length in five out of seven clocks, with adjusted mean difference estimates ranging from 0.51-day decrease (95% CI: -1.02, -0.01) per standard deviation increase for the Horvath clock to a 0.75 day decrease (95% CI: -1.26, -0.25) for the Levine clock. A similar association was not observed for fathers. No associations were found with offspring standardized birthweight. Increasing maternal epigenetic age was associated with higher risk of spontaneous preterm birth, with an adjusted odds ratio (OR) of 1.34 per standard deviation increase for the Levine clock, and adjusted ORs of 1.44 for both the Horvath and GrimAge clocks. No notable differences were seen in the risk of post-term birth, SGA, LGA or pre-eclampsia.

Conclusion: Maternal, but not paternal, epigenetic age acceleration is associated with shorter gestational length.

Sex differences in the risk of childhood cancer following ART conception: a Norwegian registry-based study

Laura Oakley[1,2], Dana Kristiansson[1], Monica Munthe-Kaas[1,3], Huong Nguyen Thu[1,4], Yunsung Lee[1], Hans Ivar Hanevik[1,5], Liv Bente Romundstad[1,6], Robert Lyle[1,7], Siri E Håberg[1,8]

[1]Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, [2]Centre for Fertility and Health, Norwegian Institute of Public Health, [3]Department of Pediatric Oncology and Hematology, Oslo University Hospital, [4]Department of Community Medicine and Global Health, University of Oslo, [5]Department of Fertility, Telemark Hospital Trust, [6]Spiren Fertility Clinic, [7]Department of Medical Genetics, Oslo University Hospital, [8]Department of Global Public Health and Primary Care, University of Bergen

Background: Previous research on the association between ART conception and childhood cancer risk has been inconclusive, and the role of child sex in this relationship has not been examined. We investigated whether the risk of childhood cancer following ART conception varies by child sex.

Methods: Cohort study including 2.5 million children born in Norway 1984-2022. Conception type was extracted from the Medical Birth Registry. Childhood cancer was defined as ≥1 diagnosis included in the International Classification of Childhood Cancer 3rd edition (ICCC-3) before age 18. Cox regression models were used to evaluate the age- and sex-specific risk of childhood cancer comparing ART-conceived children to naturally-conceived children.

Results: 5321 (0.2%) children had at least one ICCC-3 diagnosis before age 18. Although the cumulative incidence of childhood cancer was higher in ART-conceived children, there was no strong evidence for an overall association between ART conception and childhood cancer in either boys or girls. However, ART-conceived boys aged 5-9 years had a higher cancer risk compared to those naturally-conceived (aHR 1.80, 95% CI 1.13-2.89). Among boys, ICSI was associated with an increased risk of childhood cancer in boys (aHR for ICSI 1.67, 95% CI 1.15-2.44), as was the use of cryopreserved embryos (aHR 1.91, 95% CI 1.14-3.20).

Conclusion: The overall lack of association observed in this study aligns with some previous studies. However, the identification of increased risks in specific subgroups of ART-conceived boys - particularly those aged 5-9 or those conceived via the use of cryopreserved embryos – deserves further study.

Risk of stillbirth in second singleton births by gestational age in first: a population-based cohort study

Yeneabeba Tilahun Sima[1,3], Rolv Skjærven[1,2], Liv Grimstvedt Kvalvik[1], Kari Klungsøyr[1,4], Linn Marie Sørbye[3,5], Nils-Halvdan Morken[1,3]

[1]Department of Global Public Health and Primary Care, University of Bergen, [2]Centre for Fertility and Health, Norwegian Institute of Public Health, [3]Department of Obstetrics and Gynecology, Haukeland University Hospital, [4]Division of Mental and Physical Health, Norwegian Institute of Public Health, [5]Faculty of Health and Social Sciences, Western Norway University of Applied Sciences

Objective: To assess risk of stillbirth in second pregnancy by gestational age of the first pregnancy and to examine the impact of obstetric interventions on this association.

Methods: This study used linked data from 274,615 women with first two singleton births, registered in the Medical Birth Registry of Norway between 1999-2020. Perinatal losses in first pregnancies were excluded. Proportion of stillbirths were described by time periods; 1999-2009 and 2010-2020. Multivariable regression models were used to calculate relative risk with 95% confidence intervals of stillbirth by gestational age of first pregnancy (20-34, 35-36, 37-38, 39-41 and ≥ 42+) and adjusted for maternal age, education, and smoking. Additionally, we examined whether these findings differed among women with spontaneous- and iatrogenic first deliveries.

Results: Proportions of stillbirth in second pregnancy was 0.30% and 0.28% in 1999-2009 and 2010-2020, respectively. Women who delivered their first baby between 20-34 weeks had a higher risk of subsequent stillbirth compared to those who delivered a first baby at 39-41 weeks. Among women whose first birth occurred at 35-36 weeks, the increased risk of stillbirth was observed only in those who had iatrogenic first births (3.21, 95% 2.05-5.03), while no increased risk for those with spontaneous first births (0.77, 95% CI 0.41-1.43).

Conclusions: The overall rate of stillbirth following a first singleton birth surviving perinatal period remained stable. Women who delivered their first baby before 37 weeks had higher risk of experiencing stillbirth in a subsequent pregnancy except for 35-36 weeks, where risk of stillbirth was not increased.

Assessing the Risk of Major Congenital Malformations in Pregnancies Exposed to First-Trimester Antidepressants and Co-medications

Mette Østergaard Thunbo[1], Julie Hauer Vendelbo[1], Line Kolding[1,2], Agnete Larsen[3], Daniel R. Witte[4,5], Zeyan Liew[6], Lars Henning Pedersen[1,2,3]

[1]Department of Clinical Medicine, Aarhus University, [2]Department of Obstetrics and Gynaecology, Aarhus University Hospital, [3]Department of Biomedicine, Aarhus University, [4]Department of Public Health, Aarhus University, [5]Steno Diabetes Centre Aarhus, [6]Yale Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, Yale University

Background: Treatment of depression in pregnancy balances between maternal wellbeing and fetal safety. Antidepressants are a safe choice for some women, but concomitant use of other medication may result in fetal harm. This study aimed to investigate the risk of major congenital malformations (MCMs) associated with first-trimester antidepressant, alone or concurrent with other medications, during pregnancy.

Methods: This Danish registry study (2008-2018) analysed 674,154 pregnancies of which 2.2% was exposed to first trimester antidepressants. We compared the risk of MCMs in the offspring, particularly congenital heart disease (CHD), among those exposed to first trimester antidepressants, alone or combined with other medications, with non-users.

Results: First-trimester antidepressant use was not associated with changed overall MCMs risk, but associated with increased risk of CHD (adjusted odds ratio (aOR) (95% confidence interval (CI)): 1.26 (1.08-1.47). However, first-trimester co-exposures to antidepressants and antihistamines (aOR (95% CI): 1.54 (1.07-2.15)) or levothyroxine (aOR (95% CI): 1.62 (1.06-2.39)) was associated with increased MCMs risk. Conversely, the first-trimester antidepressant users who took opiods (aOR (95%CI): 0.47 (0.25-0.80) or opiods and penicillins were associated with decreased MCMs risk (aOR (95% CI): 0.15 (0.01-0.69)). Concomitant use of first-trimester antidepressants and non-steroidal anti-inflammatory/antirheumatic products was associated with increased CHD risk (aOR (95% CI): 1.85 (1.10-2.92)), and co-usage of first-trimester antidepressants, antipsychotics and hypnotics was associated increased CHD risk (aOR (95% CI): 3.37 (1.17-7.68)).

Conclusion: Combinations of first trimester antidepressants and specific medications were associated with an increased risk of MCMs. This may reflect unknown interactions, confounding or effect of multiple testing.

Childhood body mass index and risk of infertility in women

Dorthe Corfitzen Pedersen[1], Julie Aarestrup[1], Lise G. Bjerregaard[1], Allan Jensen[2], Susanne K. Kjær[2,3], Petur B. Juliusson[4,5], Kathleen M. Rasmussen[6], Jennifer L. Baker[1]

[1]Center for Clinical Research and Prevention, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Copenhagen, Denmark, [2]Virus, Lifestyle and Genes, Danish Cancer Institute, Copenhagen, Denmark, [3]Department of Gynecology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, [4]Department of Health Registry Research and Development, National Institute of Public Health, Bergen, Norway, [5]Department of Clinical Science, University of Bergen, Bergen, Norway, [6]Division of Nutritional Sciences, Cornell University, Ithaca, NY, USA

Background: Women with overweight or obesity are at greater risk of developing infertility than women with normal weight. As excess adiposity develops over time, we investigated whether body mass index (BMI) in childhood was associated with infertility in adulthood.

Methods: We studied 54,914 women born between 1955 and 1996 with information on measured height and weight at age 13 years from the Copenhagen School Health Records Register. Thinness, normal-weight, overweight, and obesity were defined according to the International Obesity Task Force (IOTF) BMI cut-offs. We identified women with infertility in the Danish National Patient Register from 1977-2017. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression. Age was used as the underlying timescale, and the analyses were stratified by birth cohorts.

Results: At age 13 years, 5.4% of the women were classified as having thinness, 83.9% with normal-weight, 8.3% with overweight, and 2.4% with obesity. During follow-up, 3,880 women (5.0%) were diagnosed with infertility. When compared to women with normal-weight at age 13 years, having thinness or overweight was not associated with infertility (HR = 0.96 [95% CI: 0.86-1.06] and 0.97 [0.84-1.11], respectively), whereas women with obesity at age 13 years had a higher risk (HR = 1.47 [1.08-2.00]).

Conclusion: Our results suggest that childhood obesity is associated with an increased risk of female infertility in adulthood. Work is ongoing with more refined information about infertility from national studies and registers.

Prenatal primary care utilization among migrant women in Norway: A nationwide register-based cohort study

Torill Alise Rotevatn[1], Nina Høy-Petersen[2], Lema Hussaini[1], Siri E. Håberg[3], Maria C. Magnus[3], Nils-Halvdan Morken[4,5], Knut-Arne Wensaas[6], Eva Marie Flaathen[7], Rannveig K. Hart[3,8]

[1]Division of Health Services, Norwegian Institute of Public Health, [2]Division of Mental and Physical Health, Norwegian Institute of Public Health, [3]Centre for Fertility and Health, Norwegian Institute of Public Health, [4]Department of Clinical Science, University of Bergen, [5]Department of Obstetrics and Gynecology, Haukeland University Hospital, [6]Research Unit for General Practice, NORCE Norwegian Research Centre, [7]Department of Nursing and Health Promotion, Faculty of Health Sciences, Oslo Metropolitan University, [8]Department of Health Management and Health Economics, University of Oslo

Background: International research highlights that immigrants, a group at higher risk of pregnancy complications, often access less prenatal care. Our study uses comprehensive Norwegian data to further explore these disparities.

Methods: We conducted a nationwide register-based cohort study of all registered deliveries to women aged ≥16 years in Norway between 2008-2018. Exclusions included multiple pregnancies, and those complicated by preeclampsia, type 1 diabetes, preterm births, or births of very small children. Logistic regression models adjusted for demographic, socioeconomic, and immigration-related factors were used to assess risks of prenatal care underutilization per trimester, defined as having fewer prenatal visits than recommended, by country of origin.

Results: We included 551,064 deliveries, 20.8% from immigrant women. Immigrants exhibited greater underutilization of prenatal care in the first trimester (21.8%) compared to the general population (16.2%), with smaller differences in later trimesters. Eritrean (OR 1.72 [95%CI 1.57-1.89]), Lithuanian (OR 1.40 [95%CI 1.28-1.53]) and Ukrainian women (OR 1.37 [95%CI 1.19-1.58]) had the highest adjusted risks of 1. trimester underutilization. Smaller risk differences were observed in the later trimesters between immigrants and the general population, with German (OR 1.24 [95%CI 1.14-1.36]) and Russian (OR 1.24 [95%CI 1.14-1.34]) women having the highest risk of underutilization in the 3. trimester after adjusting for all covariates.

Conclusion: Immigrant women, particularly from developing countries, had higher risk of underutilization in the 1. trimester, with disparities lessening but persisting among immigrants from more developed countries in later trimesters. Targeted interventions may help address these disparities in Norwegian public health program in pregnancy.

The effect of chronic inflammation on adverse pregnancy and perinatal outcomes: a two sample Mendelian Randomisation study

Gemma Clayton[1], Nancy McBride[1], Maria Carolina Borges[1], Deborah Lawlor[1]

[1]*MRC IEU, University Of Bristol*

Background: C-reactive protein (CRP), Interleukin 6 (IL6), and glycoprotein acetyl (GlycA) are serum biomarkers for chronic inflammation and hypothesised to cause adverse pregnancy outcomes. The aim of this study is to explore the potential causal effects of these inflammatory markers on pregnancy and perinatal health.

Methods: We performed two-sample Mendelian Randomisation (MR) to assess the effect of CRP, IL6, and GlycA on 15 pregnancy and perinatal outcomes, including pre-eclampsia, preterm birth, low birth weight (LBW), small size for gestational age (SGA) and admission to neonatal unit (NICU). We obtained genetic association data from the largest genome-wide association study of CRP(N=575,531), IL6(N=67,428), and GlycA(N=115,078), and for outcomes, we used the MR-PREG consortium (ranging from N=7,578 to 230,310 European women per study). We used inverse-variance weighted (IVW) MR for main analyses and MR-Egger, weighted median and weighted mode for sensitivity analyses.

Results: A 1 SD increase in genetically instrumented log transformed CRP increased the odds of LBW (OR=1.10 [1.01 to 1.20]), SGA (OR=1.06 [0.99 to 1.14]) and admission to NICU (OR=1.06 [1.00 to 1.13]). A 1 SD increase in genetically instrumented GlycA, increased LBW (OR=1.09 [0.94 to 1.25]) and SGA (OR=1.07 [0.87 to 1.33]). Results were consistent in sensitivity analyses. Evidence for effects (including IL6) on other outcomes was weaker, possibly due to limited power.

Conclusion: Higher levels of CRP and GlycA may cause fetal growth restriction. We will also investigate bias by horizontal pleiotropy. Further work will increase the sample size of GlycA to up to 500k participants.

Do birth weight-for-gestational age centiles predict severe neonatal morbidity and neonatal mortality?

Sid John[1], KS Joseph[1], Shiliang Liu[4], John Fahey[3], Sarka Lisonkova[1], Michael Kramer[5]

[1]University of British Columbia, [2]Children's and Women's Hospital and Health Centre of British Columbia, [3]The Reproductive Care Program of Nova Scotia, [4]Centre for Surveillance and Applied Research, Public Health Agency of Canada, [5]Departments of Epidemiology and Occupation Health and of Pediatrics, McGill University,

Background: Previous studies indicate that fetal- and birth weight-for-gestational age centiles (birth weight centiles) per se are poor predictors of serious neonatal morbidity and neonatal mortality (SNMM). We assessed the predictive performance of models based on birth weight centiles and maternal/pregnancy characteristics alone and in combination.

Methods: We included all live births with a gestational age of 24 to 42 weeks in the United States, 2019-2021. Data were obtained from the linked birth-infant death files of the National Center for Health Statistics. SNMM was defined as 5-min Apgar score <4, neonatal seizures, need for assisted ventilation, or neonatal death. Logistic regression was used to model SNMM with maternal/pregnancy characteristics (age, parity, chronic hypertension, gestational age, etc.) as predictors with and without birth weight centiles, based on area-under-the-curve (AUC).

Results: The study included 10,487,243 live births and 221,728 SNMM cases. Birth weight centiles alone performed poorly as predictors of SNMM (AUC 0.596, 95% CI 0.595-0.597). However, model prediction based on maternal/pregnancy characteristics alone was excellent (AUC 0.838, 95% CI 0.837-0.839) and improved only slightly after addition of birth weight centiles (AUC 0.840, 95% CI 0.839-0.841). Analysis stratified by gestational age showed similar results, although predictive performance was substantially reduced: at 39 weeks' gestation AUC=0.558, 95% CI 0.555-0.561 for birth weight centiles only; AUC=0.668, 95% CI 0.665-0.672 for maternal/pregnancy characteristics only; and AUC=0.676, 95% CI 0.673-0.680 for maternal/pregnancy characteristics plus birth weight centiles.

Conclusion: Maternal/pregnancy characteristics are strong predictors of SNMM. Predictive performance is only slightly improved by including birth weight centiles.

Genome-wide association meta-analysis of infertility

Astanand Jugessur[1,2], Yunsung Lee[1], Amy Taylor[3,4], Leslie Farland[5], Constance Turman[6], Minna K Karjalainen[7,8], Alvaro Hernaez[1,9,10], Karoline H Skåra[1], Eirin B Haug[11], Dana Kristjansson[12], Carolina Borges[3,4], Johanna Laru[13], Laurent Thomas[11], Marta Moksnes[11], Deborah A Lawlor[3], Laure Morin-Papunen[13,14], Kathryn L Penney[6], Peter L Kraft[6,15], Stacey A Missmer[6,16], Sylvain Sebert[17], Ben M Brumpton[11], Maria C Magnus[1]

[1]Centre for Fertility and Health, Norwegian Institute of Public Health, [2]Department of Global Public Health and Primary Care, University of Bergen, [3]Population Health Sciences, Bristol Medical School, University of Bristol, [4]MRC Integrative Epidemiology Unit, University of Bristol, [5]Department of Epidemiology and Biostatistics, Mel and Enid Zuckerman College of Public Health, University of Arizona, [6]Harvard T.H. Chan School of Public Health, [7]Research Unit of Population Health, Faculty of Medicine, University of Oulu, [8]Northern Finland Birth Cohorts, Arctic Biobank, Infrastructure for Population Studies, Faculty of Medicine, Finland University of Oulu, [9]Blanquerna School of Health Sciences, Universitat Ramon Llull, [10]CIBER de Enfermedades Cardiovasculares (CIBERCV), Instituto de Salud Carlos III, [11]HUNT Center for Molecular and Clinical Epidemiology (MCE), Department of Public Health and Nursing, Norwegian University of Science and Technology, [12]Department of Genetics and Bioinformatics, Norwegian Institute of Public Health, [13]Department of Obstetrics and Gynecology, Medical Research Center Oulu, Research Unit of Clinical Medicine, University of Oulu and Oulu University Hospital, [14]Medical Research Center, Oulu University Hospital and University of Oulu, [15]Trans-Divisional Research Program, Division of Cancer Epidemiology and Genetics, National Cancer Institute, [16]Department of Obstetrics, Gynecology, and Reproductive Biology; College of Human Medicine, Michigan State University, [17]Research Unit of Population Health, University of Oulu

Background: Infertility affects 15-20% of couples. Despite notable progress in identifying genetic determinants, few genome-wide studies of infertility have been published.

Methods: We performed sex-stratified meta-GWAS of infertility (defined as having tried ≥12 months to conceive) across six European-ancestry cohorts: ALSPAC (UK), HUNT and MoBa (Norway), NFBC1966 and NFBC1986 (Finland), and NHSII (USA). All cohorts included data from women (Ntotal=119,810; cases: 18,376; controls: 101,434), but only MoBa, HUNT, and NFBC1966 included data from men (Ntotal=55,681; cases: 6,627; controls: 49,054). We estimated SNP-based heritability using LD score regression and conducted a phenome-wide association study (PheWAS) of infertility-associated loci using GWAS results for 1402 traits in UK Biobank.

Results: Despite the low heritability estimated in our study (~1%), five loci were associated with infertility in women (p-value<5×10-8). The strongest signal was localized to chromosome 19p13.3, within 'RNA exonuclease 1 homolog' (REXO1) and 'KLF transcription factor 16' (KLF16). We also found associations in 'zinc finger DHHC-type palmitoyltransferase 2' (ZDHHC2; 8p22) and 'Wnt family member 4' (WNT4; 1p36.12). In men, we identified one locus in 'glutamate decarboxylase like 1' (GADL1; 3p24.1-p23). Our PheWAS analysis in women linked these findings to genital/uterine/vaginal wall prolapse, benign uterine neoplasms, uterine leiomyoma, and endometriosis. No associations were found in men.

Conclusion: Our findings indicate distinct genetic influences on infertility in women and men. However, the smaller sample size for men could have yielded less power to identify shared loci. Except for WNT4, previously associated with fertility disorders, the other genes represent novel findings requiring replication in other cohorts.

Parental BMI, gestational weight gain and associations with Juvenile Idiopathic Arthritis

Ida H Caspersen[1,2], Sigrid Valen Hestetun[2], Ketil Størdal[3], Siri Håberg[1], Helga Sanner[2]

[1]Centre for Fertility and Health, Norwegian Institute Of Public Health, [2]Department of Rheumatology, Oslo University Hospital, [3]Division of Paediatric and Adolescent Medicine, Oslo University Hospital

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatologic condition in children, but its etiology is largely unknown. We aimed to study associations between maternal or paternal BMI, gestational weight gain (GWG) and child JIA diagnosis in the Norwegian Mother, Father and Child Cohort study.

Methods: A clinical diagnosis of JIA (at least two ICD-10 codes of M08 or M09) was obtained from the Norwegian Patient Registry. The main exposures were maternal pre-pregnancy BMI (weight in kg/height in m2) and maternal gestational weight gain (GWG) through pregnancy (in kg). Paternal BMI was included as a negative control. Associations were estimated using log-binomial regression models and adjusted for parental age, parity, education, smoking, and rheumatic diagnosis. The association between GWG and JIA was also adjusted for child's sex.

Results: Our study sample included n=76 700 mother-child pairs, including 227 JIA cases, with available information on parental height and weight around the time of pregnancy. Among mothers, 31% were overweight or obese at the beginning of pregnancy. The mean total GWG was 14.8 kg. No associations were found between maternal or paternal pre-pregnancy BMI and JIA risk (RRs 1.00 and 0.98, respectively). For GWG, we found a weak positive association with JIA (RR 1.11, 95% CI 0.98, 1.25, per 1 SD increase in GWG).

Conclusion: Our findings show no association between pre-pregnancy BMI and risk of JIA but suggest a weak positive association with gestational weight gain. The role of environmental factors in JIA etiology needs further investigation.

Telomere length in relation to fecundability and use of assisted reproductive technologies: the Norwegian Mother, Father, and Child Cohort Study

Karoline H. Skåra[1,2], Yunsung Lee[1], Astanand Jugessur[1,3], Håkon K. Gjessing[1,3], Abraham Aviv[4], Ben Brumpton[5,6,7], Øyvind Næss[2,8], Álvaro Hernáez[1,9,10], Hans Ivar Hanevik[1,11], Per Magnus[1], Maria C. Magnus[1]

[1]Centre for Fertility and Health, Norwegian Institute Of Public Health, [2]Department of Community Medicine and Global Health, Institute of Health and Society, University of Oslo, [3]Department of Global Public Health and Primary Care, University of Bergen, [4]Center of Human Development and Aging, New Jersey Medical School, Rutgers, The State University of New Jersey, [5]K.G. Jebsen Centre for Genetic Epidemiology, Department of Public Health and Nursing, NTNU – Norwegian University of Science and Technology, [6]HUNT Research Centre, Department of Public Health and Nursing, NTNU – Norwegian University of Science and Technology, , [7]Clinic of Medicine, St. Olavs Hospital, Trondheim University, [8]Division of Mental and Physical Health, Norwegian Institute of Public Health, [9]Blanquerna School of Health Sciences, Universitat Ramon Llull, [10]Consortium for Biomedical Research—Pathophysiology of Obesity and Nutrition (CIBEROBN), Instituto de Salud Carlos III, Monforte de Lemos 3-5, [11]Telemark Hospital Trust, Fertilitetsavdelingen Soer

Background: Telomere length (TL) has been reported to be associated with conditions such as endometriosis and polycystic ovary syndrome in women, and with sperm quality in men. To our knowledge, no studies have investigated the associations between TL and fecundability or the use of ART.

Methods: We studied participants from the Norwegian Mother, Father, and Child Cohort (MoBa) Study. 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 TL and fecundability (the probability to conceive within each menstrual cycle), infertility (the inability to conceive after trying for 12 or more months), and the use of ART. We also repeated the analyses using instrumental variables for TL.

Results: 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 associations were observed using instrumental variables for TL.

Conclusion: Our results indicate that TL is a poor 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.

Proteomic signatures of gestational diabetes in White European and South Asian women

Nancy Sabina McBride[1], Joshua Burton[1], Deborah A. Lawlor[1], Maria Carolina Borges[1]

[1]*MRC Integrative Epidemiology Unit, University of Bristol*

Background: Gestational diabetes (GDM) is related to fetal overgrowth, preterm birth and perinatal mortality and morbidity. We used proteomics to gain biological insight and identify potential therapeutic targets for GDM, in two ethnic groups.

Methods: We explored associations of 458 maternal circulating plasma proteins (taken ~24 weeks gestation) with GDM in a subsample of women in the Born in Bradford (BiB) cohort: White European women (193 GDM, 1,807 non-GDM) and South Asian women (446 GDM, 1,552 non-GDM). Linear regression (adjusting for maternal age, ethnicity, body mass index, education status, and parity) was used to test associations in the whole cohort, with subgroup analyses and an interaction to test for ethnic differences. We applied a 5% false discovery rate correction (FDR) to account for multiple testing.

Results: In adjusted analyses, higher levels of 17 proteins associated with higher odds of GDM (e.g. IGFBPL1 (OR 1.69 (95% CI (1.36, 2.1) per 1 SD higher protein concentration, FAP (1.71 (1.25, 2.34), and GUSB (1.60 (1.28, 2.0)). Higher concentrations of 20 other proteins associated with lower odds of GDM (e.g. LEPR 0.55 (0.42, 0.73) and LPL 0.43 (0.36, 0.58)). Associations did not generally differ between South Asian and White European women, although there were exceptions.

Conclusion: We have identified novel proteins associated with GDM, as well as replicating proteins previously linked with glucose homeostasis (e.g. IGFBPL1, LPL), and oral hypoglycaemic targets (e.g. FAP). In further analyses, these results will be compared to findings from Mendelian Randomisation to identify potential mechanisms for, and targets to prevent, GDM.

Maternal BMI in early pregnancy and offspring ASD risk

Matilda Morin[1], Thomas Munk Laursen[2,3], Martina Persson[4,5], Abraham Reichenberg[6,7,8], Diana Schendel[2,3,9], Shanna H Swan[8], Weiyao Yin[1], Sven Sandin[1,6,7]

[1]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, [2]National Centre for Register-based Research, Aarhus University, [3]The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, [4]Department of Clinical Science and Education Södersjukhuset, Karolinska Institutet, [5]Department of Diabetes and Endocrinology, Sachsska Childrens' and Youth Hospital, [6]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, [7]Seaver Autism Center for Research and Treatment at Mount Sinaii, [8]Department of Environmental Medicine and Climate Science, Icahn School of Medicine at Mount Sinai, [9]A.J. Drexel Autism Institute, Drexel University

Background: Maternal pre-pregnancy obesity, increasingly prevalent globally, has been linked to higher risk of autism spectrum disorder (ASD) in offspring. However, due to the heterogeneity of existing studies, support for this association is weak. In this large, prospective cohort study, we explored the association with offspring ASD across the full range of maternal BMI.

Methods: The study included all live singleton births in Sweden between 1998 and 2019. Maternal BMI in early pregnancy was obtained from the Swedish Medical Birth Register. Diagnoses of ASD were obtained from the National Patient Register until 2022. The association was quantified using hazard ratios (HR) with 95% confidence intervals (CI) from Cox regression, adjusted for birth year and parental age, educational level, income, and psychiatric history. BMI was modeled with restricted cubic splines to account for a non-linear relationship.

Results: Among the 1,430,878 children included in the study, 43,155 (3.0%) were diagnosed with ASD. In comparison to a maternal BMI of 22kg/m², the risk of ASD exhibited a U-shaped association with gradual increase for both lower and higher BMI values, which was attenuated but remained after adjustment for confounders. For example, for BMI 15 the HR was 1.29 (95% CI: 1.15-1.44); for BMI 30 the HR was 1.56 (95% CI: 1.51-1.60) in the fully adjusted model.

Conclusion: Low and high maternal BMI in early pregnancy is associated with increased risk for ASD in the offspring even after adjustment for individual-level confounders. Next, we intend to study family-level confounders and possible mediators of the association.

Examining the Influence of COVID-19 Control Measures on Respiratory Tract Infection Hospitalizations in Vulnerable Preterm-Born Infants: Evidence from Norway and Sweden

Andreas Asheim[2,3], Kari Risnes[1,4], Jonas Valand[1], Sven Sandin[5,6], Sara Marie Nilsen[1,2]

[1]Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology, [2]Center for Health Care Improvement, Trondheim University Hospital, [3]Department of Mathematical Sciences, Norwegian University of Science and Technology, [4]Children's Clinic, Trondheim University Hospital, [5]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, [6]Seaver Center for Autism Research and Treatment, Icahn School of Medicine at Mount Sinai

Background: Respiratory tract infections (RTIs) cause stress, disturbance in parent-child relations and breast feeding, and adverse effects on quality of life. Early life RTIs may also be an important factor in the development of lung disease later in life.

Objective: Assess the impact of COVID-19 control measures on respiratory tract infection hospitalisations in vulnerable infants born preterm (< 37 weeks) in Norway and Sweden.

Methods: We used population-wide data from Norway (infants born 2015-2022) and Sweden (infants born 2015-2022). Gestational age at birth was obtained from medical birth registers and was categorised as 23-36 weeks (preterm), 37-41 weeks (term). Sub-analyses were conducted on specific sub-categories of preterm birth, further classified as 23-31 weeks (extremely and very preterm) and moderate to late preterm (32 to 37 weeks). Respiratory tract infection hospitalisations were available from national patient registries based on ICD-10 discharge codes. We conducted an interrupted time-series analyses and estimated the change in hospitalisation rates following the introduction of measures to control the spread of the COVID-19 virus.

Findings [to come]

Interpretation [to come]

COVID-19 infection and risk of venous thromboembolism in pregnancy

Anne Kristina Örtqvist[1,2], Maria C. Magnus[3], Siri E. Håberg[3], Olof Stephansson[1,4]

[1]Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, [2]Department of Obstetrics and Gynecology, Visby County Hospital, [3]Centre for Fertility and Health, Norwegian Institute of Public Health, [4]Department of Women's Health, Karolinska University Hospital

Background: Pregnancy is a prothrombotic state and immobilization, hereditary thrombophilia, or any serious infection, will increase the risk of venous thromboembolism (VTE). In Sweden and Norway, COVID-19-specific guidelines regarding thromboprophylaxis treatment for pregnant individuals were implemented early in the pandemic. This study aimed to investigate the association between COVID-19 and VTE in pregnancy while taking thromboprophylaxis treatment into account.

Method: This register-based study included all individuals in Sweden and Norway giving birth after 22 completed gestational weeks (N=323,868) with estimated conception dates between March 2020-2022. Hazard ratios for VTE according to the history of COVID-19 were estimated using Cox regression analyses, censoring for thromboprophylaxis treatment, emigration, and death, and adjusted for maternal characteristics. Analyses of 2, 4, 8, and 16 weeks of exposure windows were further assessed.

Results: Among 54,563 COVID-19-infected individuals, 80 (0.1%) were subsequently diagnosed with VTE. In Sweden, COVID-19-infected individuals exhibited an increased hazard of VTE (adjusted hazard ratio [aHR] 1.51 [95% CI, 1.14-2.02]). The corresponding aHR for Norway was 0.93 (95% CI 0.53-1.62). For both countries, the highest hazard was found within 2 weeks of exposure (meta-analyzed aHR 4.63 [95% CI, 2.71-7.90]), and subsequently decreased. In Sweden, the risk remained elevated until 16 weeks, whereas in Norway a risk of VTE was only seen for the first 2-week exposure period.

Conclusion: While the absolute numbers of VTE among COVID-19-infected pregnant individuals were low, COVID-19 infection likely adds to the already increased risk of VTE in pregnancy, and guidelines for thromboprophylaxis to COVID-19-infected pregnant individuals are important.

Severe maternal morbidity by mode of delivery in the second stage of labour: a retrospective population-based cohort study of nulliparous people in Ontario, Canada 2013-2021

Giulia Muraca[1]

[1]*McMaster University*

Background: We aimed to characterize the distribution of deliveries in the second stage of labour and to assess rates of severe maternal morbidity (SMM) by mode of delivery over time.

Methods: Population-based cohort study of all individuals in British Columbia, Canada (2004-2018) with a singleton term pregnancy who reached full cervical dilation. The definition of SMM was adapted from the Canadian Perinatal Surveillance System. Temporal trends were assessed using the Cochran-Armitage test. Multivariable regression was used to quantify the impact of changing risk factors (advanced maternal age, BMI extremes, co-morbidity) on SMM rates.

Results: The study included 391,342 deliveries. From 2004 to 2018, the rates of SSCD and forceps delivery increased among nullipara (SSCD: 7.52% to 10.1%; forceps: 9.3% to 11.5; p<0.001), while the rate of vacuum delivery decreased from 16.7% to 12.6% (p <0.0001). The overall rate of SMM was 7.2 per 1,000 with the highest rates among forceps and SSCD (19.7 and 19.3 per 1,000, respectively). Temporal increases in the SMM rate were found in forceps (13.3 to 23.0 per 1,000) and vacuum (8.9 to 14.6 per 1,000). Adjusting for several risk factors did not explain the increase in SMM with forceps (2017/18 vs. 2004/05; crude RR 1.76, 95% CI 0.94-3.16; adjusted RR 1.86, 95% CI 1.06–3.41) or vacuum delivery.

Conclusions: Rates of forceps, SSCD, and associated SMM increased between 2004-2018. Changes in risk factors could not explain the temporal increase in SMM with forceps or vacuum.

Circulatory maternal microchimerism and type 1 diabetes in boys and girls – a Danish case-control study

Gitte Lindved Petersen[1,2], Mads Kamper-Jørgensen[2], Marianne Antonius Jakobsen[3], Sofie Dolores Holm Olsen[3], Christina Ellervik[4,5,6], Lise Tarnow[7], Randi Jepsen[8], Flemming Pociot[1]

[1]Translational Type 1 Diabetes Research, Steno Diabetes Center Copenhagen, [2]Section of Epidemiology, Department of Public Health, University of Copenhagen, [3]Department of Clinical Immunology, Odense University Hospital, [4]Boston Children's Hospital, Harvard Medical School, [5]Department of Clinical Medicine, University of Copenhagen, [6]Department of Data Support, Region Zealand, [7]Steno Diabetes Center Zealand, [8]Center for Health Research, Zealand University Hospital

Background: Natural fetomaternal cell exchange can result in the presence of maternally derived cells persisting in the child's circulation. The phenomenon is called maternal microchimerism (MMc) and its presence involves a balance between increased immune surveillance and potential autoimmunity, potentially differing by sex. We aim to investigate the association between MMc and type 1 diabetes (T1D) in boys and girls.

Method: We analyzed peripheral blood samples from Danish children with T1D, controls without T1D, and their mothers. For each mother-child pair, we identified an informative indel allele. We used sequence-specific quantitative polymerase chain reaction assays to detect maternal cells in the child's blood. The MMc-T1D associations were estimated in logistic regression models. We calculated the E-value for the crude estimates to assess resilience to unmeasured confounding suggested by our directed acyclic graph.

Results: MMc was detected in 67% of boys (22/33) and 40% of girls (12/30) with T1D, and in 18% (40/219) of boys and 17% (40/240) of girls without T1D. The odds of T1D were markedly higher in MMc positive children, especially in boys (boys OR=9.0 [95% CI 4.1-20.6], girls OR=3.3 [95% CI 1.5-7.4]). For unadjusted confounding to cause spurious ORs of these sizes, it must be associated with >17-fold and >6-fold increased probabilities of testing MMc positive and of having T1D for boys and girls, respectively (E-values: boys OR=17.5 [CI 7.7], girls OR=6.1 [CI 2.4]).

Conclusion: MMc was more common in children with T1D than in controls, especially in boys, and the findings are unlikely to be explained fully by unadjusted confounding.

Acetylsalicylic acid in pregnancy and fetal growth

Julie Hauer Vendelbo[1], Håkon Gjessing[2,3], Maria Christine Magnus[4], Tine Brink Henriksen[1,5], Zeyan Liew[6,7], Agnete Larsen[8], Lars Henning Pedersen[1,8,9]

[1]Department of Clinical Medicine, Aarhus University, [2]Division of Epidemiology, Norwegian Institute of Public Health, [3]Department of Global Public Health and Primary Care, University of Bergen, [4]Center for Fertility and Health, Norwegian Institute of Public Health, [5]Department of Paediatrics, Aarhus University Hospital, [6]Department of Environmental Health Sciences, Yale School of Public Health, [7]Yale Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, [8]Department of Biomedicine, Aarhus University, [9]Department of Obstetrics and Gynecology, Aarhus University Hospital

Background: Low dose Acetylsalicylic acid (ASA) is recommended to pregnant women at high risk of developing preeclampsia or with a history of fetal growth restriction (FGR). ASA reduces the risk of small-for-gestational age newborns, but in diabetic mothers, it may increase the risk of large-for-gestational-age. We investigated differences in fetal growth patterns according to maternal use of ASA in pregnancy by subgroups.

Methods: Information on pregnancies between 2013 and 2023 with routine ultrasound scans were obtained from the Hospital Registry of the Central Denmark Region and linked to the Danish national health registries. Measures of fetal size, including abdominal circumference (AC), biparietal diameter (BPD), and femur length (FL) were standardized as residuals from the median of the total population for each gestational week of pregnancy and the weekly impact of ASA treatment was estimated in an adjusted model.

Results: A total of 140,490 singleton pregnancies were identified. Overall, ASA use was not associated with fetal growth. History of FGR in a previous pregnancy increased the risk of FGR measured by BPD, AC and FL in the index pregnancy regardless of ASA use. Pre-pregnancy diabetes was associated with increased fetal growth assessed by AC, but not BPD or FL, and ASA was associated with faster fetal growth. History of preeclampsia was not associated with any measures of fetal growth. Analyses are still ongoing.

Preliminary conclusion: ASA treatment was not associated with fetal growth. In women with pre-pregnancy diabetes, ASA appeared to be associated with faster fetal growth measured by AC.

Prenatal exposure to the Chernobyl fallout in Norway and long-term cognitive abilities measured among conscripts

Rolv Terje Lie[1,2], Elin Anita Fadum[3], Dag Moster[1,4], Allen J. Wilcox[5], Leif Aage Strand[3], Siri Eldevik Håberg[2,1]

[1]University of Bergen, [2]Norwegian Institute of Public Health, [3]Norwegian Armed Forces Health Registry, [4]Haukeland University Hospital, [5]National Institute of Environmental Health Sciences

Background: Exposure to ionizing radiation during pregnancy may cause long term effects on the developing brain. We have previously studied associations between the Chernobyl fallout and neural tube birth defects, neurodevelopmental disorders and school grades. Our analyses suggested an association with reduced mathematics grades, an association also described in Sweden. We use cognitive tests among conscripts in Norway to further investigate this association.

Methods: Radiation doses were estimated for each municipality and calendar month from May 1986 to April 1989. Total cognitive score was analyzed using a natural experiment design with pregnancy cohorts from years prior to the fallout as reference. Sub-scores for numerical, general, and verbal reasoning were available for cohorts after 1986. We used younger siblings born after the exposure period as comparison in analyses of these scores.

Results: In preliminary analyses we find no evidence of an association between total cognitive ability and level of radiation exposure. Furthermore, the sub-score for numerical reasoning was not associated with radiation exposure in our analyses of the sibling data, and no associations were found for the other two sub-scores. Sensitivity analyses are performed with alternative management of the exposure variables.

Conclusions: Our analyses have not identified any associations between the Chernobyl radioactive fallout in Norway and cognitive abilities of individuals exposed in utero. We found no support for an association with mathematics abilities. Not all Norwegians participate in the conscript testing and the possibility of selection bias is a limitation of our study.

Number of prior cesarean deliveries and adverse birth outcomes

Sarka Lisonkova[1], Sofia Nicolls[1], Julienne Van Schalkvyk[1]

[1]*University of British Columbia Faculty of Medicine*

Background: Cesarean delivery (CD) rates are increasing. Our objective was to examine the rates of uterine rupture and perinatal mortality in parous women, stratified by the number of prior CDs.

Methods: A retrospective cohort study including all parous women with singleton birth in the United States, 2016-2017, N=4,630,436. Rate of uterine rupture was contrasted between women with 1, 2, 3 and ≥4 CDs versus women with prior vaginal births only. Logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals (CI) for perinatal death; adjusting for parity, maternal age, pre-pregnancy BMI, smoking, education, race/ethnicity, etc.

Results: Overall, 75.1% of parous women had no prior CD, 17.1% had one, 5.8% had two, 1.6% had three, and 0.4% had ≥4 prior CDs. Uterine rupture (per 1000 women) in these groups increased from 0.2 (no prior cesarean delivery) to 1.0; 1.2; 1.9; and 3.4, respectively. AOR for perinatal death was 0.84 (95% CI: 0.80-0.89) in women with 1 prior CD, AOR 0.96 (95% CI: 0.89-1.04) in women with 2 CDs, AOR 1.04 (95% CI: 0.91-1.19) in those with 3 CDs, and AOR 1.59 (95% CI: 1.30-1.94) in women with ≥4 prior CDs.

Conclusions: Women with prior cesarean deliveries have higher rates of uterine rupture, particularly those with ≥4 prior cesarean deliveries. Among women with uterine rupture, perinatal mortality is lower in women with one prior cesarean delivery and higher among those with ≥4 previous cesarean deliveries compared with women who had the same number prior vaginal deliveries.

Using human biomonitoring in epidemiological studies – The Norwegian Environmental Biobank (NEB)

Line Småstuen Haug[1,2], Nina Iszatt[1,2], Mari Mohn Paulsen[1,2], Anne Lise Brantsæter[1,2], Berit Granum[1,3], Cathrine Thomsen[1,2]

[1]Centre for Sustainable Diets, Norwegian Institute of Public Health, [2]Department of Food Safety, Norwegian Institute of Public Health, [3]Department of Chemical Toxicology, Norwegian Institute of Public Health

Background: Environmental contaminants may pose a considerable threat to the health of present and future generations, however exposure data is often lacking. Human biomonitoring (HBM) is a powerful tool in epidemiological studies on health effects of environmental contaminants.

Methods: The Norwegian Environmental Biobank (NEB) is a sub-study of the Norwegian Mother, Father and Child Cohort Study (MoBa). In NEB biological samples and questionnaire data from MoBa triads of mothers, fathers and children were collected in 2016-17. Here we present results from HBM of environmental contaminants in the children's blood and urine samples (n=669) and use these data to explore associations with BMI.

Results: The participating children were 7-14 years old and evenly distributed between girls and boys, representing the whole country. We measured 81 different environmental contaminants in the children's blood and urine samples. The measured concentrations of most of the environmental contaminants were similar to those seen in comparable European surveys. Associations between several contaminants and BMI were explored, with results going in both directions.

Conclusion: The children participating in the NEB study in 2016-2017 had a wide range of environmental contaminants in their bodies, and some of them were above safe levels, which is of high concern and urge for implementing measures to reduce exposure. HBM data from NEB is useful for epidemiological studies on health effects of environmental contaminants, with follow-up assessments allowing for longitudinal analysis. The connection to Moba with the possibility of HBM on prenatal samples is a unique strength of NEB.

Second child and interbirth interval in young adults born preterm

Johanna Metsälä[1], Suvi Alenius[1], Anna Pulakka[1,2], Katriina Heikkilä[1,3], Mika Gissler[1,4,5], Eero Kajantie[1,2,6]

[1]Finnish Institute for Health and Welfare, [2]University of Oulu, [3]University of Turku, [4]Academic Primary Health Care Centre, [5]Karolinska Institutet, [6]Norwegian University of Science and Technology

Background: People born preterm are less likely to have children than those born at term. Less is known on the association of being born preterm birth with interbirth interval. We explored this association using nationwide register data from Finland.

Methods: We studied all individuals who were born alive in 1987-1992, lived in Finland at age 13 years and had at least one liveborn child/children in case of multiple pregnancy by 2018. We used Cox regression to estimate HRs and 95% CIs for having a subsequent liveborn child by March 2020 in men and women born preterm (<37 completed gestational weeks) compared with those born term (≥37 weeks). Interbirth interval was calculated as time between the date of first and second livebirths.

Results: Of the 57,823 women included, 2,347 (4.1%) were born preterm and 39,734 (68.7%) had at least two livebirths. Among the 39,444 men, 1,894 (4.8%) were born preterm and 24,808 (62.9%) had at least two livebirths. Women's or men's own preterm birth was not associated with having a second birth (unadjusted HR and 95% CI 1.00, 0.95-1.05 in women and 0.97, 0.92-1.03 in men). The median (IQR) interbirth interval was 29.0 (21.8, 40.2) months in women born preterm and 28.6 (21.4, 40.3) months in women born term and 26.6 (20.2, 37.1) months in men born preterm and 27.2 (20.8, 37.2) months in men born term.

Conclusion: Once people born preterm have their first child, being born preterm is not associated with the hazard of having a second child.

Neurodevelopmental disorders at 5.5 years of age in children born extremely preterm in Sweden 2014-2016

Anna Walås[1], Erik Wejryd[1], Thomas Abrahamsson[1], Lars Björklund[2], Magnus Domellöf[3], Anders Elfvin[4], Aijaz Farooqi[3], Lena Hellström-Westas[5], Stellan Håkansson[3], Fredrik Ingemansson[6], Karin Källén[7], David Ley[2], Erik Normann[5], Mikael Norman[8], Fredrik Serenius[5], Karin Sävman[4], Petra Um-Bergström[9], Ulrika Ådén[1,10]

[1]Department of Biomedical and Clinical Sciences, Linköping University, and Crown Princess Victoria's Children's and Youth Hospital, [2]Department of Clinical Sciences, Lund, Paediatrics, Lund University, and Skåne University Hospital, [3]Department of Clinical Sciences, Pediatrics, Umeå University, [4]Department of Pediatrics, Institution of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, Region Västra Götaland, Department of Pediatrics, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, [5]Department of Women's and Children's Health, Uppsala University, [6]Department of Pediatrics, Ryhov County Hospital, Jönköping County Council, [7]Institution of Clinical Sciences, Department of Obstetrics and Gynecology, Centre of Reproduction Epidemiology, Tornblad Institute, Lund University, [8]Department of Clinical Science, Intervention and Technology, Karolinska Institutet; Department of Neonatal Medicine, Karolinska University Hospital, [9]Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet; Sachs' Children and Youth Hospital, Södersjukhuset, [10]Department of Women´s and Children´s Health, Karolinska Institutet and Karolinska University Hopsital

Background: In the last decades survival among infants born extremely preterm has improved (1,2,3), while studies of neurological outcome have not shown a corresponding trend of improvement (1,4,5). Swedish national recommendations for follow-up were introduced in 2015. This study aims to evaluate neurodevelopmental disorders (NDD) of infants born extremely preterm at 5.5 years of age.

Method: This register-based cohort study, with prospectively collected data from the Swedish Neonatal Quality Register (SNQ), included infants born extremely preterm (before 27 weeks gestation) in Sweden 2014-2016. The main outcome was NDD, which included measures of Full Scale IQ [FSIQ], autism, attention deficit/hyperactivity disorder (ADHD), cerebral palsy (CP), speech, hearing, and vision impairment.

Results: Of the 912 infants born extremely preterm, 710 were alive at 5.5 years and of those 536 (75%) had follow-up recorded in the SNQ. WPPSI-IV was performed in 350 (49%) children with a mean FSIQ of 88 (SD 15), and an FSIQ of <70 (<-2SD) in 10.8%. Further, 10.1% of children were diagnosed with autism spectrum disorder, 3.2% with ADHD, and 9.5% had CP. Suspected or definite impairment in speech, hearing, and vision were observed in 29.3%, 5.1%, and 35.8% of children respectively.

Conclusion: At 5.5 years after extreme preterm birth NDI was common, but completeness of outcome data in the register needs to be improved. Increased efforts for survival call for comparable efforts in follow-up, in order to optimise accessibility and adherence to follow-up programs. A structured approach for follow-up enables detection, consequent management, and information on the development of NDI over time.

Do early years risk factors mediate inequalities in child mental health? Findings from eight birth cohort studies

Demetris Avraam[1,2], Gabriella Melis[2], Angela Pinot de Moira[1,3], Tim Cadman[1], Katrine Strandberg-Larsen[1], Anne-Marie Nybo Andersen[1], Daniela Schlüter[2], David Taylor-Robinson[2]

[1]Department of Public Health, University Of Copenhagen, [2]Department of Public Health, Policy and Systems, University of Liverpool, [3]National Heart and Lung Institute, Imperial College London

Background: Children growing up in less advantaged socioeconomic circumstances (SECs) are more likely to develop mental health disorders. Examining the social patterning of child mental health and its risk factors may increase our understanding of the pathways to inequalities and help identify targets for intervention.

Methods: We used data from eight birth cohorts within the EU Child Cohort Network to assess social inequalities in child mental health and how they are mediated by early-life risk factors. Maternal education level during pregnancy was used as indicator of SECs. Externalising and internalising behaviour scores around age five were used as indicators of mental health. Inequalities were quantified using the Slope Index of Inequality. Maternal smoking during pregnancy, gestational age, birth weight for gestational age, postpartum depression and breastfeeding were assessed as potential mediators using counterfactual mediation analysis.

Results: Children of lower educated mothers had 11.7 and 10.9 percentage-point increased prevalence of externalising and internalising problems respectively. The proportion mediated ranged between 19% (DNBC, Denmark) and 43% (ALSPAC, UK) for externalising and between 11% (ELFE, France) and 44% (INMA, Spain) for internalising problems, with maternal smoking in pregnancy contributing most compared to the other examined mediators.

Conclusions: There are fairly consistent inequalities in early measures of child mental health problems across the cohorts examined, whereby children from less advantaged SECs have a higher prevalence of externalising and internalising problems. These inequalities were partly explained by perinatal factors. Public health action in this period may help address the early emergence of mental health inequalities.

The role of maternal pregnancy and perinatal health in early menopause through a proteomic lens

Linda Repetto[1], Albert Navarro Gallinad[1], Maeregu Woldeyes Arisido[1], Luisa Zuccolo[1,2,3]

[1]Human Technopole, [2]MRC Integrative Epidemiology Unit, The University of Bristol, [3]Department of Population Health Sciences, The University of Bristol

Background: Adverse pregnancy and perinatal outcomes (APPOs) and early menopause (before 45) are on the rise and linked to increased cardiovascular and metabolic risk, particularly in developing countries like Bangladesh. However, we lack understanding of the genomic and proteomic architecture of women's health across the reproductive span, and of whether APPOs can predict or cause early menopause, especially in South-Asian women. This knowledge gap drives our research question: "Are there shared proteomic signatures elucidating potentially causal relationships between pregnancy and perinatal health and early menopause?"

Methods: We analyse data on N=10,000 Bangladeshi women and men (40-80yrs, with rich clinical/obstetric/reproductive data, genome-wide characterisation, 7k+ plasma proteins), to: 1)Identify menopause proteomic signatures by comparing age-related trends among men and women via functional data analysis; 2)Identify proteins predictive of pregnancy and perinatal health, and their genetic drivers; 3)Conduct causal mediation analysis of APPOs, proteins, and early menopause through Multivariable Mendelian Randomisation.

Results: We prioritise 1,400+ (20%) menopause-relevant proteins and 32 (5%FDR corrected) proteins linked to one or more APPOs, through functional analysis and regression models. While most proteins show enrichment in reproductive-related biological processes, we also identify potentially novel pathways for APPOs/menopause etiology. Ongoing population-specific genetic association analyses are pinpointing instruments for causal models (MendelianRandomisation).

Conclusions: This study elucidates the shared mechanisms between pregnancy and perinatal health and early menopause. Our results can advance our understanding of the long-term consequences of APPOs, which is critical for tackling age-related conditions through prevention efforts focused on maternal health and drug target investigation.

Consumption of organic foods during pregnancy and neurodevelopmental scores up to 5.5 years in the French nationwide ELFE cohort

Victoria Jacobsen[1], Manel Ghozal[1], Sandrine Lioret[1], Marie-Aline Charles[1], Blandine de Lauzon-Guillain[1], Manik Kadawathagedara[1]

[1]*Université Paris Cité, Inserm, INRAE, CRESS,*

Background: Consumption of organic foods may limit exposure to neurotoxic pesticides through food consumption. The objective of this work was to analyze the link between the consumption of organic foods during pregnancy and child's cognitive development up to 5.5 years of age.

Methods: Mothers of 9,946 children from the French ELFE birth cohort reported their consumption of organic foods during the last three months of pregnancy using a single 5-frequency item. Child's cognitive development was assessed using the parent-reported Child Development Index (CDI) at years 1, 3.5, and 5.5. Given the plateauing distribution of the 5.5-y CDI score, it was considered as a binary variable identifying children at risk for developmental delay. Associations of organic food consumption with CDI scores were evaluated using multivariable linear or logistic regressions, adjusted for main confounders including maternal education, income, migration history, depression, older children and diet quality.

Results: Almost half of women never consumed organic foods during pregnancy, 28% less than once a week, 17% several times per week, whereas 8% consumed them every day. The consumption of organic food during pregnancy was positively associated with CDI scores at 1 and 3.5 years old and with lower odds of being in the group of children at risk for developmental delay at 5.5 years.

Conclusion: These results suggest that frequent consumption of organic food may be associated with higher cognitive developmental scores, independently of maternal diet quality. Results were consistent after adjusting for breastfeeding. These findings need to be confirmed in other studies.

Routine antenatal corticosteroid administration and childhood respiratory morbidity: a regression discontinuity study

Jennifer Anne Hutcheon[1], Sam Harper[2], Claire Cordingley[1], Jessica Liauw[1], Amanda Skoll[1], Peter Socha[2], Myriam Srour[2], Joseph Ting[3], Erin Strumpf[2]

[1]University Of British Columbia, [2]McGill University, [3]University of Alberta

BACKGROUND: Administration of antenatal corticosteroids at 34-36 weeks' is controversial because the respiratory morbidities they are preventing at these ages are often mild (e.g., transient tachypnea of the newborn). However, mild neonatal respiratory morbidities are predictors of later childhood respiratory illnesses. We investigated if routine administration of antenatal corticosteroids was associated with lower rates of infant hospitalization for lower respiratory tract infections (LRTI) and childhood asthma, using a quasi-experimental design that better controls for confounding than standard observational designs.

METHODS: We identified maternal delivery admissions between 31+0 and 36+6 weeks' gestation in a provincial perinatal registry from British Columbia, Canada, 2000-2016. Obstetrical records were linked with population-based records of childhood hospitalizations and outpatient physician visits until 2020. We used diagnostic codes to identify infant LRTI hospitalizations and childhood asthma. We used a regression discontinuity design, which takes advantage of the fact that pregnancies presenting just before and just after the clinical cut-off for antenatal corticosteroid administration of 34+0 weeks gestation have very different rates of exposure to antenatal corticosteroids, but are otherwise similar with respect to confounder characteristics.

RESULTS: Among 21,969 deliveries, 412 (1.9%) infants were hospitalized with an LRTI, and 3939 (18%) children developed asthma. Routine exposure to antenatal corticosteroids was not associated with lower risks of LRTI hospitalization (risk ratio 0.95 [95%CI: 0.61, 1.37] or asthma (rate ratio 1.04 [95%CI: 0.88, 1.24]).

CONCLUSION: We found no evidence that routine administration of antenatal corticosteroids was linked with lower rates of childhood respiratory illnesses.

Use of ibuprofen prior to and in early pregnancy among women with and without chronic medical diseases

Line Krag Jakobsen[1], Chunsen Wu[2,3], Hanne Kristine Hegaard[1,4], Ane Lilleøre Rom[1,2]

[1]Department Of Gynecology, Fertility And Obstetrics, The Juliane Marie Centre, Rigshospitalet, [2]The Department of Clinical Research, the University of Southern Denmark, [3]Odense University Hospital, [4]Department of Clinical Medicine, University of Copenhagen

Aim: Having a chronic medical disease (CMD) may influence the need for analgesics during pregnancy, but sufficient knowledge regarding their patterns of use are lacking. We aimed to describe ibuprofen use three months prior to pregnancy and in early pregnancy among women with and without CMDs, and to assess the association between CMDs and use of ibuprofen.

Methods: We included 24,018 pregnancies from the Copenhagen Pregnancy Cohort from 2013 to 2019 to compare ibuprofen use between women with and without CMDs using patient-reported data. Descriptive statistics and multivariable logistic regression models were applied.

Preliminary results: Use of ibuprofen was significantly higher among women with CMDs prior to and in early pregnancy compared to women without (19.8% vs. 16.9% and 0.61% vs. 0.27%, respectively). Women with CMDs were 2.4 times more likely to have a frequent use of ibuprofen (daily or 1-2 times per week) three months prior to pregnancy compared to women with CMDs (aOR 2.40, CI 95% 1.96-2.94) and 2.1 times more likely to have any use in early pregnancy (aOR OR 2.08, CI 95% 1.31-3.32). Especially having endometrioses, rheumatological disease, and neurological disease were associated with a higher likelihood of frequent use of ibuprofen prior to pregnancy (aOR 4.85, CI 95% 2.14-10.99, aOR 4.57, CI 95% 2.92-7.16, and aOR 3.55, CI 95% 2.09-6.04, respectively). Similar analyses in early pregnancy were precluded due to insufficient power.

Conclusions: CMDs influenced ibuprofen use prior to and in early pregnancy and should be addressed in preconception counseling and during antenatal care.

Plant-based diet during pregnancy and child's birth weight

Yvan Njonfang Mbakop[1], Rosalie Delvert[2], Barbara Heude[1], Marie-Aline Charles[1], Blandine De Lauzon-Guillain[1]

[1]Université Paris Cité, Inserm, INRAE, CRESS, [2]Université Paris Saclay/Centre de recherche en Epidémiologie et Santé des Populations

Context: The deleterious effects on the environment and health associated with red meat are pushing for a shift towards a plant-based diet. The aim was to study the association between the level of plant-based diet during pregnancy and the child's birth weight.

Methods: The study involved 15,014 children from two French birth cohorts: the ELFE study and the EDEN mother-child cohort. Maternal diet for the last three months of pregnancy was collected at delivery using a validated Food Frequency Questionnaire. The level of plant-based diet was assessed using the Plant-based Diet Index (PDI), the healthful PDI (hPDI) and the unhealthful PDI (uPDI). Birth weight-for-gestational-age z-score was considered both as continuous and categorical variable (small (SGA), adequate, or large (LGA) for gestational age). Associations were analyzed, on the pooled dataset, using linear or logistic regressions adjusted for main confounders.

Results: The PDI, hPDI and uPDI considered as continuous variables were not related to offspring birth weight. Compared to the 1st quintile, belonging to the 5th quintile of the PDI and hPDI was associated with a higher risk of having a SGA baby (OR = 1.15 [1.02, 1.29]) and a lower risk of having LGA baby (OR = 0.86 [0.77, 0.97]), respectively, even after adjustment for pre-pregnancy BMI and energy intake.

Conclusion: High level of plant-based diet during pregnancy appeared associated with a higher risk of SGA for the child. These findings need to be confirmed in studies with prospective design and more vegetarian and vegan women.

Neurodevelopmental impairments in children following Group B Streptococcal disease: A population-based cohort study in Ontario, Canada

Romina Fakhraei[1,2], Deshayne Fell[1,2], Darine El-Chaâr[1,3], Nisha Thampi[1,2], Beate Sander[4,5,6], Kevin Brown[4,6,7], Natasha Crowcroft[4], Shelly Bolotin[4,7], Jon Barrett[8], Elizabeth Darling[8], Nahuel Fittipaldi[9], Theresa Lamagni[10], Allison McGeer[11], Michelle Murti[4], Manish Sadarangani[12,13], Kevin Schwartz[4,6,7,14], Abdool Yasseen[4,7], Matthew Tunis[15], William Petrcich[6], Kumanan Wilson[3]

[1]University Of Ottawa, [2]Children's Hospital of Eastern Ontario Research Institute, [3]Ottawa Hospital Research Institute, [4]University of Toronto, [5]University Health Network, [6]ICES, [7]Public Health Ontario, [8]McMaster University, [9]Université de Montréal, [10]UK Health Security Agency, [11]Mount Sinai Hospital, [12]University of British Columbia, [13]BC Children's Hospital Research Institute, [14]Li Ka Shing Knowledge Institute, Unity Health Toronto, [15]Public Health Agency of Canada

Background: Group B Streptococcus (GBS) is a leading infectious cause of neonatal morbidity and mortality globally, yet data on longer-term outcomes in children remain limited. We aimed to assess the risk of neurodevelopmental impairments (NDIs) among survivors of GBS disease.

Methods: We conducted a population-based cohort study of births between April 2012 to March 2018, utilizing the provincial birth registry linked with health administrative databases. GBS disease in the first year of life was ascertained through culture results and diagnostic codes. Children were followed until age 5 to assess NDIs, which encompassed cognitive, motor, sensory (hearing, vision), and social/behavioral domains, categorized by severity (mild, moderate, severe). Risks of overall, domain-specific, and multidomain NDIs were assessed, utilizing Cox regression to estimate adjusted hazard ratios (aHR) comparing children with/without GBS disease before 1 year of age.

Results: Among 764,934 children included, 771 (0.10%) had a history of GBS disease in the first year. GBS disease was associated with increased risks of any domain NDI (aHR: 2.18, 95% CI: 1.88–2.54) and multidomain NDIs (aHR: 2.09, 95% CI: 1.39–3.16). In the GBS group, 5.5% (42/771) had a moderate-severe NDI, versus 3.4% (25,732/764,163) in the unexposed group (aHR: 1.66, 95% CI: 1.21–2.29). GBS survivors were at increased risk of cognitive (aHR: 2.56; 95% CI: 2.15–3.05), motor (aHR: 7.08; 95% CI: 2.93–17.08), sensory (aHR: 1.64; 95% CI: 1.02–2.64) and social/behavioural (aHR: 1.60; 95% CI: 1.20–2.14) disorders.

Conclusion: Survivors of infant GBS disease are at an increased risk of NDIs, emphasizing the need for effective preventative strategies.

Maternal stress during pregnancy as a risk factor for childhood type 1 diabetes – a population-based Swedish cohort study

Awad Smew[1], Cecilia Lundholm[1], Tong Gong[1], Lars Sävendahl[2,3], Paul Lichtentein[1], Bronwyn Brew[1,4], Catarina Almqvist[1,5]

[1]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, [2]Department of Women's and Children's Health, Karolinska Institutet, [3]Pediatric Endocrinology Unit, Astrid Lindgren Children's Hospital, Karolinska University Hospital, [4]National Perinatal Epidemiology and Statistics Unit, Centre for Big Data Research in Health and School of Clinical Medicine, University of New South Wales, [5]Pediatric Allergy and Pulmonology Unit, Astrid Lindgren Children's Hospital, Karolinska University Hospital

Background: Previous research has shown that childhood stress may trigger type 1 diabetes development but less is known on potential fetal programming by maternal stress during pregnancy. We therefore aimed to investigate the association between a proxy of maternal stress (depression/anxiety during pregnancy) and offspring type 1 diabetes. Furthermore, the study aimed to explore potential unmeasured familial confounding, i.e., shared genetic or environmental factors.

Methods: From the Swedish population, 1.8 million offspring born 2002–2019 were linked to their biological parents and followed from preconception, during pregnancy, and childhood, through 2021. From national registers, data were available on diagnosis or medication prescription for depression/anxiety in and around pregnancy, as well as incident cases of type 1 diabetes defined through diagnosis or insulin treatment. Associations were examined using flexible parametric and Cox regression models. Familial confounding was explored using paternal exposure as a negative control and by comparing offspring exposed to maternal depression/anxiety with their unexposed siblings.

Results: Maternal depression/anxiety during pregnancy was associated with an increased risk of type 1 diabetes onset after, but not before, 8 years of age (adjusted hazard ratio [aHR] 1.21 (95% CI 1.03, 1.42]). Associations were close to the null for paternal depression/anxiety (aHR 0.95 [0.72, 1.25]), and point estimates were above 1 in sibling comparisons, albeit with wide CIs (aHR 1.36 [0.82, 2.26]).

Conclusion: Maternal stress during pregnancy was associated with childhood type 1 diabetes. Paternal negative control and sibling comparisons indicate that the findings are not entirely due to confounding from familial factors.

Associations between prenatal per- and polyfluorinated substances (PFAS) exposure and antibody response to childhood vaccines in Norwegian children

Berit Granum[1], Gro Tunheim[1], Johanna Bodin[1], Cathrine Thomsen Cathrine Thomsen[1], Marta Baranowska-Hustad[1], Azemira Sabaredzovic[1], Thea Kristine Rogne Møller[1], Kristine Gützkow[1], Line Småstuen Haug[1], Merete Merete Eggesbø[1], Nina Iszatt[1]

[1]*Norwegian Institute Of Public Health*

Background: Per- and polyfluorinated Substances (PFAS) are immunotoxicants, and there is need to study effects in populations with different exposures. We assessed prenatal PFAS exposure and vaccine antibody response in Norwegian children.

Methods: We combined two sub-populations of the Norwegian Mother, Father and Child Birth Cohort Study (MoBa, 2002-2009): HELIX (n=268, 7-10 years) and the Norwegian Environmental Biobank II (n=642, 7-14 years). PFAS were measured in maternal 2nd trimester and childhood samples (five in HELIX and 12 in NEB II). 10 persistent organic pollutants (POPs) were also measured. Antibody response (IgG) to tetanus, diphtheria and rubella was measured in childhood samples using 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. Analyses were restricted to those with recommended doses (DTP 4 doses, MMR 2 doses).

Results: In children under 12 years, per interquartile range (IQR) increase in exposure, prenatal perfluorononanoic acid (PFNA) was associated with higher diphtheria antibodies in boys (β=0.19, 95% CI: 0.02–0.36). For 12 years and over, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) were associated with lower diphtheria antibodies in girls (β=-0.39, 95% CI: -0.75– -0.02) and boys (β=-0.42, 95% CI: -0.84– -0.01), respectively. Adjustment for POPs did not affect results. Similar trends were found for tetanus and rubella antibodies.

Conclusion: Prenatal PFAS exposure may have differing effects on the immune response based on child's age and sex, possibly due to puberty. We will further investigate mixture effects and current exposure.

Antibody levels and predictors for low response to childhood vaccines among 7–14-year-old children in Norway

Johanna Bodin[1], Nina Iszatt[1], Marta Baranowska-Hustad[1], Berit Granum[1], Thea Kristine Rogne Møller[1], Tove Karin Herstad[1], Audun Aase[1], Merete Eggesbø[1], Gro Tunheim[1]

[1]*Norwegian Institute Of Public Health*

Background: Children in Norway are offered vaccination against diphtheria, tetanus and pertussis (DTP) at 2, 3 and 5 months of age, and 6 and 15 years, and measles, mumps, and rubella (MMR) at 15 months and 11 years. We analysed factors predicting low antibody responses to vaccinations.

Methods: Participants came from two sub-cohorts of the Norwegian Mother, Father and Child Cohort Study (MoBa): The Norwegian Environmental Biobank (NEB) and Human Early Life Exposome (HELIX). We measured IgG antibody levels against DTP and MMR in 901 children (7-14 years) in plasma samples using multiplex immunoassays. Data on immunization and maternal and child predictors were collected from the Norwegian Immunisation Registry (SYSVAK) and parental questionnaires.

Results: Among children with 4 doses of DTP vaccine, 5.1% and 20.6% had antibody levels below 0.1 IU/ml against tetanus and diphtheria, respectively. 14.2% and 1.7% had an antirubella concentration of <10 IU/ml after 1 dose (median age 9 years) or 2 doses (median age 12 years) of MMR vaccine, respectively. Preliminary analyses suggest that high BMI at sampling was associated with antibody levels below 0.1 IU/ml for tetanus and diphtheria and delivery by C-section associated with lower tetanus antibodies. Among children who had received 1 or 2 doses of MMR vaccine, antibody levels against rubella were lower among those breastfeed for >6 months compared to those breastfeed <6 months.

Conclusion: Despite high vaccination coverage in Norway, vaccine antibody levels were low in some children. Some modifiable risk factors may predict lower vaccine responses to childhood vaccinations.

Lifespan risk of sepsis by gestational age at birth

Jonas Valand[1], Sara Marie Nilsen[2], Erik Solligård[3,4], Tormod Rogne[3,5], Kari Risnes[1,6]

[1]Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, [2]Center for Health Care Improvement, St. Olav's University Hospital, [3]Department of Circulation and Medical Imaging, Mid Norway Sepsis Research Center, Norwegian University of Science and Technology, [4]Department of Research and Development, Møre and Romsdal Hospital Trust, [5]Yale Department of Chronic Disease Epidemiology and Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, [6]Children's Clinic, St. Olav's Hospital, St. Olav's University Hospital

Background: Preterm birth is an important risk factor for sepsis in early childhood. However, it remains unknown whether the risk persists beyond this period and whether it applies to the whole spectrum of gestational ages before full term.

Methods: We linked individual-level data for everyone born in Norway (1967-2021) to nationwide hospital data (2008-2021). Gestational age was categorized as weeks 23-27 (extremely preterm), 28-31 (very preterm), 32-33 (moderately preterm), 34-36 (late preterm), 37-38 (early-term), 39-41 (full-term), and 42-44 (post-term). Sepsis was defined as explicit or implicit based on whether a sepsis diagnosis code was used directly or whether a combination of infection and organ dysfunction codes were used, respectively. Stratified by age at follow-up (0-11 months, 1-5, 6-14, 15-29, and 30-54 years), incidence rate ratios (RRs) were estimated using negative binomial regression, adjusted for birth year, sex, maternal age, and parity.

Results: Among 3,230,926 individuals with 504,685 hospitalizations for infections, of which 49,549 with sepsis, we observed higher sepsis risks in lower gestational age groups. The association was strongest in childhood but persisted into adulthood. Comparing those born very preterm and late preterm to full-term, RRs (95% confidence interval) for hospitalization for sepsis at ages 1-5 were 4.9 (3.7-6.5) and 2.2 (1.8-2.6), respectively. At 30-54 years, the corresponding estimates were 2.1 (1.1-4.0) and 1.4 (1.2-1.7).

Conclusion: Lower gestational age at birth was linked to an increased risk of sepsis hospitalizations, and this persisted into adult life. Investigating potential mechanisms and developing effective prevention strategies are critical next steps.

Gut microbiota and sleep in 3.5-year-old children from a French birth cohort

Zeinab Houshialsadat[1], Cécile Zaros[2], MJ Butel[3], MA Charles[1,2], Gaël Toubon[1], Sabine Plancoulaine[1,4]

[1]Inserm, U1153, CRESS, [2]INED, [3]Inserm, UMR-S 1139, 3PHM, [4]Inserm, U1028, CRNL

Background: Sleep is critical to mental and physical wellbeing. Sleep disturbances are common during the preschool period a key for consolidating sleep and stabilizing the gut microbiota characteristics, but a window of opportunity to intervene at early years. We aimed to assess the association between gut microbiota and sleep at 3.5-years in the French Longitudinal Study from Infancy (ELFE).

Methods: We included 597 children with available data on stool sample and sleep at age 3.5 years. Sleep characteritics were collected using parental telephone questionnaires. Latent Class Analysis (LCA) was used to construct sleep clusters based on day and night sleep durations over the week, frequent sleep onset difficulties and night awakenings. Bacterial 16S rRNA gene sequencing was performed to profile the gut microbiota. Associations between sleep clusters and gut microbiota diversity metrics and enterotypes were assessed by multivariate logistic regressions or permutation multivariate analysis of variance, adjusting for confounding factors.

Results: Two sleep clusters were identified with more or less optimal sleep, with 25% of the children classified in the latter cluster. No significant associations were observed between sleep clusters at age 3.5 and the included gut microbiota metrics i.e., alpha diversity (Chao1 estimate and Shannon index), overall composition (beta diversity), enterotypes, or specific genera abundances. The sleep duration in both clusters was within the AASM's recommendations, possibly partially explaining the lack of associations observed.

Conclusion: While emerging evidence suggest correlations between gut microbiota and sleep in preschoolers, our results from a socioeconomically homogeneous population do not support such correlations.

The Association of Longer Breastfeeding Duration and Socioeconomic Factors, Pregnancy, Childbirth and Postpartum Characteristics

Jekaterina Kozacenko[1]

[1]*Rīga Stradins University Institute of Public Health*

Objectives: Breastmilk is the safest and most suitable food for an infant and plays a role of the first vaccine with all the essential nutrients, antibodies, hormones and antioxidants for the first months. WHO recommends exclusive breastfeeding from birth to 6 months of age, continued breastfeeding until 2 years and beyond. According to Latvian statistical data of 2022 – 88,1% of infants were breastfed for 6 weeks, 53,7% for 6 months and only 27,4% were breastfed for 12 months. The aim of this study was to investigate the duration of breastfeeding in Latvia in relation to mothers` socio-demographic factors, pregnancy, childbirth, and the postpartum period factors.

Methods: Data from the "Study on factors and habits affecting the sexual and reproductive health of the population in Latvia" carried out by Ministry of Health of Latvia, 2023, was used. Cross -sectional study with a representative sample of women who gave a birth at least once (n= 1407) aged 15 – 64 years were analyzed. Dependent variable was breastfeeding duration. Binary logistic regression was used to detect factors independently associated with the breastfeeding duration. Variables with statistically significant association in univariate analysis were included in a binary logistic regression model. R

Results: Multivariate analysis shows that not smoking during pregnancy (aOR=2.1), two childbirths (aOR= 1.5), maternal higher education (aOR=2.0), breastfeeding initiation immediately after childbirth (aOR=1.7) are associated with longer breastfeeding duration.

Conclusions: Identification of factors promoting longer breastfeeding in Latvia is useful in planning and organizing targeted public health activities.

Use of antimigraine medication before pregnancy and in the first trimester. A cross-sectional study

Stine Wieland[1], Marie Stampe Emborg[1], Mie Gaarskjær de Wolff[2,3], Peter Damm[1,4], Mona Ameri Chalmer[5], Hanne Kristine Hegaard[1,4], Ane Lilleøre Rom[1,6]

[1]Department of Gynecology, Fertility and Obstetrics, Juliane Marie Centre, Copenhagen University Hospital, Rigshospitalet , [2]Department of Obstetrics and Gynecology, Amager- Hvidovre Hospital, [3]University of Southern Denmark, Department of Public Health, Section for Health Promotion, [4]Faculty of Health Sciences. Department of Clinical Medicine, University of Copenhagen, [5]Department of Neurology, Danish Headache Centre, Rigshospitalet, [6]Research Unit of Gynecology and Obstetrics, Department of Clinical Research, University of Southern Denmark

Background: Knowledge of use of antimigraine medication before and during pregnancy is needed to ensure optimal migraine treatment and minimize potential teratogenic risk. We aimed to describe the prevalence of use of antimigraine medication three months before pregnancy and in the first trimester among women with migraine, and to assess maternal characteristics associated with a frequent use (daily or 1-2 times/week) in the first trimester.

Methods: We used patient-reported data from the Copenhagen Pregnancy Cohort October 2013 - May 2019 and included all women with migraine. The prevalence of antimigraine medication use before and in the first trimester was assessed descriptively, and associations with maternal characteristics were analysed using logistic regression.

Results: We identified 1586 pregnancies of women with migraine corresponding to a prevalence of 6.6%. Among these, 78% reported any use before pregnancy and 22% in the first trimester. Before pregnancy, paracetamol was the most used medication, followed by ibuprofen and sumatriptan. In the first trimester, paracetamol was the most common used drug, followed by sumatriptan. Five per cent reported a frequent use of antimigraine medication in the first trimester. Characteristics associated with frequent use were short education and other chronic somatic or mental diseases.

Conclusion: Most women with migraine reported use of antimigraine medication before pregnancy, but usage was reduced in the first trimester. Only few women used medication frequently in the first trimester. Women with a short education, chronic somatic diseases or mental illness were more likely to use antimigraine medication than women without.

The risk of adverse pregnancy outcomes across generations in a high-income country

Maria Jeppegaard[1,2,3], Steen Rasmussen[1,3,4], Lone Krebs[1,2], Anne Marie Nybo Andersen[5]

[1]Department of Gynecology and Obstetrics, Copenhagen University Hospital - Amager and Hvidovre, [2]Department of Clinical Medicine, University of Copenhagen, [3]Department of Gynecology and Obstetrics, Copenhagen University Hospital-Holbaek, [4]Centre of Diagnostic Investigation, Copenhagen University Hospital-Rigshospitalet, [5]Section of Epidemiology, Department of Public Health, University of Copenhagen

Background: There are studies suggesting that women with a maternal history of pregnancy complications have higher risk of pregnancy complications in their own pregnancies, but is it a risk factor that should be considered in the antenatal care if a pregnant woman report that her mother had a perinatal death? The aim of this study is to investigate if a maternal family history with perinatal death increases the risk of perinatal death for a pregnant woman.

Methods: This is a nationwide register-based cohort study. All women giving birth in Denmark between January 1,2010 and December 31, 2021 were included if they were born in Denmark after January 1, 1978 and registered in MBR. The maternal family history of perinatal death (stillbirth and early neonatal death) was registered. To account for clustering in the included women, we conducted a robust sandwich model in the analysis. We adjusted for smoking, BMI>30 and education.

Results: This study included 507,240 children delivered by 305,865 women. A total of 2910 cases of perinatal death were included and 90 of these had a maternal family history of perinatal death. The proportion of lower education level, smoking and BMI>30, preterm birth and growth restriction was higher in cases of perinatal death. We found an increased risk of perinatal death in women with a maternal history (OR 1.35, 95%CI 1.07-1.71 (aOR 1.35 (95%CI 1.06-1.72)).

Conclusion: Women with a maternal family history of perinatal death has a higher risk of experiencing perinatal death.

Are mothers with multiple sclerosis at higher risk of a postpartum depression? A nationwide cohort study

Mette Louise Andersen[1,2,3], Line Riis Jølving[1,2], Elsebeth Stenager[4], Egon Stenager[4,5], Thomas McElrath[6,7], Bente Mertz Nørgård[1,2]

[1] Center for Clinical Epidemiology, Odense University Hospital, Kløvervænget 30, entrance 216, DK-5000 Odense, Denmark, [2] Research Unit of Clinical Epidemiology, Department of Clinical Research, University of Southern Denmark, [3] Department of Gynecology and Obstetrics, University Hospital of Southern Jutland, Esbjerg, [4] Department of Regional Health Research, University of Southern Denmark
[5] Multiple Sclerosis Clinic of Southern Jutland, University Hospital of Southern Jutland, [6] Brigham and Womens Hospital, Department of Maternal-Fetal Medicine and Harvard Medical School, Boston, Massachusetts, US, [7]Harvard T.H Chan School of Public Health, Boston, Massachusetts, US

Objective: Postpartum depression (PPD) is the most common mental disorder in relation to childbirth with a global estimated prevalence among mothers of 10-15%. Women with multiple sclerosis (MS) are shown to have increased risk of depression, but whether this involves motherhood is not clarified. We aimed to investigate if women with MS have increased risk of postpartum depression.

Methods: We used the Danish national health registers to establish the study cohort of all births by women with MS born from 1995 to 2019. In logistic regression models we estimated odds ratios (OR) and 95 % confidence intervals (95% CI) of antidepressant prescriptions in the 12 months following childbirth. The risk estimates were adjusted for relevant confounders such as maternal age, parity, BMI, calendar year of birth, adverse obstetrical outcomes, and hospitalizations during pregnancy.

Results: The study cohort consisted 1,461,283 childbirths, including 2,655 childbirths in women with MS from 1 January 1995 until 31 December 2018. We found that women with MS are at increased risk of a postpartum depression with adjusted OR 1.94 (95% CI 1.65-2.28). The risk estimate was adjusted for maternal age, BMI, calendar year of birth, birth complications, and hospitalization during pregnancy.

Conclusion: Women with MS are at increased risk of postpartum depression. This is independent of adverse obstetric outcomes, and without any medically treated depression prior to pregnancy. The results of this study is important in order to facilitate support, screening and timely treatment of this special group of women, since severe PPD is preventable.