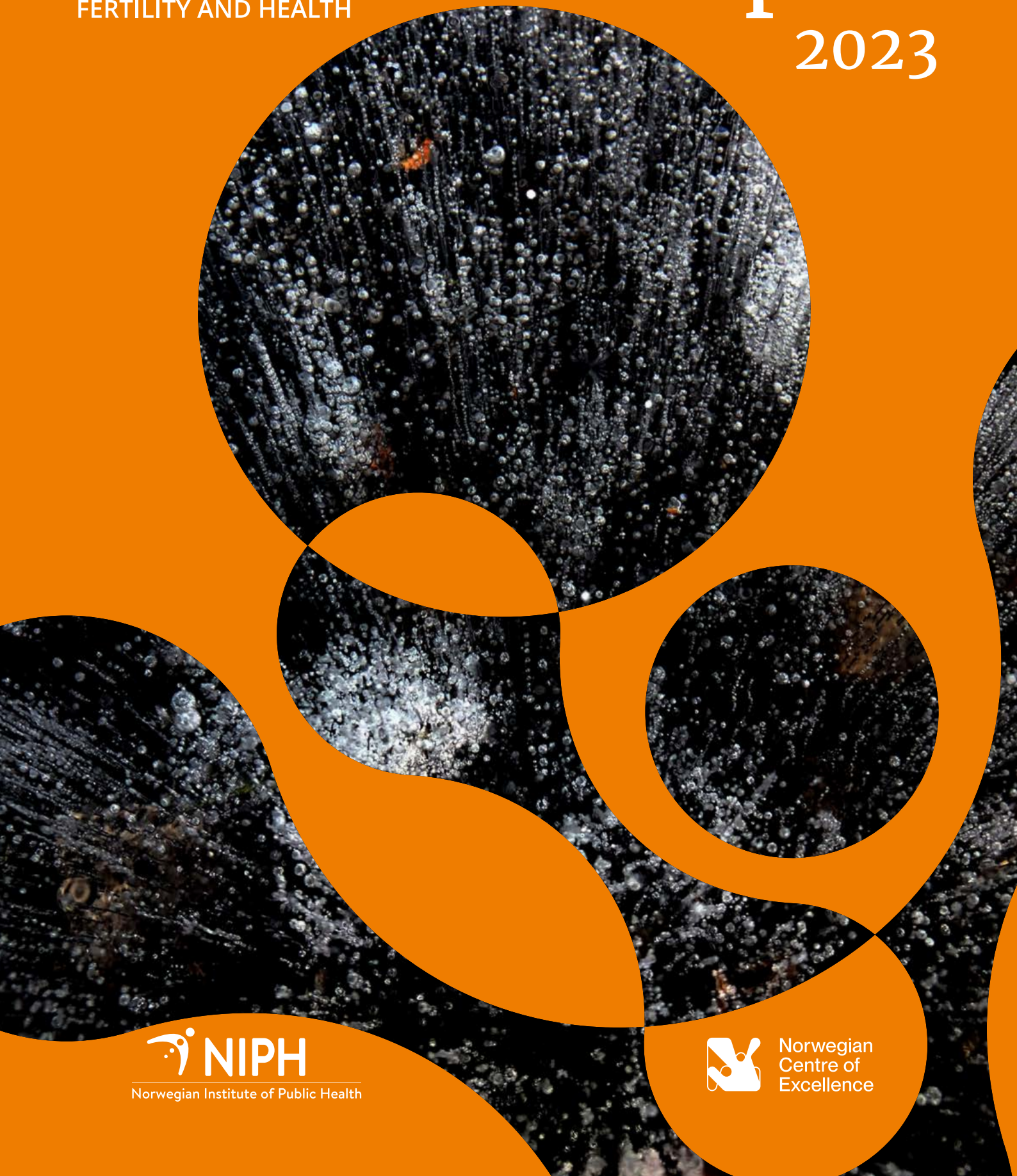
CENTRE FOR
FERTILITY AND HEALTH

Annual report 2023



NIPH
Norwegian Institute of Public Health

Norwegian
Centre of
Excellence

Contents

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Introduction from the Centre Directors

For CEFH, 2023 has been a year with continued success. Our team counts around 60 researchers. In 2023, we moved again to new offices. We hope to stay in these offices for the remaining period of the Centre of Excellence (CoE) funding and beyond.

Since the inception in 2017, we have produced over 500 scientific papers, with a considerable number in leading journals. Our scientific success is a result of extensive and active collaboration with researchers in more than 50 national and international institutions.

2023 – a challenging year for our host institution
Our host institution, the Norwegian Institute of Public Health, went through major changes in 2023. Severe budget cuts led to a reduction in the workforce. A restructuring of the central health administration in Norway also brought changes. CEFH has been successful in securing external funding for research over the last years. Therefore, we are less affected by the internal budget cuts than other units in our institute. The changes did not lead to a downsizing of the Centre, but we had to adjust some of our ambitions.

Successful early career researchers
In 2023, three of our talented PhD candidates successfully defended their theses: Dana Kristjansson, Ellen Øen Carlsen and Kristine Løkås Haftorn. PhD candidates Kristine Løkås Haftorn, Hans Fredrik Sunde and Kathryn Beck received prizes for their presentations at conferences and events. Several of our early career researchers obtained media attention. It is a pleasure to see that the postdocs are successful in securing new permanent positions at NIPH or at other institutions. We are also pleased that the PhD candidates move on to postdoc and researcher positions.

In 2023, several visitors came to the Centre. Two Fulbright scholars, Michael Betz and Darci Johnson, came for longer stays, and two researchers, Florence Martin and Amanuel Gebremedhin, were granted the Gro Harlem Brundtland Visiting Scholarship. Three other researchers, Lara Tavares, Bernardo Lanza Queiroz and Weiqian Xia, came to work with the Dimjob project. In addition, we have had many other guests for shorter stays. These visits to our centre are tools for developing scientific collaborations. Members of our team are appointed as hosts to be responsible for introducing the guests, to facilitate presentation of ongoing collaborative work, and to set up meetings with relevant persons at CEFH during the visits.

External funding
A main goal of the Centre is to ensure high-quality, innovative research within fertility and health through continued investment in state-of-the-art technologies, methodologies, and interdisciplinary collaboration. With successful research proposals to highly competitive calls, we ensure that our research holds the highest standards.

Since 2017, researchers at the Centre have submitted around 90 proposals for external funding as principal investigators and participated in numerous proposals as collaborators. Of these 90 proposals, 24 have been funded so far, with a total funding budget of around 400 MNOK. All applications are assessed for relevance to our research themes and for budgetary constraints before submission. A key to success is writing proposals as a team effort. For every grant proposal an appointed administrative person is part of the team.

Projects ending in 2023
The research project *"Health-gap"* was wrapped up with an open seminar at Litteraturhuset on March 16 with over 250 participants. The seminar included a panel discussion with the Minister of Health and other stakeholders. The event had over 2000 views online. The project started just after the inception of the Centre and has been a remarkable success. The project's topic, gender differences in school performance, has recently received much attention. The research is followed up through several other projects. Read more about this research in the impact case presented on page 19.

Projects starting up in 2023
Our new ERC Synergy Grant project *"BIOSFER"* was launched at an event in September at the Max Planck Institute for Demographic Research in Rostock, Germany. We have established the first phase of data collection in the project and recruited several PhD and postdocs. Other projects that started in 2023 are *"Parment – Parenthood, childlessness, and mental health in times of falling fertility"*, *"SCOPE2 – Studies of COVID-19 in pregnancy"* and *"ART and cancer – Risk of breast cancer in persons born after assisted reproductive technologies (ART)"*.

Beyond the Centre of Excellence period
The Centre has four more years of funding from the CoE grant. Presently, we are planning for our afterlife. The portfolio includes externally funded projects that continue beyond the end date of the CoE funding. With our accomplishments in achieving funding, we expect several projects to start in the coming years. The aim is to keep our team of researchers and continue to develop the fruitful scientific environment of CEFH. We will continue the interdisciplinarity that has developed over the years. This environment is vital for a continued success. The main topic at our annual Centre gathering in March was ideas for a CoE proposal, with the aim of submitting a new application to the Research Council of Norway in 2025. The work on this application has started. We continue to develop other grant proposals. The advantage of having ambitious researchers from as diverse fields as sociology, demography, economics, medicine, genetics, biology, and statistics, is that we can benefit from critical internal reviews and discussions before submission.

We look forward to another exciting year in 2024!

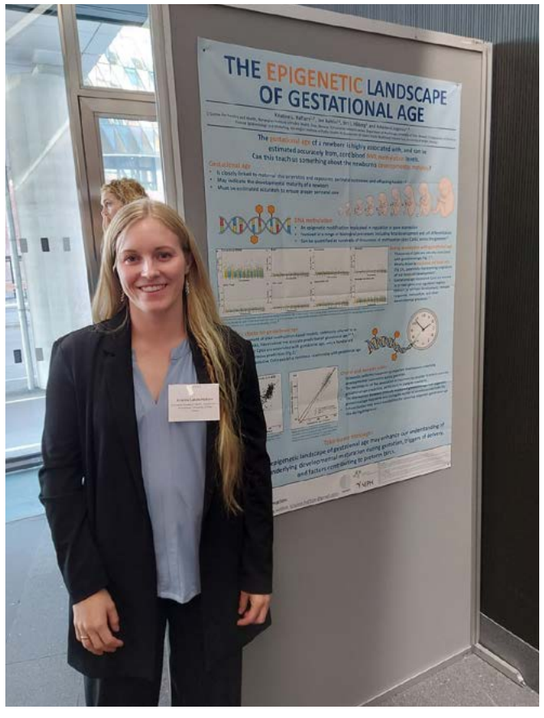
Siri E. Håberg, Centre Director

Per Magnus, Centre Deputy Director

Highlights 2023

A strong interdisciplinary team

By the end of 2023, 29 women and 32 men were associated with the centre including researchers in full- and part-time positions and administrative personnel. The centre also has many national and international visiting researchers and other associated collaboration partners.



Selected publications

Carlsen EØ, Wilcox AJ, **Magnus MC**, **Hanevik HI** and **Håberg SE**. (2023). Reproductive outcomes in women and men conceived by assisted reproductive technologies in Norway: prospective registry based study. *BMJ Medicine* 2(1), e000318.

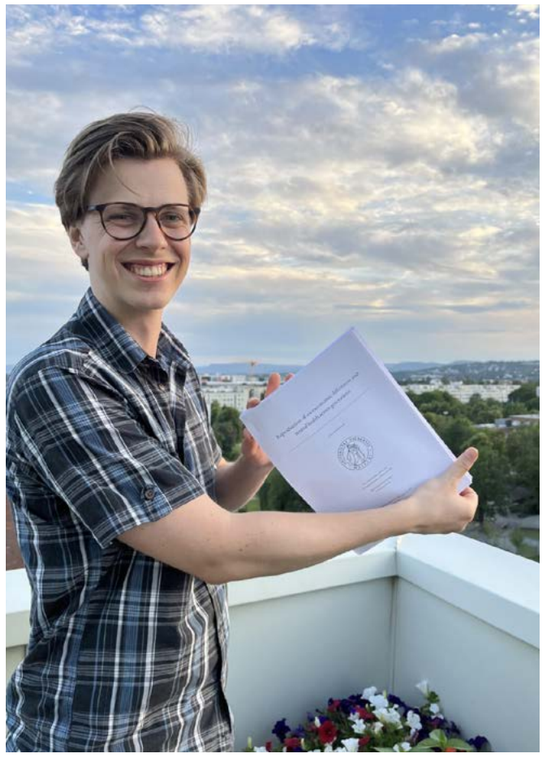
Haftorn KL, Romanowska J, Lee Y, Page CM, Magnus PM, Håberg SE, Bohlin J, Jugessur A and Denault WRP. (2023). Stability selection enhances feature selection and enables accurate prediction of gestational age using only five DNA methylation sites. *Clinical Epigenetics* 15, 1, 114.

Kravdal Ø and Wörn J. (2023). Mental and Physical Health Trajectories of Norwegian Parents and Children before and after Union Dissolution. *Population and Development Review* 49, 1, 71-103.

Magnus MC, Fraser A, **Håberg SE**, Rönö K, **Romundstad LB**, Bergh C, Spangmose AL, Pinborg A, Gissler M, Wennerholm UB, Åsvold BO, Lawlor DA and Opdahl S. (2023). Maternal Risk of Cardiovascular Disease After Use of Assisted Reproductive Technologies. *JAMA Cardiology*.

Romanowska J, Nustad HE, **Page CM**, **Denault WRP, Lee Y, Magnus MC, Haftorn KL, Gjerdevik M**, Novakovic B, Saffery R, **Gjessing HK, Lyle R, Magnus P, Håberg SE** and **Jugessur A**. (2023). The X-factor in ART: does the use of assisted reproductive technologies influence DNA methylation on the X chromosome? *Human Genomics* 17, 1, 35.

Skodvin SN, Gjessing HK, Jugessur A, Romanowska J, Page CM, Corfield EC, **Lee Y, Håberg SE** and **Gjerdevik M**. (2023). Statistical methods to detect mother-father genetic interaction effects on risk of infertility: A genome-wide approach. *Genetic Epidemiology* 47, 7, 503-519.



Theses

Ellen Øen Carlsen. Determinants of perinatal outcomes in Norway: 1982-2020.

Kristine Løkås Haftorn. The role of DNA methylation in gestational age.

Dana Kristjansson. Historical and Phylogeographic Influences on Mitochondrial DNA Diversity in Norwegians.

New externally funded projects

10 million NOK were granted to the project *"Pubertal timing and inequalities in education"* led by **Martin Flatø**. The project is funded by the Research Council of Norway through a thematic priority call on education and competence.

11,9 million NOK were granted to the project *"YoungWork: Young adults' mental health and labor market exclusion - causes, consequences, and trends"* led by **Jonas Minet Kinge** together with **Jonathan Wörn and Bjørn-Atle Reme**. The project is funded by the Research Council of Norway through a thematic priority call on welfare, culture and society.

8 million NOK (to be confirmed) were granted to the project *"YoungPsych: Drivers and implications of the mental health decline among the young"*, led by **Jonathan Wörn**. This Young Research Talents project is funded by the Research Council of Norway through FRIPRO.

Prizes and awards

Katryn Beck won the prize for best presentation at the *29th Norwegian Epidemiological Association (NOFE) conference* for her presentation of "*The Manipulation of Birth Timing and a Novel Approach to School Starting Age and ADHD".*

Kristine Løkås Haftorn won the prize for best poster at the *European Perinatal and Pediatric Epidemiology Conference (EPEC)* for her poster "*The epigenetic landscape of gestational age*".

Hans Fredrik Sunde received the *Behavior Genetics Associations Thomson Award* for best oral presentation about "*Assortative mating increases genetic similarity among distant relatives: evidence from polygenic scores".*

Major events

- Health-gap ending seminar. Mar 16, 2023.
- Centre seminar. Mar 29-30, 2023.
- 6th Annual CEFH Symposium 2023. May 15-16, 2023.
- CEFH summer garden party. June 15, 2023.
- BIOSFER kickoff meeting. Sep 20-22, 2023.
- European Perinatal and Pediatric Epidemiology Conference (EPEC). Sep 28, 2023
- Centre moving to new offices. Oct 2023.
- Hosting the Demography Breakfast at CEFH. Dec 14, 2023.
- Centre Christmas lunch. Des 19, 2023.
- PhD seminars and courses
- Various project specific seminars and over 50 weekly seminars.

Ambitions towards 2027: Our research themes

The overarching scientific goal of the Centre is to advance the understanding of the factors that influence fertility and elucidate the social and biological pathways through which fertility affects health across the lifespan.

In addition to this overarching goal, we aim to increase our knowledge about the determinants and health consequences of union formation and dissolution, which are closely linked with fertility.

To address these issues, the Centre combines expertise from epidemiologists, geneticists, physicians, psychologists, demographers, statisticians, sociologists and economists.

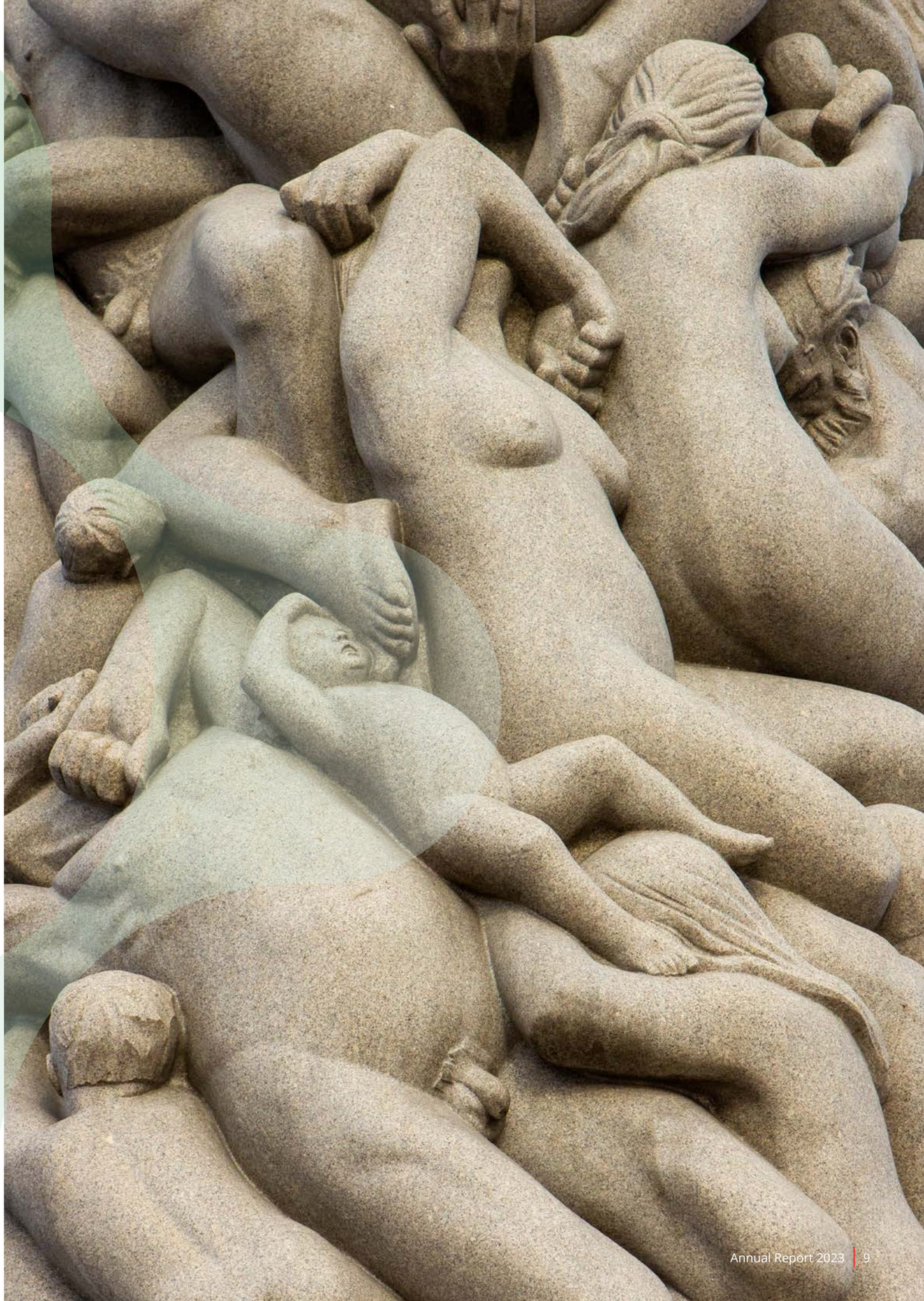
As the Centre has evolved, new research ideas have been added to the ones originally described in our CoE proposal. They reflect advances in the field and new ideas are spawned by the growing number of Centre team members and collaborators.

Ongoing research projects are aiming to understand how maturation and education influence health, how biological age can be measured and what is shaping fertility in young adults today. The pandemic has also provided new research opportunities.

We have defined six main research themes. The research themes are an underlying framework for our research. Many of our research projects and activities are intertwined and integrated parts in several of these main themes.

Our six current research themes are:

- Maternal and paternal age
- Infertility, subfertility and reproductive technologies
- Fetal life, adolescence and fertility outcomes
- Fertility, family structure and transmission of health across generations
- New statistical methods for analysing family and transgenerational data
- Covid, vaccination and its implications on pregnancy, young adults, education, partner formations and fertility



Maternal and paternal age

Age is perhaps the most important predictor of fertility and health. Maternal and paternal age influence the ability to become pregnant and has consequences for pregnancy outcomes and for health. Aging processes differ between individuals, as some appear to age faster and some slower than people of the same chronological age.

Our research is at the forefront of developing biological aging clocks, which we use to study how differences in chronological and biological age are associated with fecundity, fertility and risk of disease.

We investigate the impact of maternal and paternal age at childbirth on subfertility, pregnancy outcomes, and consequences for parental and child health. We also analyse the factors behind the increasing age at childbearing.

KEY AIMS

- To understand how maternal and paternal age affect pregnancy outcomes and children's health through social and biological mechanisms.
- To improve biological clocks of ageing, including gestational age clocks, and to use them in ongoing research on fertility and ageing.
- To understand which factors influence age at childbearing in young adults today.

PRESENT ACHIEVEMENTS

Magnus MC *et al.* (2019). Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. *BMJ* 364, 1869.

Haftorn KL *et al.* (2023). Nucleated red blood cells explain most of the association between DNA methylation and gestational age. *Communications Biology* 6(1), 224.

Lee Y *et al.* (2020). Blood-based epigenetic estimators of chronological age in human adults using DNA methylation data from the Illumina MethylationEPIC array. *BMC Genomics* 21(1), 747.

Basso O *et al.* (2022). Parents' age at birth and daughters' time to pregnancy: a study within the Norwegian Mother, Father and Child Cohort. *Human Reproduction* 37(8), 1896-1906.

Infertility, subfertility and assisted reproductive technologies

Assisted reproductive technologies can help many subfertile couples to become pregnant. Studies indicate that children conceived with assisted reproductive technologies are at increased risk of some adverse health outcomes in childhood and young adulthood. However, whether this is related to the technologies themselves or to underlying heritable aspects of subfertility is difficult to disentangle.

We use genetic, epigenetic and registry data to investigate causes and consequences of infertility and health consequences of subfertility and assisted reproductive technologies in parents and children.

KEY AIMS

- To investigate the social and biological causes and consequences of subfertility and the use of assisted reproductive technologies.
- To understand the nature of the relationships between infertility, various diseases, and health status.
- To understand how genetic influences and epigenetic differences are associated with subfertility and the use of assisted reproductive technologies in parents and children.

PRESENT ACHIEVEMENTS

Håberg SE *et al.* (2022). DNA methylation in newborns conceived by assisted reproductive technology. *Nature Communications* 13, 1896.

Goisis A *et al.* (2020). The demographics of assisted reproductive technology births in a Nordic country. *Human Reproduction* 35(6), 1441-1450.

Bratsberg B *et al.* (2021). Fathers of children conceived using ART have higher cognitive ability scores than fathers of naturally conceived children. *Human Reproduction* 35(6), 1461-1468.

Lee Y *et al.* (2022). Associations between epigenetic age acceleration and infertility. *Human Reproduction* 37 (9), 2063–2074.

Magnus MC *et al.* (2021). Growth in children conceived by ART. *Human Reproduction* 36(4), 1074-1082.

Fetal life, adolescence and fertility outcomes

Starting with conception and fetal life, we investigate how factors in early life affect maturation, puberty, later fertility and health. Central topics include educational pathways, mental health in social interactions and partner formation.

In the last decades there has been a steep increase in gender dysphoria. We need to understand both social and biological aspects of this increase. We will investigate whether environmental substances in fetal life can disturb development and influence sexual identity.

KEY AIMS

- To understand causes and consequences of gender differences in school performance and examine whether they are explained by differences in timing of physical maturity between girls and boys.
- To understand the interplay between education, labour market participation, family formation and health.
- To understand how social, biological and psychological forces shape the emerging fertility patterns in young adults, and investigate the role of social and biomedical factors on low fertility.
- To understand the short and long-term consequences of medication use and endocrine disrupting substances in pregnancy.

PRESENT ACHIEVEMENTS

ERC Synergy Grant BIOSFER: Untangling the biologic and social causes of low fertility in modern societies.

Beck KC *et al.* (2024). Distressing testing: A propensity score analysis of high-stakes exam failure and mental health. *Child Development* 95(1), 242-260.

Nordmo M *et al.* (2022). The educational burden of disease: a cohort study. *Lancet Public Health* 7 (6), e549-e556.

Kinge JM *et al.* (2021). Parental income and mental disorders in children and adolescents: prospective register-based study. *International Journal of Epidemiology*; 50(5): 1615-1627.

Fertility, family structure and transmission of health across generations

We investigate the causes and health consequences of various aspects of fertility such as number of children, number of siblings, childlessness, age at first birth, birth intervals, union formation and dissolution.

We analyse determinants and health effects of union formation and dissolution, which are closely linked with fertility

We explore how health and disease are transmitted across generations.

KEY AIMS

- To understand how fertility, union formation and union dissolution is related to health of children and adults.
- To understand how socioeconomic and ideational factors affect reproduction among women and men.
- To understand the role of mental health in the reproduction of socioeconomic differences.
- To understand associations in occurrence of pregnancy outcomes, health and disease across generations.

PRESENT ACHIEVEMENTS

Kravdal Ø *et al.* (2023). Mental and Physical Health Trajectories of Norwegian Parents and Children before and after Union Dissolution. *Population and Development Review.*

Carlsen EØ, *et al.* (2023). Reproductive outcomes in women and men conceived by assisted reproductive technologies. *BMC Medicine.*

Kravdal *et al.* (2020). Association of Childbearing With a Short-Term Reduced Risk of Crohn Disease in Mothers. *American Journal of Epidemiology* 189(4), 294-304.

Torvik FA *et al.* (2022). Modeling assortative mating and genetic similarities between partners, siblings, and in-laws. *Nature Communications* 13, 1108.

Bonsang E *et al.* (2022). Does Childbearing Affect Cognitive Health in Later Life? Evidence From an Instrumental Variable Approach. *Demography* 59(3), 975-994.

New statistical methods for analysing family and transgenerational data

We develop novel advanced statistical models to analyse genetic data from large-scale genome-wide association studies, integrating SNP and methylation data, and focusing on nuclear families and transgenerational data.

A large number of projects at the Centre will also benefit from extending methodology such as time-to-event data, correlated data, and multilevel data to studies of pregnancy and fertility-related outcomes within families.

KEY AIMS

- To develop and extend methods to analyse large-scale genetic association data, particularly in nuclear families and outcomes related to the use of artificial reproductive technologies.
- Develop and investigate new ways to define and measure heritability and intergenerational transmission of health.
- Develop new, general methodology for analysing correlated and multilevel data.
- Extend time-to-event methodology to comprehensively analyse pregnancy outcomes under time-dependent exposure.
- Introduce and apply novel methods to analyse COVID-19 and other infectious disease data to provide real-time descriptions and short-term predictions of disease spread.

PRESENT ACHIEVEMENTS

Gjerdevik M *et al.* (2020). Design efficiency in genetic association studies. *Statistics in Medicine* 39(9), 1292-1310.

Skrondal A *et al.* (2022). The Role of Conditional Likelihoods in Latent Variable Modeling. *Psychometrika* 87, 799-834.

Gjerdevik M *et al.* (2019). Haplin power analysis: A software module for power and sample size calculations in genetic association analyses of family triads and unrelated controls. *BMC Bioinformatics* 20.

Kravdal Ø. (2020). Are Sibling Models a Suitable Tool in Analyses of How Reproductive Factors Affect Child Mortality? *Demographic Research* 42, 777–98.

Berentsen GD *et al.* (2021). Heritability Curves: A Local Measure of Heritability in Family Models. *Statistics in Medicine* 40(6), 1357–82.

Covid and its implication on young adults, education, partner formations and fertility

The COVID-19 pandemic had a huge impact on health, living conditions, education and fertility. Pregnant women were especially vulnerable and at higher risk of adverse outcomes. People had an abrupt change in social interactions, work life and lifestyle changes. A surprising surge in births was seen 9 months after lockdown. However, a current corresponding downswing in births is now observed.

We study the impact of the COVID-19 pandemic on health, living conditions, education and fertility.

KEY AIMS

- To explore the underlying causes in the changing fertility patterns during and after the COVID-19 pandemic.
- To understand the role of long COVID in fertility and pregnancy.
- To examine whether effects of the pandemic vary across social strata and contribute to larger social inequalities in fertility and health.
- To understand how the COVID-19 pandemic and vaccinations have affected pregnancy outcomes and the health of pregnant women and their offspring.

PRESENT ACHIEVEMENTS

Magnus MC *et al.* (2021). Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage. *New England Journal of Medicine* 385, 2008-2010.

Magnus MC *et al.* (2023). Infection with SARS-CoV-2 during pregnancy and risk of stillbirth: a Scandinavian registry study. *BMJ Public Health* 1, e000314.

Carlsen EØ *et al.* (2022). Association of COVID-19 Vaccination During Pregnancy With Incidence of SARS-CoV-2 Infection in Infants. *JAMA Internal Medicine* 182(8), 825-831.

Wörn J *et al.* (2023). Job loss and psychological distress during the COVID-19 pandemic: a national prospective cohort study. *BMC Public Health* 23, 1447.

Partnerships and funding

Adequate funding is essential to CEFH's ability to reach our ambitious research plans.

CEFH has developed a culture striving for high quality research and renewal. Key to this development are strong collaborations with international and national researchers to develop new research proposals and projects. Both formal and informal collaborations with other researchers contribute to enhance the quality of our research and to improve the chances for funding.

Thorough analyses of calls for proposals, a support system for proposal writing and budgeting and fostering an open research environment are important steps taken at CEFH to help ensure successful funding. In CEFH, researchers and administrative staff liaise to ensure compliance and coordinate research with funders and collaborators.

Since the inception of the Centre in 2017, researchers at CEFH have submitted around 90 applications for external funding. Of these, 24 have been funded, totalling around 400 million NOK. In addition, we are partners and collaborators in many other project proposals.

The Centre has secured funding from a many different funders. Ongoing projects are funded by The Research Council of Norway, the European Research Council (ERC Synergy Grant and Starting Grant), Nordforsk and The Norwegian Cancer Society.

Funded by The Research Council of Norway

NORWEGIAN CANCER SOCIETY

European Research Council
Established by the European Commission

Funded by the Nordic Council of Ministers

The Gro Harlem Brundtland Visiting Scholarship 2023

Florence Z. Martin

Flo is a PhD student in the MRC Integrative Epidemiology Unit at the University of Bristol in the UK. She studies pharmacoepidemiology in pregnancy, primarily focusing on antidepressant use, using a range of causal inference methods in electronic health record data. Her main interest lies is focused on improving the evidence base for people needing to use medication during pregnancy.

During her research stay at the Centre in 2023, she studied antidepressant use during pregnancy and a range of adverse birth outcomes, including stillbirth and preterm delivery. Previous studies have shown that antidepressant use during pregnancy is associated with such outcomes, but there is weaker evidence for more uncommon antidepressants and timing of exposure. The study used Norwegian data from NorPreSS (primarily, the Medical Birth Registry and the Norwegian Prescription Database) to triangulate with analyses from the UK and Sweden, utilising a range of analyses including a paternal negative control and discordant sibling analysis.

Amanuel Gebremedhin

Amanuel is a post-doctoral Research Fellow at Curtin School of Population Health, Curtin University, Australia. His research interests encompass maternal and perinatal health with a particular focus on adverse pregnancy outcomes, their immediate and long-term morbidity, pre-conception exposures and post-conception outcomes, discovery and application of maternal biological clock and application of causal methods and quasi-experimental epidemiological designs. During his stay at the Centre in 2023, he examined the association between pregnancy timing and adverse pregnancy outcomes and clarify the independent effects of chronological age, biological age, waiting, and time to pregnancy (TTP) on adverse pregnancy outcomes.

Previous studies indicate that prolonged time to pregnancy is associated with higher risks of adverse pregnancy outcomes, and long post-partum intervals may reduce fecundability. However, the specific impacts of biological aging and the partition effect of pregnancy spacing on these outcomes have not been explored. The study used Norwegian data from MoBa and the Medical Birth Registry. Analyses are still ongoing.

The Gro Harlem Brundtland Visiting Scholarship

We are strongly committed to the education and engagement of early career researchers and have established the Gro Harlem Brundtland Visiting Scholarship. This scholarship helps CEFH host early career researchers from Norway and abroad to engage in collaborative research and to participate in and enrich the research community at the Centre and at the Norwegian Institute of Public Health. The scholarship was announced for the first time in May 2018, and we plan to solicit new applications on an annual basis.

Impact cases

The Centre for Fertility and Health was one of the administratvie units in the evaluation of medicine and health sciences conducted by the Research Council of Norway in 2023-2024.

The primary aim of the evaluation is to reveal and confirm the quality and the relevance of research performed at Norwegian Higher Education Institutions (HEIs), the institute sector and regional health authorities and trusts. The evaluation shall result in recommendations to the institutions, the Research Council and the ministries.

The Centre prepared four impact cases for the evaluation. Edited versions of these impact cases are presented here:

- Gender, education and health
- Assisted reproductive technologies and impact on women's and children's health
- The role of chronological and biological aging in fertility
- Understanding potential consequences of infection with and vaccination against Covid-19 during pregnancy

Impact case: Gender, education, and health

Summary of the impact

Boys perform worse than girls in school, and men obtain lower education and have higher mortality than women. A group of researchers in our Centre has fundamentally changed how issues facing boys and men are viewed and discussed in the Norwegian society. They have brought attention to gender differences in school performance and education, created public awareness that biological differences in development contribute to these outcomes, raised concerns for health impacts of gender differences in schooling, and presented evidence-based solutions to the issues. The change has come about through wide-spread media participation, engagement with policymakers, and contributions to several government commissions and white papers.

Underpinning research

Boys perform worse than girls in school and men obtain lower education than women in Norway. This societal challenge has implications for health, one of many implications of which are the large and growing differences in male mortality by education and income.

Gender differences in school performance and education in Norway were well documented by the Stoltenberg commission (NOU 2019:3). Brandlistuen et al. (2021) in addition contributes with research on gender differences in early school performance, development, and behaviour among 5-year-old children. Using the Norwegian Mother, Father, and Child Cohort Study (MoBa), the researchers found gender differences favouring girls for all outcomes except internalising behaviour, including a .31 standard deviation difference in school readiness.

A second research endeavour has been to explore biological differences in development between the sexes. Using data on 13,477 British twins in the Twins Early Development Study (TEDS), Torvik et al. (2021) found that sex differences in pubertal maturation were important and accounted for up to half of the sex difference in academic achievement, whereas genetic influences on pubertal development explained 7-8% of the variation in academic achievement.

The third group of findings relates to impacts of gender differences in school performance and education on health and family formation. Beck et al. (2023) uses propensity score matching to study impacts of failing a final exam on mental health diagnoses in the following year. They find a 31% increased risk for boys compared to 11% for girls,

and 64% of the impacted were male. Reme and Torvik (2023) finds that males and females with low school grades have a three-to-fourfold higher mortality between ages 13 and 30 compared to children with high grades (0.06% vs 0.02%). Suicides, accidents, and overdoses are the main sources of excess mortality among males with low school grades. Bratsberg et al. (2023) find larger differences in fertility and childlessness by income for males than for females. Lack of family network may be one contributing factor to excess male mortality. Taken together, this research suggests that school performance may affect men's health both in the short and the longer term.

Fourth, the group has been concerned with studying policies that can improve boys' performance in school. Flatø et al. (2023) evaluates effects of introducing school psychology offices in Norway, that promoted delayed school start for children based on a screening test in the 1960s and 1970s. They find positive effects of the offices during this period on adult income, and negative effects for male education when the practice was abandoned.

Details of the impact

The initiative started on 10 February 2017 with a newspaper column by Camilla Stoltenberg in Morgenbladet that highlighted the large gender differences in school performance and education at the disadvantage of boys and men, and launched the hypothesis that biological differences in development are contributing to these outcomes. It was followed up through two mutually reinforcing tracks. A policy track, in which the Ministry of Education on 25 August 2017 established a government commission on gender differences in school performance chaired by Stoltenberg, and a research track with the RCN-funded project "Health Gap: Health, Maturity, and Gender Gap in Education" which started on 1 May 2018. The research project was placed at the Centre for Fertility and Health, which had several advantages. CeFH is an interdisciplinary centre, and a combination of medical and social scientists were needed to properly address the research questions. Furthermore, it enabled studies of the role of reproductive maturation for school performance and impacts of education and income for male fertility.

Martin Flatø and Fartein Ask Torvik were hired in August 2018 and, together with Stoltenberg, the team worked closely with the Ministry of Education to contribute to the commission report and at the same time get input to develop research that would be relevant for policy. The close connection between policy and research has been key to achieving the impact in this case. The report made top headlines in most Norwegian news outlets when it was published, and the team gave more than 100 presentations on the work. This included dissemination to an audience outside Norway through Stoltenberg's presentations to Unesco and OECD, and her TED talk in 2019. The impact of changing the awareness in the general public as well as among policymakers can be dated to the 2017-2019 period.

After the turn of the decade, initial results and publications emerged from the group. Additional funding was secured, including the projects "Reproduction of socioeconomic differences and mental health across generations (REMENTA)" led by Torvik and "Lost in transition? Uncovering social and health consequences of sub-optimal transitions in the education system" as well as "Pubertal Timing and Inequalities in Education" led by Flatø. We were also partners in the project "Determined to Succeed? Maturation, Motivation and Gender Gaps in Educational Achievement" led by the Institute for Social Research. Kate Beck, Thomas Kleppestø, Magnus Nordmo, Bjørn-Atle Reme, Hans Fredrik Sunde and Jonathan Wörn were recruited, and the group expanded.

The findings from the Health-Gap project was presented at an open seminar attended by the Minister of Health and Social Affairs Ingvild Kjerkol on 16 March 2023, and followed up with a newspaper article in Morgenbladet on 17 March 2023 and with a presentation for all staff in the Ministry of Education on 3 May 2023. In addition to documenting the gender differences in school performance and their preschool origins, the group's research showed that differences in pubertal timing could partially explain the gender differences. The results also showed strong associations between school performance, boys' mental health, and mortality among young men. This widened the policy debate beyond the education sector and triggered interest within the health authorities in the school problems that are facing many boys. The group has also provided research on potential policies for a more maturity-sensitive and male-friendly school system.

The research is continuously being referred to and acted upon in policymaking. The Stoltenberg commission's report was followed up by Reports to the Parliament on early learning (Meld. St. 6 (2019–2020)) and upper secondary education (Meld. St. 21 (2020–2021)). Research from the group was presented in a parliamentary hearing on lower secondary school reform in 2022 and has thus uniquely impacted policies for all levels of education in Norway. The group has successfully managed to also communicate the gaps in current knowledge and called for further research that uses person-identifiable register data. This has been instrumental for a new government enquiry on improved data collection from schools and kindergartens, to which the group has contributed with expert advice.

The group has also conveyed the research to the government commission on male equality where Stoltenberg is an appointed member, and the government commission on social differences in school performance where Torvik is member. Our research was cited by the Commission on quality assurance and development in schools (NOU 2023:27).

CeFH has spearheaded research and dissemination on gender, education, and health through leading several research projects, engaging in policy dialogue, and hosting several events. The research has been conducted in collaboration with other research organisations, in particular the Institute for Social Research and the The Ragnar Frisch Centre for Economic Research. The end beneficiaries of our impact are boys in the Norwegian educational system, and girls who face similar problems as those that on average are affecting more boys. However, it will take years before any tangible impacts may be measured for boys, and it may not be likely that researchers will be able to identify research from the group as its cause. Nonetheless, the group has over a relatively short time period managed to fundamentally change public discourse on males in the education system and has engaged with policymakers to improve male equity in education and reduce adverse health consequences.

To our knowledge, no other country has had a similarly broad and balanced public debate and high number of policy processes addressing gender differences at the disadvantage of men. Nearly all OECD countries, and an increasing number of other countries, are facing similar gender differences in schools and education, family formation, health, marginalisation, and socioeconomic differences. At the moment, Norway appears to be at the forefront, however, the need for research and policies on these issues will hopefully soon be acknowledged internationally.

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Impact case: Assisted reproductive technologies and impact on women's and children's health

Summary of the impact

Women using Assisted Reproductive Technologies (ART) and children born after ART have been found to have increased risk of some adverse health outcomes. Our studies find that the actual ART procedures may play a role, and that some risks may vary with procedures, while others do not. Our research informs fertility clinicians and couples considering ART about potential risks, and helps clinicians and couples consider the safest ART method for them.

Underpinning research

With interdisciplinary teams, international collaborations and data from health registries and the Norwegian Mother, Father, and Child Cohort Study (MoBa), we have shown that:

1. Women using ART differ in characteristics from women conceiving naturally.
2. The long-term risk of cardiovascular diseases is not increased in women using ART, and there are small cardiovascular differences in children born after ART.
3. There is increased risk of preterm delivery and neonatal death after ART.
4. ART-conceived children have increased risk of respiratory infections and are different in growth up to age 7 but not at age 18. The differences in birth weight were partly mediated through DNA methylation.
5. ART-conceived offspring have fewer children as young adults, but not higher risks of pregnancy complications.
6. ART conceived children have DNA methylation differences at birth in 176 known genes, including differences in the *BRCA* promotor gene and in genes on the X chromosome.

We are now following up and exploring if DNA methylation differences persist into childhood, and whether they are associated with RNA expression, sex differences in DNA methylation, and effects on outcomes.

Underpinning projects and funding
Our work underpinning the impact of our ART research, is based on several research projects and funding:

- The Norwegian Research Council's Centre of Excellence funding scheme (#262700): Researcher time, PhD, Costs for analyses of DNA methylation
- The European Research Council Starting Grant INFERTILITY (#947684): Data collection, researcher time
- The Norwegian Cancer Society) (#244291-2022: Data collection, researcher time, analyses of RNA and DNA methylation
- Norwegian Institute of Public Health (own funding): Data collection, researcher time, infrastructure

More than 10 million children have been born worldwide after ART. The number is rapidly increasing, also in Norway, where more than 50.000 children have been conceived through ART since 1984. Studies have found that these children have lower birthweight, higher risk of neonatal complications and increased risk of certain diseases, such as metabolic and neurodevelopmental disorders as well as some cancers.

It has been difficult to study whether these increased risks are related to the ART procedures or to the underlying conditions causing subfertility. Most studies have had methodological shortcomings, such as limited sample sizes and relatively short follow up time. A challenge in studying potential links between ART and risk of cancer beyond childhood is the relatively young age of the ART-conceived group. Although current evidence suggests a higher risk of some cancers in children born after ART it is emphasized that it is still unknown whether this is due to the ART treatment, to birth outcomes associated with ART, or to other factors associated with the use of ART, including parental subfertility. Our research is aimed at resolving these questions.

Details of the impact

The nature and extent of the impact
Our research increases knowledge about risk factors for cancer and consequences of ART treatments. More information on potential risks will enable couples to make more informed choices about reproduction and use of ART. This is important as use of ART is increasing. Our results identify risks according to different ART methods and in specific subgroups of women. This may guide medical practice and help tailor treatments.

The results increase the understanding of the role of genetics and epigenetics in breast cancer and other *BRCA*-associated cancers. Better knowledge on longer term health risks in persons conceived by ART will provide opportunities for closer follow-up and tailored screening and may inform preventive measures and early detection of cancer. This may improve the prognosis and potentially give rise to personalized treatment.

Researchers at our Centre have collaborated with several institutions in the described work. One collaboration was through the CoNARTaS – the Committee of Nordic Assisted Reproductive Technology and Safety. Our collaborative work with ConARTAS has been presented at scientific conferences:

- Magnus MC et al. Maternal risk of cardiovascular disease after use of assisted reproductive technologies: a Nordic registry linkage. *Society of Pediatric and perinatal Epidemiological Research, Chicago, June, 2022. Poster Presentation 0093.*
- Westvik KJ et al. Maternal and treatment contributions to perinatal outcomes after transfer of fresh and cryopreserved embryos in assisted reproduction: A Nordic sibling study. *European Society of Human Reproduction (ESHRE) virtual meeting in 2020. Oral Presentation O-029.*

Our Centre's work with epigenetics after ART have been disseminated at several scientific meetings as posters and oral presentations:

- Lyle R et al. START: The STudy of Assisted Reproductive Technologies. *European Society of Human Genetics (ESHG) Conference (2020). Interactive e-poster P01.005.B*
- Lyle R et al. DNA methylation in newborns conceived by assisted reproductive technology. *European Society of Human Genetics (ESHG) Conference (2022). Hybrid Poster P01.024.D.*
- Lyle R et al. Assisted Reproductive Technology is associated with DNA Methylation in Newborns Conceived by Assisted Reproductive Technology. *Wellcome Genome Campus, UK, November 2021. Oral Presentation.*
- Lyle R et al. DNA methylation in newborns conceived by assisted reproductive technology. *Genetics of Reproduction Meeting. The Royal Society, London (2022). Poster P01.*

Beneficiaries of the impact
Scientific community: Research findings have been communicated to the international scientific community through publications in high impact journals and by presentations at scientific conferences. The findings generate future research questions and collaborations with the obstetric community and perinatal epidemiologists, as well as with researchers in cancer, assisted reproduction, genetics, and epigenetics.

Policy makers: The Norwegian Institute of Public Health (NIPH) is in direct frequent contact with governmental agencies, and we communicate relevant findings to policy makers, such as the Directorate of Health and the Ministry of Health and Care Services. Our research has had an impact through public media. By identifying robust

modifiable factors that influence the risk of breast cancer or other cancers after ART, this knowledge can be used to guide interventions and develop screening tools and treatments. The results will help guide future research efforts in this direction.

Clinicians: We collaborate closely with two public and one private fertility clinic in Norway. These collaborators have central roles in the medical field of ART in Norway, and they ensure close contact and communication of results to clinicians and obstetricians. Presentations have been given to clinicians participating in annual meetings of the National Association for Assisted Reproduction (NOFAB). We have also presented our work at a network conference to clinicians and researchers within breast cancer research.

The general public: We participate in open popular science meetings to communicate research findings, for example the "Women's health conference". Also, we communicated our findings through open popular research websites specifically designed to communicate science to a general audience (project descriptions at www.fhi.no and www.cefh.no).

Subfertile women, women using ART and breast cancer patients: Our clinical collaborators are in close contact with representatives from the Norwegian Association for Fertility and Unwanted Childlessness "Ønskebarn" and will be involved in communicating results to women who struggle to conceive. This will ensure the right communication to those who consider ART or are treated with ART and to those who may face increased risk of adverse effects and adverse health conditions as a consequence of their infertility. Our results have been presented to patients through user participation at Women's health conference and NOFAB.

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Impact case: The role of chronological and biological aging in fertility

Summary of the impact

Age is undoubtedly one of the most important factors in fertility. People age with different speed, and both the ability to become pregnant and health vary greatly within people of the same chronological age. Some genetic measures, including DNA methylation and telomere length, are surprisingly good indicators for biological aging. Accurate estimation of biological age can advance our understanding of biological mechanisms linking age to fertility, development, health and disease. Also, we have shown that gestational age can be predicted by genetic measures, which is particularly valuable in gauging fetal and newborn's development.

Underpinning research

Leveraging genetic, epigenetic and telomere data from the Norwegian Mother, Father and Child Cohort Study (MoBa), we present here a selection of key findings from our research on the importance of chronological age, epigenetic aging and telomere length on fertility:

1. With Norwegian registry data we could show that the risk of miscarriage increases steeply with maternal age over 35 years, and around half of all pregnancies in women above age 40 end in a miscarriage.
2. Building on previous work we show that an epigenetic gestational age clock built on DNA-methylation data from the more recent Illumina MethylationEPIC BeadChip (EPIC) platform estimates gestational age more precisely than previously published clocks based on data from earlier Illumina platforms.
3. There were strong correlations between DNA-methylation and gestational age across seven main cell-types in cord blood, most of which was attributable to nucleated red blood cells (nRBCs). These correlations were closely related to genes involved in erythropoiesis, immune response, and the transition from fetal to adult hemoglobin.
4. Our gestational age clock showed a similar performance when applied to samples from children born after assisted reproductive technologies and after natural conceptions.
5. We found that telomere length is associated with 823 CpG sites using an epigenome-wide association study (2019) and have submitted a paper that shows that polygenic scores for

telomere length predict the observed telomere length equally well for newborn children and adults.
6. We found a significant difference in the epigenetic age acceleration in adults calculated by the DunedinPoAm clock between in vitro fertilization (IVF) and non-ART mothers after adjustment for potential confounders.

The above findings warrant further investigations and are already seeding new initiatives and exciting applications. Examples include the use of the Cytometry by time of flight (CyTOF) instrument at NIPH to disentangle specific contributions from different cell types to gestational age. This will enable us to map the roles of different cell types in biological processes related to the postnatal period. Another application pertains to measuring DNA methylation levels of extracted cell-free fetal DNA in maternal blood as an alternative to cord-blood DNA, given the invasiveness and ethic-legal limitations of sampling biologic specimens before a baby is born.

The bulk of the work underpinning the impact of our research into gestational age and biological aging is based on funding from several research grants, including the following:

- The Norwegian Research Council of Norway's Centre of Excellence funding Scheme (grant no. 262700): Researcher time, PhD, Costs for analyses of DNA methylation
- The National Institutes of Health (NIH; grant no. R01 1HL134840-01NIPH): "Telomeres and female fecundity": Researcher time, PhD, Costs for analyses of telomere measurements
- The Research Council of Norway's FRIPRO call (grant no. 262043): "Telomere length, epigenetic age and T cells in women who give birth at an older age".

Details of the impact

Our research has mainly focused on generating new knowledge to advance the field of chronological aging and biological aging in growth, development, fertility and health. Although it has been well known that women's age affects their ability to become pregnant, we were able to provide solid evidence quantifying the risk of miscarriage with maternal age. This study has proven valuable for other research groups around the world and has been highly cited in international publications since 2019.

We are in the forefront in developing and using biological aging clocks. Our team developed the first gestational age clock and have refined this gestational age clock and excelled the work around using DNA methylation in gestational age prediction. It has added significant value to both clinical and research settings by providing crucial insights into a newborn's developmental stage. Previous research has shown a link between preterm birth and several negative outcomes in neonates, extending into later life. The precise determination of gestational age is critical for effective perinatal care. Traditional methods, such as calculations based on the last menstrual period or ultrasound estimates, are fraught with limitations. With focus on cell-type specific relationships between gestational age and DNA methylation in cord blood we have identified strong correlations across seven main cell types found in cord blood, particularly in nucleated red blood cells (nRBCs). The DNA methylation markers (CpGs) we discovered were linked to genes crucial in the development of red blood cells, various developmental processes, and the preparation for birth and adaptation to life outside the womb. These findings not only contribute to our scientific understanding of these vital processes, but also highlight the potential for practical applications in neonatal care and developmental research. Promising new research based on our work in this field includes the potential of generating new methods for gestational age determination based on blood samples.

Our team has also worked extensively on refining and using DNA methylation clocks in adults as markers of accelerated biological aging and its implications for lower fertility and how the rate of biological aging in adults is relevant for later risk of disease. Prior to our work, a variety of epigenetic clocks had been developed and associated with various environmental exposures and diseases in the elderly, but these were mostly based on older methylation platforms. Our research, based on the newer methylation platform has provided numerous insights regarding the importance of the additional epigenetic marks included on this platform.

Several studies have suggested that epigenetic age acceleration in mothers who conceived using ART may be associated with low oocyte yield and poor ovarian response. However, the difference in epigenetic age acceleration between non-ART and ART mothers (or fathers) had not been examined previously. We filled this gap in knowledge by comparing epigenetic age derived from various epigenetic clocks between non-ART and ART mothers and fathers. We found a significant difference in the epigenetic age acceleration between in vitro fertilization (IVF) and non-ART mothers after adjustment for potential confounders. A plausible biological mechanism for the observed association is that mothers who undergo IVF may be nearer to menopause compared to mothers who do not use ART.

We are now at a stage where it is possible to delve deeper into the significance of the findings in terms of their relevance for translational applications. Accordingly, we will seek funding to investigate cell-specific methylation profiles using state-of-the-art instruments (CyTOF) in-house at the NIPH, in addition to extracting cell-free fetal DNA in the maternal circulation to determine methylation profiles at an earlier stage than at birth.

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Impact case: Understanding potential consequences of infection with and vaccination against Covid-19 during pregnancy

Summary of the impact

During the Covid-19 pandemic, we conducted a range of studies looking into the potential consequences of infection with and vaccination against Covid-19 during pregnancy. These studies became very important in the generation and continuous update of national guidelines for vaccination of pregnant women during the pandemic and contributed to the international knowledge base on covid-19 and pregnancy. The findings were also communicated to the public through press releases and to important international stakeholder such as the World Health Organization and the European Medicines Agency.

Underpinning research

During the pandemic, we conducted a range of studies looking into the consequences of infection with and vaccination against Covid-19 during pregnancy. We used national health registries, and collaborated with researchers in Sweden and Denmark, to conduct high-quality studies and produce robust evidence using data from these three Nordic countries. With our unique registry linkages, we were able to perform research which is not possible in most other countries. Our work was made possible by the Emergency preparedness register for Covid-19 (BEREDT C19) at the Norwegian Institute of Public Health (NIPH). This register includes data from all the central health registries, including the Medical Birth Registry of Norway, the Norwegian Patient Registry, the Vaccination Registry, the Norwegian Surveillance System for Communicable Diseases and several other important data sources. In addition, with used rich data collected by questionnaires from participants in the Norwegian Mother, Father, and Child Cohort Study (MoBa) and the Norwegian Influenza Cohort (NorFlu). The regularly updated data in BEREDT C19 was invaluable to the conduction of this work. The research conducted within this topic at the CEFH has been funded by the Research Council of Norway and NordForsk. Some of our major findings include:

1. In a study using information from Norwegian health registries, pregnant women were not more likely to be infected with the coronavirus SARS-CoV-2. Still, pregnant women with COVID-19, especially those born outside of Scandinavia, were more likely to be hospitalised. This supports the notion that pregnant women are at greater risk of severe disease from COVID-19 if they get infected. These findings supported vaccination of pregnant women.
2. The rate of fetal death (miscarriage and stillbirth) did not change after the implementation of COVID-19 pandemic mitigation measures in the three Nordic countries. This provided preliminary reassuring evidence that pandemic mitigation measures, or the general psychosocial stress throughout the pandemic, did not appear to impact the rate of fetal death.
3. Using unique population-based data on first-trimester miscarriages in Norway, we found no evidence of an increased risk of first-trimester miscarriage after Covid-19 vaccination, which added to findings from smaller reports of more selected samples indicating no increased risk of early pregnancy loss following vaccination.
4. Based on findings from a large population-based study of births in Sweden and Norway, vaccination against SARS-CoV-2 during pregnancy, compared with no SARS-CoV-2 vaccination during pregnancy, was not significantly associated with an increased risk of adverse birth outcomes, such as stillbirth, preterm birth, small-for-gestational age, low Apgar score etc. This study provided important evidence of the safety of vaccination against Covid-19 during pregnancy.
5. Results from Norway suggested a lower risk of a positive test for SARS-CoV-2 during the first 4 months of life among infants born to mothers who were vaccinated during pregnancy. Maternal COVID-19 vaccination may therefore provide important passive protection to young infants, for whom COVID-19 vaccines are not recommended.
6. Using MoBa, we followed 70.000 participants with and without SARS-CoV-2 infection and found an excess risk of 13.6% for fatigue 12 months after infection. Two main underlying factors explained 50% of the variance in the 13 symptoms that were associated with infection (long COVID symptoms). Brain fog, poor memory, dizziness, heart palpitations, and fatigue had high loadings on the first factor, while shortness-of breath and cough had high loadings on the second factor.

Grants

We have received four grants to facilitate the completion of the described research. The research has primarily come out of a Nordic research collaboration funded by NordForsk, which enabled us to study the risk of more rare pregnancy complications.

- NordForsk – Scandinavian studies of Covid-19 in pregnancy (SCOPE) : 105545
- NordForsk – Scandinavian studies of Covid-19 in pregnancy 2 (SCOPE 2): 135876
- NordForsk – Tobrisk-Cov grant no. 105544.
- Research Council of Norway – Safety of Covid-19 vaccination in pregnancy (SAFETY): 324312

Details of the impact

Description of relevant stakeholders

There are several important stakeholders regarding the described research:

1. Government agencies responsible for developing guidelines for vaccination of pregnant women against Covid-19 and monitoring of potential side effects.
2. Pregnant women contemplating vaccination.
3. General practitioners responsible for the routine antenatal care of pregnant women.
4. Other researchers.

Description of dissemination activities

1. Meetings with government agencies. Throughout the pandemic, we have continuously informed the ***advisory group at the Norwegian Institute of Public Health (NIPH)*** about our findings, in order to inform their development and updated recommendations for vaccination of pregnant women against Covid-19. The evidence that we have made available has been critically important to inform the existing national recommendations for vaccination of pregnant women. Therefore, we had regular meetings with the advisory group at the NIPH and informed them about our findings. Furthermore, we have presented our findings to a sub-committee at the ***World Health Organization (WHO)*** responsible for their official guidelines of vaccination of pregnant women against Covid-19. Together with evidence from large-scale studies originating from other countries, our findings have therefore also contributed to the official WHO recommendations. Finally, we have presented findings from our studies on vaccination for the ***Norwegian and European Medicines Agencies***. These agencies are responsible for monitoring all evidence regarding potential side effects of vaccines. Our reassuring findings of no adverse effects of vaccination during pregnancy based on Nordic data has been critically important both national and internationally for this purpose.

2. Our findings have been of interest to the ***general population of pregnant women*** trying to decide whether they should get vaccinated against Covid-19. We have been able to show that pregnant women appear to be at an increased risk of severe disease, and that there is no evidence of adverse effects of vaccination, supporting the general recommendation of vaccination for pregnant women. The described research has been disseminated widely through press releases and news articles to reach the general population of pregnant women. Specifically, we have written press releases together with the NIPH communications department which have been published on our website. Furthermore, we have contacted/and been contacted by major national newspapers, which has further contributed to the wide dissemination of our

findings to the general population.

3. Our findings have also been of interest to ***all general practitioners responsible for the antenatal care of pregnant women***. As general practitioners are those who meet pregnant women and must answer their questions about whether or not they should get vaccinated against Covid-19, it has been vitally important to have evidence from large well-conducted studies that they can lean on when communicating with pregnant women. General practitioners heavily relied on the summary of evidence and existing recommendations from the NIPH, and as our findings contributed to these, they were also vitally important for these health-care workers.

4. Our findings have also been important for ***other researchers both nationally and internationally***. For example, our analytical strategies to minimize bias leading to spurious findings have been adopted by other researchers on other/independent datasets. This has been important as similar evidence across different populations are necessary to increase confidence in the robustness of findings.

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Key projects

Reproduction, partner disruption and health

The aim of this project is to gain more insight into how partnership disruption, number of children, parents' age at birth, and birth interval lengths affect the health of parents and offspring. Four sub-projects are defined:

- How does maternal/paternal age at birth, number of siblings, and age interval between siblings affect children's health?
- How does the number of children (including childlessness), age at first birth, and interval between births affect adult health?
- How does disruption of parental relationships, and possible parental re-partnering, affect children's health?
- How does disruption of relationships, and possible re-partnering, affect the health of the involved adults?

This project was initiated in 2017 to answer many of the research questions described in our original Centre of Excellence application. It is based on a rich linkage of data from registers and surveys.

In 2023, we initiated several new collaborations with national and international partners in this project. The project now involves collaborations with researchers from 30 national and international research institutions. The first publications are published, and many publications are in progress. In 2023, we started the process of obtaining updated data from some of the data sources. The project will continue until the end of 2028.

The project is funded by the Research Council of Norway through the Centre of Excellence grant.
Project managers: Per Magnus and Øystein Kravdal

START – Study of assisted reproductive technology

The main aim of the project is to understand causes and health consequences of subfertility and use of assisted reproductive technologies in women and men. We examine the role of genes, age and environment, and whether there are differences in epigenetic markers associated with subfertility and the use of assisted reproductive technologies (ART). The Centre of Excellence funding provided the opportunity to establish the largest dataset to date of DNA methylation in mother-father-child trios with a child conceived with ART and naturally conceived children.

In 2022 we published our findings on epigenetic differences in children born through ART compared to naturally conceived children. Differences were found in 176 known genes, many of which were related to health outcomes associated with ART in other studies. With new funding from the Norwegian Cancer Society, we are now investigating if these DNA methylation differences at birth persist into older ages, and whether the DNA methylation differences are associated with differences in gene expression at birth. We also found that DNA methylation mediates differences in birth weight with ART and are now looking into outcomes at older ages. With the data in START we have expanded our work on biological aging clocks based on DNA methylation, exploring cell type specific patterns and different CpG sites in the aging clocks. The role of genetics in subfertility, and interaction between parent's genes are also investigated.

The project is funded by the Research Council of Norway through the Centre of Excellence grant and by the Norwegian Cancer Society.
Project manager: Siri E. Håberg

ART (Assisted Reproductive Technologies) – Pregnancy and childhood outcomes

This project combines Norwegian registry data and questionnaire data from the MoBa cohort study to investigate causes and consequences of subfertility and assisted conceptions. Main outcomes include fetal growth, gestational length, fetal loss, 'vanishing' twins, and causes and consequences of subfertility and use of ART in parents and children.

Our research has provided knowledge on causes of miscarriages, such as the role of maternal age, and also on the link between underlying chronic diseases and mental health in miscarriages. We are also investigating short- and long-term health effects in women who used ART. Several PhD candidates at CeFH are involved in this project and in studies of subfertility and miscarriages. We have shown that children's growth and health after ART is different at birth and in preschool ages. Our international collaborators include senior researcher Gavin Pereira from Curtin University in Perth, Australia, and several members of his team. In this collaboration we are investigating the role of interpregnancy intervals, and how short and long intervals between children influence risk of miscarriages and fertility outcomes. With Olga Basso at McGill University in Canada we have studied intergenerational risks on fertility outcomes, and the role of parents' age in offspring fertility.

The project is funded by the Research Council of Norway through the Centre of Excellence grant.
Project manager: Siri E. Håberg

Metabolomic profile and IVF, pregnancy, perinatal and longer-term outcomes

In this collaborative MoBa-project we work with researchers in Bristol, UK, and combine metabolic profiles, genome-wide genotypic data, and clinical factors to understand causal mechanisms for adverse pregnancy, perinatal and postnatal outcomes in in vitro fertilisation (IVF) and spontaneously conceived pregnancies. Differences in pregnancy metabolic profiles are likely to be important, but it is only recently that studies of pregnant women have acquired detailed measurements of metabolic profiles during pregnancy.

We are now adding metabolomic profiles (250 metabolites in total) to pregnancy samples in 11000 women and 5000 of their male partners in MoBa who have genome-wide genotypic data on trios. The results from the analysis of these data will enhance our understanding of the role of pregnancy metabolism on pregnancy and perinatal outcomes. We will use machine learning methods to develop prediction algorithms for each adverse outcome, also for 'healthy' pregnancies, and test the discrimination and calibration of these, as well as compare them to similar metrics for prediction using established risk factors collected at the first antenatal clinic.

The project is funded by grants to Deborah A Lawlor (ERC Advanced Grant and UK National Institute of Health Research Senior Investigator award).
Key personnel at the Centre: Maria C. Magnus, Siri Eldevik Håberg, Per Magnus

InPreSS – International Pregnancy Drug Safety Studies. Short and long-term safety of drug use in pregnancy.

InPreSS is a multinational collaboration to study the safety of drug use in pregnancy. The overarching objective is to understand the consequences of in-utero drug exposure on fetal development, birth defects and longer-term outcomes (neurodevelopment outcomes and academic performance) in the child, comparative drug safety, as well as maternal social and health consequences of discontinued drug treatment. The project uses several population-based nationwide health registers from all 5 Nordic countries and administrative healthcare data from the US and New South Wales, Australia, which enables us to study rare exposures and outcomes.

This has been a very ambitious, extensive and demanding project. 2023 was the final year with funding from RCN. We have completed the project and achieved good scientific results with >20 publications in high impact journals and 7 more papers will be completed in 2024. Our research has provided very important knowledge to the international community and various stakeholders about short- and long-term safety of exposure of antiseizure drugs, antidiabetic drugs and antipsychotics in pregnant women. One example of impact: In 2023 the European Medicine Agency introduced further restrictions in the use of the antiseizure drug topiramate in pregnant women together with a pregnancy prevention programme based on our publication in JAMA Neurology 2022. In the letter to health personnel in Europe, three of our InPreSS publications on antiseizure drug exposure in pregnancy were cited. Epidemiological studies of such a size we have been able to include in InPreSS are crucial and the only way that can give us more reliable knowledge about the consequences of drug use and higher precision in the risk estimates.

The project is funded by the Research Council of Norway through the BEDREHELSE programme.
Project manager: Kari Furu

ADHD medication in pregnancy: understanding the population and outcomes related to treatment use and discontinuation

This project sets out to understand risks associated with use or discontinuation of drug treatment for ADHD during pregnancy. The project uses existing data sources, including population-based national health registries from Norway and Sweden and MoBa. We are collaborating with researchers in Canada and Sweden for high quality studies that aim to generate new knowledge that will empower women with ADHD to make informed treatment choices and advance research on the safe use of medicines during pregnancy.

In 2023, we presented results from two studies at international perinatal- and pharmacoepidemiology conferences and published a study on trajectories of ADHD medication use surrounding pregnancy. The PhD candidate in the project, Chaitra Srinivas, completed the educational component of the PhD program and worked on her second study on risk of preterm birth. We obtained additional funding from the ADHD Research Network (Oslo University Hospital) to expand the project to study potential effects of prenatal exposure to ADHD medication on neurodevelopment. We also held a project team meeting in Stockholm to plan for the remaining work in the project.

The project is funded by the Research Council of Norway's FRIPRO - Young Research Talents programme.
Project manager: Jacqueline Cohen

Dimjob – Social, demographic and health dimensions of technology-induced job loss

This project will study Norwegian population registries and surveys on occupation and business data, education, cognitive test performance, personality, coping, health, intergenerational data, social isolation, as well as physiological and mental health trajectories. We will study how these factors relate to how individuals respond in terms of demographic, social and health outcomes, including quality of life, re-employment, disease incidence, training and demographic outcomes (e.g., partnership stability, childbearing, internal migration).

The project is funded by the Research Council of Norway's VAM programme.
Project manager: Vegard Skirbekk

National Historical Population Register for Norway (HPR) 1800–2024

In December 2021, the Research Council of Norway awarded a new substantial grant to continue this project, now under a new name 'Historical Registers'. This grant will secure the completion of the HPR within a few years. The project is coordinated by the Norwegian Computing Center, with extensive contribution by CeFH researchers in all work packages. Progress on digitalization and linkage of sources from 1900-1960 has progressed particularly well, and we expect major deliverables in 2024. We are still committed to facilitate full linkage of the historical registers and datasets with existing modern microdata. Under the new grant we will also work to set up an infrastructure were also other historical thematic sources with person-data can be fully integrated with HPR and modern data. Norwegian archives are full of valuable sources that can realistically be digitalized and linked to HPR with modest resources.

The project is funded by the Research Council of Norway's FORINFRA programme since 2013.
Project manager at CEFH: Kåre Bævre. The project is coordinated by Lars Holden at the Norwegian Computing Center.

Health-gap. Health, maturity and the gender gap in education

The primary objectives of this project are to understand the health consequences of gender differences in educational attainment and school performance, and to examine whether the difference in timing of physical maturity between girls and boys is a major explanation for the observed gender gaps in education. Educational attainment is likely to affect fertility and health because more educated men and women have increased fertility compared to their less educated peers. In addition, the health risks of low educational attainment may be particularly damaging in the combination with little social support in terms of

family network, and perhaps especially for men's health.

The project was concluded in the spring of 2023 with a public seminar attracting roughly 250 in-person attendees, including the Minister of Health. The project resulted in 9 academic papers and 109 dissemination pieces within its timeframe. This project created public awareness of biological differences in development, changed how issues facing boys and men are viewed in the Norwegian society, and contributed policy relevant knowledge to government commissions.

The project is funded by the Research Council of Norway's BEDREHEL-SE programme.
Project manager: Fartein Ask Torvik

Lost in transition? Uncovering social and health consequences of sub-optimal transitions in the education system

The overarching aim of this project is to understand the effects of transitions in the educational system on later labour market participation, family formation, and health. The project considers how starting school at a suitable age, attending an upper secondary school of choice, and managing to complete upper secondary education affect later social participation and health.

In a first publication (Beck et al., 2024), we used propensity score matching and found that students who failed a final exam had a 21% higher risk of receiving a psychological diagnosis and a 57% lower odds of having graduated with a diploma 5 years later. Boys and students with a high teacher-assessed grade in the subject experienced particularly high risks of receiving a psychological diagnosis compared to the control group.

The project is funded by the Research Council of Norway's FRIHUM-SAM programme.
Project manager: Martin Flatø.

Rementa – Reproduction of socioeconomic differences and mental health across generations

The aim of this project is to understand the role of mental health in the reproduction of socioeconomic differences. Children of parents with low socioeconomic status do less well in school and are at higher risk of dropping out, of lower education, unemployment, and social exclusion than their peers. It is not adequately understood why social differences 'reproduce'. There is a close relationship between socioeconomic status and mental health, suggesting that mental health could be key for a better understanding of the reproduction of social differences and mobility.

Important publications in 2023 include a study on the association between common mental disorders among parents and the school performance of their children (Nordmo et al., 2023) and a study on causes of parent-child resemblance in ADHD symptoms (Kleppestø et al., 2023). Hans Fredrik Sunde, who was a PhD candidate in this project, handed in his thesis in June 2023, and was awarded the Thompson Memorial Award for the best presentation at the Behavior Genetics Association's annual meeting the same month. The project utilizes survey and genetic data from MoBa and register data on health, demography and school performance in combination with administrative register data from the entire population of Norway.

The project is funded by the Research Council of Norway's VAM programme.
Project manager: Fartein Ask Torvik

Maternal effects of asthma – Revisiting and dissecting the maternal effect of asthma

It is well established that childhood asthma is more common when the mother has asthma than when the father has it. Although this has been reproduced by many researchers, none have come up with a good explanation for the effect. At present there is no efficient primary prevention of childhood asthma, due to lack of etiological insight. We aim to discover the biology behind the maternal effect using data from a large pregnancy cohort, MoBa, as well as data from nationwide registries.

We have established a collaboration with Klaus Bønnelykke and his team at Den Selvejende Institution - Dansk BørneAstma Center. In 2023, standard contractual clauses (SCC) were signed with Rutgers University in the US in order to ship biological samples for analysis. We have discovered a genetic locus that may be responsible for a parent-of-offspring effect. We found that the risk of childhood asthma is increased when a specific allele is transmitted from the mother, but not when it is transmitted from the father.

The project is funded by the Research Council of Norway's FRIMEDBIO programme.
Project manager: Per Magnus

Women's fertility – an essential component of health and well-being

More couples than before seek treatment for infertility. Women's fertility and the number of children born is associated with her health throughout life. Subfertility and childlessness are associated with increased risk of early chronic disease and death. The mechanisms behind these associations are poorly understood. Underlying causes of subfertility may contribute to later disease risk. Not having been pregnant, breastfeeding or having children may directly affect physiology, but also the lifestyle and social support of women, and thereby increase the risk of adverse health outcomes. Understanding the causes and consequences of infertility is important for understanding women's health and well-being.

This project is currently involved in a new data collection in MoBa, in which young second-generation participants are invited to a clinical examination at collaborating fertility clinics. So far, around 400 women have been examined. Our aim is to examine 1250 young women and with additional funding also include 1250 young men, and study whether measures for fertility in young adulthood can be associated with early life and prenatal exposures. The role of heritability in fertility measures and age at menarche and menopause will be part of the study. Women's health related to puberty, fertility and menopause are key interest areas, and conditions such as endometriosis, PCOS and various symptoms related to menopause will be explored. This study was crucial for obtaining the ERC Synergy Grant BIOSFER which expands on this project.

The project is funded by the Research Council of Norway's KVINNEHEL-SE funding scheme.
Project manager: Siri E. Håberg

Telomere and female fecundity

This project is founded on the observation that women with delayed menopause and those who give birth to children later in life have a lower risk of cardiovascular disease and live longer than other women. Moreover, women with longer telomere length (TL) have delayed menopause, less cardiovascular disease, and live longer than other women. A central hypothesis of this project posits that women who bear children later in life, without the use of assisted reproductive technologies (ART), may have a longer TL than their peers. The aims of the study were therefore to: 1) measure TL in 1700 mothers who gave birth at ages 18 years or older, including 1000 mothers who gave birth at the age 32 years and older; 2) measure TL in 300 mothers who gave birth at the age of 32 years or older with the assistance of ART; 3) measure TL in the 2000 fathers (the sexual partners) of the mothers in aims 1 and 2); and 4) measure TL in newborns of these parents.

The first two years of Kristine Haftorn's PhD work was supported by funding from this project. Haftorn defended her thesis successfully in 2023 at the University of Oslo. Her thesis also dealt with epigenetic gestational clocks, which are DNA methylation-based predictors of gestational age. Currently, we are in the process of analyzing the TL data that have been gathered thus far. One manuscript, on the effect of polygenic scores of TL alleles on TL in newborns and parents, is currently under review. Another manuscript on the relationship between TL and fecundity is currently being drafted for submission.

The project was initially funded by the US National Institutes of Health (NIH) (grant R01 1HL134840-01) and later by the Research Council of Norway through the Centre of Excellence grant. Key personnel at the Centre: Astanand Jugessur, Per Magnus, Yunsung Lee, Håkon Gjessing.

The intrauterine redox state and telomere length in the newborn

The aim of the project is to examine the associations between (1) newborn's leukocyte telomere length (LTL) and mitochondrial haplogroups and (2) newborn's LTL and maternal smoking during pregnancy. The main hypothesis is that the redox state during early gestation has a considerable impact on LTL dynamics in utero and therefore LTL at birth. If the results of the proposed research support the main hypothesis, then this work will bring into focus the role of inherent and extrinsic factors within the intrauterine milieu in fashioning LTL in the newborn, and thus usher telomere epidemiology into a new era of mitochondrial genomics.

After having successfully gone through a tender application to contract a suitable core sequencing facility, we were finally able to ship DNA samples to a core facility in Bonn – Life and Brain GmBH – for the sequencing of approximately 1000 children from MoBa. At the time of writing, all samples have been sequenced, except for one of the plates, but we anticipate all the sequencing to be finalized by the end of March 2024. After the data have been quality-controlled, we will start the planned analyses to achieve the aims set forth in the project.
Dana Kristjansson's PhD work was funded by this project, and she successfully defended her thesis in 2023 at the University of Bergen, Norway.

The project is funded by the Research Council of Norway's FRIMEDBIO programme.
Project manager: Astanand Jugessur

INFERTILITY: Understanding the causal nature of the relationship between infertility and cardiovascular disease.

The INFERTILITY project aims at filling several existing knowledge gaps in our understanding of the nature of the relationship between infertility and cardiovascular disease. The working hypothesis is that both infertile men and women have an increased risk of cardiovascular disease, and that this might at least partly reflect a greater burden of cardiovascular disease risk factors. The project uses data from the MoBa, HUNT, the Avon Longitudinal Study of Parents and Children (ALSPAC), and the national health registries.

Findings so far have confirmed an increased risk of cardiovascular disease among infertile women in both MoBa and HUNT, while there appears to be no robust evidence of an increased risk among infertile men. Using genes as instrumental variables in Mendelian randomization analyses, we have found an increased risk of infertility among obese women and men, while there appears to be no strong relationship between smoking and infertility in either sex. The project continues to study the causal relationship between other known cardiovascular disease risk factors and their impact on infertility, including blood pressure, lipids levels and glucose levels. We have further shown that there appears to be no increased risk of cardiovascular disease among women who delivered after using assisted reproductive technologies compared to those who delivered after conceiving spontaneously. Currently, we are expanding this to investigate whether there are any differences according to the number of cycles of in vitro fertilization a woman has undergone. One PhD candidate, Karoline Hansen Skåra, and one postdoctoral researcher, Álvaro Hernaéz, were hired to work on the project when it started in 2021. A second postdoc, Huong Thu Nguyen, started in February 2023.

The project is funded by the European Research Council's Starting Grant funding scheme.
Project manager: Maria C. Magnus

Sickness in the Family: A register Study on the Short- and Long-Term Effects of Severe Sickness on Family Members

Even with a well-developed welfare scheme like the one in Norway, severe sickness can have significant negative effects on the life trajectory of both the patient and their close family members (i.e., parents, children, siblings). The main aim of this project is to investigate the effects of severe sickness on family members' labor market participation, educational achievements and health, both in the short and long term. The focus is on young families, where the offspring are particularly dependent on their parents.

The project was established in the fall of 2021, with research activities starting in January 2022. As of 2023, several analyses in the project are at an advanced stage, and several research papers have been presented at (inter)national conferences, are under review, or accepted for publication. Ongoing work addresses both intergenerational spillover effects from parents to children and from children to parents, but also intragenerational spillover effects from children to their siblings and from parents to their partners. Completed and ongoing work includes studies of (1) Effects from parental suicide and from parental cancer (and possible cancer death) on children's mental health, (2) Consequences of teenage mental health problems for the health of their parents and siblings, (3) Consequences of child disability on parental relationship stability, fertility, and employment careers, (4) Long-term spillover effects of losing a close family member in childhood on entries into the labor market ("NEET") in early

adulthood and health service use as an adult later in life, (5) Spillover effects of a partner's cancer on health, welfare use and labor market participation.

The project is funded by the Research Council of Norway's VAM programme.
Project managers: Bjørn-Atle Reme and Jonathan Wörn

SCOPE2 - Studies of COVID-19 in pregnancy - A framework to secure reproductive, maternal and child health during societal crises

This project builds on our expert network and established infrastructure established in SCOPE-1 and the continued collaboration with Karolinska Institutet in Sweden and the University of Copenhagen in Denmark. Our overall aim and purpose in this project is to increase knowledge on how crisis like a pandemic affects pregnant women and their infants, who are especially vulnerable during most societal crises. We are investigating medium- and long-term effects of the COVID-19 pandemic, including vaccinations, on pregnant women and their children. We will investigate how the COVID-19 pandemic influenced fertility patterns, reproductive health, pregnancy, and infant outcomes. Pregnant women and infants are especially vulnerable during crises, whether it is pandemics, disasters, or war. We will use our experience from SCOPE 1 and SCOPE 2 to inform preparedness for how to gain knowledge during ongoing crises to improve management of pregnant women and children in future societal crises.

The project is funded by NordForsk's Societal Security Beyond COVID-19
Project managers: Siri E. Håberg, Olof Stephansson and Anne-Marie Nybo-Andersen

Safety of COVID-19 vaccination in pregnancy

In this project, we study safety of COVID-19 vaccination in pregnancy. We build on the established Scandinavian and international collaborations in our covid-in-pregnancy studies and use our updated registry data to provide rapid results on vaccine safety in pregnant women. The aim is to investigate potential health consequences of Covid vaccination in women's health, pregnancy outcomes and health in newborns and early childhood.

The project has provided important knowledge to the international community. A letter to the editor of the New England Journal of Medicine was accepted in October 2021 reporting no evidence of an increased risk of early pregnancy loss after COVID-19 vaccination. The project has studied potential adverse pregnancy outcomes such as preterm births, stillbirths, neonatal health, and we have not found indication of adverse effects after vaccination. The reassuring results have been published in several high impact journals, including several publications in JAMA. Women are still recommended vaccination in pregnancy, and we continue to follow outcomes in women who have been pregnant during the covid-19 pandemic, investigate short- and long-term impact of vaccination on women's risk of disease pregnancy outcomes, and health in children who were born to vaccinated women. We are also continuing to study potential adverse effects of infection during pregnancy on health outcomes in women and their children.

The project is funded by the Research Council of Norway through the FRIPRO-scheme.
Project manager: Siri E. Håberg

Addressing the smoking paradox in the etiology of COVID-19 through population-based studies

The role of tobacco use (smoking and snus) on the incidence and prognosis of COVID-19 has raised much international interest, due to contrasting findings in the scientific literature. Given the public health importance of tobacco use as a major risk factor for morbidity and mortality it is urgent to provide both the scientific and the broad lay community with sound information from large population studies.

Together with our Nordic collaborators, we have analysed the association between tobacco use and the occurrence of COVID-19 using existing longitudinal population studies in Finland, Norway and Sweden. So far, 6 scientific papers have been published from the project. Our studies have shown that there is an inverse association between smoking and COVID-19 before the roll-out of vaccination, also in the Nordic registry data. This association seems to be linked to recent behavior (i.e., being a smoker at the time of the pandemic). However, our findings using snus as an exposure suggest that nicotine does not have a protective effect on the risk of contracting COVID-19

The project is funded by NordForsk's Nordic Health Data Research Projects on Covid-19 programme
Project manager: Maria Rosaria Galanti (Karolinska Institutet) and Per Magnus

BIOSFER: Untangling the biologic and social causes of low fertility in modern societies

BIOSFER is an interdisciplinary collaboration between our Centre and researchers at Aarhus University in Denmark and the Max Planck Institute for Demographic Research in Germany. The aim of the project is to investigate how social, biological and psychological forces influence fertility patterns in young adults, and to what extent the fertility decline and polarization of fertility in socioeconomic groups can be attributed to social vs. biomedical factors. We use data from the two richest population-based longitudinal pregnancy and pubertal cohorts in the world, The Norwegian Mother, Father and Child Cohort Study and the Danish National Birth Cohort. The project will establish clinical examinations in young adults in Norway and Denmark, recruit young couples to a pregnancy planner cohort, and perform a randomised controlled trial of fertility knowledge among young adults.

The project started on March 1, 2023. We have established the first phase of the new data collection, and several PhD candidates and postdocs have been recruited. A successful kick-off event has taken place and the scientific output is underway as published and accepted articles.

The project is funded by the European Research Council (ERC) through an ERC Synergy Grant.
Project managers: Siri E. Håberg, Mikko Myrskylä, Cecilia Ramlau-Hansen

Parment - Parenthood, childlessness, and mental health in times of falling fertility

The overarching aim of this project is to understand how mental health is linked with reproduction among men and women. The specific aims are to understand: 1) how mental health leads to selection into partnership and parenthood 2) the effects of reproduction on mental health and 3) how patterns of partner selection influence mental health (assortative mating). We use of register data on the entire population of Norway that includes longitudinal information on kinship, mental health, education, and economic activity.

The project started in August 2023. One postdoc, Hans Fredrik Sunde, and one PhD candidate, Maria Lyster Andersen, have been hired.

The project is funded by the Research Council of Norway's FRIPRO programme
Project manager: Fartein Ask Torvik

Risk of breast cancer in persons born after assisted reproductive technologies (ART)

The Centre of Excellence funding from the Research Council of Norway enabled us to study epigenetic differences in newborns conceived by ART compared to naturally conceived children. In this project we follow up our recent finding that children conceived with ART have substantially different epigenetic patterns at birth, especially in the promotor of the *BRCA1* gene. In this project we investigate the potential role of ART and DNA methylation at birth in risk of breast cancer by 1) using registry data to explore if persons born after conception with ART has an increased risk of cancer, and especially risk of *BRCA*-related cancers, 2) explore whether differences in epigenetic marks at birth in *BRCA1* persist into older ages and 3) explore whether epigenetic differences in *BRCA1* at birth is associated with gene-expression in newborns. Currently, samples are being analysed and the registry-based study is ongoing.

The project is funded by The Norwegian Cancer Society's Rosa sløyfe call.
Project manager: Siri E. Håberg

New externally funded projects

Pubertal timing and inequalities in education

9 999 000 NOK

Research Council of Norway

Within a typical classroom, the onset of puberty occurs four years earlier for the first developing girl than for the latest developing boy. However, it is not clear how these large inter-personal differences affect school performance and educational trajectories, with previous studies finding negative effects of both early and late pubertal timing on school performance. This project therefore aims to provide new knowledge on how variation in pubertal timing affects school performance during adolescence and inequalities in education later in life, and to assess policies that could mitigate adverse consequences of such relationships.

The project will start formally on April 1, 2024.

The project is funded by the Research Council of Norway through a thematic priority call on education and competence.

Project manager: Martin Flatø

YoungWork: Young adults' mental health and labor market exclusion - causes, consequences, and trends

11 993 000 NOK

Research Council of Norway

Increasing rates of mental health problems in young persons – especially depression and anxiety – have caused concerns about young adults' well-being as well as their ability to contribute to the labor force. The YoungWork project examines whether society has become more or less inclusive of young persons with mental health problems and whether young adults with mental health problems today are more (or less) likely to complete education and to be active in the labor force. We will also study whether school pressure, stressful employment, and widespread use of social media contribute to recent changes in mental health. Not least, we will assess to what extent more openness about mental health problems and changing norms related to help-seeking contribute to observed increases in reported mental health problems.

The project will start formally on April 1, 2024.

The project is funded by the Research Council of Norway through a thematic priority call on welfare, culture and society.

Project manager: Jonas Minet Kinge

YoungPsych: Drivers and implications of the mental health decline among the young

7 990 000 NOK

Research Council of Norway

During the last decade, depression and anxiety have been on the rise among adolescents and young adults in Norway and other countries. This trend has been referred to as a "teen mental health crisis" and caused concerns regarding the immediate impact on well-being as well as the long-term consequences for affected individuals and society at large. The aim of this project is to identify causes and implications of this development. Several explanations have been brought forward, and this project will focus on some of the most prominent, including (i) the medicalization hypothesis: emotional distress previously considered "normal" being to a larger extent labelled as disease, (ii) the pressure hypothesis: a stronger perceived pressure to perform in all areas of life, including the school context, and (iii) the social media hypothesis: more widespread use of social media leading to mental health declines via changing sleep patterns, social comparison, altered leisure time activities, and online bullying.

The project is planned to start formally on September 1, 2024.

This Young Research Talents project is funded by the Research Council of Norway through FRIPRO.

Project manager: Jonathan Wörn

PhD and postdoc projects in 2023

Completed dissertations for the PhD degree

Dana Kristjansson
"Mitochondrial DNA and Norwegians". Dana successfully defended her thesis on January 13, 2023.

Ellen Øen Carlsen
"Determinants of perinatal outcomes in Norway: 1982-2020". Ellen successfully defended her thesis on June 14, 2023.

Kristine Løkås Haftorn
"The role of DNA methylation in gestational age". Kristine successfully defended her thesis on October 5, 2023.

Ongoing PhD fellowships

Kathryn Beck
"School entry and exit: understanding the consequences of transitions in education"

Espen Beer Prydz
"Fertility, Aging, and Income: Poverty and Inequality under Demographic Change"

Marianne Hopen Rørholt
"Revisiting and dissecting the maternal effect on childhood asthma, and its impact"

Siri Nærland Skodvin
"Statistical methods for genetic interactions in family trios"

Karoline Hansen Skåra
"Understanding the causal nature of the relationship between infertility and cardiovascular disease"

Chaitra Srinivas
"Trajectories of ADHD medication use before, during and after pregnancy in Norway and Sweden and the risk of miscarriage and preterm birth among women with ADHD"

Hans Fredrik Sunde
"Mental health and intergenerational transmission of social differences"

Rishabh Tyagi
"Social, health & demographic consequences of technologyinduced job loss"

Mari Landås Warp
"Is the reproductive potential in young women today influenced by that of their mothers? A study of mothers and daughters in the Norwegian Mother, Father and child Cohort Study".

Lise Andrea Arge
"Miscarriage history and subsequent fecundability: Results from the Norwegian Mother, Father and Child Cohort Study"
Medical Student Research Program at the University of Oslo

Ongoing postdoc fellowships

Sara Abrahamsson
"Intergenerational effects and transmission of health, welfare and fertility over the last century"

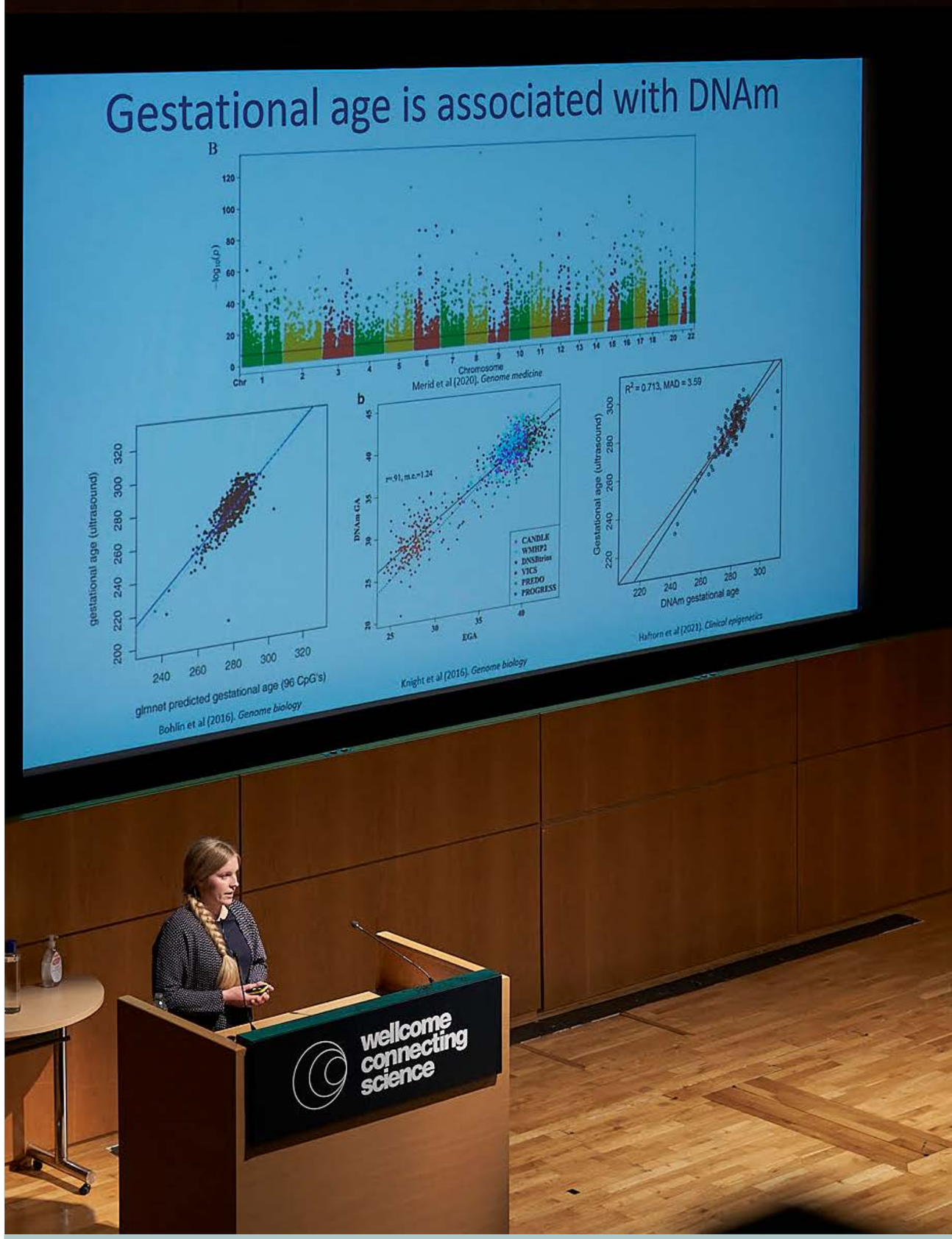
Thang Dang
"Institutions, policy interventions, and health inequalities in Norway"

Thea Grindstad
"Determinants of fecundity across generations in modern developed society"

Álvaro Hernáez
"Understanding the causal nature of the relationship between infertility and cardiovascular disease"

Huong Thu Nguyen
"Assisted reproductive technologies and risk of cardiovascular disease"

Magnus Nordmo
"Reproduction of socioeconomic differences and mental health across generations"



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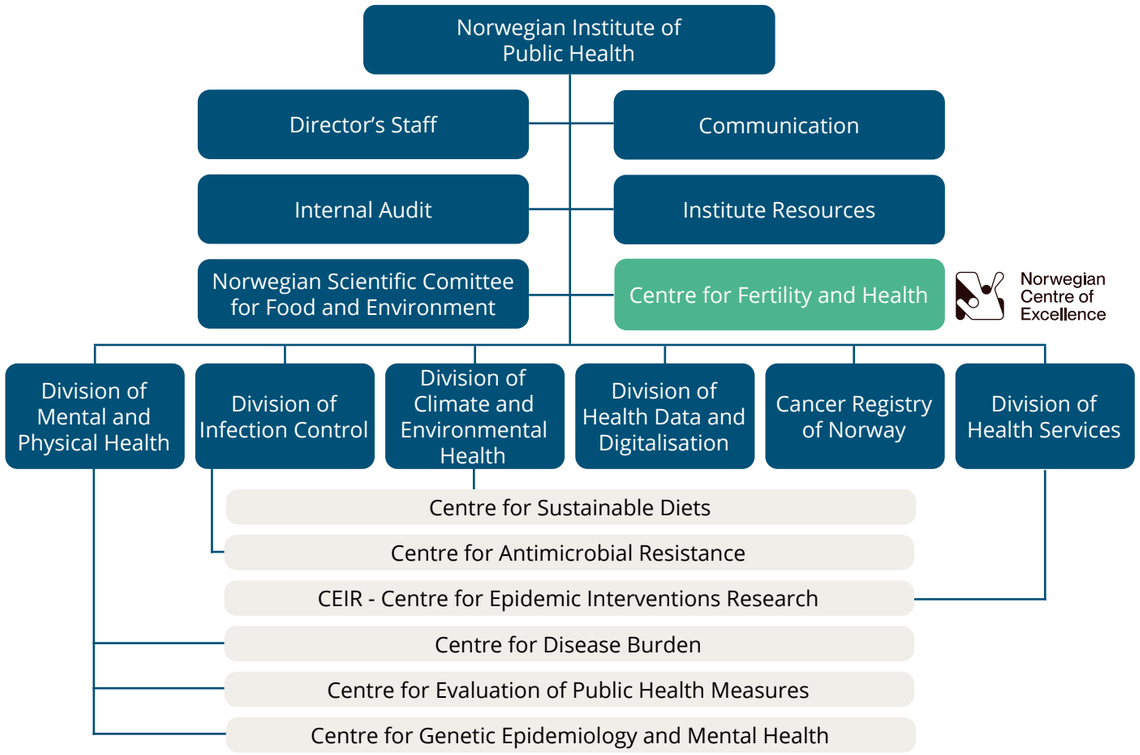
The Scientific Advisory Committee (SAC) ic constituted by international scholars who are specialists in research fields relevant to the Centre.

The mandate of the SAC is to:

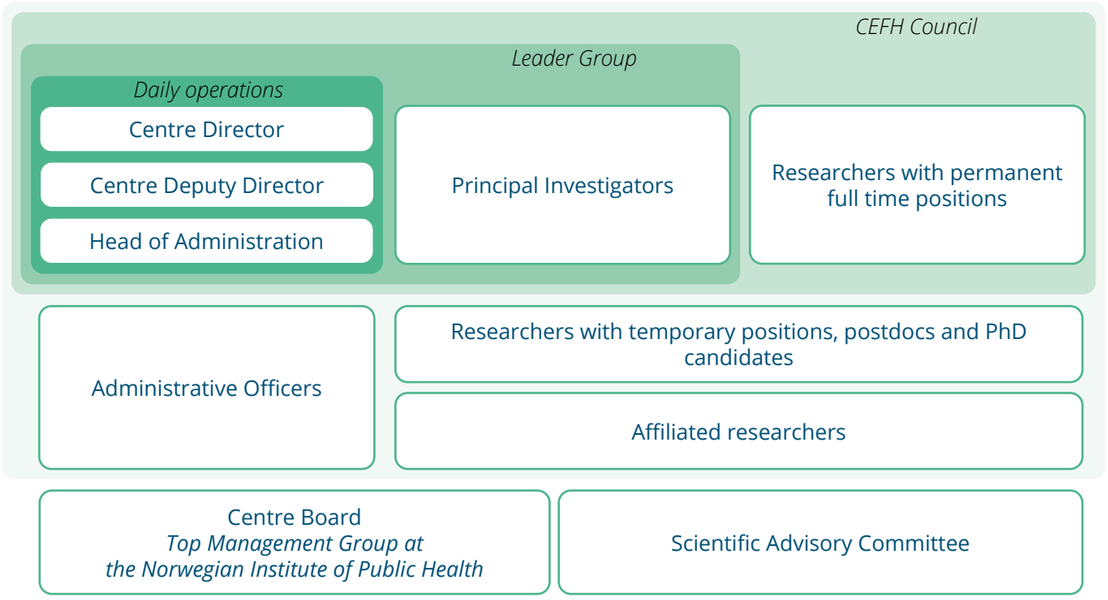
- Partake in discussions of the Centre's research strategy and scientific challenges throughout the project period. The committee may also provide advice on other types of issues.
- Provide strategic advice to the Centre, based on international trends and scientific development within the field of fertility and health. As far as possible, the SAC should also be able to provide advice that is directly relevant to Norwegian needs and strategies.
- Assume an active role in monitoring the performance and scientific excellence of the Centre.
- Provide annually a short status report on the development of the Centre, drawing on annual reports and other material made available by the Centre.

Organisation

Organisation chart of the Norwegian Institute of Public Health

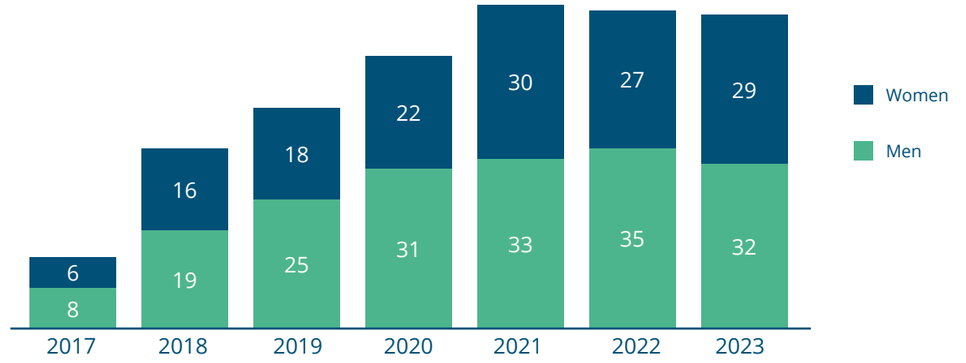


Organisation of the Centre for Fertility and Health

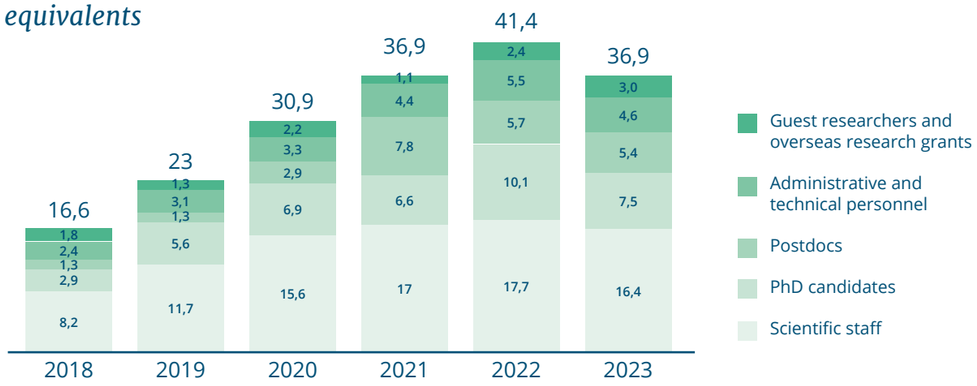


Indicators 2017–2023

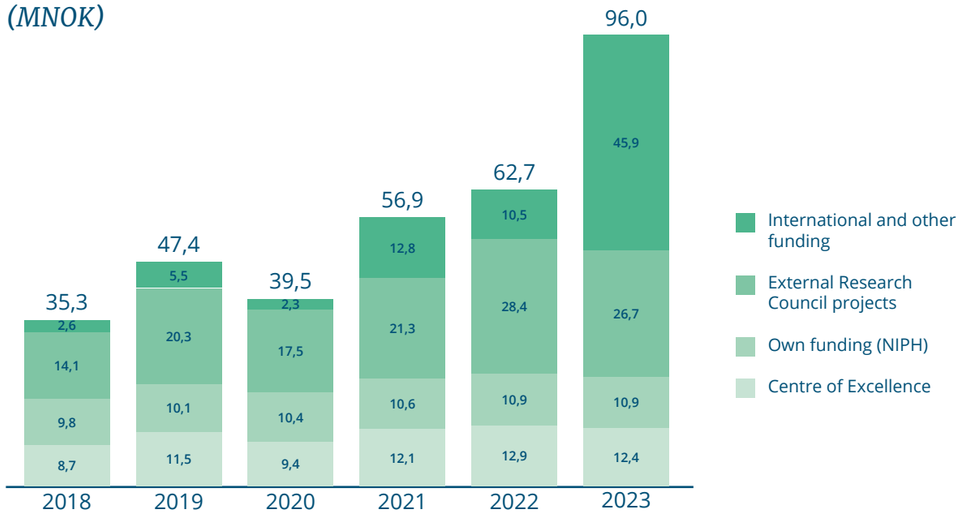
CEFH personnel



Full-time equivalents



Financing (MNOK)



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Letters

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Seminars 2023

The Centre has initiated several series of seminars to foster scientific exchange.

CeFH Lunch Seminars
Our lunch seminars are informal research seminars held every Friday. Both researchers at the Centre and researchers from other parts of the world present interesting topics in fertility and health. The presentations include new research ideas, projects, results and methods as well as possible collaborative projects. The seminars are also open to other researchers outside of the Centre.

CeFH Genetic Fridays
Genetics Fridays are held every Friday. This is an informal venue for all employees at the Norwegian Institute of Public Health and collaborators who work in genetics, plan to implement genetics in their work, or merely have an interest in genetics. There is ample room for presentations and/or discussions, where participants can share their knowledge and experience, come up with ideas, and discuss projects and methods.

Lunch Seminars and Genetic Fridays in 2023

***Ingrid Huitfeldt*.** Breast Cancer Screening and Mortality. *January 13.*

Alba Fernández-Sanlés. Characterizing the causal effects of cytokines on human health: a phenome-wide approach. *January 13.*

***Thea Grindstad*.** Environmental exposures and time to pregnancy: a MoBa study. January 27.

Kristine L. Haftorn. Epigenetic clocks: an overview. *January 27.*

Julie Røgler Langås. Lifestyle across the life course and health outcomes at an advanced age: does age at menopause matter? *February 3.*

William Denault. Empirical Bayes methods for modern genomic data. February 10.

Leticia Spindola. Exploration of brain-heritable methylation in schizophrenia cases and controls. *February 10.*

David Hugh-Jones. Trading social status for genetics in marriage markets. *February 17.*

Zichen Deng. Revealed Preference or Forced to Leave: Internal Migration Responses to Pollution Information in China. *March 3.*

Kathryn Beck. The Causal Effect of School Starting Age on School Performance and ADHD Diagnosis. *March 10.*

Nikolai Eftedal. Explaining correlations between nonimmediate relatives on Norwegian national tests. *March 10.*

Agnes Fauske. The influence of societal changes on the nature and nurture of fertility behavior: A study of the 1940-77 Norwegian birth cohorts. *March 17.*

Suzan Carmichael. Preventing Severe Maternal Morbidity & Maternal Health Inequities in the US: Contributions of Population-Level Research. *March 24.*

Christian M. Page. The MoBa epigenetic cohort. *March 24.*

Kathrine Frey Frøslie. Hard facts in soft materials. *March 31.*

Cathrine Ebbing. Fetal circulatory physiology. Conimpreg and DiaDoppler; Two carefully characterized cohorts with serial measurements throughout pregnancy and a rich biobank. *April 14.*

Kåre Bævre & Hans Fredrik Sunde. ChatGPT - Friend or foe? *April 21.*

Karl Trygve Kalleberg. Epigenetic signatures for seropositive and seronegative rheumatoid arthritis. *April 21.*

Kristine L. Haftorn. Stability selection enhances feature selection and enables accurate prediction of gestational age using only five DNA methylation sites. *April 28.*

Anders Skrondal. Should you share your good ideas? *May 5.*

Hans Fredrik Sunde. Assortative mating strongly increases genetic resemblance between distant relatives. *May 5.*

Rolv Terje Lie. New smokeless tobacco data from the Medical Birth Registry of Norway. May 12.

Thijs van den Broek. The contribution of fertility patterns to ethnic differences in mothers' body mass index in the Netherlands: A decomposition approach. *May 26.*

Pauline Kleinschlömer. Exploring the Influence of Adaption and Anticipation Effects: The Impact of Changing Family Structures on Children's Educational Outcomes. *June 2.*

Kristine L. Haftorn. Cell-type specific DNA methylation in newborns conceived by assisted reproductive technologies. *June 2.*

Jakko Kaprio. Twins, epigenetics and the exposome. *June 9.*

Astrid de Linde. The impact of maternity ward closures on infant health outcomes, maternal health outcomes, and birthing procedures in Norway. *June 16.*

Rolv Skjærven. Longterm Maternal CVD risk should not be based on 1st pregnancy complications only. *August 25.*

Liv Bente Romundstad. Eggs, love & DNA. *September 1.*

Amanuel Gebremedhin. Interpregnancy interval and pregnancy complications in a high-income context. *September 8.*

Stein Emil Vollset. Forecasting fertility and more. *September 15.*

Kristine L. Haftorn. The role of DNA methylation in gestational age. *September 15.*

Tonje Lien. Precision medicine methods in cancer clinical practice. *September 22.*

Tam Mai. Separate but Not Equal: The Uneven Cost of Residential Segregation for Network-Based Hiring. *September 29.*

Rosa Cheesman. The genetics of educational fields. *October 6.*

Ingrid van Dijk. Family Differences in Mortality and Health. *October 13.*

Mette Haug Stensen. Assisted Reproductive Technologies: in the laboratory. *October 20.*

Anna Matysiak. Adoption of industrial robots and fertility. *October 27.*

Sarah Gust. Global Universal Basic Skills: Current Deficits and Implications for World Development. *November 3.*

Oddvar Myhre. BRAIN HEALTH project: New Approach Methodologies (NAMs) to study developmental glial cell toxicity of food toxicants (BRAIN HEALTH). *November 10.*

Maria Magnus. Project update on the INFERTILITY project: understanding the causal nature of the relationship between infertility and cardiovascular disease. *November 17.*

Yunsung Lee. Recent research into the genetics of asthma. *November 17.*

Rannveig Kaldager Hart. Use of prenatal primary care among immigrants in Norway. *December 1.*

Hans Fredrik Sunde. Genetic similarity between relatives provides evidence on the presence and history of assortative mating. *December 1.*

Flo Martin. Antidepressant use during pregnancy: what are the outcomes? *December 8.*

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