





# Introduction from the Centre Directors

Reflecting on 2024, the Centre for Fertility and Health (CEFH) has continued to thrive as an interdisciplinary research hub. We continue our mission to advance knowledge on fertility and its long-term health implications.

This year, we have made remarkable progress in research, collaboration, and expanded our engagement with policymakers and institutions.

### A strong research community

Our early career researchers have flourished, fostering creativity and independent thinking. We actively participated in the 3<sup>rd</sup> KUPP workshop, a career development program at the University of Oslo which has helped raise awareness about career growth and strengthened our support for it. Our commitment to interdisciplinarity remains unwavering, with increasing collaboration between disciplines reinforcing our research strategies and methodological approaches.

As a Norwegian Centre of Excellence, we benefit from international recognition, increased research and funding opportunities, the ability to attract top talents and great freedom to explore high-reward research. Our funding has enabled us to generate world-class data, benefiting our team and other

researchers in Norway and abroad. In 2024, we developed new research grant applications, including initiating the process of a Centre of Excellence grant application for the 2025 call.

### Research with societal impact

Our research continues to inform policy, particularly regarding fertility trends and health disparities. We have made significant progress in understanding declining birth rates through clinical examinations of participants in the Norwegian Mother, Father, and Child Cohort Study (MoBa), with expanded collaborations at Haukeland University Hospital enhancing the scope of this work. We are now collaborating with fertility clinics in three locations across the country: Trondheim, Porsgrunn and Bergen. The ERC Synergy Grant project BIOSFER has reached critical milestones, including extensive

data collection, more than 47 published papers, and clinical examinations of more than 1,600 participants.

### Institutional engagement and evaluation

The preparation for the Research Council of Norway's evaluation of medical and health research (EVALMEDHELSE) encouraged us to assess and refine our organisation. In March, we presented key research highlights in epigenetics, infertility and cardiovascular disease, assisted reproduction, gender disparities, and BIOSFER during a site visit by the Research Council of Norway. In addition to an overview of our scientific progress, discussions focused on gender balance in recruitment, building careers of young researchers, financial sustainability, and ethical considerations in research.

Researchers in the centre are highly attractive for their expertise. Beyond conducting research, we actively contribute to knowledge dissemination. For instance, our team members contributed to the Public Health Report, published by the Norwegian Institute of Public Health, which provides insights and statistics on Norway's health status. Notably, Rannveig Kaldager Hart was appointed chair of a government committee on birth rates. We also organised several project specific seminars to disseminate results.

### New research and external funding

Several new externally funded projects will contribute to strengthen our research. These include Maria C. Magnus's study on endometriosis, Vegard Skirbekk's research on men's health and employment, Kathryn Beck's project on neurodevelopmental diagnoses, Rolv Terje Lie's work on preventing newborn brain damage, and Robert Lyle's study on assisted reproduction and cancer risk.

### Doctoral defences and visiting scholars

We celebrated the doctoral defences of three PhD candidates: Kathryn Beck on educational transitions and health, Hans Fredrik Sunde on socioeconomic differences and mental health, and Karoline Hansen Skåra on infertility and cardiovascular disease. In addition to these successes, we welcomed visiting scholars from Finland, Denmark, the Netherlands, USA, Austria, and Australia, strengthening our international collaborations and broadening our knowledge exchange. Their contributions have enriched ongoing research efforts.

### Looking ahead

As we move forward, our commitment to high-quality, interdisciplinary research remains strong. We aim to deepen our understanding of fertility and health dynamics, secure new funding, and further expand our international collaborations. The dedication of our researchers, collaborators, and institutional partners continues to drive our success.

With enthusiasm and ambition, we look forward to another year of impactful scientific contributions.



Siri E. Håberg, Centre Director



## Highlights 2024

### A strong interdisciplinary team

In 2024, 29 women and 31 men were associated with the centre including researchers in full- and part-time positions, postdoctoral fellows, PhD candidates, and administrative staff. Additionally, the center has several national and international guest researchers and collaborators associated through formal collaboration agreements.

### **Selected publications**

Our study of children born to mothers who had COVID-19 or were vaccinated against it during the first trimester of pregnancy showed reassuring results, specifically that the children did not have a higher risk of birth defects. The study was published in *BMJ*, and the results received significant attention.

Magnus MC, Söderling J, Örtqvist AK, Andersen A-MN, Stephansson O, Håberg SE and Urhoj SK. 2024. Covid-19 infection and vaccination during first trimester and risk of congenital anomalies: Nordic registry based study. *BMJ*. 386, e079364.

In a study on assortative mating published in *Nature Communications*, we found that people often choose partners with similar educational levels. Partner selection may be one of the reasons why we see increasing social inequalities in Norway.

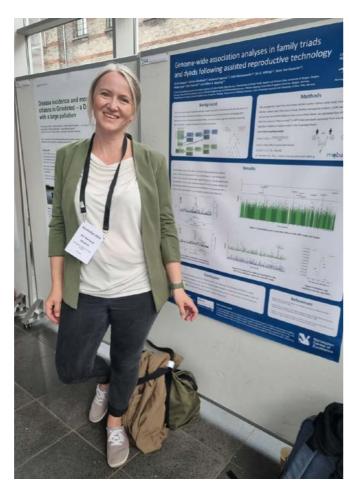
Sunde HF, Eftedal NH, Cheesman R, Corfield EC, Kleppesto TH, Seierstad AC, Ystrom E, Eilertsen EM and Torvik FA. 2024. Genetic similarity between relatives provides evidence on the presence and history of assortative mating. *Nature Communications*. 15, 1, 2641.

In a study published in *Demography*, we showed that the age at which individuals complete their education and their career development are important mechanisms for delayed fertility.

**Beck KC**, **Hart RK** and **Flatø M**. 2024. School Starting Age, Fertility, and Family Formation: Evidence From the School Entry Cutoff Using Exact Date of Birth. *Demography*. 61, 6, 1999-2026.

A paper published in *Nature Human Behaviour* showed that low education is associated with early death, and this is particularly linked to accidents and poisonings.

**Reme B-A**, Røgeberg O and **Torvik FA**. 2024. School performance and the social gradient in young adult death in Norway. *Nature Human Behaviour*. 9, 84-89.



### New externally funded projects

FRIPRO funds awarded to **Maria C. Magnus** for the project "ENDOHEALTH" and research on endometriosis and adenomyosis.

ERC Advanced Grant to **Vegard Skirbekk** for the project "HOMME" concerning health, cognition, family, and employment among men.

Funding from the Regional Competence Service for Autism, ADHD, and Tourettes Syndrome in Health Southeast to **Kathryn Beck** for the project "Stable Life Trajectories for Young People with ADHD and Other Neurodevelopmental Diagnoses".

The Trond Mohn Foundation is supporting a collaborative project with the University of Bergen, "ProBND," on prediction and prevention of brain damage in newborns. The project is led by **Rolv Terje Lie**.

Kreftforeningen is supporting a collaborative project with Oslo University Hospital on "Assisted reproductive technologies and cancer risk in later life". The project is led by **Robert Lyle**.

### **Nominations and awards**

**Rannveig Kaldager Hart** was appointed as the chair of the Government's committee on birth rates. **Vegard Skirbekk** is a member of the committee.

**Hans Fredrik Sunde** received the Outstanding Associate Member Poster Presentation Award at the 2024 BGA Annual Meeting.











### **Theses**

**Kathryn Beck**. School Entry and Exit: Understanding the Consequences of Educational Experiences.

**Hans Fredrik Sunde**. Reproduction of socioeconomic differences and mental health across generations.

**Karoline Hansen Skåra**. The complex interplay between infertility and cardiovascular disease.

### **Major events**

- Annual Centre retreat Sundvollen. Feb 29 Mar 1, 2024
- Mito-project ending seminar. May 13-14, 2024.
- Puberty & Education kickoff meeting. May 14, 2024.
- 7th Annual CEFH Symposium 2024. May 15-16, 2024.
- BIOSFER synergy camp. May 27-30, 2024.
- CEFH summer garden party. June 19, 2024.
- European Perinatal and Pediatric Epidemiology Conference (EPPEC). Sep 16-17, 2024.
- Open seminar on MoBa and cancer. Oct 7, 2024.
- Rementa ending seminar. November 20, 2024.
- Centre Christmas Lunch. Dec 11, 2024.
- PhD seminars and courses.
- Various project seminars and over 50 weekly seminars

### 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.

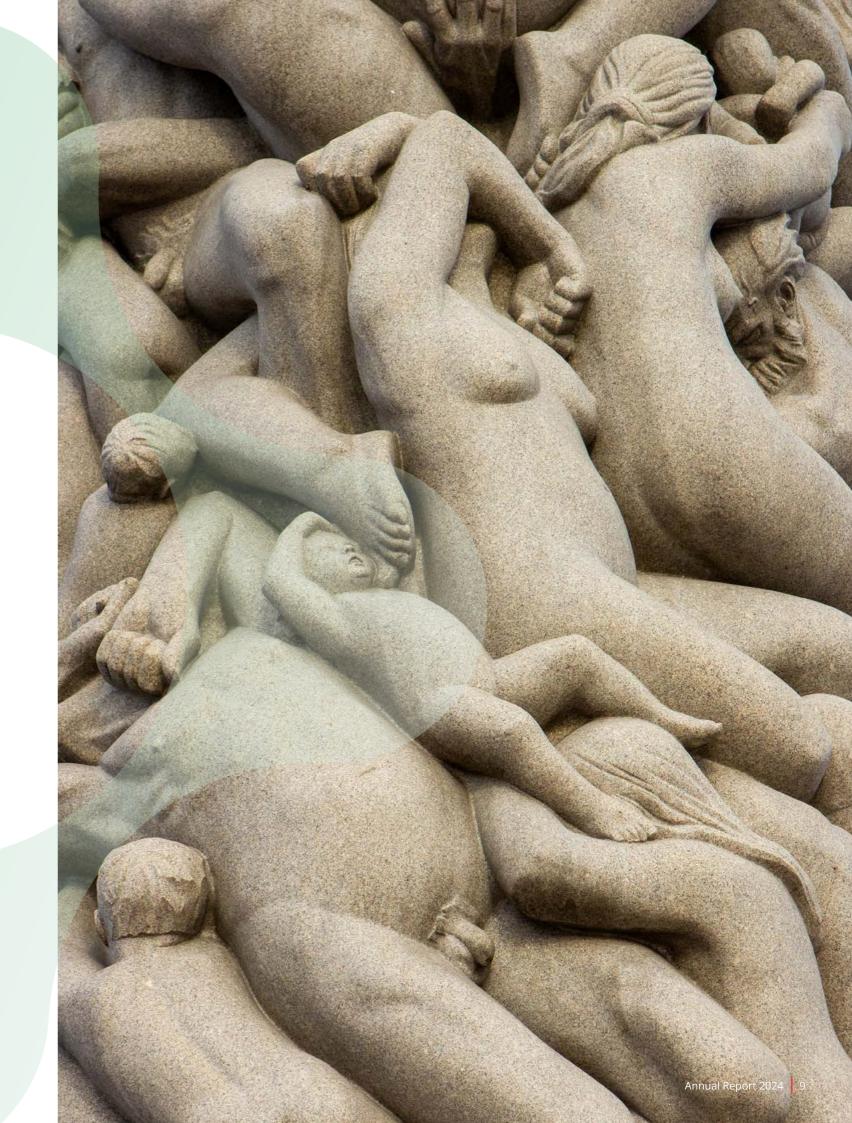
As the Centre has evolved, new research ideas have been added to the ones originally described in our CoE proposal. They reflect advances in the field and new ideas are spawned by the growing number of Centre team members and collaborators.

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.

## 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

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),

### **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
- 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.

## 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
- 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.

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), 242Nordmo M et al. 2022. The educational burden of disease: a cohort study. Lancet Public Health 7 (6), e549-e556.

Beck KC et al. 2024. School Starting Age, Fertility, and Family Formation: Evidence From the School Entry Cutoff Using Exact Date of Birth. Demography. 61, 6, 1999-2026.

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

Reme B-A et al. 2024. School performance and the social gradient in young adult death in Norway. Nature Human Behaviour. 9, 84-89.

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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.

Sunde HF et al. 2024. Genetic similarity between relatives provides evidence on the presence and history of assortative mating. Nature Communications. 15, 1, 2641.





## 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. <u>Heritability</u> 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

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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.

Magnus MC *et al.* 2024. Covid-19 infection and vaccination during first trimester and risk of congenital anomalies: Nordic registry based study. *BMJ.* 386, e079364.

### 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 100 applications for external funding. Of these, 25 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, The Norwegian Cancer Society and Oslo University Hospital.







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## The Gro Harlem Brundtland Visiting Scholarship 2024



### Claudia Bruno

Claudia is a post-doctoral Research Fellow at the Medicine Intelligence Research Program, University of New South Wales, Australia. She is a pharmacoepidemiologist interested in the safety and quality use of medicines among high-risk and underserved population groups, including pregnant women and children. Her research aims to promote best-practice healthcare through public health policy and clinical practice changes.

During her research stay at the Centre in 2024, she studied the use of medicines used to treat attention deficit hyperactivity disorder in pregnancy and child neurodevelopmental disorders. The study used Norwegian, Swedish and Danish data from NorPreSS (mainly, Medical Birth Registry, Prescription Database and Patient Registers, and utilised a range of analyses including a discordant sibling analysis and paternal data for confounding control.



**Marie-Caroline Compans** 

Marie-Caroline Compans is a postdoctoral researcher at the University of Vienna (Wittgenstein Centre) and the French Institute for Demographic Studies (Ined). Her research focuses on delayed childbearing and late fertility, experiences of infertility, the use and legislation of assisted reproduction, and miscarriages.

During her stay at the Centre in 2024, she examined maternal and paternal factors associated with time to birth since trying to conceive among infertile individuals, distinguishing between spontaneous and ART births and over time. Previous studies indicate that the general tendency to start a family later has prompted an increase in infertility prevalence and in the use of reproductive health services. At the same time, assisted reproductive technologies (ART) have developed and improved considerably. However, little is known about whether people with infertility problems who use ART ultimately take less or more time to achieve a birth than those who do not use ART, and whether those who use ART now have a child faster than in the past. The study used Norwegian data from the HUNT study and the Medical Birth Registry.

### 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.

## 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 subprojects 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 2024, many papers from this project were published in reputable journals such as Nature Communications, Nature Human Behaviour and Demography. The project involves collaborations with researchers from 30 national and international research institutions. The project will continue until the end of 2028.

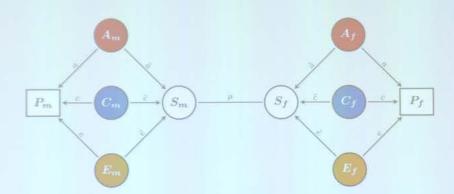
Project managers: Per Magnus and Øystein Kravdal

### 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. We have expanded the epigenetic data with additional random trios and have now the world largest dataset to date with triodata of DNA methylation combined with genetics.

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 funding from the Norwegian Cancer Society, we are 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

### Indirect assortment



How can we estimate  $\tilde{a}$ ,  $\tilde{c}$ , and  $\tilde{e}$ ?

Solution: Twins-in-law



in the aging clocks, and in 2024 we investigated parental biological aging in relation to pregnancy outcomes. The role of genetics in subfertility, and interaction between parent's genes are also investigated. We have also studied genetic effects on telomere length, and the relation between telomere length, fecundity and use of ART. Another advancing area is combining our triodata on genetics, and we have published novel statistical methods to detect mother-father genetic interaction effects, with infertility as an example.

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 have now received all metabolomic profiles (250 metabolites in total) to pregnancy samples for approximately 11 000 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. Our research has provided very important knowledge to the international community and various stakeholders about shortand long-term safety of exposure of antiseizure drugs, antidiabetic drugs and antipsychotics in pregnant women. Large-scale epidemiological studies are essential for reliable knowledge and precise risk estimates. This new knowledge has benefitted healthy women of childbearing age (pregnant or planning), their partners, health personnel, regulatory authorities, and advisory bodies. Our Nordic and International research collaboration has been carried forward, leading to new safety studies using the InPreSS data set and



Common Data Model. The InPreSS project also had a positive impact on junior researcher careers: The two positions (postdoc and researcher) fully financed by InPreSS, secured permanent positions at NIPH. The researcher also managed to receive a Young Research Talent funding from RCN.

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 2024, we presented results at two international and one national conference. The PhD candidate in the project, Chaitra Srinivas, finalized the study on preterm birth, carried out analyses for her final study on miscarriage, and worked on her thesis (to be submitted in 2025). Guest researcher Claudia Bruno from Australia (UNSW) carried out analyses on risk of neurodevelopmental disorders. We established a new collaboration with researchers from University of Southern Denmark to extend the study on postpartum depression to include results from Denmark and developed the study protocol. Finally, we received data from the Norwegian Prescribed Drug Registry, which had been delayed by the establishment of the new drug register. These data will be linked with data from the MoBa cohort to study prenatal health behaviours and self-reported measures of perinatal mental health in women with ADHD.

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

### 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.



Digitalization of all sources 1900-1960 is now basically completed. This work, using various Al-techniques, has been conducted by CeFH. The focus now turns to linking together these sources, validation, and integration of HPR 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.

## 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.

New results published in 2024 show that both men and women who start school one year later postpones their fertility, resulting in later first, second and higher order births (Beck, Hart & Flatø, 2024). Delayed income growth and education are plausible mechanisms for this. School starting age was, however, not associated with lower total cohort fertility, as delayed fertility was recuperated towards the end of the reproductive age. The Phd candidate in the project, Kathryn Beck, successfully defended her thesis in December 2024.

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 more likely to achieve low education themselves, and experience unemployment or social exclusion. It is not adequately understood why social differences 'reproduce'. The close relationship between socioeconomic status and mental health could suggest that mental health is important to understand the reproduction of social differences and mobility.

This project ended in 2024 and by the end of the project, we have published 25 scientific articles, in addition to preprints that have not yet undergone peer review. Below, we highlight some key findings.

In one publication (Kinge *et al.*, 2021, International Journal of Epidemiology), we documented how parental income was associated with children's mental health. The study concluded that mental disorders are 3 to 4 times more common among children whose parents are in the lowest earning percentiles compared to those in the highest percentiles, and that the association between income and mental disorders holds across the entire income distribution. We also found that these differences could not be explained by factors such as parental education or parental mental health. The same pattern was observed among adoptive children, indicating that genetic factors alone could not fully account for the association.

We have also documented that children of parents with mental disorders achieve lower school performance. In one article (Nordmo *et al.*, 2023, npj Science of Learning), we show that when adjusting for factors that are constant within a family, parental mental disorders still have a small but statistically significant effect on final grades in lower secondary school.

Further, we investigated how children's health is linked to their own school performance (Nordmo et al., 2022, The Lancet Public Health). We examined all possible diagnosis codes in primary health care and subsequent grades in lower secondary school. Among all examined types of health conditions, mental health contributed by far the largest share of health-related inequalities in school performance, followed by non-specific and endocrine conditions. Among specific diagnoses, ADHD contributed the most to reduced educational attainment in the population.

Another topic in the project was how assortative mating can lead to social inequality. Previous studies of assortative mating have focused primarily on the partners themselves. However, assortative mating also has consequences for the next generation. Researchers typically expect a genetic similarity between siblings of 50 percent. Yet, because children can inherit genes variants with the same effects from both parents, we found that the similarity in education-related genes was as high as 68 percent. In other words, there is greater genetic similarity within families than expected and greater differences between families (Torvik et al., 2022, Nature Communications). We have also compared close relatives with more distant relatives, whose similarity appears to be more strongly influenced by partner choice than close relatives. Remote relatives are connected through historical partner choices, allowing us to observe how these patterns have evolved. The results indicated increased variation in genetic variants associated with education over time (Sunde et al., 2024, Nature Communications). Additionally, we found strong partner selection across multiple traits (Torvik et al., 2024, Nature Communications).

We have also participated in the public debate on social inequality through lectures, interviews, podcasts, and opinion pieces.

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.

We use data from linkages between registries, but also data from the Norwegian Mother, Father, and Child Cohort Study. Many mechanisms may explain the maternal effect. Some of the mechanisms are related to genetic factors while others are determined by environmental factors. As yet, we have found a gene that confers higher risk of asthma to the child when the gene is inherited from the mother than from the father. Epigenetic mechanisms (imprinting) is a possible explanation for this. We are also looking at sequencing of mitochondrial genes (inherited solely from the mother) and telomere length analyses (higher mother-child than father-child correlations).

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. We have recently published how environmental toxins may affect time to pregnancy in parents in the Norwegian Mother, Father, and Child Cohort Study (MoBa), and are following up on several studies on environmental toxins and endocrine disruptors on pregnancy and fertility outcomes.

This project was the basis of in an ongoing new data collection in MoBa, in which young second-generation participants are invited to a clinical examination at collaborating fertility clinics. So far, around 500 women have been examined. With additional funding from the BIOSFER-project, we build on this project aiming at examining 1250 young women and 1250 young men. With the new data we can study whether measures for fertility in young adulthood are associated with current lifestyle, early life or prenatal exposures. The role of heritability in fertility measures and age at menarche and menopause have been published.

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 are currently being 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, was published in the journal Aging Cell in 2024 (Lee et al.). A second manuscript, on the relationship between TL and fecundity was published in the journal BMC Medicine in 2024 (Skåra et al.) is currently being drafted for submission. Regarding our work on epigenetic aging, we submitted a preprint on a project where we examined the effect of prenatal stress on gestational epigenetic age (Murgatroyd C et al.)

The project was initially funded by the US National Institutes of Health (NIH) (grant R01 1HL134840-01) until 2022 and subsequently 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.

Approximately 1000 DNA samples from children in MoBa have now been sequenced at Life and Brain GmBH in Bonn, Germany and the results transferred to our account at the Services for sensitive data (TSD) at the University of Oslo. The data have been quality-controlled, and the analyses to achieve the aims set forth in the project have started. In 2024, we organised a research workshop on mitochondrial DNA sequence analysis in this project.

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. Beyond this, results from this project from 2024 include that telomere length does not seem to differ among women and men who are infertile compared to those who are fertile and that epigenetic age acceleration does not seem to influence the likelihood of infertility among women and men. We have previously provided evidence that women who delivered after using assisted reproductive technologies do not appear to have an increased risk of cardiovascular disease. We are now conducting follow-up studies looking into the number and types of cycles of assisted reproductive technologies that a women has undergone. One PhD candidate who was working within the project, Karoline Hansen Skåra, defended her PhD in 2024. A postdoctoral researcher, Álvaro Hernaéz, has also completed his postdoc and resumed a faculty position at Blanguerna School of Health Sciences in Barcelona. A second postdoc researcher, Huong Thu Nguyen, has been working in the project since 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 2024, the analyses in the project are either at a final stage, in review processes, or accepted for publication. Ongoing work focuses particularly on describing the prevalence of disease within families across socioeconomic status. Living with severely sick family members can add strain and stress, which could affect health, school performance and labor market outcomes. This work aims to shed light on the extent to which members of families from less resourceful backgrounds also are exposed to an additional burden from sick family members.

The project is funded by the Research Council of Norway's VAM pro-

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 the early phase of the COVID-19 pandemic with Karolinska Institutet in Sweden and the University of Copenhagen in Denmark with funding from NordForsk. Our overall aim and purpose in this project is to increase knowledge on how international crisis like a pandemic affects pregnant women and their infants, who are especially vulnerable during most societal crises. Also for pandemics, pregnant women and their infants are high risk groups. After the initial studies on COVID-19 and COVID-vaccinations in SCOPE 1, we continue the Scandinavian collaboration investigating medium- and long-term effects of COVID-19 infections and vaccinations on pregnant women and their children. We investigate how the COVID-19 pandemic influenced fertility patterns, reproductive health, pregnancy, and child outcomes in the first years of life after their mothers were exposed to pandemic infections or were vaccinated while pregnant. 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 CO-

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 aims to study safety of COVID-19 vaccination in pregnant women and children born to mothers who were vaccinated while pregnant. So far, 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.

In 2024 we published together with our Scandinavian collaborators reassuring results on COVID-19 vaccination during pregnancy, with no indications of increased risk of congenital anomalies when women were vaccinated during first trimester. We also showed reassuring findings on neonatal outcomes in children born after maternal vaccination while pregnant. The reassuring results from this project have been published in

several high impact journals, including publications in BMJ and JAMA. Women are continuing to be recommended a COVID-19 vaccination in pregnancy, although vaccine uptake is decreasing. 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 collaborate with Canadian and US researchers on these topics. We continue 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

## 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 includes new survey and clinical data collected through clinical examinations of young adults, and through pregnancy planner cohorts, in Norway and Denmark. We also investigate fertility knowledge among young adults, and whether information on fecundity may affect fertility plans in young adults.

In 2024 we carried out two BIOSFER-research camps, with around 50 participants brainstorming and developing research ideas. We have initiated several new interdisciplinary collaborations across the research teams, and developed materials for new data collections. Several new PhDs and postdocs have been recruited in 2024. After publishing 17 papers in 2023, more then another 20 papers were published in 2024, ranging from biological processes in puberty and fertility to the impact of educational differences, partnering patterns and childlessness.

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



## Young Dyad: Romantic partners in the young adulthood - A dyadic perspective on childbearing plans and values

One of the main reasons for the recent decline in fertility in Norway and other Nordic countries is that men and women are having children later. Even though young adults are central to understanding the decline in fertility, we know little about fertility determinants and desires in this life phase. Over 90% of Norwegian children are born to mothers who are married or cohabiting. Although the decision to have children is usually always made by couples, most studies only have access to information from one partner.

In this project, we will examine how young adults, and their partners/boyfriends think about parenthood, child plans and equality. The project will use data from the Norwegian Mother and Child Cohort (MoBa) and the "Young Health" data collection, as updated from time to time, on fertility determinants in MoBa. We invited their boy/ girlfriends to fill in a similar form. This gives us data on how young couples think about family formation, equality and values, and how such agreement or disagreement affects when and if they have children.

The project is funded by the Research Council of Norway through the Centre of Excellence grant and closely connected to the BIOSFERproject.

## 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.

Since the start of the project in August 2023, we have published two papers on partner formation in Nature Communications. In Sunde et al. (2024), we compare genetic similarity between close and distant relatives. Similarity between close relatives is due to recent partner choices, while similarity between distant relatives reflects partner choices made further back in time. This allows us to understand how partner selection has evolved across generations. The results show that people increasingly choose partners with similar genetic predispositions towards education, contributing to rising social inequality. In Torvik et al. (2024) we investigate how education relates to partner choice along with mental and somatic health. Additionally, we have released a preprint on the mental health

Project manager: Rannveig Kaldager Hart along with mental and somatic health. Additionally, we have released a preprint on the mental health

28 | Centre for Fertility and Health | Centre for Fertility and Heal



effects of parenthood (Hart *et al.*, 2024). The findings indicate that more individuals seek healthcare for mental health issues after having children, compared to their mental health before becoming parents. The results are most pronounced for men but are also present for women. We have also released a preprint on the associations between parenthood and mental health throughout the life-course and how this association has changed over time (Andersen *et al.*, 2024). The disparity between parents and non-parents increased over the study period, suggesting stronger selection into parenthood. Our findings highlight parenthood as a significant indicator of mental health inequalities, with its importance growing over time.

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 funded by the Norwegian Cancer Society, 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. We investigate the potential role of ART and DNA methylation at birth in risk of breast cancer and other cancers by 1) using registry data to explore if persons born after conception with ART has an increased risk of cancer, whether there are sex differences in cancer risk after ART, 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.

The first papers have been published, showing sex differences in childhood cancer risk in children born after ART, and also showing sex differences in DNA methylation at birth in children born after ART compared to naturally conceived. Currently, we are analysing data on repeated measurements from children born after ART and naturally conceived children, comparing methylation at older ages to methylation at birth to investigate if the methylation differences shown at birth persists up to age 22. We are currently also performing lab analyses of RNA samples and will continue analyses of the generated data in 2025.

The project is funded by The Norwegian Cancer Society's Rosa sløyfe call.

Project manager: Siri E. Håberg

### Pubertal timing and inequalities in education

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 started formally on April 1, 2024. In 2024, we have hosted an inaugural seminar and hired one postdoc in the project, Kathryn Beck.

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

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 and stressful employment 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 started formally on April 1, 2024. In 2024, we hired one postdoc in the project who will start in 2025.

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

Project managers: Jonathan Wörn, Bjørn-Atle Reme and Jonas Minet Kinge

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

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 one of the most prominent, 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 will produce novel insights about the links between social media use and mental health. These relate to pathways, buffering characteristics of individuals and families, associations between extensive use of social media with functioning in other life domains, and the role of age restrictions.

The project started formally on September 1, 2024.

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

Project manager: Jonathan Wörn

## New externally funded projects

Endohealth: Endometriosis and adenomyosis throughout the life-course

Research Council
of Norway
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ADHDStab
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People wit

ADHDStability: Stable Life Trajectories for Young People with ADHD and Other Neurodevelopmental Diagnoses Regional kompetansetjeneste for autisme, ADHD og Tourettes syndrom Helse Sør-Øst

Despite the large number of women living with endometriosis and adenomyosis, there is a limited understanding of the causes and consequences of these conditions. The ENDOHEALTH project aims to mitigate these knowledge gaps. First, we will identify genetic, prenatal and childhood/adolescent determinants of endometriosis and adenomyosis. The more than 20 years of follow-up from the fetal period will enable us to identify vulnerable periods for environmental exposure in the risk of endometriosis and adenomyosis. Second, we will examine the health and psychosocial status of young women defined as having high risk of endometriosis/adenomyosis. Third, we will identify social and health consequences of endometriosis and adenomyosis. Our focus also on educational attainment, work force participation and sexual health as broader aspects of the consequences of these conditions will help shed light on the lives of the women living with these disorders. To answer

these objectives, we will study ~95,000 mothers and

~45,000 adult female offspring participating in the Norwegian Mother, Father and Child Cohort Study and a large national registry linkage of all women of reproductive age in Norway (~1 million). Our evaluation of endometriosis and adenomyosis in combination as well as separately is a strength of the project, allowing us to identify both common and independent causes and consequences, to better

In 2024, we recruited one PhD candidate and one postdoc who will start in 2025.

This Researcher Project for Scientific Renewal is funded by the Research Council of Norway's FRIPRO programme

Project manager: Maria C. Magnus

understand their relatedness.

This project aims to understand how the life trajectories of neurodivergent youth and young adults develop across education, employment, and family formation, and to access factors which promote positive trajectories, both assessed in traditional terms and in less traditional ones, like stability, among young adults with neurodevelopmental diagnoses.

The project is funded by the Regional kompetansetjeneste for autisme, ADHD og Tourettes syndrom Helse Sør-Øst (RKT) and will start formally in 2025.

Project manager: Kathryn Beck

## ProBND: Predicting and preventing brain damage in newborns

Trond Mohn Research Foundation

## Assisted reproductive technologies and cancer risk in later life

Norwegian Cancer Society

During birth, most newborns are exposed to a period of shortage of oxygen. Most newborns seem to be well adapted to this shortage, but for some, severe asphyxia appears to disrupt normal brain development. The project aims to identify markers of vulnerability for brain damage that may be used to improve clinical management. The project involves strong collaboration between the Centre for Translational Research in Epidemiology (TRACE) at the University of Bergen and the Centre for Fertility and Health.

In 2024, we established a collaboration agreement with the University of Bergen and initiated the process of analysing biological samples. The project will conduct new DNA methylation analysis that will be integral to the START-project.

The project is funded by the Trond Mohn Research Foundation and managed from the University of Bergen

Project leader group: Rolv Terje Lie, Dag Moster (UiB) and Astanand Jugessur.

More and more children are being conceived through assisted reproduction. Studies have shown that this technology can cause genetic changes and a possible increased risk of cancer. In this project we will examine these genetic changes more closely and see how they can affect health later in life. The project involves close collaboration between the Department of Medical Genetics at Oslo University Hospital and the Centre for Fertility and Health.

The project will conduct new RNA analysis that will be integral to the START-project. In 2024, we initiated the process to analyse samples from children born after assisted reproduction and compare with children are conceived naturally.

The project is funded by the Norwegian Cancer Society and managed from Oslo University Hospital

Project manager: Robert Lyle

## PhD and postdoc projects in 2024

## Completed dissertations for the PhD degree

### **Hans Fredrik Sunde**

"Reproduction of socioeconomic differences and mental health across generations".

Hans Fredrik successfully defended his thesis at the Department of Psychology, Faculty of Social Sciences at the University of Oslo on April 30, 2024.

### **Kathryn Christine Beck**

"School Entry and Exit: Understanding the Consequences of Educational Experiences".

Kate successfully defended her thesis at the Department of Sociology and Human Geography, Faculty of Social Sciences at the University of Oslo on December 2, 2024.

### Karoline Hansen Skåra

"The complex interplay between infertility and cardiovascular disease".

Karoline successfully defended her thesis at the Institute of Health and Society, Faculty of Medicine at the University og Oslo on December 5, 2024.

### PhD fellowships

### **Espen Beer Prydz**

"Register-based research on effects of severe illness on the family"

### **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"

#### **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"

#### 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

### Maria Lyster Andersen

"Parenthood, childlessness, and mental health in times of falling fertility"

### **Postdoc fellowships**

### Sara Abrahamsson

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

### **Thang Dang**

"The long-term and intergenerational impacts of traditionalism versus modernism on demographic, health and economic outcomes."

#### 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"

## People

### **Leader group**



Siri E. Håberg Centre Director



Per Magnus Deputy Director



Håkon Gjessing Principal Investigator



Øystein Kravdal



Vegard Skirbekk Principal Investigator Principal Investigator



Fredrik Swift Head of Administration



Haakon Nustad



Christian Page



Bjørn-Atle Reme Liv Bente Romundstad





Anders Skrondal Fartein Ask Torvik

### Researchers



Jon Bohlin



Bernt Bratsberg



Kåre Bævre





Ida Caspersen Jacqueline Cohen Kim Danielsson





Aage Tverdal



Jonathan Wörn

Martin Flatø



Kari Furu







Miriam Gjerdevik Hans Ivar Hanevik Jennifer Harris





Rannveig Kaldager Hart

Dena Treider

Alavi

**Postdocs** 



Kathryn Beck



Ellen Øen Carlsen



Thea Grindstad



Arno van Hootegem



Anil (Astanand) Jùgessur



Birgitte Heiberg



Dana Kristjansson



Yunsung Lee



Huong Thu Nguyen Maria C. Magnus



Karoline Hansen Skåra



Hans Fredrik Sunde



Pekka Vartiainen

### PhD candidates



Andersen



Lise Andrea Arge



Kristina Wikiord Dreiås



Marianne Rørholt Grefslie



Sunniva Marie Nydal



Siri Nærland Skodvin

## Scientific Advisory Committee



Rishabh Tyagi



Mari Landås Warp

### **Administrative staff**



Frida Løvlie Bråttum Office Coordinator



Anina Falch Research Finance



Research Administration Officer





Katrine Kranstad Randi Sekkeseter Project coordinator



Linda Selje Sunde Project coordinator

David Leon Professor of Epidemiology Faculty of Epidemiology and Population Health London School of Hygiene & Tropical Medicine, London, UK.



Roberta B. Ness Rockwell Professor of Public Health University of Texas, Houston, USA.



Torkild Hovde Lyngstad Professor of Sociology Department of Sociology and Human Geography, University of Oslo, Norway.



Susan Sawyer Professor of Adolescent Health at The University of Melbourne and Director of the RCH Centre for Adolescent Health, Australia.



Dag Erik Undlien Professor of Medical Genetics Department of Genetics, Oslo University Hospital, University of Oslo, Norway.



Matthijs Kalmijn Professor of Sociology and Demography at the University of Amsterdam, Netherlands and Senior Researcher at Netherlands Interdisciplinary Demographic Institute.

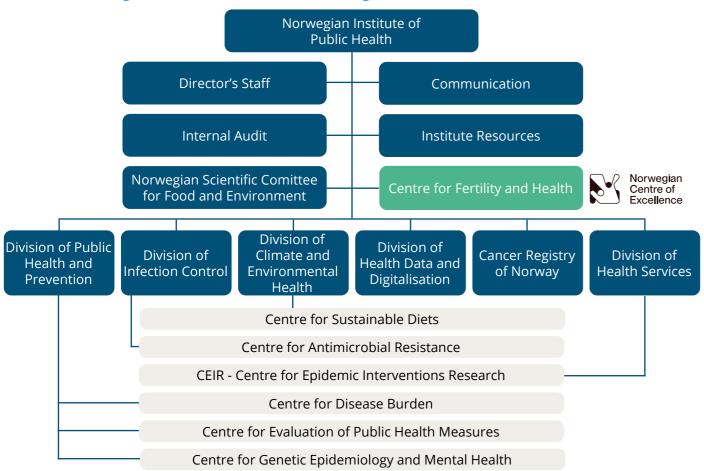
The Scientific Advisory Committee (SAC) ic constituted by international scholars who are specialists in research fields relevant to the Centre.

### The mandate of the SAC is to:

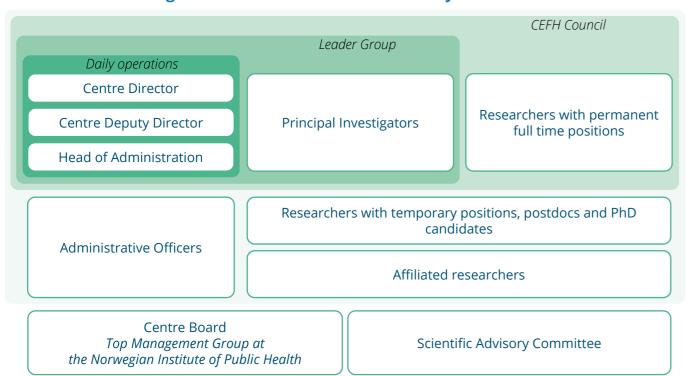
- Partake in discussions of the Centre's research strategy and scientific challenges throughout the project period. The committee may also provide advice on other types of issues.
- Provide strategic advice to the Centre, based on international trends and scientific development within the field of fertility 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**

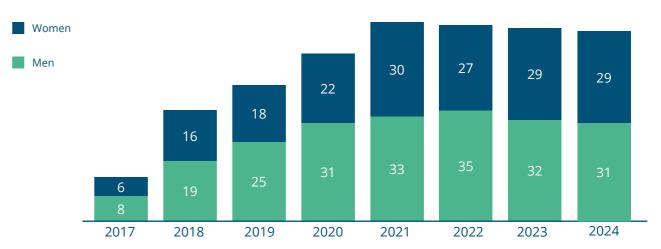


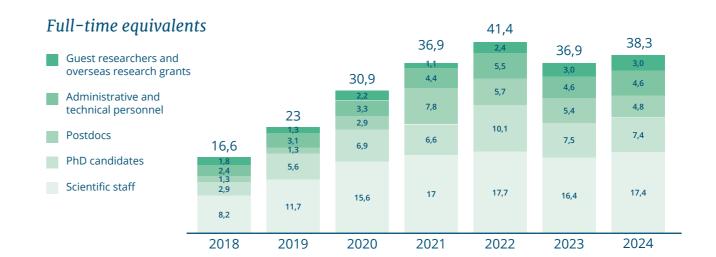
### **Organisation of the Centre for Fertility and Health**

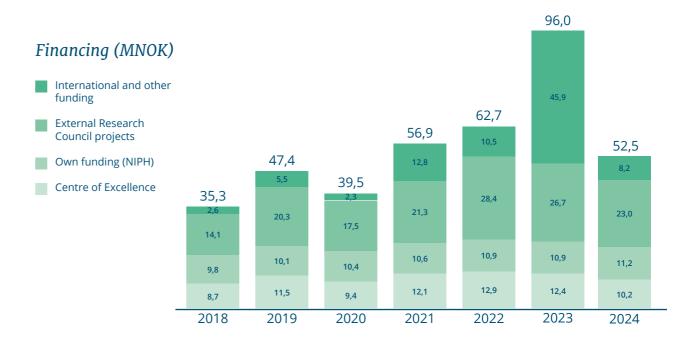


## Indicators 2017-2024

### **CEFH** personnel







## **Publications 2024**

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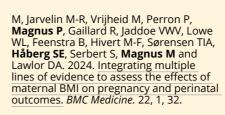
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### **Thesis**

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### **Books and book chapters**

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### Other

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## Seminars 2024

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 2024**

Øystein Kravdal. Biomedical determinants of second birth. January 12.

Henrik-Alexander Schubert. Religion and fertility decline in Finland: A dyadic perspective. January 19.

Espen Beer Prydz. Accounting for Demographic Change in the Measurement of Global Poverty and Inequality. January

Arno von Hootegem. Social Origins and Socioeconomic Outcomes: A Combined Twin and Adoption Study. February 2.

Leila Torgersen/Per Magnus. "Født i feil kropp": definitions, prevalence, and comorbide psychiatry in young people with gender dysphoria. Presentation of three ongoing studies. February 9.

Gregor Duncan Gilfillan. Structural genetic variants – the next big step in genetic analysis? February 9.

**Ida Caspersen.** The Risk of COVID-19 among tobacco users: highlights from the Tobrisk-Cov project. *February 16.* 

Jennifer Harris. Genetic and psychosocial effects on IBS: a twin study collaboration through 25 years. March 8.

Jon Bohlin. Epigenetics in development and health. March 8.

Dag Moster. Predicting and preventing brain damage in newborns. March 15.

Simen Markussen. Not a flying start after all? Maternity leave benefits and long-run outcomes. March 22.

Christopher Murgatroyd. Prenatal stress and epigenetic gestational age. March 22.

Sara Cools. Growing apart. Fertility consequences of an increasing educational gender gap. April 5.

Kate Beck. The Later the Better? A Novel Approach to Estimating the Effect of School Starting Age on ADHD and Academic Skills. April 12.

Tilmann von Soest. Increase in mental health problems and trends in psychosocial factors among children and adolescents. April 19.

Vidar Ulset. Using GIS data to investigate social and geographical inequalities in greenspace exposure. April 19.

Jonas Kinge. Forecasting and decomposing total and cause-specific health expenditures for 116 health conditions in Norway, 2022-2050. April 26.

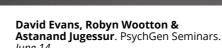
Darci Johnson. The Social Determinants of Maternal Health: A Norwegian Perspective.

Mona Bekkhus. Re-thinking the programming Hypothesis. Prental stress, DNAm and child psychopathology findings from MoBa and Sofus study. *May 3.* 

**Anil Jugessur** Assessing the reliability of the EPIC platform for measuring DNA methylation. May 24.

Karoline Hansen Skåra. Preliminary characteristics of the BIOSFER data. May

Kristine Vejrup. Monitoring the health of the Armed Forces' personnel: Insights into the Armed Forces' Health Register. June 7.



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Kine Pedersen. Prevention and Eradication of Cervical Cancer - Analyses Using Simulation Models. June 21.

Ellisif Nygaard. Genome-wide gene-bymethylation interaction analyses. August

Christina Bergh. The health of children born after assisted reproductive technology and their mothers. August 30.

Raya Muttarak. Assessing the impact of climate change on fertility behaviour. September 6.

Pekka Vartiainen. Genetic predisposition for severe respiratory infections and RSV in young children. September 6.

Claudia Bruno. ADHD medication use in pregnancy and neurodevelopmental disorders: preliminary results. September

Pekka Vartiainen. Which children need RSV immunisation the most? Some examples on Al applications on Finnish registry data. September 20.

**Tormod Rogne.** How does heat exposure during pregnancy affect the mother and child? September 27.

**Jon Bohlin.** So, did it come from the lab?? Molecular and epidemiological evidence for the origin of SARS-CoV-2. October 4.

**Mads Larsen.** Stories of Love from Vikings to Tinder: The Evolution of Modern Mating Ideologies, Dating Dysfunction, and Demographic Collapse. October 11.

Adrian Farner Rogne. Work before and after first birth - changes in employment, part-time work, wages and job flexibility.

Øystein Kravdal. Is low fertility really a problem? October 25.

**Pol Solé Navais.** Parity in genetic studies of gestational duration. November 1.

Martin Blomhoff. Savings and demographic change. November 8.

Josefina Bernardo. A Simulation Study on Resolving Cultural Transmission And Sibling Interaction Using Polygenic Scores. November 15.

Siri Skodvin. Genetic effects associated with infertility and assisted reproductive technology. November 15.

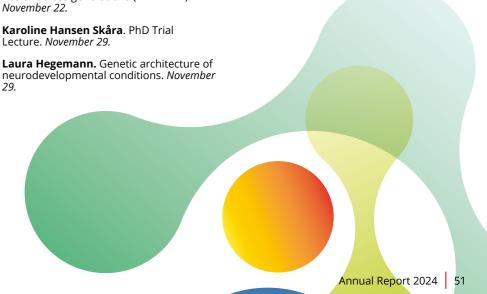
Fartein Ask Torvik. Reproduction of socioeconomic differences and mental health across generations (REMENTA). November 22.

Lecture. November 29.

neurodevelopmental conditions. November

Yunsung Lee. Epigenetic estimator as a biomarker of fetal growth restriction. December 6.

Martin Flatø. How CeFH researchers engage in communication. December 13.







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