Annual report 2022

CENTRE FOR FERTILITY AND HEALTH







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Introduction from the Centre Directors

Siri E. Håberg, Centre Director Per Magnus, Centre Deputy Director

In 2022, we celebrated the five-year anniversary of our Centre for Fertility and Health (CeFH) which has grown from just a handful to approximately 60 researchers. We also finally started to see the end of the pandemic, allowing us to return to physical meetings and conferences in Norway and abroad.

We are pleased that CeFH has expanded its national and international collaborations and continues to produce research at the international forefront. More than 450 papers have been published, including a significant number in leading journals.

We have also developed future research themes that build on our previous achievements.

Research data and infrastructure

We have established a research infrastructure with large registry linkages combining social, demographic and medical data. More than 200,000 participants in the Norwegian Mother, Father, and Child Cohort Study (MoBa) have now been genotyped. As part of the Centre of Excellence funding, we have established the world's largest epigenetic dataset with mother-father-child trios. Combined with our growing interdisciplinary expert team this will enable us to achieve our ambitions of excellent research in the final five years of our funding period.

External funding

We are delighted that we have by far exceeded our initial goals for acquiring additional funding during the first phase of CeFH, with grants awarded from the Research Council of Norway, the European Research Council, the U.S. National Institutes of Health, and other sources. This funding has given us the opportunity to expand the data infrastructure, recruit new expertise, pursue novel research and build research careers for PhDs, postdocs, and early career researchers.

New offices

CeFH moved to a new building in the summer of 2022. The move went smoothly, and the new premises include generous



workspaces, guest offices to host visiting scientists as well as meeting rooms and social space used for weekly seminars. These are important qualities that we hope will be maintained when we have to relocate again by the end of the year.

Career development

One of our main goals is to help develop the careers of junior researchers. To this end, we have established a career review program, developed a streamlined administrative and scientific support-team for grant applications, and facilitated project leadership. We have also continued with our *Gro Harlem Brundtland visiting scholarship* for young researchers, which continues to successfully attract international talent and expands our international collaborations.

New research opportunities

The COVID-19 pandemic was a stress test for the Norwegian Institute of Public Health (NIPH) because of its central role in handling the pandemic. The analytical expertise and experience in using registries and cohort data in CeFH helped provide rapid answers to urgent questions. In addition to the effects of vaccination and infections on fertility and on somatic complications, we are studying the impact of the pandemic on young people's education and social life.

Research – the way forward

Looking ahead at the coming five years, we have revised our research strategy. In addition to our existing topics, we aim to investigate the etiology of fertility changes in young adults and exploit our unique data even more by developing advanced statistical methods. We are excited to embark on this new phase of our Centre of Excellence and hope to make groundbreaking scientific contributions.



Siri E. Håberg, Centre Director



Per Magnus, Centre Deputy Director

Key achievements 2022

A strong interdisciplinary team

By the end of 2022, 27 women and 35 men were associated with the centre including researchers in full- and part-time positions and administrative staff. The centre also has many national and international visiting researchers and other associated collaborators.

Selected publications

We showed differences in methylation of 176 known genes in children born after assisted reproduction compared to children born after natural fertilization. The results support the hypothesis that assisted reproduction induces DNA methylation alterations that may impact health and disease risk later in life.

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

We discovered genetic similarity between partners for educational attainment, height, and depression and elevated genetic correlations between siblings. The genetic similarity extended to in-laws and co-inlaws.

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

We showed faster epigenetic aging in mothers who need assisted reproduction. A plausible biological mechanism behind the reported association is that mothers who need in vitro fertilisation could be closer to menopause than mothers who don't.

Lee Y *et al.* (2022). <u>Associations between epigenetic age</u> acceleration and infertility. *Human Reproduction*, 37(9), 2063–2074. We introduced a new indicator, the educational burden of disease, to quantify the link between health and school performance. The indicator could provide a simple metric to guide researchers and policy makers.

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

We demonstrated that parents' mental health declines before the union dissolution and subsequently improves, while children's mental health deteriorates more after the break-up than before.

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

We found a reduced risk of Covid-19 in infants of women who have taken the vaccine during the second or third trimester of their pregnancy.

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

We found that there was no increased risk of adverse pregnancy outcomes after vaccination against SARS-CoV-2 during pregnancy.

Magnus MC *et al.* (2022). Association of SARS-CoV-2 Vaccination During Pregnancy With Pregnancy Outcomes. *JAMA*, 327(15), 1469-1477.

We showed how childbearing affects cognitive health - having three or more versus two children negatively affects late-life cognition. This effect is strongest in Northern Europe.

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

New externally funded projects

ERC Synergy Grant

14 million EUR were granted to the project "BIOSFER: Untangling the biologic and social causes of low fertility in modern societies". This project will investigate how social, biological and psychological factors affect fertility in young adults. It is led by Siri E. Håberg at CeFH in collaboration with Cecilia Ramlau-Hansen at Aarhus University in Denmark and Mikko Myrskylä at the Max Planck Institute for Demographic Research in Germany. The project will continue and develop further the data collection that started in 2021 in the RCN-funded project "Young women's fertility".

Research Council of Norway

9,6 million NOK were granted to the project *"Parment: Parenthood, childlessness, and mental health in times of falling fertility"* led by Fartein Ask Torvik. This is a researcher project for scientific renewal in the ground-breaking research theme (FRIPRO).

The Norwegian Cancer Society

8 million NOK were granted to the project "*Risk of breast cancer in persons born after assisted reproducti-ve technologies (ART)*" led by Siri E. Håberg. This project aims to study the association between assisted reproduction and cancer. It follows up on our 2022 finding showing altered methylation of the breast cancer gene *BRCA1* in children born after assisted reproduction.

Nordforsk

9 million NOK were granted to the project "SCOPE2: Studies of Covid-19 in pregnancy – A framework to secure reproductive, maternal and child health during societal crises" led by Olof Stephansson at Karolinska Institutet, Sweden together with partners Siri Håberg at CEFH and Anne-Marie Nybo Andresen at the University of Copenhagen. The overall aim of this project is to understand how the COVID-19 pandemic has influenced fertility patterns, reproductive health, pregnancy, and infant outcomes, in the medium- and long-term, and to use this knowledge to inform better preparation and management for future similar societal crises.



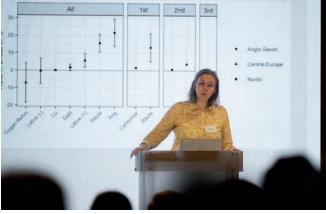


Major events

- Centre seminar. Mar 2, 2022.
- Covid-19, Vaccination and Pregnancy seminar. *Mar 9, 2022.*
- Instrumental variable & Mendelian randomization seminar series. *Mar-May 2022.*
- 5th Annual Symposium 2022. Jun 7-8, 2022.
- Workshop: How can we use genetics in fertility research? *Jun 9, 2022.*
- Workshop: Understanding fertility change Studying the determinants of childbearing trends in low fertility contexts. Sep 27, 2022.
- 5 Year Anniversary seminar. Nov 1, 2022.
- PhD seminars and courses
- Various project specific seminars and over 50 weekly seminars.

Differences in epigenetic age acceleration between ART and non-ART parents





Ambitions towards 2027: Our research themes

The overarching goal of the center 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 Centre of Excellence 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 aim 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.

Entering the sixth year of the 10-year Centre of Excellence period, we have defined six new main research themes representative of our ongoing research and in line with the most promising new directions of research ahead. 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. The six research themes are presented over the next pages in this annual report:

- 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 and its implications on 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. Lee Y *et al.* (2020). <u>Blood-based</u> epigenetic estimators of chronological age in human adults using DNA methylation data from the Illumina <u>MethylationEPIC array. *BMC Genomics*</u>, 21(1), 747. Basso O *et al.* (2022). <u>Parents'</u> age at birth and daughters' time to pregnancy: a study within the Norwegian Mother, Father and Child <u>Cohort. Human Reproduction</u>; 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

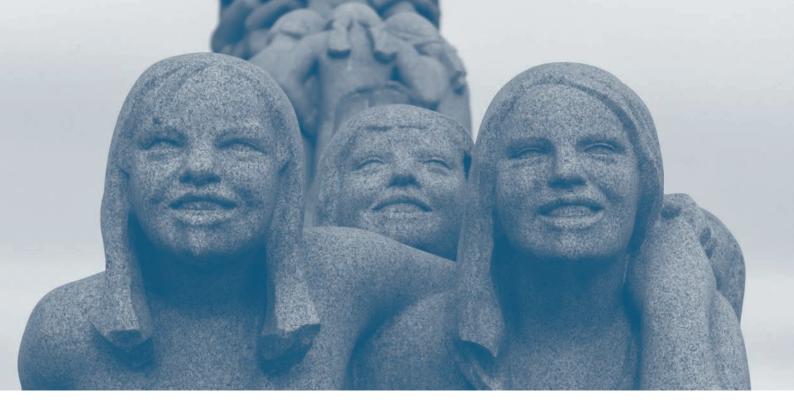
- To investigate the social and biological causes and consequences of subfertility and the use of assisted reproductive technologies.
- To understand the nature of the relationships between infertility, various diseases, and health status.
- To understand how genetic influences and epigenetic differences 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). <u>Associations</u> 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. Nordmo M *et al.* (2022). <u>The</u> educational burden of disease: a <u>cohort study</u>. *Lancet Public Health*; 7 (6): e549-e556. 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.



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.

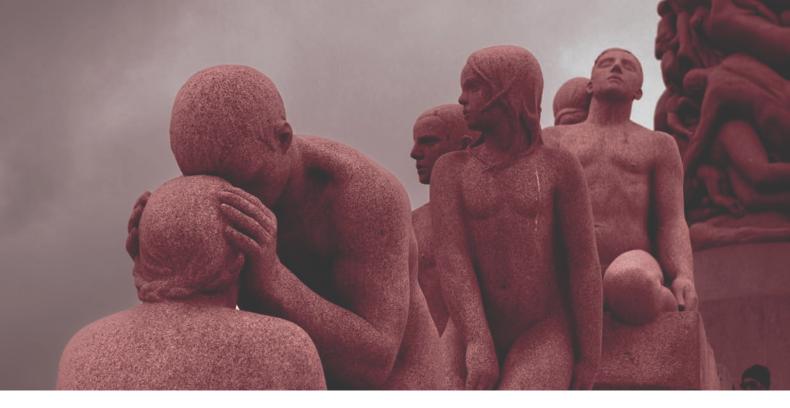
PRESENT ACHIEVEMENTS

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). <u>Does</u> 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). <u>Design</u> efficiency in genetic association <u>studies</u>. *Statistics in Medicine*, 39(9), 1292-1310.

Skrondal A *et al.* (2022). <u>The Role</u> of Conditional Likelihoods in Latent Variable Modeling. *Psychometrika*, 87, 799-834. Gjerdevik M *et al.* (2019). <u>Haplin</u> 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

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

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. In 2022, the total funding to CEFH exceeded 60 million NOK, where 41 million NOK came from the Research Council of Norway, approximately 11 million from the Norwegian Institute of Public Health and 10,5 million NOK from ERC and Nordforsk.

The Centre has secured funding from a many different funders. Current 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







European Research Council Established by the European Commission



Funded by the Nordic Council of Ministers

The Gro Harlem Brundtland Visiting Scholarship 2022

Katrin Wolfova

Katrin is a medical doctor and researcher at the Czech National Institute of Mental Health and Charles University in the Czech Republic. She studies risk factors for brain disorders in older adults using epidemiological methods. Her main interest lies in the influence of a variety of social and biological factors on cognitive aging.

During her research stay at the Centre in 2022, she studied sex differences in the relationships between fertility history, parents' cognition and risk of dementia. Previous studies suggests that fertility histories, which include number of children and the timing of births, influence other postreproductive outcomes such as mortality and longevity. The pathways by which pregnancy, parenthood, and childrearing affect cognition may involve both biological and social mechanisms and may differ between males and females. The study uses data from the Trøndelag Health Study (HUNT), the Medical Birth Registry and Statistics Norway. 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.



Previous visitors



Robyn Wootton (2018-2019)



Gizachew Tessema (2020)



Gemma Sharp (2018-2019)



Anne Sofie Dam Laursen (2020-2021)

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 2022, the dataset incuding register and survey data was completed. The project involves collaborations with researchers from over 20 national and international research institutions. The first publications are published, and we expect many more publications from this project in the coming years. In 2022, an extension of the project period until the end of 2028 was approved by the Regional Committees for Medical and Health Research Ethics (REK).

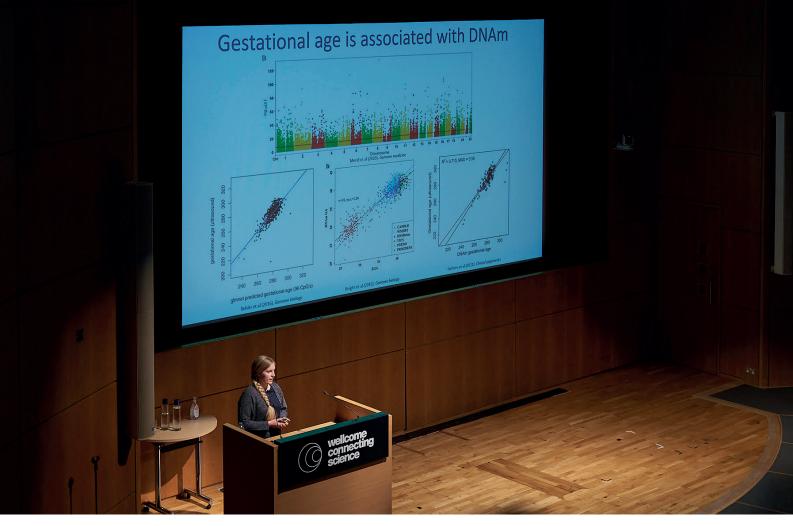
Project managers: Per Magnus and Øystein Kravdal

START – Study of assisted reproductive technology – epigenetic mechanisms

The main aim of the project is to understand causes and health consequences of subfertility 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 methlyation in trios conceived with ART and naturally conceived.

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. We have obtained further funding to follow up and investigate 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 project is funded by the Research Council of Norway through the Centre of Excellence grant. 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. It was initiated in 2014 and has been updated since then. Main outcomes include fetal growth, gestational length, fetal loss, 'vanishing' twins, and health in children and parents with subfertility and after use of ART.

Our research has provided more knowledge on the link between underlying chronic diseases and miscarriages, and the relationship between mental health in women and miscarriages. Several of the PhD candidates at CeFH are involved in this project and in studies of subfertility and miscarriages. We have also shown that children's growth and health after ART is different at birth and in preschool ages. Lise Arge, a medical student, is pursuing her PhD in this project investigating risk factors of subfertility. Our international collaborators include senior researcher Gavin Pereira from Curtin University in Perth, Australia, and several members of his team, and Olga Basso at McGill University in Canada who is interested in intergenerational risks on fertility outcomes.

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 to pregnancy samples in 16 000 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.

In 2022, we hosted a doctoral candidate from Australia for an 8-month exchange to carry out a study on exposure to antipsychotic drugs in utero and risk of learning disorders and poor academic performance. We published papers on both short- and longterm outcomes associated with pregnancy use of antiseizure medication (Cohen JM et al., Bjørk MH et al.) and antipsychotic medication (Huybrechts KF et al., Hálfdánarson Ó et al.). We presented a study on ADHD medication safety at the International Conference on Pharmacoepidemiology and Drug Safety and a study on 2nd-line glucose lowering non-insulin drugs in early pregnancy and risk of major congenital malformations at the conference for the European Association for the Study of Diabetes (EASD). Analyses are ongoing for additional studies.

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 2022, we carried out user consultations with members of the organization ADHD Norway to inform the research questions, interpretation of the data, and later dissemination activities. We presented results from two studies at international perinatal- and pharmacoepidemiology conferences and published a study on ADHD medication use in pregnancy in Norway and Sweden, 2010-2019. We found that use during pregnancy more than doubled in both countries during the last decade and most discontinued ADHD treatment during pregnancy. The PhD candidate in the project, Chaitra Srinivas, completed her first study on ADHD medication use trajectories surrounding pregnancy and initiated her second study.

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 2023 and 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

Project manager at CEFH: Kare 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 notes important publications in 2022, including on the association between mental and somatic health conditions and later educational performance (Nordmo M *et al.*), the associations of ADHD with school performance in different social groups (Sunde HF *et al.*), and how interactions between genetics and school environments shape performance (Cheesman, R *et al.*). We will see even more publications in the project in the upcoming year as the project is reaching its end in 2023.

The project is funded by the Research Council of Norway's BEDREHELSE 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.

The project started in 2021. In 2022, the project hosted a workshop and preliminary results have been presented at international conferences. One paper shows an increase in mental health disorders and low prospects for completing upper secondary education for students who fail their final exam in upper secondary school.

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

CeFH 5th Annual Symposium June 2022

CHEO

of Epidemiology & Public Health, University of Ottawa of Eastern Ontario Research Institute

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 2022 include a study of the consequences of assortative mating for genetic and phenotypic similarities between extended family members (Torvik *et al.*). 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 and prepared shipping of biological samples for analysis at Rutgers University in the US. We aim at shipping the samples in 2023, pending legal arrangements for executing the material transfer agreement between MoBa and the University of Pennsylvania in the US. 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 women 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.

In 2021, we established a new data collection in MoBa, in which young second-generation participants are invited to a clinical examination at collaborating fertility clinics. We have ongoing data collection and in 2022, around 200 women were examined. Our aim is to examine 800 young women 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. 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 KVINNEHELSE funding scheme. Project manager: Siri E. Håberg

Telomere and female fecundity

This project is based 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.

In 2022, Kristine Løkås Haftorn presented her second paper at the "Epigenomics of Common Diseases" meeting at the Wellcome Trust Campus in Hinxton, UK. The paper was accepted for publication in the Nature portfolio journal "Communications

Biology" in Feb 2023.

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.

The aftermath of the Covid-19 pandemic has continued to have major consequences in 2022 in acquiring the mitochondrial DNA sequences in the project. The original plan was to generate sequence data at the University of Pennsylvania, a collaborating partner and R&D-supplier in the project. In addition to Covid-19 impeding progress in securing the necessary paperwork for the material transfer agreement, a verdict from the EU Court of Justice on the Schrems II in July 2020 also halted the transfer of any sensitive personal information from Europe to third-party countries. Despite numerous attempts, the project was not successful in securing the necessary agreements for material transfer in 2022. We are currently investigating other options for sequencing DNA using genetic core facilities in Europe.

Due to these unforeseen hindrances, the PhD candidate hired into the project (Dana Kristjansson) was not able to pursue the goals set out in the original grant proposal. Instead, another research project closely related to the aims in the original proposal was developed, but with the research focus still aimed at elucidating mitochondrial DNA energetics. Kristjansson used publicly available mitochondrial DNA sequences as a basis for the three articles in her thesis. She published the first paper in her PhD thesis in Sept 2021, in the American *Journal of Physical Anthropology*. Her second paper was published in BMC Genomics in Dec 2022 and her third paper in the American Journal of Biological Anthropology in Nov 2022. Finally, Kristjansson successfully defended her thesis in Jan 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 are currently also investigating the impact of use of assisted reproductive technologies on women's risk of cardiovascular disease. 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. In 2022, the project delivered a publication on the relationship between parental suicide and adolescents' healthcare utilization and a paper examining the relationship between parental cancer and child health (under review). Furthermore, new studies were initiated, including among others: (1) A study of the mental health development of parents and siblings of teenagers with mental health problems, and (2) a study of long-term health consequences on family members following the early death of a sibling or child.

The project is funded by the Research Council of Norway's VAM programme.

Project managers: Bjørn-Atle Reme and Jonathan Wörn

SCOPE – Scandinavian studies of COVID-19 in pregnancy

Combining data from the three Scandinavian countries give us the ability to study the impact of COVID-19 in pregnant women. We have studied whether pregnant women are at higher risk of being infected or are at higher risk of severe COVID-19 illness. With access to the total Scandinavian female population, we can study rare outcomes.

The Scandinavian countries have had different courses of the pandemic, and this enables us to compare results from different contexts with similar data resources. With daily updated data from our registries, results from this project have contributed knowledge on the risks of COVID-19 related to pregnancy, identified susceptible subgroups among pregnant women, shown how health care in pregnant women changed during lockdown, and presented consequences of infection and lockdown for pregnant women.

The project is funded by NordForsk's Nordic Health Data Research Projects on Covid-19 programme. Project manager: Siri E. Håberg

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 started in August 2021. 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. Since August 2021, it is recommended that pregnant women in Norway should also be vaccinated. The project has studied



potential adverse pregnancy outcomes such as premature births, stillbirths, Apgar-scores, transfers to intensive care etc., and found no adverse effects. The reassuring results are published in *JAMA* in 2022. 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 benefits of vaccination on women's risk of disease pregnancy outcomes and health in children who were born to vaccinated women, and potential adverse effects of vaccination in pregnancy on 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 populationbased 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 reported so far 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.

We have analysed the association of tobacco use with the occurrence of COVID-19 using existing longitudinal population studies in Finland, Norway and Sweden. Our preliminary 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

New externally funded projects

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

14 000 000 EUR

European Research Council

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 produce the emerging fertility patterns in young adults, and to what extent the fertility decline and polarization 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 conduct clinical examinations, a pregnancy planner cohort and a randomised controlled trial of fertility knowledge among young adults. The project was granted in 2022 and will start formally on March 1, 2023.

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

9 600 000 NOK

Research Council of Norway

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. We also use genetic data from The Trøndelag Health Study (HUNT). The project starts in August 2023.

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

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

9 000 000 NOK

NordForsk

This project builds on our expert network and established infrastructure established in SCOPE and is a collaboration with Karolinska Institutet in Sweden and the University of Copenhagen in Denmark. Our overall aim and purpose in this project is to understand medium and long term effects of the COVID-19 pandemic 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 call

Project managers: Siri E. Håberg, Olof Stephansson and Anne-Marie Nybo-Andersen



8 000 000 NOK

Norwegian Cancer Society

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. This project will follow up our recent finding that children conceived with ART have substantially different epigenetic patterns at birth. One surprising finding was differences in the BRCA1 gene. In this project we will follow up on this finding investigating the potential role of ART and BRCA1 methylation at birth in risk of breast cancer by exploring 1) the overall cancer risk and especially risk of breast cancer in register data, 2) whether differences in epigenetic marks at birth in BRCA1 persist into older ages and 3) whether epigenetic differences in BRCA1 at birth is associated with gene-expression and risk of breast cancer. The project was granted in 2022, and will start formally in 2023

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



Siri E. Håberg (*right*) receiving the the Norwegian Cancer Society's Rosa sløyfe grant from Ellen Harris Utne (*left*), chair of the Norwegian Breast Cancer Association (Brystkreftforeningen)

PhD and postdoc projects in 2022

Completed dissertations for the PhD degree

Dana Kristjansson

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

Ongoing PhD fellowships

Kathryn Beck

"School Entry and Exit: The Health Consequences of Sub-Optimal Transitions in Education"

Ellen Øen Carlsen

"Determinants of perinatal outcomes in Norway: 1982-2020"

Kristine Løkås Haftorn

"The role of DNA methylation in gestational age"

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"

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

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

William Denault

"Development of new causal inference methods in epidemiology, with an application to studying the effect of ART on health outcomes"

Álvaro Hernáez

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

Thomas Kleppestø

"Health Gap: Health, maturity, and the gender gap in education"

Magnus Nordmo

"Reproduction of socioeconomic differences and mental health across generations"

Thea Grindstad

"Determinants of fecundity across generations in modern developed society"

Fellowships

William Denault receives the Eric and Wendy Schmidt AI in Science Postdoctoral Fellowship from the University of Chicago.

After sucessfully defending his thesis at the University of Bergen, William started in a 2-year postdoc position at the University of Chicago, USA. The Centre funded the third postdoc year and William is commuting between the two positions.

In 2022, William was selected to become a <u>Eric and</u> <u>Wendy Schmidt AI in Science Postdoctoral Fellowship</u> <u>Program</u> at the University of Chicago.

The fellowship is a unique recognition of highly promising junior researchers who seek to apply Al methods to enable discovery in the science, technology, engineering, and mathematics.

This fellowship will enable William to pursue independent research and collaborate widely across the University of Chicago and its affiliate institutions and receive support for research and travel activities. He will also be a part of the global cohort of Schmidt AI in Science Fellows and will attend Schmidt Futures conference to establish wide-ranging international collaborations.



People

Leader group





Siri E. Håberg Centre Director

Per Magnus Centre Deputy Director



Håkon Gjessing Principal Investigator



Øystein Kravdal Principal Investigator



Vegard Skirbekk Principal Investigator



Fredrik Swift Head of Administration

Researchers



Jon Bohlin



Bernt Bratsberg



Aline Bütikofer



Kåre Bævre



Ida Caspersen



Jacqueline Cohen



Jon H. Fiva



Martin Flatø



Kari Furu



Miriam Gjerdevik





vik Hans Ivar Hanevik Jennifer Harris



Rannveig Kaldager Hart



Dana Kristjansson



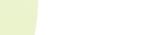
Anil (Astanand) Jugessur



Jonas Minet Kinge Yunsung Lee



Rolv Terje Lie



30 Centre for Fertility and Health













Jo Thori Lind

Robert Lyle

Maria C. Magnus

Haakon Nustad

Christian Page

Bjørn-Atle Reme











Jonathan Wörn

Postdocs



Sara Abrahamsson



Thang Dang



William Denault



Thea Grindstad



Álvaro Hernáez



Thomas Kleppestø



Huong Thu Nguyen



Magnus Nordmo

PhD candidates





Lise Andrea Arge

Kathryn Beck



Ellen Øen Carlsen



Kristine Løkås Haftorn



Espen Beer Prydz



Marianne Hopen Rørholt



Siri Nærland

Skodvin



Skåra



Chaitra Srinivas



Sunde

Hans Fredrik Rishabh Tyagi





Mari Landås Warp

Administrative staff



Frida Løvlie Bråttum Office Coordinator Officer

Anina Falch

Research Finance



Katrine Kranstad Research Administration Officer



Randi Sekkeseter Project coordinator



Linda Selje Sunde Project coordinator

Affiliated researchers

These scholars supported our application for status as Centre of Excellence, have formal roles as affiliated researchers or are formal project partners.

Abraham Aviv Rutgers University, New Jersey, USA

Allen Wilcox NIEHS/NIH, North Carolina, USA

Anne Sofie Dam Laursen Aarhus University Hospital, Denmark

Asgeir Skålholt The Nordic Institute for Studies of Innovation, Research and Education (NIFU), Norway

Berit Lødding The Nordic Institute for Studies of Innovation, Research and Education (NIFU), Norway

Catherine Bowen University of Vienna, Austria

Cecilia Ramlau-Hansen Aarhus University

Deborah Lawlor University of Bristol, UK

Emily Grundy University of Essex, UK

Gavin Francis Pereira Curtin University, Australia

Julia Romanowska University of Bergen, Norway

Kari Vea Salvanes The Nordic Institute for Studies of Innovation, **Research and Education** (NIFU), Norway

Katrin Wolfova National Institute of Mental Health, Czech Republic

Laura Oakley London School of Hygiene and Tropical Medicine, UK

Liza Reisel Institute for Social Research, Norway

Marcin Stonawski Statistics Denmark

Marianne Røed Institute for Social Research, Norway

Maya Rossin-Slater Stanford University, California, USA

Mikko Myrskylä Max Planck Institute for Demographic Research, Rostock, Germany

Miriam Evensen Institute for Social Research, Norway

Nicoletta Balbo Università Commerciale Luigi Bocconi, Italy

Ole Røgeberg Ragnar Frisch Centre for Economic Research, Norway

Pål Schøne Institute for Social Research, Norway

Theodore Shurr University of Pennsylvania, USA

Wendy Sigle London School of Economics, UK

Wendy Nilsen OsloMet, Norway

Scientific Advisory Committee



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.



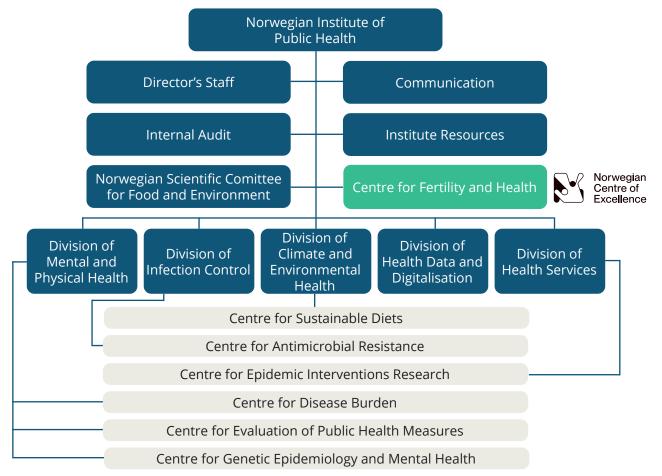
Matthijs Kalmijn Professor of Sociology and Demography at the University of Amsterdam, Netherlands and Senior Researcher at Netherlands Interdisciplinary Demographic Institute. The Scientific Advisory Committee (SAC) ic constituted by international scholars who are specialists in research fields relevant to the Centre.

The mandate of the SAC is to:

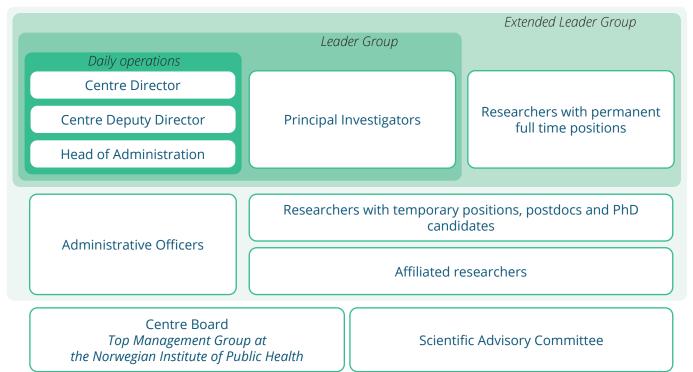
- Partake in discussions of the Centre's research strategy and scientific challenges throughout the project period. The committee may also provide advice on other types of issues.
- Provide strategic advice to the Centre, based on international trends and scientific development within the field of fertility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

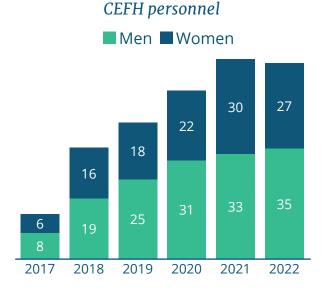
Organisation chart of the Norwegian Institute of Public Health



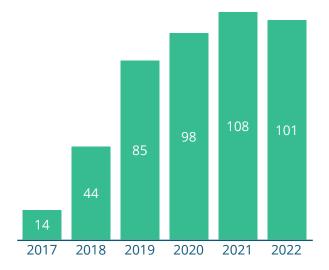
Organisation of the Centre for Fertility and Health



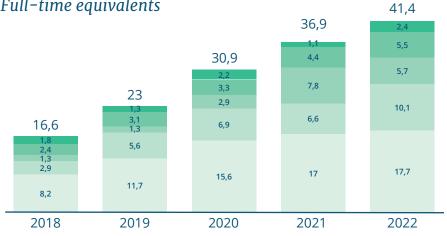
Indicators 2017-2022



Peer-reviewed scientific articles

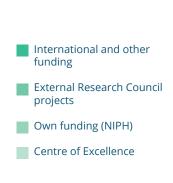


Full-time equivalents









Publications 2022

Peer-reviewed articles in scientific journals

Ahmed MA, Bailey HD, **Pereira G**, White SW, Wong K, & Shepherd CCJ. (2022). Trends and burden of diabetes in pregnancy among Aboriginal and non-Aboriginal mothers in Western Australia, 1998–2015. *BMC Public Health*, 22(1), 263.

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Bekkhus M, **Lee Y**, Samuelsen SO, Tsotsi S, & **Magnus P**. (2022). <u>Maternal and</u> paternal anxiety during pregnancy: Comparing the effects on behavioral problems in offspring. *PLOS ONE*, 17(10), e0275085. Bélanger SM, Stene-Larsen K, **Magnus P**, Reneflot A, Christiansen SG, & Hauge LJ. (2022). Employment status and bereavement after parental suicide: a population representative cohort study. *BMJ Open*, 12(9), e064379.

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Borud EK, Fadum EA, **Carlsen EØ**, & **Håberg SE**. Health at age 17 in Norwegian adolescents: Mental and physical status in the national cohort born in 2001. *Scandinavian Journal of Public Health*, 50(8), 1148-1154.

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Corrections

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Seminars 2022

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 2022

Ann Kristin Knudsen. SYBY presentation. *January 7.*

Nicolas Todd. Socioeconomic development predicts a weaker contraceptive effect of breastfeeding. *January 14.*

Morten Mattingsdal. The genetic structure of Norway. *January 14.*

Baptiste Coulmont. Naming for Kin during World War I: Baby Names as Markers for War. January 21.

Tina Tellum. Adenomyosis and endometriosis: their implications for reproductive health and blank spots on the research-map. *January 28*.

Guy Hindley. Charting the landscape of genetic overlap between mental disorders and related traits beyond genetic correlation. *January 28.*

Anne Sofie Dam Laursen. SnartForaeldre. dk: A danish preconception cohort - Description and an example of ambient air pollution and risk of spontaneous abortion. *February 4.*

Ida Lykke Kristiansen. Consequences of serious parental health events on child mental health and educational outcomes. *February 11.*

Kristiina Hutttunen. School Starting Age, Maternal Age at Birth, and Child Outcomes. *February 18.*

Ole-Jørgen Bekkevold. The causal role of C-reactive protein and Interleukin-6 on symptoms of anxiety, depression and life satisfaction. A Mendelian Randomization study in HUNT. *March 4.*

Vidar Sandsaunet Ulset. Links between prenatal dietary inflammation, language problems and ADHD symptoms in 8-yearolds: A moderated mediation model. *March 11.*

Stefania Benonisdottir. Genome scan of study participation. *March 11.*

Dinka Smajlagic. Parent-of-origin effects in aggressive behaviour in MoBa children: explorative analyses using genetic and epigenetic data. *March 18.*

Håkon Gjessing. What happens to your paper after it has been submitted to a journal? Some insights from an editor... and a few suggestions what (not) to do when submitting. *March 25.*

Kristine Løkås Haftorn. Differentially methylated cell types in epigenome-wide association studies. *March 25.*

Álvaro Hernaéz. What Mediterranean diet can teach us of causal inference in Nutrition. *April 1*.

Hans Fredrik Sunde. ADHD and school performance across sex, parental education, and school subjects. April 8.

Pol Solé-Navais. Genetic architecture of gestational duration and preterm delivery. *April 8.*

Thea Grindstad. At home testing for male fertility. *April 22.*

Rannveig Kaldager Hart. A discussion of differences in differences with variation in treatment timing. *April 29.*

Ugochinyere Vivian Ukah. Severe maternal morbidity and the risk of long-term health outcomes in women. *May 6.*

Childlessness and psychological well-being

has Hansen icide, NIPH 4/OsloMet

Nancy McBride & Carolina Borges. Leveraging MR and omics to reveal mechanisms influencing pregnancy complications. *May 6.*

Elsje van Bergen. Decoding the Gene-Environment Interplay on Learning. *May 13.*

Bettina Hünteler. Intergenerational family positions and wealth trajectories in different life phases. *May 20.*

Shai Carmi. The potential and limitations of screening human IVF embryos for polygenic diseases. *May 20.*

Ana Rodriguez-Gonzalez. The Impact of the Female Advantage in Education on the Marriage Market. *June 3.*

Simona Tudor. Hospital-Acquired Infections and Neonatal Health: The Underestimated Costs of Medical Fraud. *June 10.*

Anders Husby. Gestational age and cognitive outcome. June 10.

Linea Hasager. Sick of Your Poor Neighborhood? Quasi-Experimental Evidence on Neighborhood Effects on Health. *June 17.*

Ian Colman. Public health implications of stress and mental health measured in Norwegian survey data. *August 19.*

Isa Steinmann. Between-country variation in achievement gender gaps. *August 26.*

Julia Romanowska. Impact of ART procedures on DNA methylation on X-chromosome. August 26.

Erich Striessnig. How much time is left? International trends in parental lifespan. *September 2.*

Finn Egil Skjeldestad. Infertility in Norway - data from Tromsøundersøkelsen 2015-16. *September 9.*

Inger Johanne Bakken. Tips and tricks when working with large data sets in R. *September 16.*

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Thang Dang. The Dynamic Effects of Gender on Adolescent Mental Health. September 23.

Jared Balbona. Estimation of Parental Effects Using Polygenic Scores. September 26.

Christopher Murgatroyd. Investigating the epigenetics of maternal and early-life stress using animal models and human studies. *September 30.*

Kathryn Beck. The effect of high stakes exam failure on mental health. *October 7.*

Dorret Boomsma. (Epi)genetics and the extended twin design, including twinning as an outcome phenotype. *October 7*.

Fanny Lundaud. Getting Lucky: The Long-Term Consequences of Exam Luck. October 14.

Irene Voldsbekk. Brain health and mental health related to pregnancy and childbirth. *October 21.*

Nicolas Fragoso. Epigenome wide association study of objectevely measured physical activity during pregnancy. *October 21.*

Sarah Wilkins Laflamme & Nitzan Peri-Rotem. Normative aspects of reproductive behaviour & Does spirituality matter for fertility? October 28. *Elizabeth Corfield.* The Norwegian Mother, Father, and Child cohort study (MoBa) genotyping data resource: the MoBaPsych-Gen pipeline. *November 4.*

Toumas Pekkarinen. Pre-College Skills and Educational Wage Differentials. *November 11.*

Hans Fredrik Sunde. Using children-oftwins to distinguish genetic and social transmission of mental health indicators. *November 18.*

Sascha Becker. Economic Growth and Belief systems. November 25.

Øystein Kravdal. A brief discussion of a couple of methodological issues in a sibling analysis of how maternal age affects birth weight. *December 2.*

Ellen Christine Røyrvik. A genetic population structure potpourri: geno-geographic signatures, Vikings and ART. *December 2.*

Thang Dang. The Effects of Investments in Refugees' Human Capital. *December 9.*

Marta Hernandez. Gene-psychoactive drug interactions on birthweight. *December 16.*

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