

Annual report 2021





The Research Council of Norway



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Introduction from the Centre Directors

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

The Centre has continued to grow in 2021 and many new talented team members have been recruited. There has also been an increasing number of publications stemming from key projects that were initiated through the Centre of Excellence grant.

Another year of pandemic

Another extraordinary year has passed, with lockdowns, social distancing, and extensive use of home office. These are not optimal conditions for a growing research environment. Many new team members have started during the year. To get to know each other in a time of digital meetings, we have kept and further developed our weekly Thursday "Centre lunch" as a place for informal exchanges, brief scientific presentations, and communication about new publications from the Centre team.

The pandemic has also provided new research opportunities. Periods of lockdown and challenges in work and schooling have taken a severe toll on our society. Surprisingly, birth rates in Norway have increased during the pandemic, but we do not know why. Our Centre has also been vital for the Norwegian Institute of Public Health during the pandemic. Our methodological experts have contributed heavily to predicting hospitalization for Covid-19. We have provided updated and

essential information about Covid-19 related risks to pregnant women and their newborns, and we have investigated potential demographic, disease- and pregnancy-related risk factors for Covid-19. Our ongoing studies are investigating consequences on births, family, school performance, job loss, family structure and health.

The Centre team

By the end of 2021, 30 women and 33 men were formally associated with CeFH. Our staff includes full-time and parttime researchers, international researchers with whom we have established collaboration agreements, and administrative personnel. In addition, the CeFH team collaborates closely with researchers in Norway and at acclaimed research institutions abroad. Now that in-person meetings are possible, we are happy to again welcome collaborators and colleagues outside of the Centre to spend time with us in Norway. Formal and informal meetings are important to exchange ideas and initiate exciting new research.

To facilitate successful careers for our researchers, we developed and piloted a Career Development Review scheme in 2021 to provide valuable guidance to our increasing number of early-career researchers. This scheme allows scientists at the Centre to openly share their views about performance, achievements, and contributions with one or several of the more senior scientists. We will evaluate and further develop the scheme in 2022.

Promising research

The Centre of Excellence grant allowed us to invest in analysis of DNA methylation in samples from mother-father-child trios in the Norwegian Mother, Father and Child Cohort Study (MoBa), spearheading groundbreaking research in the Study of Assisted Reproductive Technologies (START) subproject. This project has sparked a growing interest in genetics, and a large group of

team members with interest in genetics and genetic epidemiology is now involved. Several promising publications are underway aimed at improving our understanding of genetic and epigenetic causes and consequences of subfertility and assisted reproduction. The DNA methylation data are also used to construct new biological clocks as well as improve previously published ones. The family trio study design of the START dataset also enables developing new statistical methods for epigenetic and genetic analysis of motherfather-child trios.

In 2021, we started a new data collection in MoBa targeted at further exploring women's fertility and health. This includes data from both questionnaires and clinical examinations. These data will provide a basis for research on the fertility status of young women. We will be able to follow women from the fetal stage until they are in their early 20s and examine how exposures during pregnancy and childhood may affect later fertility.

We are at the forefront of research into the effects of physical and mental maturation during adolescence as well as school performance in relation to later health and social circumstances.

We also investigate how biological and social conditions are transmitted over generations through couple formation, family structures and exclusion from working life and school.

Grant applications

We submitted grant proposals to the ERC and the Research Council of Norway among other funding sources in 2021. At the core of our grant proposal approach is excellent administrative support and the facilitation and involvement in the grant writing process by all members of the Centre team. By including early career researchers in the grant application process, we provide them with training and opportunities to develop own ideas for future research.

Towards the midway evaluation and beyond

We have started to prepare for the midway evaluation of the Centre and to plan our future after current funding of the Centre of Excellence expires. We are now reassessing our research themes and have started the process of identifying promising new directions of research. Suggested new directions include exploring the consequences of covid-19 on pregnancy and fertility and how transitions into childhood and youth are linked to family formation and health in later life. We will continue this work in 2022 and involve everyone at the Centre.



Siri E. Håberg, Centre Director



Highlights 2021

Selected publications

Bratsberg, B., Rogeberg, O., & Skirbekk, V. (2022). Technologyinduced job loss risk, disability and all-cause mortality in Norway. Occupational and environmental *medicine*, 79(1), 32-37.

Haftorn KL, Lee Y, Denault WRP, Page CM, Nustad HE, Lyle R, Gjessing HK, Malmberg A, Magnus MC, Næss Ø, Czamara D, Räikkönen K, Lahti J, Magnus P, Håberg SE, Jugessur A, Bohlin J. An EPIC predictor of gestational age and its application to newborns conceived by assisted reproductive technologies.

Clin Epigenetics, 13(1), 82.

Kinge JM, Øverland S, Flatø M, Dieleman I, Røgeberg O, Magnus MC, Evensen M, Tesli M, Skrondal A, Stoltenberg C, Vollset SE, Håberg S, & Torvik FA. (2021). Parental income and mental disorders in children and adolescents: prospective register-based study. International Journal of *Epidemiology, 50(5)*, 1615-1627.

Magnus MC, Gjessing HK, Eide HN, Wilcox AJ, Fell DB, Håberg SE. (2021). Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage. New England Journal of Medicine,

Magnus MC, Wilcox AJ, Fadum EA, Gjessing HK, Opdahl S, Juliusson PB, Romundstad LB, & Håberg SE. (2021). Growth in children conceived by ART. Human Reproduction, 36(4), 1074-1082.

PhD defenses

385, 2008-2010.

Christina H. Edwards, Yunsung Lee and William Denault have successfully defended their theses in 2021.

New funding

We secured funding from the Research Council of Norway's groundbreaking research programme for the project "Safety of Covid-19 vaccination in pregnancy", led by Siri E. Håberg. Additional funding includes the 'Infrastructure Programme' for the project "Historical Registers", led by Kåre Bævre.

Recruitment

We recruited one researcher, five postdocs and six doctoral research fellows in 2021. In addition, while being primarily employed by other institutions, two doctoral research fellows are also part of our Center of Excellence. The new team members with new positions are Yunsung Lee, Kathryn Beck, Espen Beer Prydz, Marianne Hopen Rørholt, Siri Nærland Skodvin, Karoline Hansen Skåra, Chaitra Srinivas, Rishabh Tyagi, Mari Landås Warp, Sara Abrahamsson, Thang Dang, Álvaro Hérnaez, Magnus Nordmo, and William Denault.



Major events

- CeFH Digital seminar for everyone in the Centre, Teams. April 20.
- CeFH autumn kick-off seminar, Soria Moria. August 25-26
- CeFH 4th Annual Symposium 2021. September 29-30
- Over 50 seminars















Our research

The scientific goal of the Centre is to greatly advance the understanding of causes and health consequences of changes in patterns of fertility and family structure. The changing trends may influence child and adult health through social and biological pathways. To achieve this goal, the Centre combines expertise from epidemiologists, geneticists, physicians, demographers, statisticians, and economists.

In this annual report, we provide a synopsis of our research in **five integrated themes** of research. We also present selected research findings and projects. Most of our research projects and activities are intertwined and form part of several research themes.

Maternal and paternal age

We investigate the impact of advanced maternal and paternal age at childbirth on the risk of subfertility, adverse pregnancy outcome, and consequences for parental and child health.

Fertility and family structure

We investigate the causes and health consequences of many components of reproductive history, such as the number of children/siblings, childlessness, the age at first birth, the interval between births, and family instability.

Intergenerational transmission of health

We investigate how health and disease are transmitted between generations through examining pertinent biological and social pathways.

Fertility problems

We investigate causes of fertility problems and health consequences of subfertility and assisted reproductive technologies in parents and children.

Statistical methods

We develop advanced statistical methods that help address research questions in the Centre.

Theme

Maternal and paternal age

Parental age at first birth is increasing in most countries. In Theme 1, we investigate the impact of advanced maternal and paternal age at childbirth on subfertility, pregnancy outcomes, and diseases in offspring. We study how differences in chronological and biological age is associated with fecundity and risk of disease.

Parental age at first birth is rising in most countries. For example, in Norway, the mean age of mothers at first birth increased from 23.3 years in 1970 to 30.1 years in 2021. The mean age of men at first birth has also increased. In the same period, the total number of children born to each woman has declined across the world, and this is not only because of the later entry into motherhood. One of the Centre's goals is to add to the knowledge about how higher maternal and paternal age affect pregnancy outcomes and children's health, through social and biological mechanisms. Surprisingly, during the Covid-19 pandemic, the number of births has increased in some countries (like Norway), but not in others. This "natural experiment" offers an excellent opportunity to explore causes and consequences of fertility.

One of several possible biological mechanisms that are studied in the Centre involves epigenetics and telomere biology. As people age at a different pace, their biological age may differ from their chronological age. This accelerated or decelerated biological aging can be measured using epigenetic markers, and our Centre is at the forefront of such research involving the use of DNA methylation data to construct various types of biological age clocks.

The social pathways are also diverse and influence age at childbearing. For example, one reason why parental age may affect child health is that older parents are more likely to have higher economic resources to spend on their children. They may also have accumulated more knowledge and may be more mature. On the other hand, they are less likely to survive until the child reaches adulthood.

Another issue, addressed under Theme 3, is that the age when a person becomes a parent (for the first time) has implications for his or her health, through both biological and social pathways.

In 2021, we published a paper describing resource advantages associated with advanced parental age (Sigle W et al.), and two visiting researchers at the centre were either first- or co-authors of three papers on how short birth interval length affects various child health outcomes (Dhamrait GK et al., Pereira G et al., Tessema GA et al.). At the end of the year, a pan-Nordic analysis of how maternal age affects birth weight was revised for a major epidemiology journal.

A paper presenting the first predictor of gestational age based on the Illumina Infinium EPIC array was published in 2021 (Haftorn et

Theme 2

Fertility problems

The use of assisted reproduction technologies (ART) is continuously increasing. We investigate the causes and health consequences of subfertility and assisted reproductive technologies in parents and children. To this end, we employ advanced (epi)genetic analysis and statistical models.

In parallel with the increased age of mothers and fathers at first birth, we have also witnessed increased fecundity problems in the population. There has been a steady increase in the use of ART since its introduction in Norway in 1984. Because the total number of births per woman has also decreased, the proportion of children conceived through ART is steadily increasing. Today, around 3000 children are born in Norway each year through ART, and around 9 million children have been born through ART worldwide.

While most mothers treated with ART and most children born through ART are healthy, there is some evidence pointing to adverse effects. Some studies have found ART to be associated with adverse pregnancy outcomes and increased risk of congenital malformations, infant morbidity and mortality. ART has also been linked to several childhood diseases, as well as cardiovascular

diseases and cancer in mothers.
One proposed mechanism
for the detrimental effects of
ART procedures is epigenetic
modifications of the DNA during
gametogenesis, fertilisation, and
early embryonic development.
However, it is not clear whether the
observed adverse effects of ART
are caused by the procedure itself
or if it is caused by the underlying
subfertility or higher age of the
mother.

We will estimate short and longterm health consequences of ART for women and offspring using a combination of data from registers, cohorts and biological samples. We are interested in health consequences of subfertility in women and men. Thus, we will also examine epigenetic changes induced by ART in their offspring and determine their possible role in diseases.

In 2021, we published a paper on growth in children conceived by ART (Magnus MC et al.). Our findings provide reassurance that offspring conceived by ART are not different in height, weight or BMI from naturally conceived children, once they reach adolescence. In a letter to the New England Journal of Medicine (Magnus MC et al.), we show no evidence of an increased risk for early pregnancy loss after Covid-19 vaccination. This adds to findings from other reports supporting Covid-19 vaccination during pregnancy

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Fertility and family structure

Our goal is to contribute to a better understanding of how the number of children, age at first birth, length of birth intervals, and partnership disruptions affect the health of parents, and how the number of siblings, birth interval lengths and parental disruption affect offspring health.

As age at first birth has increased and the number of children born to each woman has decreased over the past decades, more people are ending up childless. Additionally, there have been marked changes in marriage, divorce and cohabitation patterns over the last half century. For example, the age at marriage and the proportion of people who never marry have increased, while divorce rates have escalated. Couples living together in consensual unions have The reproductive factors such as largely compensated for this shift away from marriage, but these unions are much more unstable. In combination with an increase in the proportion of children born outside of marriage, and most commonly to cohabiting parents, these patterns and trends in partnership instability have led to a sharp rise in the proportion of children who experience parental disruption. For example, 39% of 17-year-old children in 2015 did not live with both of their parents. Because many parents form new partnerships after disruption, and often have children in these partnerships, families are becoming more fragmented and complex.

The changes in marriage, divorce, cohabitation and family structure have been influenced by (and contributed to) the fertility changes, and the two sets of changes have also been driven by many of the same forces. Because of this close relationship between fertility and family behaviour, it is reasonable to take both into account in studies of health implications.

the number of children, age at first birth, length of birth intervals, and partnership disruptions may affect the parents' health through both biological mechanisms (linked to physiological processes during pregnancy or lactation) and social pathways. As examples of social pathways, the number of children born is likely to affect a person's lifestyle and may be important for access to support in old age, whereas early entry into parenthood may disrupt education or work careers, with later implications for health. Comparisons between 'fertility-health' associations among women and men may shed light on the relative importance of biological and social mechanisms.

A methodological paper published late in 2020 (Kravdal Ø) about how sibling models can be used to estimate effects of birth interval lengths when there are only two siblings spurred an interesting discussion in the journal Paediatric and Perinatal Epidemiology. Three letters to the editor were published. A paper about the association between time-to-pregnancy (also a reproductive factor) and cardiovascular disease among women and men was published in a major epidemiology journal (Magnus MC et al.), and researchers at the Centre contributed to two papers about birth interval lengths and hypertensive disorders of pregnancy (Gebremedhin et al., Gebremedhin et al.). Finally, a paper about effects of cohabitation and marriage on mental health was finalized and accepted by Population Studies (to be published in 2022). A paper on effects of partnership disruption on parents' and children's mental and physical health was submitted in 2021.

Statistical methods

We develop advanced statistical methods that help address research questions in the Centre.

The Centre's interdisciplinary approach to understand health implications of the recent changes in fertility patterns and family structure requires close collaborations across different disciplines, as well as coordination and development of research methodology. While the different disciplines at the Centre have different traditions, different terminology and different approaches to research methodology, statistical modelling is a unifying theme across all these disciplines. The figure below illustrates some of the many interdisciplinary links rooted in statistical science.

The methods research activity during 2021 has been strongly influenced by the acute need for new approaches to analyse Covid-19 registry data in real time. In particular, predictions of the expected number of infections and hospitalizations some weeks ahead (short-term predictions) have been a special focus, and resulted in about 60 reports published online as "Korttidsframskrivninger". The results have in several cases been

central to the NIPH's decision strategies. Additionally, the Centre's extensive experience in analysing pregnancy outcomes has been put to use in developing specific strategies for investigating the possible effects of vaccination and infection on numerous pregnancy outcomes and pregnancy-related conditions, resulting in several publications (Magnus MC et al.).

In parallel to the Covid-19 methods development, work has continued on methods in genetic epidemiology. This includes methods for developing and estimating "heritability curves", i.e., a measure of non-linear heritability, as well as extensive applications

of wavelet-transforms to analyzing GWAS and EWAS data (as part of William Denault's PhD work), and novel parental interaction models in ART data analyses (as part of Siri Skodvin's PhD work and Miriam Gjerdevik's postdoc project).

Additionally, extensive research is being done on general methodology for multilevel and longitudinal data, resulting in a new edition of the book Multilevel and longitudinal modeling using Stata by Rabe-Hesketh and Skrondal. Methods for dependent data are ubiquitous, both in most research at the Centre, as well as in the general research community.

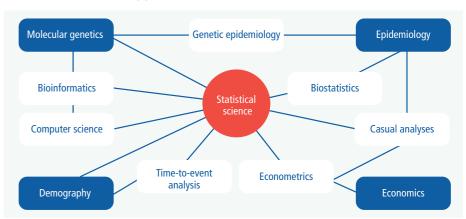


Figure: Statistical methodology at the Centre.

Intergenerational transmission of health

We investigate how health and disease are transmitted across generations through biological and social pathways.

Health factors can be transmitted to subsequent generations in several ways. First, certain characteristics of the parents that are important for their own health, such as their socioeconomic transmissions of disease and risk resources, lifestyles and attitudes, may be passed on to their children through various types of "social transmission". Second, traits from the parents can be inherited through genes. Third, the parents' health may affect the daily life in the home, their ability to care for children, and the children's education and income, all of which in turn may be important for the children's health.

Relative importance of genes and environmental factors

We will estimate the relative importance of genes and environmental factors in transmission of certain diseases and indicators of wellbeing. We will use GWAS data from MoBa to calculate genetic risk scores for both adults and offspring. Thus, we can examine the interaction between genetic and social factors with respect to the risk of specific diseases.

Transmissions of disease and risk

Using data from two large cohort studies. Cohort of Norway (CONOR) and MoBa, we will analyse factors (such as smoking, high caloric intake diets, and low levels of physical activity) across three generations, from grandparents via parents to children. Detailed questionnaire data, physiological measures and physical tests will allow us to consider a broad range of biological and socio-economic factors that can be involved.

Analyses across multiple generations

We further plan to extend perspectives on intergenerational transmission of health to more than three generations by using historic demographic data that include seven to nine generations. We will assess whether the health of children today is related to the health of their ancestors. We will consider the longevity of past generations and explore influences via family size and structures, socioeconomic resources and environmental contexts. For these studies, we will make use of the

National Historical Population Register. The National Historical Population Register is a project to register and link information from various sources, and thus construct a register of the whole Norwegian population since 1801.

Intergenerational transmissions of norms and social values related to reproduction

Reproduction and lifestyle decisions have become a matter of personal choice and subjected to idiosyncratic circumstances, yet influences from families, parents and grandparents can remain important. One important example is the rapid secularization related to the fertility decline observed in Norway from 1970 to 2020. Parental religiosity has also been found to be linked to offspring religiosity – which in turn affects reproductive decisions.

In 2021, we published a paper showing that mental disorders were 3- to 4-fold more prevalent in children whose parents were in the lowest compared with the highest income percentiles (Kinge et al.). Parents' own mental disorders, other socio-demographic factors

and genetic confounding did not fully explain these associations. Furthermore, we studied polygenic risk scores and phenotypic data from pairs of partners, siblings, siblings-in-law and co-siblings-inlaw. Our study, published in 2022 in Nature Communications (Torvik et al.), shows genetic similarities between extended family members and that assortative mating has taken place for several generations.



Research projects

Projects with external funding and key projects

Reproduction, partner disruption and health

The aim of the 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 paren-tal re-partnering, affect children's health?
- How does disruption of relation¬ships, and possible repartnering, affect the health of the involved adults?

The project was initiated in 2017 to establish a data linkage to be used to answer many of the research questions described in our Centre of Excellence original application. The project is based on register and survey data. In 2021, we received conscription data and data from the Norwegian Labour and Welfare Administration on diagnoses underlying various social benefits

and pensions. Additionally, we established a system for linkage to the Trøndelag Health Study (HUNT) surveys. Data from the Norwegian Patient Register, the Medical Birth Register, the Norwegian Cause of Death Register and MoBa were still lacking at the end of 2021 because of various formal hurdles and delays in getting access to data.

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 if there are differences in epigenetic markers associated with subfertility and the use of assisted reproductive technologies (ART). In 2021 we continued our investigations of whether there are epigenetic differences in children born through ART compared to naturally conceived children, and we have finalized the main analyses to be published in 2022. We are following up with further analyses on our main results. We are also looking into the mediating effect of DNA methylation on birth outcomes and expanding analyses to include health and development

in children at older ages. There is an extensive international interest in the data and results, and the manuscript related to our epigenome-wide association analysis (EWAS) of ART has been accepted for publication in *Nature Communications*.

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

In this project, we combine Norwegian registry data and questionnaire data from the MoBa cohort study to investigate causes and consequences of subfertility and assisted conceptions. The project was initiated in 2014 and has been updated with new datasets in 2018, 2019 and 2020. 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 international collaborators in this project include senior researcher Gavin Pereira from Curtin University in Perth, Australia, who has been a guest researcher at our Centre for 2 years, and his postdoc who

visited us as a Brundtland visiting scholar, Gizachew Tessema. In this collaboration, we have continued to publish results on interpregnancy intervals and shown that the interval matters in relation to adverse birth outcomes (Dhamrait et al., Pereira et al., Tessema GA et al.). 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 our PhD students 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 (Magnus MC et al.).

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 longerterm outcomes

We will combine metabolic profiles, genome-wide genotypic data, and clinical factors to understand causal mechanisms for, and accurately predict, 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 plan to add metabolomic profiles to pregnancy samples on a subgroup of 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.

In 2021, we experienced several Covid19-related delays. However, the analysis of 9000 parental plasma samples is now completed, and we will finish the remaining analyses in 2022.

The project is funded by grants to Professor Deborah A Lawlor (ERC Advanced Grant and UK National Institute of Health Research Senior Investigator award).

Key personnel at the Centre: Siri Eldevik Håberg, Per Magnus, Maria C. 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 better 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 national health registers from all 5 Nordic countries which enables us to study rare exposures and outcomes (Hálfdánarson Ó et al, Cesta C et al, Cohen J et al.). Data were updated during 2021. Analyses and the writing of manuscripts are ongoing

In May 2021, we arranged a 2-day international webinar (200 participants from 17 countries worldwide) titled "Antiepileptic drugs in pregnancy and risk for the mother and child". Results from InPreSS and other international research efforts in perinatal

pharmacoepidemiology/neurology were presented and discussed. This provided important contributions to increased knowledge and awareness regarding the consequences and challenges of using drugs, especially antiepileptics, before and during pregnancy.

The project is funded by the Research Council of Norway through the BEDREHELSE program.

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 populationbased 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 2021, we employed a PhD candidate, Chaitra Srinivas, started analyses of already linked health registry data, and applied for a new data linkage which includes MoBa. We also invited patients to share their personal experiences of ADHD medication and pregnancy with our research group to inform the research questions, interpretation of the data, and later dissemination activities.

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 technologyinduced job loss

The 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).

An important part of the project's work in 2021 was to measure the health effects of job loss, both related to plant closures generally, but also during Covid-19. This work represents an important input for building a better understanding of how job loss affects the individual and his/her family members.

In 2021, a paper was accepted in Occupational and Environmental *Medicine (Bratsberg B et al.)*. The study shows that individuals in occupations characterised by high routine intensity are less likely to remain employed in the long term and have higher rates of disability and mortality.

One PhD candidate, Rishabh Tyagi, was hired in the project in a joint effort between CeFH and the Max Planck Institute for Demographic Research in Germany. The two postdocs working on the project were hired in permanent positions at the Norwegian Institute of Public Health and will continue to contribute to the project.

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

Project manager: Vegard Skirbekk

Changing lives, changing brains: How modern family and work life influences ADRD risks

The prevalence of Alzheimer's disease and related dementias (ADRD) is projected to triple by 2050. Currently, there is no known effective medical treatment for ADRD. Prevention through behavioural changes affecting ADRD risk is therefore of utmost importance. Rapid changes that characterise modern family life and work are two critical domains that likely impact ADRD risk. A shift to "modern" family structures and work tasks have occurred relatively early in Norway, and unique data availability allows these changes to be studied prospectively to predict coming changes in ADRD in the US and other countries.

The project is funded by the U.S. National Institutes of Health Research Project Grant Program

Project manager: Biørn Heine Strand together with Vegard Skirbekk

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

The main aim of the project is to build a longitudinal population register including all persons who lived in Norway in the period 1800-1964, and which will be integrated with the National Population Register. This register will be very valuable in studies of the population over the life course and for the research in the Centre. The Historical Population Register is constructed from linking data from censuses, church books and other primary sources.

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 2022 and 2023. 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 program since 2013.

Project manager at CEHF: Kåre Bævre. The project is led by Lars Holden at Norwegian Computing Center.

Health-gap. Health, maturity and

the gender gap in education The primary objectives of the 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 in several ways. First, more educated men and women have increased fertility compared to their less educated peers. Second, combining health risks of low educational attainment with little social support in terms of family network may be particularly damaging for health, and perhaps especially for men's health. Third, assortative mating among people with low education may further exacerbate individual health risks in this group.

Members of the project marked the international men's day with an op-ed calling for more research on men's health issues, one of several appearances in public debates this

year. The project notes important publications in 2021, including on the association between pubertal timing and gender differences in educational performance (Torvik FA 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 program.

Project manager: Fartein Ask Torvik

Schooling and children with ADHD

Children with ADHD perform, on average, poorer in school than other children. It is still unclear how large this disadvantage is, and which subjects these children struggle with the most. It is also unclear to what extent different prevalence of ADHD between boys and girls contributes to boys' poorer performance in school. We investigate these questions by using unique register data for the entire Norwegian population, which includes diagnoses, results from national tests and grades in upper secondary school.

The project was organized as part of the main project Health-gap and ended in 2021. Data were analysed and a paper was submitted and accepted for publication in JCPP Advances in 2022. The paper showed that the ADHD deficit in school performance was large and not easily attributable to other factors. Because the ADHD deficit was large in all school subjects, interventions should ideally address factors that affect school performance broadly.

The project is funded by the Oslo University Hospital's NevSom funding.

Project manager: Fartein 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. An initial workshop was held in 2021 and a PhD student, Kathryn Beck, was recruited into the project.

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

Project manager: Martin Flatø

Rementa - Reproduction of socioeconomic differences and mental health across generations

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

The project will utilize survey and genetic data from MoBa and register data on health, demography and school performance. We will use 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.

In 2021, Marianne Rørholt started as a PhD candidate in the project. 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 2022, pending legal arrangements for executing the material transfer agreement between MoBa and the University of Pennsylvania in the US.

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

Project manager: Per Magnus

Women's fertility – an essential component of health and wellbeing

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 completed the pilot phase and aim now at examining 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.

The project is funded by the Research Council of Norway's KVINNEHELSE funding scheme.

Project manager: Siri E. Håberg

Telomere length, epigenetic age and T cells in women who give birth at an older age

A major aim of this project is to investigate female fecundity in the context of three major indices of biological age: telomere length (TL), epigenetic age, and immune status (as expressed by the ratio of naïve to memory CD8+ T cells). The main hypothesis is that women with longer TL, younger epigenetic age, and a healthier immune status than their peers have an increased ability to give birth to their first child at an older age.

DNA samples of 2000 motherfather-newborn trios from MoBa were selected for this project. Rutgers University in the US (a collaborating partner and R&D-supplier in the project) has completed TL measurements on 1557 trios to date.

Concurrently, DNA methylation in 1000 of the mothers aged ≥32 years (from the above 2000 trios) was measured at Erasmus MC in Rotterdam, the Netherlands. These data have now been merged with the larger (but similar) EPIC-derived DNA methylation dataset from the Study of Assisted Reproductive Technologies (START) at CeFH.

Regarding the TL data, preliminary analyses have been carried out to replicate known characteristics of TL in the available subset of trios with TL measurements. The research group is currently in the process of finalizing analyses of the association between maternal smoking and newborn leukocyte TL, and a manuscript is currently being drafted.

Results from the project propose precise epigenetic estimators of chronological and gestational age in humans (Lee Y et al. 2020, Haftorn KL et al. 2021). Furthermore, they supplement the current knowledge base by providing epigenetic determinants of leukocyte TL in adults. The epigenetic estimators of age have important implications for other research fields, including geroscience and forensics. For example, the output of our research may allow a better assessment of an individual's biological aging status in relation to the onset of elderly disease. Also, the epigenetic estimators can be used to accurately predict the chronological age of victims in the field of forensics.

The project was funded by the Research Council of Norway's FRIMED program (grant 262043) and ended in 2021.

Project manager: Astanand Jugessur

Telomere and female fecundity

The background and several aims of this project overlap largely with the above project. 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 constitutively long TL have delayed menopause, show less

cardiovascular disease, and live longer than other women. Thus, a central hypothesis of this project is that women who bear children later in life, without the use of ART, may have a constitutively longer TL than their peers. Accordingly, the aims of the study are 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 and older with the aid 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 2020, the PhD candidate in the project, Kristine Løkås Haftorn, submitted her first paper and presented her work at two PhD conferences. The paper was published in 2021 in the journal *Clinical Epigenetics* and received some media attention (Haftorn KL et al.).

The project is funded by the US National Institutes of Health (NIH) (grant R01 1HL134840-01) and by the Research Council of Norway through the Centre of Excellence grant (grant 262007).

Key personnel at the Centre: Astanand Jugessur, Per Magnus, 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. This project focuses on key intrinsic and extrinsic factors that are likely to affect LTL dynamics in utero. Mitochondria - the organelles responsible for energy production in the cell – are a key intrinsic source of reactive oxygen species (aka free radicals). These free radicals may affect LTL because the 'GGG' nucleotides in the hexanucleotide telomeric repeats are sensitive to free radicals. Maternal smoking is also important to examine in this context because tobacco smoke is a rich extrinsic source of free radicals. 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 Covid-19 pandemic has continued to have major consequences in 2021 in acquiring the mitochondrial DNA ('mtDNA' hereafter) sequences on the 1000 MoBa children that are central to the original aims of the project. The original project plan was to generate mtDNA sequence data at the University of Pennsylvania (UPENN), a collaborating partner and R&D-supplier in the project. In addition to Covid-19 severely impeding progress in securing the necessary paperwork for the material transfer agreement (MTA), 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 thirdparty countries (e.g., USA). The new privacy regulations have significantly delayed data collection and processing for European researchers. The legal counsel at NIPH is currently assisting the project administrators in solving these issues and enable biologic

specimens to be sent to UPENN within the current legal framework.

Due to these unforeseen hindrances in the project, 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 mtDNA energetics. Kristjansson used publicly available mtDNA sequences as a basis for the three articles in her PhD thesis. She published the first paper in her PhD thesis in 2021, in the journal American Journal of Physical Anthropology. Her second paper is under review in BMC Genomics, and her third paper is currently being reviewed by the coauthors.

The project is funded by the Research Council of Norway's FRIMEDBIO program (grant 287961).

Project manager: Astanand Jugessur

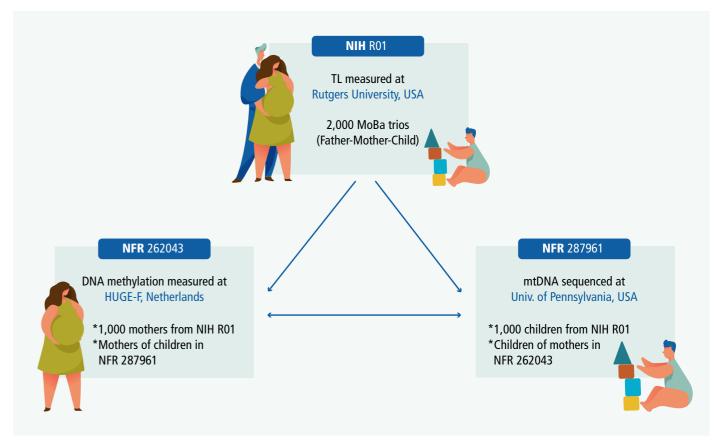


Figure: Telomere-related projects at CeFH. The figure shows how the above three projects on telomeres are related to each other.

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, in addition to a causal effect of body-mass index on infertility using Mendelian randomization analysis. The project continues to study the causal relationship between other known cardiovascular disease risk factors and their impact on infertility. One PhD candidate and one postdoctoral researcher were hired to work on the project when it started in 2021.

The project is funded by the European Research Council's Starting Grant funding scheme.

Key personnel at the Centre: Maria C. Magnus, Álvaro Hernáez, Karoline Skåra.

SCOPE – Scandinavian studies of Covid-19 in pregnancy

Combining results from the three Scandinavian countries provide us with the ability to study 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. We have identified susceptible subgroups. With access to the total Scandinavian female population, we can study

non-frequent 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 up-to-date data from our registries, results from this project have provided more knowledge on the risks of Covid-19 related to pregnancy (Magnus MC et al.), how health care in pregnant women changed during lockdown (Oakley LL et al.), and consequences of infection and lockdown for pregnant women (Magnus MC et al.).

The project is funded by NordForsk's Nordic Health Data Research Projects on Covid-19 programme.

Project manager: Siri E. Håberg

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 by getting the administrative setup ready and organizing brainstorming sessions. The project has initiated close collaborations with renowned researchers from several national and international research institutions. The starting date for research activities is January 2022.

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

Project managers: Bjørn-Atle Reme and

Re-thinking the programming hypothesis: Prenatal maternal anxiety/depression, DNAmethylation and child psychopathology. A sibling design Depression and anxiety disorders are among the most common disorders to inflict the expecting mother during pregnancy. Mothers-to-be are continuously warned about the potential hazard that could inflict the unborn child. We aim to gain new knowledge about some of the mechanisms underlying the link between prenatal anxiety and depression and later outcomes in the child.

In this study we will examine the role of DNA methylation in the association between prenatal maternal anxiety/depression and child psychopathology from infancy to middle childhood, using a discordant sibling design. We expect that our findings will extend current knowledge on the role of prenatal programming and DNA methylation on pathways to healthy and aberrant development and provide new knowledge about how epigenetic mechanisms may render some infants more susceptible to adversity and simultaneously more likely to benefit from supportive experiences.

In this study, we will use a quasiexperimental approach with genotype information and DNA methylation to address some of the current challenges in research examining exposure to prenatal stress or adversity on child psychopathology. CeFH collaborates on this project with the Department of Psychology, University of Oslo on data and method sharing, research ideas and development and supervision and mentoring of two postdoctoral fellows.

The project is funded by the Research Council of Norway and is led by Mona Bekkhus at the University of Oslo.

Key personnel at the Centre: Christian Page.

The Burden of Obesity in Norway

The main aim of the project was to study the impact of obesity on morbidity, mortality, health service use and social insurance benefits in Norway. The project aims to gain a deeper understanding of the total burden of obesity in Norway by estimating individual trajectories and cost of illness by different demographic and social characteristics. The project also aims to elucidate the causal impact of obesity on health and health service use by employing genetic markers as natural experiments.

In 2021, the project produced two articles (Edwards CH et al. 2021 and Edwards CH et al. 2022). The PhD candidate in the project, Christina Hansen Edwards, was awarded her PhD.

The project, which was funded by the Research Council of Norway's FRIMEDBIO program (Young Research Talents), was finalised but some of the publications are still under review in various journals.

Project manager: Jonas Minet Kinge

YoungGrowth. Evaluation of free school fruit on childhood growth and obesity: a natural experiment

The primary objective of the project is to estimate the effect of the free school fruit program on childhood growth and obesity.

In the period 2007 to 2014, pupils in junior high schools and combined primary and junior high schools were given a free fruit/ vegetable every day, while pupils in primary schools were not. We have measured height and weight among 13-year-olds in more than 150 schools to evaluate the effects of this natural experiment. The main finding is that free fruit/ vegetables in a school setting does not influence the incidence of obesity in children.

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

Project manager: Per Magnus

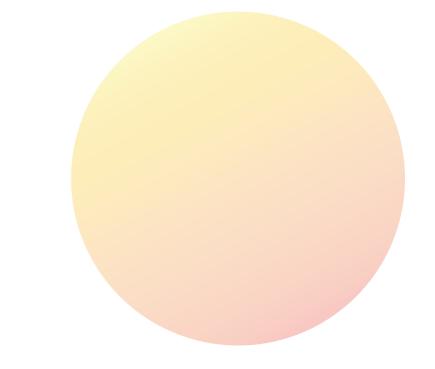
Addressing the smoking paradox in the etiology of Covid-19 through population-based studies

The role of tobacco use (smoking and snus) in 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 will analyse the potentially causal association of tobacco use with incidence and prognosis of Covid-19 using existing longitudinal population studies in Finland, Norway and Sweden.

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



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New projects in 2021

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 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 (Magnus MC et al.).

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 (Magnus MC et al., 2022).

The project is funded by the Research Council of Norway through the FRIPRO-scheme.

Project manager: Siri E. Håberg

Historical Registers

In December 2021, the Research Council of Norway awarded a new substantial grant to continue the project National Historical Population Register for Norway. The project will continue under a new name, Historical Registers. See above for more details about the project.



PhD projects in 2021

Completed dissertations for the PhD degree:

Christina Hansen Edwards

"Economic Consequences of Elevated BMI in Norway" Christina successfully defended her thesis on March 4, 2021

William Denault

"Wavelet-based methods in genetic epidemiology" William successfully defended his thesis on September 3, 2021

Yunsung Lee

"Human aging, DNA methylation, and telomere length: Investigation indices of biological ageing" Yunsung successfully defended his thesis on May 26, 2021

Ongoing PhD fellowships:

Kathryn Beck

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

Ellen Øen Carlsen

"Parental age and subfertility as risk factors for adverse pregnancy outcomes"

Kristine Løkås Haftorn

"Using DNA methylation for estimation of gestational age, and its application to ART-pregnancies"

Dana Kristjansson

"Mitochondrial DNA and Norwegians"

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 Tyaqi

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

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

Postdoc projects in 2021

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 Hérnaez

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

Thomas Kleppestø

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

Vera Mitter

"Risk of infections and chronic immune-mediated diseases among children conceived by assisted reproductive technologies"

Magnus Nordmo

"Reproduction of socioeconomic differences and mental health across generations"

Bjørn-Atle Reme

"The DIMJOB project: Impact of technological progress on the labor market"

Jonathan Wörn

"The DIMJOB project: Consequences of unemployment for families and children"

New team members 2021



Researcher Yunsung Lee

Yunsung started in a full-time researcher position at the Centre in May 2021. Yunsung obtained a master's degree in statistics from the University of Oslo and a PhD degree in epigenetics and telomere biology from the same university in 2021. At the Centre, he continues to pursue his research interests in epigenetic aging and telomere biology in relation to fertility, using MoBa data.



PhD candidates

Kathryn Beck

Kathryn joined the Centre in August 2021. She holds a master's degree in Global Health from the Norwegian University of Science and Technology (NTNU), where she studied the link between educational attainment and adult all-cause mortality and interventions to reduce child health inequalities. As a PhD candidate in the 'Lost in Transition?' project, Kathryn will investigate the long-term health and social consequences of sub-optimal transitions within the educational system.



Siri Nærland Skodvin

Siri joined the Centre in March 2021. She holds a master's degree in applied statistics from the Norwegian University of Life Sciences. In her PhD project, Siri aims to develop new methodology for investigating genetic influences on fertility as well as the potential effects of assisted reproductive technology on epigenetic reprogramming. She also works on various projects related to Covid-19.



Karoline Hansen Skåra

Karoline joined the Centre in January 2021. She holds a master's degree in physiology from the Norwegian University of Science and Technology (NTNU), where she specialized in thermoregulation and metabolism in bats. Karoline will be working in the infertility project, investigating whether there is an association between infertility and cardiovascular disease using data from HUNT.



Chaitra Srinivas

Chaitra started a PhD position at the Centre in May 2021. She is a pharmacist and has a master's degree in public health sciences from Karolinska Institutet in Stockholm, Sweden. Her research focus is in pharmacoepidemiology. She is currently working on a project to understand the treatment patterns and outcomes related to ADHD medication use in pregnancy in Norway and Sweden.



Espen Beer Prydz

Espen joined the Centre as a doctoral research fellow in February 2021. His research focuses on changes in living standards and well-being and how these are impacted by demographic factors, changes in family structures and health shocks. Espen is pursuing a PhD in Economics at the University of Oslo and holds a master's degree from Harvard University and a BSc from the London School of Economics. Previously, he worked with the World Bank on global measurement of children's health, poverty and inequality.



Marianne Hopen Rørholt

Marianne joined the Centre in November 2021 as a PhD candidate. She is a trained medical doctor from the Royal College of Surgeons in Ireland, and has clinical experience within oncology, paediatrics, and ENT (ear, nose, and throat). She has a special interest in paediatric medicine, and much experience in treating asthmatic children and children with other airway diseases. She will investigate the maternal effect on offspring asthma, the duration of this effect, whether the risk of asthma in the offspring is related to severity of maternal asthma during pregnancy, and whether having asthma in childhood may predispose towards or protect against other childhood illnesses.



Rishabh Tyaqi

Rishabh joined the Centre in May 2021 and is aiming to work as a labour demographer in developing countries to close the gender and wage differentials in labor market. He has previously worked at the National Institute of Medical Statistics, India and holds both M.Sc. & M.Phil. degrees in Biostatistics & Demography. Currently, he is a PhD candidate in the Research Group 'Labor Demography' at Max Planck Institute for Demographic Research, Rostock, Germany and in the DIMJOB project at the Centre. In his doctoral research, he is investigating the social, health & demographic consequences of technology-induced job loss.



Mari Landås Warp

Mari joined the Centre in October 2021. She is a physician and graduated from the Medical University of Łódź in Poland. She also holds a bachelor's degree in nutrition physiology from Atlantis Medical College in Oslo. Mari is specializing in gynecology and obstetrics, with a special interest in female fertility.

As a PhD candidate, she is a part of the Women's fertility project where she investigates the reproductive potential of young women born to MoBa mothers. She shares her time between Telemark Hospital where she is currently employed, and the Centre.

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Postdocs

Sara Abrahamsson

Sara joined the Centre as a postdoc in August 2021. Her main research interests are to understand changes in patterns of health, fertility, family structure and education, with a focus on identifying causal effects of different social policies, such as infant health care and changes in technological adaptation at schools. She was previously a PhD Student in Economics at the Centre for Experimental Research on Fairness, Inequality and Rationality (FAIR) at the Norwegian School of Economics.



Thang Dang

Thang started his postdoc position at the Centre in April 2021. Thang is an applied micro-economist working on policy-relevant topics in labor, education, family and health economics. His current research focuses on the long-term and spillover impacts of health and human capital shocks, and cultural origins of social mobility and inequality. Thang received a PhD in economics from the University of York, North Yorkshire, England.



Álvaro Hernáez

Álvaro started in the Centre as a postdoctoral researcher in January 2021. He holds a PhD in Food Science and Nutrition from the University of Barcelona, Spain. Before joining the Centre, he specialised in nutritional and cardiovascular epidemiology. Álvaro works in the Infertility project, in which he is studying the relationship between cardiovascular disease and decreased fertility in MoBa. He also contributes to the study of the genetic predisposition to fertility problems in several European cohorts.



Magnus Nordmo

Magnus was hired as a postdoc at the Centre in February 2021 to work in the Rementa project. He is a trained psychologist with a PhD from the University of Oslo (2020). The work presented in his PhD research deals with patient recovery following psychotherapy. In addition to his academic work, Magnus has several years of experience working as a clinical psychologist, particularly related to the development of low-threshold interventions for common mental health problems.



William Denault

William started as a postdoc at the Centre in May 2021. He holds a PhD in biostatistics from the University of Bergen (2021) and the work in his thesis was done primarily at the Centre. His main research focus is on developing alternative methods for GWAS analysis to improve the statistical power for studying complex traits. William's 1-year postdoc position at the Centre will complement a 2-year postdoc position with Prof. Matthew Stephens at the departments of Human Genetics and Statistics of the University of Chicago, USA.



New part-time position in 2021

Mads Melbye

Mads Melbye is a physician and scientist with a deep interest in population health data science. He holds a position of senior advisor to the Norwegian Institute of Public Health and is a professor at the Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU). He is also affiliated with the Department of Genetics at Stanford University in the US and the Department of Clinical Medicine at the University of Copenhagen in Denmark. He was involved in uncovering the cause and spread of the AIDS epidemic and has major interests in infectious disease and vaccine research, in research on the etiology of cancer, in genetic and molecular epidemiology, and in perinatal epidemiology. He founded and headed the Department of Epidemiology for many years at Statens Serum Institute in Denmark, founded the Danish National Biobank and co-founded the Danish National Birth Cohort. He has held previous academic positions as senior investigator at the National Cancer Institute, NIH, USA, Danish Research Council Professor, NORFA professor, and Foreign Adjunct Professor at Karolinska Institute in Sweden. He has authored more than 600 publications.



Guest researchers in 2021

Gavin Pereira

Gavin is a perinatal epidemiologist, environmental health researcher and biostatistician in the discipline of Epidemiology and Biostatistics at the School of Public Health, Curtin University, Australia. He was a visiting professor at the Centre in 2020-2021, working on several projects and research topics such as algorithms for predicting stillbirth and perinatal morbidity, maternal and environmental exposures, and of interpregnancy intervals. He is also developing a pre-pregnancy cohort in Western Australia.



Vera Mitter

Vera is a pharmacist by training and holds a MSc in Demography and Health from the London School of Hygiene and Tropical Medicine, UK. In June 2020, she finished her PhD in epidemiology on obstetric and perinatal outcomes of assisted reproductive technologies (ART) at the University of Bern, Switzerland. Vera obtained a mobility grant from the Swiss National Science Foundation (SNF) and a 4-month extension financed by Foundation Fridericus to conduct a postdoc at the Centre. Since September 2020, she has worked with Maria Magnus and Siri Håberg on the long-term health of children born after ART, using MoBa and Norwegian Registry data.

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The Gro Harlem Brundtland Visiting Scholarship

The Centre for Fertility and Health is strongly committed to the education and engagement of early career researchers and has established the Gro Harlem Brundtland Visiting Scholarship. This scholarship helps to 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 primarily but also the Norwegian Institute of Public Health overall. The scholarship was announced for the first time in May 2018, and we plan to open for new applications on an annual basis.

Anne Sofie Dam Laursen

Anne Sofie holds a Masters' degree in Human Nutrition from the University of Copenhagen, Denmark. She was awarded a PhD degree in Nutritional Epidemiology from Aarhus University, Denmark, in September 2019. She has recently transitioned into the field of reproductive epidemiology at the Department of Clinical Epidemiology, Aarhus University Hospital. There, her main interest is in investigating preconceptional risk factors for miscarriage and gestational diabetes.

During her research stay at the Centre in 2021-2022, she used data from MoBa to model maternal gestational weight gain trajectories across different levels of fertility, including women who conceived after assisted reproduction. She also investigated the association between subfertility and gestational diabetes.

People

Leader group



Siri Håberg, Centre Director



Per Magnus, Deputy Centre Director



Håkon Gjessing, Principal Investigator



Øystein Kravdal, Principal Investigator



Vegard Skirbekk, Principal Investigator



Fredrik Swift, Head of Administration



Robert Lyle Maria C. Magnus



Mads Melbye



Christian Pag



Gavin Pereira, Bjørn-Atle Reme Visiting Professor

Researchers



Jon Bohlin



Bernt Bratsberg



Aline Bütikofer



Kåre Bævre



Ida Caspersen



Jacqueline Cohen



Liv Bente Romundstad

Postdocs



Rolv Skjærven



Anders Skrondal



Fartein Ask Torvik Aage Tverdal



Jonathan Wörn

Espen Moen Eilertsen

Jon H. Fiva





Martin Flatø



Kari Furu



Hans Ivar Hanevik Jennifer Harris





Sara Abrahamsson



Thang Dang



William Denault



Miriam Gjerdevik



Thea Grindstad



Álvaro Hernáez



Rannveig Kaldager Hart



Astanand Jugessur



Jonas Minet Kinge



Yunsung Lee



Rolv Terje Lie



Jo Thori Lind



Thomas Kleppestø



Vera Mitter



Magnus Nordmo

More people

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PhD candidates



Lise Andrea Arge



Kathryn Beck



Ellen Øen Carlsen



Kristine Løkås Haftorn



Dana Kristjansson



Espen Beer Prydz



Marianne Hopen Rørholt



Siri Nærland



Karoline Hansen



Chaitra Srinivas



Hans Fredrik Sunde



Rishabh Tyaqi



Mari Landås Warp

Administrative staff



Frida Løvlie Bråttum, Office Coordinator



Randi Sekkeseter, Project Coordinator



Anina Falch.

Officer

Research Finance

Linda Selje Sunde, Project Coordinator



Katrine Kranstad. Research Administration Officer



Project Coordinator

Affiliated researchers

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

Abraham Aviv, Rutgers University, New Jersey, USA

Catherine Bowen, independent researcher and University of Vienna

Ian Colman, University of Ottawa, Canada

Haakon Nustad, Deepinsight AS, Norway

Anne Sofie Dam Laursen, Aarhus University Hospital,

Julia Romanowska, University of Bergen, Norway

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

Laura Oakley, London School of Hygiene and Tropical Medicine, UK

Allen J. Wilcox, NIEHS/NIH, North Carolina,

Wendy Sigle, London School of Economics,

Marcin Stonawski, Statistics Denmark, Denmark Emily Grundy, University of Essex, UK

Scientific Advisory Committee (SAC)



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 Melbourneand 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 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

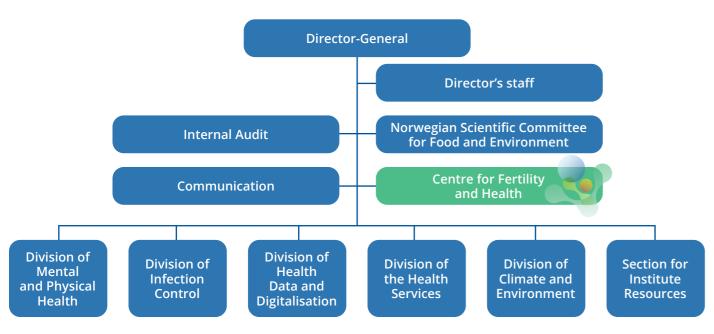
Denmark

• Provide annually a short status report on the development of the Centre, drawing on annual reports and other material made available by the Centre.

List of people updated as of April 2022

Organisation





Organisaton Chart of the Centre



Leader Group Centre Director

Deputy Centre Director Principal Investigators Head of Administration

Leader Group Researchers and Staff **Affiliated Researchers**

Centre Team

Extended Leader Group

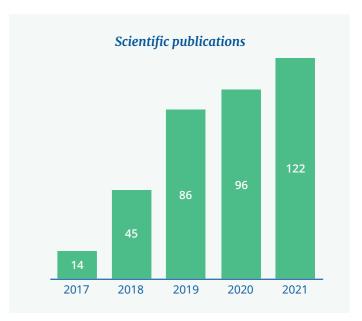
Centre Director Deputy Centre Director Principal Investigators **Head of Administration**

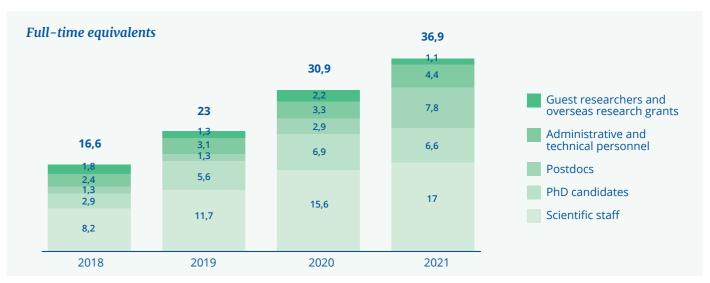
Researchers with permanent positions



Indicators 2017-2021









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Seminars 2021

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

CeFH Lunch Seminars Our lunch seminars are informal research seminars that are normally 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. Although primarily aimed at researchers at the Centre, the seminars are also open to other researchers.

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 2021

Jon Bohlin. What is driving the epigenetic clocks? January 22.

Andreas Nydal. Confounding, causality and confusion applications to multigenerational effects. January 29.

Torstein Tengs. A genetic element in the SARS-CoV-2 genome is shared with multiple insect species. January 29.

Maria Magnus. Are pregnant women at higher risk of COVID? February 5.

Hein Stigum. Standardization: Stratified versus Model based. February 12.

Kaja Kristine Selmer. TeraEpi: Teratogenicity of antiseizure medication: the roles of epigenetics and folic acid supplements. February 19.

Pieter Vanhuysse. Pro-elderly welfare states within child-oriented societies. March 5.

Sigrid Børte. Maternal relatedness and mitochondrial DNA. March 5.

Eva Beaujouan. Studying inability to ever have a child by age with contemporary data. March 12.

Per Magnus. Using genetics to understand the maternal effect on asthma. March 12.

Vera Mitter. Methodological challenges in ART cycle data analysis. March 19.

Lars Christian Stene. Overview of machine learning for simple epidemiologists. March 26.

William Denault. Wavelet-based methods in genetic epidemiology. March 26.

Berkay Ozcan. Age at Marriage and Divorce: Causal Evidence from a Legal Reform in China. April 9.

Siri Håberg. When sibling analyses lead you astray. April 16.

Laurie Hannigan. Psychiatric genetic epidemiology and the null hypothesis. April 16.

Hans Fredrik Sunde. Mental health and intergenerational transmission of social differences. April 23.

Bjørn-Atle Reme and Jonathan Wörn. Did mental health inequalities decrease during the COVID-19 pandemic in Norway? April 30.

Ziada Ayorech. Which metabopsychiatric factors affect the risk of anorexia nervosa? A Mendelian randomization study. April 30.

Veronika Siegl. The biopolitics of assisted conception in Russia; from demographic anxieties to demographic desires. May 7.

Yunsung Lee. Human aging, DNA methylation, and telomere length: Investigating indices of biological aging. May 7.

Thang Dang. Welfare Reform and Mental Health. May 21.

Bernt Bratsberg. Male Fertility: Facts, Distribution and Drivers of Inequality. May 28.

Ida Elken Sønderby. Using rare CNV carriers to gain insight into neurodevelopment and disease. May 28.

Karoline Hansen Skåra. The association between infertility and cardiovascular disease: The HUNT study, Norway. June 4.

Thomas Hansen. Does having children make people happier? A review of folk theories versus empirical evidence. June 11.

Morten Valberg. Inequality in genetic cancer risk suggests bad genes rather than bad luck. June 11.

Felix Tropf. Genetic discovery and heterogeneity in the social sciences. June 18.

Francesca Azzolini. Heritability curve: a local measure of heritability in family structures. August 6.

Tormod Rogne. Climate changes pregnancy. August 13.

Thang Dang. Does Religiosity Link to Family Formation and Fertility? August 20.

William Denault. Wavelet-based methods in genetic association analyses. August 20.

William Denault. Polygenetic score in clinical risk prediction. August 27.

Sara Abrahamsson. Distraction or Teaching Tool: Do Smartphone Bans in Schools Help Students? September 10.

Jon Bohlin. SARS-CoV-2: from viral genomics to host epigenetics – Case studies in genomic epidemiology from the Nordic countries. September 17.

Hermine Maes. Using genetic data to better understand the nature of substance use and related behaviors. September 24.

Kayleigh Easey. Using data on fathers/partners to study associations between prenatal parental exposures and child health. October 1.

Christine Sommer. Findings from the EPIPREG sample: Epigenomewide association study of HOMA-IR. October 1.

Daniel Ciganda. Demographic models of the reproductive process: past, interlude, and future. October 8.

Siri Håberg. ERC Synergy Grant. October 15.

Marc Vaudel. Changes in the educational gradient of fertility not driven by changes in preferences. October 15.

Astri Syse. Associations between health and fertility in administrative data. October 22.

Maria Magnus. Covid-19 Vaccination during Pregnancy and First-Trimester Miscarriage. October 29.

Dinka Smajlagic. Parent-of-origin effects in ADHD. October 29.

Mirjam Wentzel. Surviving a Mass Shooting. November 5.

Rene Karadakic. Health Effects of Information Diffusion. November 12.

Helge Ræder. The role of gonads in health and disease. November 12.

Hans Fredrik Sunde. What's up with statistical control: when to use. when not to use, and when it's not enough. November 19.

Stefan Öberg. The casual effect of fertility: The problems with natural experiments and how to fix them. November 26.

Rosa Cheesman. Schools moderate effects of ADHD symptoms and genetic risk on achievement. November 26.

Kenneth Wiik. Origin and residential influences on the first partnership choices of the children of immigrants in Norway. December 3.

Nis Brix. Maternal lifestyle, puberty and semen quality. December 10.

Perline Demange. Using genetics and pedigree to investigate the effects of parental psychopathology on children's school performance. December 10.







Other CeFH events:

CeFH Digital seminar for everyone in the Centre, Teams. April 20.

CeFH Start-up after summer seminar, Soria Moria. August 25-26

CeFH 4th Annual Symposium 2021. September 29-30

- Álvaro Hernáez, CeFH: Body mass index, smoking, cardiovascular risk factors and subfertility: Mendelian randomization analyses in the Norwegian Mother, Father and Child Cohort Study
- Hans Fredrik Sunde, CeFH: Are highly educated parents good for • Espen B. Prydz, CeFH: Child your mental health?
- Siri N. Skodvin, CeFH: Genetic interaction as a cause of infertility in couples
- Chaitra Srinivas, CeFH: Use of ADHD medication in pregnancy in Norway (2010-2018) and Sweden (2010-2019)
- · Jonathan Wörn, CeFH: Paternal plant closures and children's health care usage
- Kathryn Beck, CeFH: School Entry and Exit: The Health Consequences of Sub-Optimal Transitions in Education
- Magnus Nordmo, CeFH: The Effects of Parental Anxiety and

Depression on Child Educational Performance

- Vera Mitter, CeFH: Early childhood respiratory tract infections according to parental subfertility and conception by assisted reproductive technologies
- Karoline H. Skåra, CeFH: Risk of cardiovascular disease in subfertile women and men: findings from the Trøndelag Health Study
- Sara Abrahamsson, CeFH: Intergenerational Effects of Access to Infant Health Care
- Cancer and Parental Labor Outcomes
- Thang Dang, CeFH: Understanding Mechanisms Behind the Link Between Religiosity and Fertility
- · William Denault, CeFH: Assisted reproductive technology reduces fetal growth and alters maternal and fetal DNA methylation
- Bjørn-Atle Reme, CeFH: Developments in primary health care utilization: a populationwide registry study from Norway 2006-2019
- Håkon Gjessing, CeFH: Short term prediction of Covid-19 hospitalization rates

- Fartein Ask Torvik, CeFH: How genes and mental health create social differences
- **Deborah Lawlor**, University of Bristol: ART-HEALT a new collaboration exploring the effects of ART on perinatal and future offspring and maternal health
- Martin Kolk, Stockholm University: Religion and fertility in Finland - evidence from longitudinal register data
- Alice Goisis, University College London: Antidepressant purchases and medically assisted reproduction: a 24-years longitudinal analysis using Finnish register data
- · Virpi Lummaa, University of Turku: Intergenerational effects on fertility in historical Finnish families
- Stefania Benonisdottir, University of Oxford: The Genetics of Study Participation
- *Kjell G. Salvanes*, Norwegian School of Economics: First generation elite: the role of school social networks (with Sarah Cattan and Emma Timiney)
- Maria Magnus, CeFH: Covid-19 and pregnancy - research at CeFH

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