

Healthy choices and the social gradient

1. Relevance relative to the call for BEDRE HELSE proposal

Why do we observe increasing inequality in health – even in welfare societies where all citizens should have equal access to health services? This proposal is the result of a research environment that has the infrastructure, data sources and the competence to explore the conditions of inequity in health. Our vision is not only to seek to explain inequality, but we also see our social responsibility as a research community to contribute to evidence-based actions that can bring positive consequences for the society.

This proposal addresses key thematic health priorities and the majority of goals and sub-goals of the BEDREHELSE program using novel and innovative approaches. We will develop new and applicable knowledge on the impact of modifiable traditional risk factors on inequalities in health through the life course. Using data from several cohorts we will study these factors through transition phases in life. This allows us to identify specific risk factors and subgroups of the population that can be targeted for actions to reduce social inequalities in health. Furthermore, our cohorts include information on ethnicity enabling us to address sensitive groups in particular.

The proposal includes ongoing and planned research on health behavior and social inequalities in health at UiT – the Arctic University of Norway, national and international partners and research networks. By interdisciplinary joint research and extensive sharing of research ideas, data, methodologies and results, we will develop novel insights into the interrelationships between an individual's health related behavior and social position at different age periods. This will serve as a knowledge-based background for our targeted intervention efforts and strategies. The findings will be communicated in novel ways to policy makers and the public ensuring informed decision-making.

Furthermore, we will develop and actively use new ways of communicating targeted public health messages to risk groups identified through our research. We will use large existing cohort data that include teenagers and adults with up to 45 years of follow-up. Many of these individuals have provided self-reported information on childhood living conditions. We will link these data sets with national health registries on a number of health parameters and demographic information, using innovative tools for data sharing and tracing. Ongoing partly funded qualitative research projects will supplement the cohort-based research to better understand determinants of health and life-long health trajectories. We will use the research results as a guide for developing new questionnaires, and choosing clinical examinations and biological measures to be included in future surveys to be carried out by our research network. By involving students in all phases of planning a new student health survey we aim to address important research questions in an important transition phase as well as integrating research even more into training and education. However, the funding of new data collections as such is not a part of this proposal. The boldness, ambition and large international networks in this trans-disciplinary research endeavor will provide vital knowledge for public health actions.

2. Aspects relating to the research project

2.1 Background and status of knowledge

Norway has two main public health objectives; improve public health in terms of increased longevity and health-related quality of life and reduce social inequalities in health.

Numerous reports have shown large and persistent social gradients within Norway measured by traditional indicators of socioeconomic status (SES). According to the EUROTHINE project, cardiovascular disease (CVD) has contributed to most of the socioeconomic health inequality in Norway – due to the social class-dependent prevalence of smoking [1], underscoring the fact that health related choices follow a social gradient.

Policy makers need improved knowledge on the *causes* of the non-satisfactory health in Norway, as well as better knowledge of which *interventions* are effective. There is a need to improve the knowledge base concerning the causes of the inequalities in health determinants observed along a social gradient. How much can be explained by health-related behaviour, and how much by initial childhood and even pre-birth

circumstances? Early life experiences have an impact on health throughout life. Children and adolescents with multiple adverse childhood experiences are at a major risk for a number of physical and mental adverse health conditions as adults, including increased premature mortality [2]. It is therefore crucial to acknowledge the life-course dimension in public health strategies, and thereby give special attention to the next generation.

There is growing evidence that social-biological transitions are detectable in the epigenome, and both early life and life course changes in socioeconomic status have been shown to affect the epigenome and the transcriptome [3, 4]. To encompass the overall impact of social adversities on biology, the concept of human social genomics has been put forward [5]. New insights into mechanisms by which the environment affects epigenetic processes in the developing offspring enables identification of early life biomarkers and mechanisms of future risk, and tracing of signals of disease development that start in early life. Furthermore the fact that epigenetic modifications can be stable during cell division and can be transmitted to the next generation, calls for new efforts to promote health literacy as well as healthy lifestyle choices in young adults and their children [6]. By including in our analyses intermediate biomarkers potentially involved in diseases, we expect to reveal some common and currently unknown roots of several NCDs, and improve our ability to implement successful interventions.

Worldwide, the prevalence of adult obesity has nearly tripled since 1975, and overweight and obesity is now responsible for more deaths than underweight [7]. The worldwide increase in overweight and obesity prevalence among children is one of the most serious public health challenges in the 21st century due to several immediate and long-term health problems related to this condition. Tromsø Study data also shows an increase in the prevalence of obesity in adults [8, 9]. The same trend has also been found among young children in Finnmark and Troms [10, 11]. The Fit Futures Study found that children with a high birth weight had higher odds of later overweight/obesity [12]. Chronic lifestyle diseases have emerged quite recently in indigenous populations and are prevalent among the Sami population [25-29]. A recent Lancet review addressing health among indigenous people worldwide includes SAMINOR data, and describes a wide range of poor health outcomes such as high infant mortality rate and maternal mortality [13]. The SAMINOR study show alarming results concerning obesity, metabolic syndrome and type 2 diabetes in the Northern rural population.

There has been a global dietary shift towards increased intake of energy-dense foods high in fat and sugar, but low in vitamins, minerals and other healthy micronutrients [7, 14]. This was also observed in the Fit Futures Study. The global trend of decreasing level of physical activity related to occupation, educational level, and mode of transportation is a major public health challenge. In Norway, less than 30% of the adult population achieve the national recommendation of 30 minutes of moderate-intensity daily physical activity [15], and for children the activity levels are decreasing with increasing age [16]. The trends in overweight/obesity, low levels of physical activity, increasing sedentary behavior and shift towards an unhealthy diet are determined by changes in society. Unlike adults, children and adolescents do not freely choose the environment in which they live, and the food they have access to. Furthermore, they have limited ability to understand the long-term consequences of unhealthy behaviors.

Mental health problems constitute a major public health challenge in Norway [17]. It is estimated that 15-20% of children and adolescents have reduced function caused by anxiety, depression and behavioral problems [18]. Nearly 10% of adults have considerable mental health problems, and 30-50% will experience such problems during the life course [18]. More than half of high school dropouts could be seen as related to mental health problems. The “Ungdata” survey has reported alarming figures of mental health problems such as loneliness and social isolation among children and adolescents [19]. The 2014 Student Health and Wellbeing Study (SHoT survey) showed that university students with low academic self-efficacy or delayed academic performance are more likely to experience serious symptoms of mental distress [20]. Compared to 2010 [21], mental distress had increased and 19% in 2014 reported serious complaints about their mental health [20]. Students’ report of drop out, alcohol and drug abuse, and lack of social relationships and loneliness are worrisome [20]. We need an active focus on preventive and health promotion measures to reduce mental health problems among children, adolescents and adults.

2.2 Approaches, hypotheses and choice of methods

Hypothesis

Inequalities in socioeconomic status and social relations interact with modifiable risk factors and influence health throughout life. Appropriate actions and knowledge building during transition periods can improve population health and reduce health inequalities, ensuring healthy aging for all.

Objectives

The main objective is to provide new insight into the complex interrelationships between health-related choices, the social gradient and modifiable risk factors, as well as building actionable knowledge among people and decision makers to reduce inequalities in health.

Secondary objectives:

- Transfer research data to novel data handling tools (EUTRO)
- Improve knowledge on health related behavior along the social gradient and different measures of SES, in order to design effective interventions tailored to socioeconomic groups and transition phases
- New knowledge on links between people's social relationships (friends, family and community connectedness) and their health and well-being, especially in the elderly
- Develop and implement new ways of communicating public health knowledge
- Build a research program together **with** students, **for** students and **of** students
- Explore epigenetic and transcriptomic alterations in blood in relation to SES

Rationale

The research program at the Institute of Community Medicine has been recognized as excellent in previous RCN-evaluations. This status is based on longstanding research using rich data from large population-based studies and biological samples; intervention study capacity; a broad range of research methods and statistical tools, new methods combining omics analyses; and a strong publication record in world-leading journals. We are therefore capable of developing novel research communication tools, blend research and education, and educate student ambassadors in public health.

The determinants of health in a life course perspective are complex and interrelated, as visualized in Figure 1. Childhood circumstances have a major influence on adult health related behaviour, socioeconomic position, and the quality of their social relationships. Education plays a key role, in that it critically affects the range of occupational opportunities and income, and hence social status. Furthermore, a fortunate social position generally impacts positively on health habits and social relationships. Conversely, for adolescents with a low level of education, the causal pathway involves limited occupation opportunities, low income, low status, unhealthy habits and less stable social relationships.

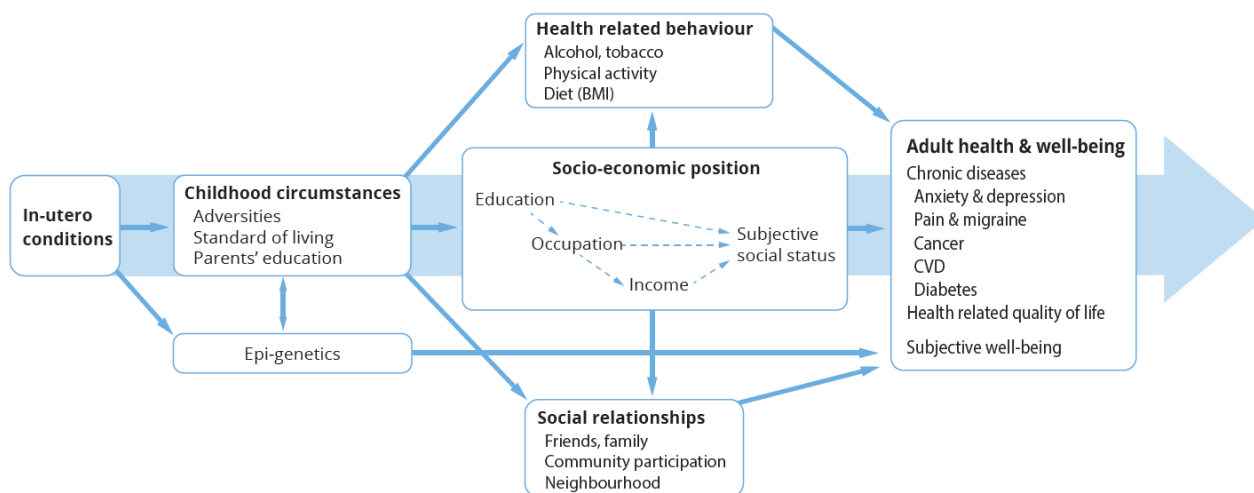


Figure 1. Life course framework on determinants of inequalities in health and wellbeing

Through this proposal we will address and explore general relationships between SES and health determinants, while we simultaneously will perform in depth similar analyses of the population of Finnmark, including the indigenous Sami population. Historically this population has been subject to more poverty and hardships than any other population groups in Norway. In 1899, Norwegian authorities decided that boarding schools were to be built in all Finnmark municipalities. Until the 1960s, a large proportion of the child population therefore lived away from their family for weeks at a time from the age of 7 years, and the Sami language was not allowed to be used at school. During World War 2, two thirds of the county population was forced to leave the county while the rest avoided evacuation by hiding during the withdrawal of German troops in 1944. After the war, most of the evacuees returned and had to rebuild the county that had been almost completely destroyed. The fact that the Finnmark Study and SAMINOR are among the cohorts included in this research proposal gives this network a unique opportunity to address vulnerable groups and the effects of structural and individual traumas.

We have accessible data based on the combination of observed health measures in population-based surveys (clinical tests and biomarkers), and subjects' own reporting of health-related behaviour, health-related quality of life (HRQoL), and subjective well-being. We have a longstanding experience in linking population-based data with national registries, i.e. the Cancer Registry and the Norwegian Cause of Death Registry. We will extend this by linking to other registries as the Medical Birth Registry of Norway, the Norwegian Prescription Database and The Norwegian Armed Forces Health Registry to gain a picture of the determinants that shape people's health trajectories, and which logically also may explain inequalities in health: childhood circumstances, socio-economic position, health-related behaviour and social relationships. It is crucial to distinguish between what are completely exogenous (e.g. gender and age) versus modifiable lifestyle factors, i.e. those which policy makers can influence, e.g. alcohol and tobacco habits, anthropometry, dietary habits, and physical activity. Given the wide range of health determinants, there is a need to enhance the knowledge-base on causes of the inequalities observed along the social gradient.

We will address current challenges in public health by acknowledging the systematic differences in health-related behaviour (i.e. substance use, diet, physical activity) over the life course across socioeconomic groups. The *Healthy Choices* research network will use unique epidemiological data from large population-based studies, with the possibility to link epigenetics to extensive exposure and outcome information. We will use our expertise in both observational epidemiology and intervention trials to gain evidence-based knowledge on what works, i.e. which interventions are most effective to improve overall population health and reduce health inequalities, using state-of-the-art statistical methods. Furthermore, we will consolidate and strengthen our status as an excellent research environment (RCN evaluations in 2003 and 2011) by extending collaboration to additional research groups within and beyond our Department. The research network will strengthen and increase our national and international collaboration on health equity through collaboration with recognized, established research groups, and by offering targeted adjunct positions to international partners.

3. The project plan, project management, organisation and cooperation

The Healthy Choices Research Network

The Healthy Choices Research Network is based on research groups at the Department of Community Medicine (ISM), UiT. The network includes researchers with a range of health professional backgrounds and related specialty fields (statistics, molecular genetics, health economy, psychology, environmental medicine, sociology, philosophy). Our research activity is based on large population studies and biobanks as well as RCTs and is well embedded in the UiT strategy towards 2020. Several of the scientists of the proposed *Healthy Choices* Research Network are leaders of health professional study programs on the BSc, MSc and PhD (National Research School in Population based Epidemiology) levels. This provides us with unique possibilities to blend teaching and research in novel ways by incorporating research issues and results into the various study program, including identifying topics and data that are relevant and suitable for student research; bachelor and master- theses.

The ISM employs a total of 200 staff, of whom 160 are academic staff, responsible for close to 100 ongoing external funded projects. Our research is based on well-established national and international networks and

institutional agreements and is far more extensive than described in this application. The research environment at ISM was graded as excellent by the RCN in 2003, and the two epidemiological research groups - System Epidemiology (SE) and Chronic Diseases Epidemiology (CDE) received excellent grading at the RCN evaluation in 2011. These groups are in charge of the NOWAC Study and the Tromsø Study. PubMed listed publications from the researchers at ISM in 2013- April 2018 numbers more than 900. This research platform introduces several novel concepts by including a large WP on novel science communication that will build knowledge among individuals that need it the most and provide decision makers with applicable knowledge. In addition we will, through WP 6 on Student knowledge, involve students in the planning, data handling, and analysis of a new research project on student lifestyle and health, providing them with unique hands-on research experience. Research findings will also be much more efficiently included in teaching and dissemination activities building interdisciplinary knowledge.

The research groups behind this proposal will act as a consortium that explores a number of unresolved issues on health and equity, including the suitability of traditional markers of SES. We will address the research questions through a number of work packages built on defined sub-projects. Each sub-project will have external academic collaborators on a national /international level, as well as collaboration with municipal and county health authorities as deemed necessary and adequate (Figure 2).

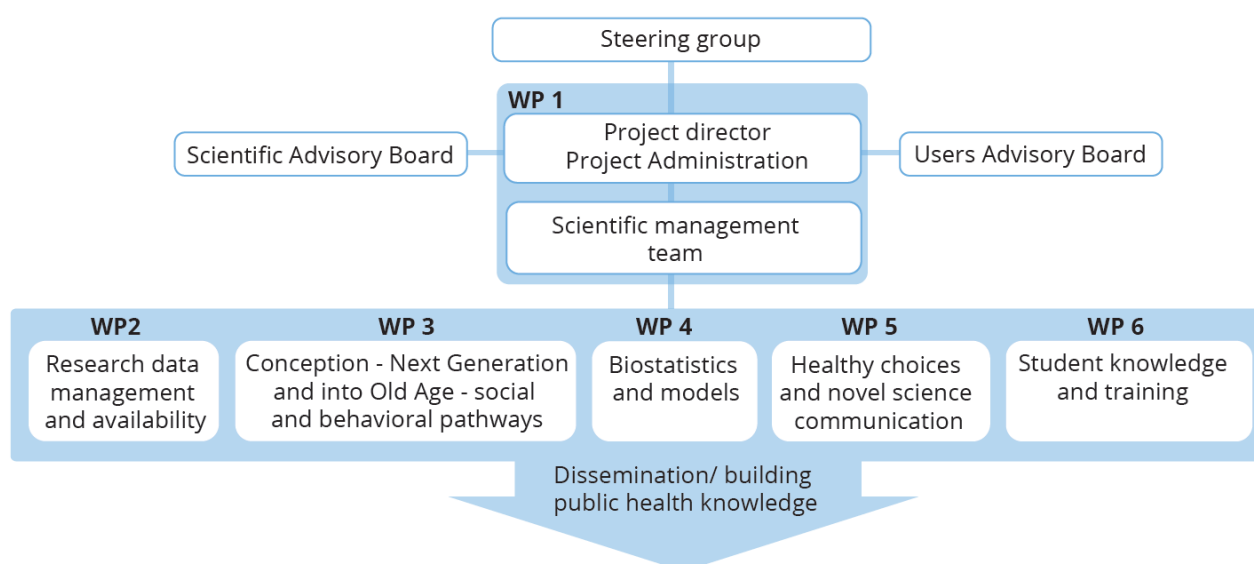


Figure 2. Project organization and administration

WP 1 Management

Steering group: The Board of the Dept. of Community Medicine will act as Steering Group for this project. The **Project director**, Prof. Inger Njølstad, has a clinical background as a primary health care physician, and has extensive research experience from the Tromsø Study and the Finnmark Study and several large RCTs since 1990. She was Head of the Tromsø Study 2005–2017, which included the planning and conducting of two large surveys, i.e. Tromsø 6 (12,000 participants) and Tromsø 7 (21,000 participants and 54 collaborating research sub-projects). She introduced important changes in the Tromsø Study regarding access to research data by means of the EUTRO/NESSTAR application and new policy for data delivery. This revolutionized research output from the Tromsø Study, from some 50 PhD theses 1974 – 2004 to 80 completed and 60 ongoing PhD projects 2005–2018. Njølstad was the first leader of the EPINOR research school (2007–9) and was a Faculty Vice Dean of education 2009–2017, a period with great institutional changes. Mergers between UiT and two regional university colleges in 2009 and 2015 did not only increase the number of health professional study programmes from 2 (medicine and pharmacy) to 13, but represented

a merger of different institutional cultures for education and research. Njølstad led a full revision of the 6-year medical study program and has introduced and implemented educational and pedagogical improvements, as evidenced by several awards (see CV).

The project administration will assist the project director and will be responsible for budget, reporting and arranging seminars and meetings.

Scientific Management Team: The scientific management team will assist the project director in coordinating the research and research-related activities as described in WPs 2-5. The team will include the leaders of work packages, core research facilities (EUTRO, biobank), and the population studies included.

Scientific Advisory Board (SAB): The SAB will advise the steering group and project director on scientific priorities and methods, and will be consulted on a yearly basis. The board will include representatives from collaborating national and international research institutions including the Life path consortium and the Västerbotten Intervention study.

Users Advisory Board (UAB): The UAB will advise the steering group and project director on the overall management and scientific progress of the project. The board will include partners and end users of the research output; i.e. representatives of municipality and county health authorities in Troms and Finnmark, the Arctic Student Welfare Organization, and the Student Parliament. The Users Advisory Board will be consulted regularly and will be invited to seminars arranged by *Healthy Choices*, along with politicians and key institutional representatives.

WP 2 Research data management and availability (Lead: ISM/Tom Wilsgaard, NIPH)

Main objective: To provide easy access to research data, including online analysis of data.

2.1 Data sources for research

Data sources	Sample characteristics			Data characteristics					Lifecourse questionnaire data			
	Year	Age groups	Repeated measurem.	Questionn.	Blood samples	Physiological measurem.	Clinical measurem.	Biobank material	Childhood	Youth	Adults	Elderly
Tromsø 1-7	1974-	20-104	X	X	X	X	X	X	X	X	X	X
Fit Futures 1-2	2010-	15-19	X	X	X	X	X	X	X	X		
Saminor 1-2	2003-	18-79	X	X	X	X		X	X	X	X	X
NOWAC	1991-	30-70	X	X	X			X	X	X	X	X
Norw. conscripts ¹	1968-	17-19		X		X				X		
Finnmark 1-3	1974-88	20-62	X	X	X	X			X	X	X	
TROFINN	2002	40,45		X	X	X			X	X	X	
40-yr programs ²	1988-98	40-42									X	

¹ Norwegian Armed Forces Health Registry

² Finnmark, Troms, Nordland

Figure 3. Major population based datasets to be used by the Healthy Choices project

The Tromsø Study is conducted in the municipality of Tromsø (current pop. 75,000), and is Norway's most longstanding and comprehensive cohort study [22, 23]. It comprises questionnaire data, biological specimens, clinical measurements and disease endpoint registries which are updated annually (national death and cancer registries). It was initiated in 1974 to study risk factors, causes and prevention of CVD.

Throughout seven consecutive surveys over the past 44 years, it has expanded to cover a wide range of risk factors, chronic diseases, use of health care services and disease endpoints. Clinical examinations comprise echocardiography, carotid ultrasound, electrocardiograms, body composition, retinal photography, pain sensitivity, spirometry etc. Altogether 45,473 persons have participated at least once and 18,510 have participated at least three times. Attendance rates between 65-77 % are among the highest in Norwegian cohort studies.

Fit Futures is a part of the Tromsø Study, was initiated in 2010 and invited all high school students in Tromsø and the neighboring Balsfjord municipalities. A total of 1,038 (93% response rate) first year students participated in 2010 and 870 took part in the follow-up examination two years later. The study comprises questionnaire data, anthropometric and clinical measurements, and biological samples.

The SAMINOR Study is a population-based study addressing the deficiencies of health information on ethnic groups in Finnmark municipalities and other municipalities with Sami and Norwegian populations [24]. SAMINOR 1 included inhabitants aged 30 and 35 – 79 years in 24 selected municipalities. The SAMINOR 2 Questionnaire Survey [25] was performed in the same areas as SAMINOR 1, and was followed

by a clinical survey in 10 selected municipalities. Questions on ethnicity were identical in all three surveys, and the study design included both self-perceived ethnicity and identity and objective and subjective criteria on Sami language, enables categorization of participants into indigenous versus non-indigenous groups [26-31].

The Norwegian Women and Cancer Study (NOWAC) is a randomly sampled, nationally representative prospective cohort study of 30-70 year-old (at entry) women initiated in 1991 [32], with study participants enrolled in 1991-92 (n=57 561), 1995-97 (n=44,836), and 2003-05 (n=70,081). The majority have filled in at least two follow-up questionnaires. The questionnaire includes detailed lifestyle information including SES and childhood conditions. Venous blood, and normal and pathological breast tissue, were collected in the 2003-2005 enrollees. The detailed and repeated information for each participating woman in a national representative study population, gives a unique opportunity to estimate population attributable fractions (PAFs) for possible single and/or combined risk factors for cancer and other non-communicable disease endpoints [33-36].

Norwegian Armed Forces Health Registry

The Norwegian Armed Forces Health Registry has since 1968 stored data on the health status of more than 1.3 million conscripts (8000 of these were women) born between 1950 and 2000. All conscripts have been subject to a thorough physical examination in addition to physical and mental performance tests.

The Finnmark Study

A total of 7 surveys in the county of Finnmark were carried out between 1974 and 2003 and provide very rich data material for analyses. The screening program structure ensured repeated measurements in a large number of attendees.

Other data sources are available through linkage between studies using the personal identification number: **National health registries:** Cause of Death registry, Cancer Registry, Medical Birth Registry, Norwegian Patient Registry, Norwegian Prescription Registry and others.

Historical population register (HBR) includes information on the Norwegian population from 1800-1964 and is administered by the Historical Registration Unit, at the Faculty of history, social sciences and teaching, UiT. Data are stored in EUTRO.

2.2 Easy access to research data: online data shopping and data analysis (Lead: Hans-Henry Jacobsen)

Data harmonization is crucial for research across population studies. [EUTRO](#) is a module-based unique database solution for research, developed at the Dept of community medicine, UiT. It is used for data registration, storage and retrieval, administration of biobank samples, and project administration. EUTRO is built on the Oracle database system and uses QBE Vision as a programming tool. This e-infrastructure was approved by the Norwegian Data Protection Authority in 2006, and was recommended for ISO certification. By using EUTRO combined with the NESSTAR WebView system developed by NSD, variables and metadata can be presented on the Internet. EUTRO is in use at UiT to manage data from the Tromsø Study (<http://tromsundersokelsen.uit.no/tromso/>), SAMINOR, and other large-scale research datasets. The Cohort of Norway Network (CONOR) (<http://conor.uit.no/conor/>) dataset is also presented by NIPH through the EUTRO/NESSTAR solution. Health Registries for Research (HRR) (RCN-funded infrastructure project) is using EUTRO to present variables and metadata from national health registries (<http://HRR.uit.no/hrr>). EUTRO thus fulfils the EU criteria for *technology readiness level 6* and GDPR requirements. Data from all seven surveys in the Tromsø Study have been harmonized, and researchers can access variables online for approved research projects. As a part of this proposal, we will harmonize research data of the NOWAC Study with the Tromsø and Finnmark Studies as well as SAMINOR to facilitate analyses across cohorts. We will use EUTRO/NESSTAR to present the variables at our *Healthy Choices* online portal. We are working closely with the Directorate of e-health to make research data available at a national online Health Analysis Platform (Helseanalyseplattformen). The platform is under construction, using IT architecture principles developed by our EUTRO system developers. We anticipate that it will be possible to link data from the cohort studies to national health registries and the Historical Population Registry, and will use the current EUTRO solution to prepare our datasets for future online analyses at the Health Analysis Platform at helsenorge.no.

WP 3 From conception to next generation and into old age – social and behavioral pathways

Lead: ISM/Sameline Grimsgaard, Torkjel Sandanger

Main objective: To provide novel insights on the complex interrelationship between the social and behavioral pathways that shape health over the life course, identify key modifiable risk factors at transition phases and across social gradients, and identify vulnerable groups for selected interventions.

Description of work: This WP will investigate the associations between traditional SES markers and modifiable risk factors in our different data sources, linked to hard endpoints (diabetes, cancer, CVD, total mortality). We will examine the appropriateness of traditional markers of SES, and critically evaluate the validity of these markers in a society where, for example, the achieved general level of education has increased substantially. We will use the comprehensively phenotyped Tromsø study cohort which has undergone measurements of **frailty, physical activity, impaired vision, cognitive function, renal function, osteoporosis, sleep disturbances, mental health**, etc. i.e. **functional components of ageing** to understand the ageing processes across the social gradient. Extensive transcriptomic and epigenomic data are available for the NOWAC cohort. These cohorts have follow up data from early adolescence to old age, and also include information from questionnaires concerning the participants' childhood conditions. Studies based on data from the SAMINOR study and the Finnmark County study will be included. In addition, a new youth study among high school students will be developed to complement the same age groups that were included in the Fit Future study. WP 3 also includes two sub-studies already partly funded by NFR and the Regional Research Fund.

Tasks:

3.1 Identify the best markers of inequality in health and healthy aging *(PI Jan Abel Olsen)*

We will describe and compare different measures of inequalities in SES (education, income, occupation) in the different cohorts and time periods, and link these factors with health outcomes (cancer, CVD, metabolic syndrome, self-reported health, mental health) and healthy aging.

3.2 Assess the relationship between key modifiable lifestyle factors over the social gradient and their impact on health and disease during transition phases *(PI Tonje Braaten)*

The contribution of selected modifiable risk factors (diet, physical activity, obesity, alcohol, and smoking) to inequality in health outcomes will be calculated using Comparative Risk Assessment methods and risk prediction models that are tailored to the target population.

3.3 Examine factors affecting self-reported health and different health trajectories *(PI Geir F Lorem)*

We will investigate the relationship between physical activity, diet, anthropometry, self-reported health (SRH,) health outcomes and survival. Analyses include the Tromsø, NOWAC, and SAMINOR studies, who contribute cohorts with repeated measurements. Latent trajectory models will be used to assess SRH changes over time, and to identify subgroups with different trajectories.

3.4 Identify resilient and vulnerable individuals and develop targeted interventions *(PI Sameline Grimsgaard, Ann-Ragnhild Broderstad)* Identify, describe and explore resilient and vulnerable individuals and groups within the NOWAC, SAMINOR and Tromsø study cohorts, and expand this knowledge to develop targeted interventions. A piloted intervention to improve lifestyle and physical function in elderly individuals with a low SES and a high disease risk will be further developed and tested, and we will include social networks and NGO's in the follow-up to improve sustainability of potential effects.

3.5 Assess the association between modifiable risk factors and “omic” markers *(PI Torkjel Sandanger)*

The association between modifiable risk factors and the transcriptome and the epigenome will be investigated using existing omics data in the NOWAC cohort. We will further explore how parental and individual lifestyle can possibly impact on alterations of the transcriptome and the epigenome, including the epigenetic clock. The possible impacts of social inequalities and social relations on epigenetic alterations in blood will be examined in the Tromsø and SAMINOR studies.

3.6 Examine the relationship between SES, anthropometry and epigenetic factors *(PI Inger Njølstad)*

A critical appraisal of the validity of traditional SES indicators (income and education length) and their temporal relationship to epigenetic markers and anthropometry (height, weight, waist circumference) will be explored in data derived from regional (Finnmark, Tromsø SAMINOR) and national (NOWAC) cohorts.

3.7 Fill the knowledge gap on youth health in Finnmark County *(PI Ane Kokkvoll, Tore Christoffersen)*

We will plan a youth study in Finnmark to include high school students (15-19 years) similar to the Fit Futures study.

3.8 Study CVD risk and cognitive function by SES and local environment (PI Maja-Lisa Løchen)

In a joint project using Australian and Tromsø Study data, we will study the interactive effects of physical activity, diet, smoking, alcohol consumption and sleep quality on cognitive function, CVD risk factors and disease, and whether these effects vary across SES. We will explore adding environmental data (physical and social characteristics of geographical areas) to the Tromsø Study to investigate the effects of direct, or lifestyle behaviour-mediated environmental exposures on CVD and cognitive health.

Ongoing and partly funded projects included in WP 3:

Tracing causes of inequalities in health and well-being: Analysis of rich longitudinal data (PI Jan Abel Olsen) (Research project ES 592437):

Objective and subjective measures of health in the Tromsø Study, including sudden health events, allow us to study how “health shocks” may lead to changes in health-related behaviors and job market participation. By linking data on health and well-being with information on early life events, health-related behavior, socio-economic characteristics, and social support, we will explore how individuals' early life circumstances and life course impact on their ability to cope with adverse health events. How people can partake through own efforts to improve their health, is of central importance for healthcare planners worldwide.

Sociocultural and structural factors determining health, illness and survival in Finnmark (PI Jorid Anderssen) (Regional Research Funds)

We will combine qualitative and quantitative research methods in two sub-studies to:

I) Study determinants and variation of survival over 30 years, linking population-based survey data from Finnmark III in 1987-88 with the Norwegian Cause of death Registry. We will explore how geographic, socioeconomic and cultural inequalities influence long-term survival, and employ a theoretical model comprising social and structural aspects, health perceptions, reported disease and illness experience with CVD-risk and behaviors as health risks. II) Investigate how social, structural and cultural factors influence people's perception of their health and well-being. We will use in-depth interviews of young and older adults in different (coastal, urban, Sami) municipalities in Finnmark, and focus on how informants perceive and experience their own health, and describe how it relates to their life situation, lifestyle and living conditions.

WP 4 Biostatistical methods and models (ICL/INSERM, UiT)

Objectives: The overarching goal of this WP is to explore available data to characterize the social exposome (the measure of all the exposures of an individual in a lifetime and how those exposures relate to health), relying on the definition of a clear, general and translatable methodological framework to

- Identify health relevant components of the social exposome
- Quantify exposome components' health effect
- Improve the understanding of their actual effects and their relationship to established (molecular) biomarkers and modifiable risk factors
- Assess biological consequences by exploring molecular profiles available in the cohorts
- Better understand their downstream consequences and disentangle the exposure, behavioral and physiological factors they capture.

Description of work:

Data from all cohorts will be used once collected, recoded, harmonized, and curated by WP2. A primary focus of the WP will be to develop statistical models to explore how socioeconomic status (SES), social capital, psychosocial and behavioral factors and biological markers are interrelated and related to health outcomes in a life course framework combined with the characterization of all risk factors including biological markers.

Task 4.1 Identify health-relevant and reproducible socioeconomic factors

Lead: Inserm (Participants: ICL, UiT)

Using the collated and curated data from WP 2, this task will first focus on the identification of social determinants and confounding/mediating factors of healthy ageing within each cohort, and will propose harmonization strategies to the database WP 2. Harmonization procedures will ensure comparability across populations and will account for the biological, and functional nature of these indicators and will also include their clinical relevance. Causal modelling including mediation analyses and structural equation models will

be used to assess the relative contribution of biological, environmental, psychosocial and behavioral components to i) the overall social exposome and ii) various health outcomes. Joint modeling of longitudinal and survival data will be applied to combine repeatedly measured exposure data with outcomes as diabetes, cancer, CVD, and total mortality.

Task 4.2 Characterization of the social exposome

Lead: ICL (Participants: INSERM)

The main objective of this task is to use life course socio-economic and psychosocial factors and examine their downstream biological consequences as measured by (possibly targeted) OMICS profiles. Life course analyses will first be carried out to understand the relative importance of SES and social factors at different time points on the outcomes, using a nested regression models approach. Due to the complex nature of socio-economic factors which capture a complex mixture of economic, psychosocial, environmental, and behavioral factors, these analyses raise interpretability challenges. Full results interpretation will rely on disentangling which (combinations) of factors directly or indirectly affect biology, and will be facilitated by exploring OMIC signatures of the social environment. Consistent and theorized socio-economic metrics developed in the first task will be related to health outcomes and molecular data. In a final step, multi-OMIC data (from the consortium and from publicly available data bases) will be related to reconciled SE indicators, in a life course context, to seek for biologically effective and interpretable molecular signatures of past SE experiences. Such analyses will rely on the combination of profiling techniques (e.g. univariate analyses, dimensionality reduction techniques, or variable selection approach) and network topologies. Envisaged network approaches will be either unsupervised (e.g. correlation network) or supervised (e.g. differential network).

Task 4.3 Combining life course approaches and exposome science to healthy ageing

Lead: ICL & INSERM

This task will combine social factors and related sets of (i) risk factors and (ii) molecular markers into longitudinal models of ageing to evaluate their respective contribution to individual ageing trajectories. We will develop individual-based dynamic models to reconstruct health individual trajectories using multi-state models. These models will incorporate life course features of the social exposome including OMIC markers of exposures and socio economic experiences. Accounting for these time-resolved risk drivers would improve the prediction of disease progression and add a dynamic element to the classical case/control discrimination problem. Specifically we will use established sequence analyses and hidden Markov Models and include selected OMIC and exposome signals in the models' parameter. Model selection approaches will identify step(s) of the health trajectories where the potential risk drivers are exerting their effect.

These approaches can be combined to micro-simulation approaches, and in order to perform health impact assessment, these will include counterfactual analyses to simulate interventions within and across cohorts. This last step will help identify modifiable factors of vulnerability and resilience that may define prioritised policy-relevant targets for future interventions.

WP 5 Healthy choices and novel science communication (Torkjel M Sandanger ISM, UiS, NIPH, key experts)

The main objective is to develop and implement new ways of communicating evidence from public health research to people and decision makers, which enable them to make more informed decisions about healthy choices and health care, reducing inequalities in health.

Description of the work: This WP will be led by UiT in close collaboration with science communicator and professor at UiS Jo Røislien. The work will also be monitored by Sarah Rosenbaum (Informed Health Choices) and Professor in Scholarly Communication Charlotte Wien (SDU). Tasks 5.1, 5.2 and 5.3 will be carried out in collaboration with a panel consisting of media students, SoMe-experts from the private sector and/or independent film production companies (e.g. Bulldozer Film) alongside with YouTube pioneers like Nordic Screens. We will also include representatives from the mass media prioritizing large national channels. In order to explore new and creative ways of promoting public health knowledge we will in particular collaborate with OsloMet researcher Ingrid Tolstad and projects like "Unge Kokker", using innovative strategies for gaining interest from, and interaction with, adolescents and young adults. All these experts will go through various health messages of core interest for the project, and target groups, and help

prioritize key messages and communication strategies. The risk factors and target groups will be based on findings from WP 3.

Task 5.1 Targeted use of Social Media for healthier choices

The aim is to build knowledge through targeted use of social media and create an arena for public health knowledge. We will explore the use of Social Media (Facebook/Instagram algorithm, others like Google algorithm, Snapchat etc.) to reach selected groups in specific case studies. In the complexity of online information; it is hard to reach the target groups with group-tailored information. Currently, the largest online companies within social media have the most control of what information goes to which target group – even when limited to the Norwegian population. Together with information designers (e.g. Astromaria.no Maria Hammerstrøm), health science bloggers (e.g. medical statistician Kathrine Frey Frøslie) and Snapchat communicators (as Helsesista) we will establish a format that is recognizable and trustworthy, focusing on short graphics transferable between different SoMe platforms. We will thus build knowledge in target groups and position ourselves and our collaborators as the social media source of informed decision making for public health topics in Norway.

Task 5.2 Use of entertainment in Mass Media

We will take further innovative steps in knowledge-building over the social gradient by actively using entertainment channels to integrate scientific knowledge into decision-making scenarios in drama and comedy series and other media channels targeted to adolescents and young adults. In close cooperation with producers of drama series we want to integrate the act of making choices, based on what we know from health research, into the fiction story of e.g. a Web-TV series, podcast etc. The target groups will indirectly learn about public health decision-making through their own choice of entertainment. The characters can give voice to typical healthy choices and behavior. The (Web-) TV series-campaign will in addition include the use of social media, blogs and tailored YouTube clips (as in task 5.1). Emphasis will be put on no “finger pointing” – only illustrative, real life, examples.

Task 5.3 Improving seniors’ health knowledge

It is important to reach vulnerable groups at their own frame of understanding. We will produce information tailored to their level of understanding. Information to support more informed decision-making will be distributed as short films on screens, billboards, Social Media advertisement, campaign for health apps and handouts at doctors’ offices, Norwegian Labour and Welfare Administration (NAV) offices, and in local newspapers. This action will be done in cooperation with the NAV (Tromsø) and Municipal MD Offices. Meeting points: NAV, Facebook, Healthy Choice Apps, Doctor’s office (Pasientsky) and local news papers

Task 5.4 Tracing public health knowledge building

We want to investigate our ability to reach target groups by designing specific questions in the follow-up of the cohorts involved where we ask specifically about knowledge communicated as part of this project. Tracing knowledge and skills in making informed decisions will be emphasized in the future planning of cohorts.

WP 6 Education and transition phases, student knowledge and training (Lead Kristin B. Borch, Student Parliament, The Arctic Student Welfare Organization, the municipality of Tromsø)

The main objective is to build a research program together **with** students, **for** students and **of** students in order to increase knowledge of the transition from youth to adult during the important years in which young people start their studying carrier at universities, and integrate education and research in student active learning.

Description of work: The program leader for the Master in Public Health program will lead this WP in close collaboration with the Student Parliament, the Arctic Student Welfare Organization and the Faculty of Health. In the project period we will develop the student’s welfare study for Troms and Finnmark together with the students and integrate the planning of this study and smaller pilot studies into different study programs at bachelor and master level, using PhD students as supervisors.

Task 6.1 The UiT Student Welfare Study

The aim for this task is **to plan and develop a study on student welfare** at UiT, the Arctic University of Norway at all 11 campus sites in Troms, Finnmark and Nordland. The Student Parliament, the Arctic Student Welfare Organization, Tromsø municipality and ISM will take part in the planning process. An important task is to write applications for external funding of data collection. The UiT Student Welfare Study will emphasize factors contributing to health and well-being as social network and relationships, empowerment

and resilience, mental health, lifestyle behaviors (physical activity, anthropometry, healthy diet, alcohol and smoking habits and sexual health), and issues related to study situation and completing a degree.

Task 6.2 Public Health in education

The specific aim for this task is **to integrate the research program into students' learning process** with the opportunity for students of several disciplines at UiT to take part in the research program i.e. Master in Public Health, medicine, PhD research schools, other health professional studies and other study programs relevant in public health. We aim to educate **student ambassadors in public health**. One task will be active involvement of students in performing small pilot studies on dietary interventions; i.e. master students in nutrition will plan menus, students from cook (chef) education will prepare meals in collaboration with the Arctic Student Welfare Organization, nurses, bioengineers and medical students will be involved in blood sampling, and analysis of markers in blood (lipids and immunomarkers) will be done by the bioengineers/biochemistry students. PhD students in epidemiology will help plan, implement and perform statistical analysis of the study. A second task is to integrate and develop student-centered research projects in the KRAFTFORSK facilities. This is comprehensive student exercise facility at UiT campus, that has an incorporated municipal general practice (GP) health center and associated laboratory facilities.

PARTNERS:

Imperial College London (ICL) -Department of Epidemiology and Biostatistics, School of Public Health, London, UK (Dr. Marc Chadeau-Hyam, Prof. Paolo Vineis, and postdocs) The group of Paolo Vineis includes world leading experts in Cancer and Molecular Epidemiology, Biomarkers, Biostatistics – Bioinformatics, Computational Epidemiology - Omics analyses. The group is responsible for a number of large EU projects and Paolo Vineis is responsible for EPIC Italy. Marc Chadeau-Hyam is the lead biostatistician in the group with an impressive track record in statistical methods and will be responsible for WP 4 in this project.

INSERM, the French institute for health and medical research, Toulouse, France. (Michelle K Irving and Cyrille Delpierre) INSERM is a public research organization in France entirely dedicated to human health and the research focus of this unit aims to increase knowledge about the pathophysiological and social determinants, patterns of care and the consequences of chronic diseases. Michelle Irving and Cyrille Delpierre will be responsible for the statistical methods development (WP4) and involved in statistical analysis in WP3 and supervision of postdocs.

University of Stavanger, Prof. Jo Røislien, Department of Quality and Health Technology, aims to provide end users and patients a higher quality health care. Their scientific profile emphasizes an interdisciplinary approach and involvement of students, patients, end users and health personnel. Jo Røislien has an impressive track record in Research Dissemination and use of mass media and will have a key position in WP 5.

National Institute of Public Health (NIPH), is in charge of the Finnmark Study and a number of national health registries. Division director Gun Peggy Knudsen represents the NIPH and will collaborate on data set harmonization.

Centre for Informed Health Choices, NIPH (Sarah Rosenbaum) The Centre develops and evaluates ways to make it easier for people to use research in decision making. The Centre was established by NIPH to conduct research on how to make research findings more understandable and accessible for everyone by developing and evaluating interventions. Sarah will participate in the forum for dissemination activities in WP 5.

The Arctic Student Welfare Organization and **The Student parliament**, at UiT will be involved in the planning and implementation of the Student Survey.

Researcher recruitment and career development

The research groups behind this proposal have a steady production of PhD candidates. However, positions as post docs and associate professors are few, and the age profile of the academic staff clearly indicates the need for recruitment in the coming 5-year period. Therefore, recruitment of young scientists at the postdoc level is a specific and important goal for this proposal. Six postdoc positions will be allocated to the research groups that participate in the proposed network. The young scientists will be hired for 3-4 years, to qualify for a position as an associate professor at ISM and other departments.

National and international collaboration

Through ongoing projects we have well-established and extensive national and international collaboration beyond the partners listed in this application. Examples of key national partners are UiO, NTNU, UiB, Nord University and HUNT. The international network is extensive in Europe, the US, and Australia, examples being EPIC, ERFC, MORGAM, IARC. The *Healthy Choices* research network will establish a Scientific Advisory Board with representatives from our collaborators and international partner institutions. We will also engage international collaborating scientists in 20% adjunct positions. We will encourage international young scientist exchange through dedicated funds for travelling and short stays.

4. Key perspectives and compliance with strategic documents

The national public health goals set out in the **White paper on public health** (Meld St. 19 (2014-2015)), to *Reduce social inequality in health and increase life expectancy and quality* are at the core of our project. It fits closely with the **Health&Care21 strategy** by using *Health data as a national competitive advantage*, to contribute *Knowledge mobilization in, for and around the municipalities*, *Develop human resources*, and feed *Strategic knowledge and quality-based governance*. The network activities support the national **Program for public health in the municipalities 2017-2027** that emphasizes quality of life and the importance of mental health, especially among children and youths. We will make national health data accessible according to the **National strategy on access to and sharing of research data**. The research focus on student health blended with student involvement in research will contribute new and vital knowledge to feed goals in the **White paper on quality in higher education** (Meld. St. 16 (2017-18)). We acknowledge the effects and potential impacts on the society and will develop novel strategies for research communication and dialogue in accordance with the **Responsible Research and Innovation (RRI)** framework put forward by the European Commission.

This *Healthy Choices* Research Network and the underlying WPs and projects complies with the **Strategy at UiT and Faculty of Health Sciences 2018-2022**, to develop *Cutting-edge knowledge on public health, preventing and curing disease, and improving living conditions for all age groups*. It extends the strategic project “*Population studies in the north*” that has received extensive funding from the UiT board in 2018-2021. The proposed network will provide further scientific renewal and recruitment that enables consolidation and development of our unique population studies, biobanks and methodological competence. Strengthening our international research collaborations will contribute to place us in a favorable position to *Attract national and international research funding*, which is a key strategic goal at UiT and the Faculty of Health Sciences. The **Department of Community Medicine** has pointed out *Molecular epidemiology* as a strategic area where we need to build competence to exploit the potential in our rich data sources.

Relevance and benefit to society

Identification of key modifiable risk factors, their interplay, and understanding of at what time in the life course a factor or combination of factors best can be targeted for intervention, can provide the relevant knowledge base needed for intervention. In addition the project will develop the necessary, up-to-date tools for such intervention both at the political, public health administrative and individual level.

Environmental impact

We have not identified any negative impacts on the environment.

Ethical perspectives

The research proposal is based in an environment that aims to explore conditions of health inequality. We also acknowledge our social responsibility as a research community to contribute to evidence-based actions that can bring positive consequences for the society.

The population based studies referred to, are defined as health registries for research and have been approved by the Data Inspectorate and the Regional Ethics Committee for Medical Research. This proposal will

address topics at the very core of those surveys. Data is stored in secure servers. Biological material is stored in the Department biobank, in accordance with the Norwegian Act on Biobanking. For the epidemiological analyses, individual researchers will not have access to personal identification number, name or address of study participants. Special attention will be given to research on vulnerable groups and sensitive issues. We will adhere to the proposed ethical guidelines for Sámi Health Research and Research on Sámi Human Biological Material, to be decided by the Sámi Parliament in 2018.

Gender issues (Recruitment of women, gender balance and gender perspectives)

Our network is well balanced with regard to gender throughout the project organization. The project leader is a woman, and both genders are represented as Work Package leaders and sub-task leaders.

Except for the one-gender NOWAC study, all datasets include both genders. In general, the network members promote and encourage gender-specific analyses in research whenever feasible.

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