MASTER'S THESIS IN HEALTH SCIENCE

# Physical activity and cognitive function in older adults

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# ACKNOWLEDGEMENT

This master thesis is written as a completion of the master degree "Health Science" at the Norwegian University of Science and Technology. The inspiration for this master thesis came from my engagement in physical activity and from my bachelor degree in public health. I have always liked being in activity, and based on that, developed an interest in how the activity is affecting our body. After finishing my bachelor degree in public health the interest for the health promotion aspect got bigger, especially regarding how physical activity could help in association with mental health and brain health.

In this master thesis I wanted to focus on the older adults as they are a group that easily is forgotten in the health promotions aspect. It also gave the opportunity to further investigate my interest for brain health and physical activity.

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# SUMMARY

The present thesis consists of two papers. The first paper is investigating the literature on the association between physical activity and cognitive function from a health promotion perspective. The second paper investigates the association between objectively measured physical activity and mild cognitive impairment by using data from the ongoing study "The Generation 100 study".

Demographical changes lead to new public health related challenges as a larger percentage of the population is getting older. To be able to face the challenges, knowledge about health promotion among older adults will become important. To achieve a healthy aging, it is important to find factors that can serve as resistance resources so health can be maintained or even improved in late life stage. One of the challenges connected to aging is the cognitive decline which will threaten the independency and quality of life for older adults, lead to increased burden for relatives, and increased health care and costly impacts on the society. Physical activity is brought up as a health promotion strategy as brain health and brains regions connected to cognitive decline, also seems to be affected by physical activity. Empirical research has shown promising findings regarding physical activity serving as a resistance resource for cognitive impairment, but some of the evidence are weak and some are even equivocal.

Multivariable analysis from the Generation 100 study (n=701) suggested that there was no beneficial effect of achieving the recommendations for weekly physical activity recommendations regarding cognitive impairment measured 3 years later, but considering other health benefits, the groups achieving the recommendations had significantly lower BMI. The results however, showed an increased risk of developing mild cognitive impairment for the participants having the lowest daily activity level compared to those having the highest level of activity, thus suggesting there is an association between daily physical activity level and development of cognitive impairment. More research on characteristics and modalities of physical activity and development of cognitive impairment in older people are needed.

# NORSK SAMMENDRAG

Denne masteroppgaven består av to artikler. Den første artikkelen undersøker litteraturen på sammenhengen mellom fysisk aktivitet og kognitiv funksjon og har et helsefremmende perspektiv. Den andre artikkelen undersøker sammenhengen mellom objektivt målt fysisk aktivitet og mild kognitiv svikt ved å bruke data fra den pågående forskningsstudien "Generasjon 100".

Demografiske endringer fører til nye folkehelserelaterte utfordringer da en større prosentdel av populasjonen blir eldre. For å kunne møte disse utfordringene vil det bli viktig å tilegne seg kunnskap om helsefremmende arbeid blant eldre. For å oppnå en sunn aldring er det viktig å finne faktorer som kan fungere som motstandsressurser, slik at helsen kan opprettholdes og kanskje også forbedres ved aldring. En av utfordringene tilknyttet aldring er kognitiv svekkelse, noe som vil være en faktor som svekker de eldres uavhengighet og livskvalitet. Videre kan kognitiv svekkelse føre til økt byrde hos pårørende, økt press på helsevesenet og sånn sett by på økonomiske utfordringer. Fysisk aktivitet er fremhevet som en helsefremmende strategi for kognitiv svikt da det kan se ut som regioner i hjernen og ulike reaksjoner i hjerneområder tilknyttet kognitiv svikt også blir påvirket av fysisk aktivitet. Empiriske forskning har vist lovende funn der fysisk aktivitet har fungert som motstandsressurs for kognitiv svekkelse, men noen av bevisene er svake og noen er også tvetydige.

Multivariate analyser fra studien Generasjon 100 (n=701) antydet at det ikke var en klar fordelaktig effekt av å oppnå de ukentlige anbefalingene for fysisk aktivitet med tanke på utvikling av kognitiv svekkelse målt tre år senere, men andre helsemessige fordeler tatt til følge, hadde gruppen som oppnådde anbefalingene for fysisk aktivitet statistisk signifikant lavere kroppsmasseindeks. Resultatene viste imidlertid en økt risiko for utvikling av mild kognitiv svikt for de deltakerne som hadde det laveste daglige aktivitetsnivået sammenlignet med de med høyest daglig aktivitetsnivå, hvilket antyder at det er en sammenheng mellom daglig nivå av fysisk aktivitet og utvikling av kognitiv svekkelse. Mer forskning på egenskaper og modaliteter av fysisk aktivitet og utvikling av kognitiv svekkelse hos eldre er derfor nødvendig.

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# MAIN INTRODUCTION

The main aim of the thesis was to investigate the association between physical activity and cognitive function in older adults. The populations are growing older and the percentage of the population over 65 is increasing. Strategies to maintain or improve the health in this group and find health promoting strategies will be important to keep up their quality of life.

This master thesis is divided into two connecting articles. The first article is a theoretical article which contains the theoretical and empirical foundation article two is based upon. The first article aims to give a theoretical framework for health promotion, physical activity and cognitive function. It also looks at empirical foundations for the association between physical activity and cognitive function. The article is based upon theoretical and empirical foundations retrieved from literature search. Databases used in the study was mainly PubMed, Science Direct, and Cochrane, and the most used search words in the databases were physical activity, exercise, training, cognition, cognitive impairment, cognitive decline, healthy aging, and demographic changes. In addition to literature search, the "snowball" method was used to find similar articles listed in the reference lists from studies retrieved from the databases. Last, books based on the same search words were used to lay the theoretical foundation.

The second article is an empirical article investigating the association between objectively measured physical activity and cognitive impairment. The study is quantitative and based upon data from the Generation 100 study, which is an ongoing project governed by Cardiac Exercise Research Group (CERG) at the Institute of Medical Imaging and Circulation at Norwegian University of Science and Technology (NTNU).

The Publication Manual of the American Psychological Manual (APA 6<sup>th</sup>) has been used as a writing and reference guide. The articles are written for a possible publication in Journal of Mental Health and Physical Activity, an international peer-reviewed journal approved by the Norwegian Register for Scientific Journals, Series and Publishers.

**ARTICLE 1** 

# "Physical activity, cognitive function and health promotion"

#### Abstract:

As the demographical change continues resulting in an older population, the health promotion work in the group of older adults will become necessary. It is important to acknowledge that the health of older adults might be perceived as good even though they have different health issues. In this context, this article focuses on healthy aging, and addresses the relevance of physical activity as prevention of one of the largest health challenges in the group of older adults: mild cognitive impairment and dementia. According to literature, physical activity seems to have an effect on cognition, in addition to affect structural mechanisms in the brain resulting in a preventive state of cognitive decline. However, metaanalyses conclude that more research is needed to strengthen the evidence, and to address which type and dose of physical activity behavior is most beneficial for preservation of cognitive function in older adults.

Keywords: aging, demographical changes, exercise, cognitive impairment, dementia, brain

#### Abbreviations:

PA – Physical Activity, AD – Alzheimer's Disease, MCI – Mild Cognitive Impairment, MoCA – Montreal Cognitive Assessment, MMSE – Mini Mental State Examination, MVPA-Moderate-to-vigorous physical activity, RCT -Randomized Controlled Trial.

# **1.0 Introduction**

Demographical data shows an increase in the share of people over 60 years old, and by 2050 the share is predicted to be over 21% (Norwegian Directorate of Health, 2015). This development will result in new public health related challenges due to an increase of the prevalence of diseases commonly for the elderly.

Genetic factors and disease development are well-known factors that affects the aging process. Factors like physical activity (PA) and exercise can help prevent and reduce age related physical and psychical changes. PA is also important in maintaining a respectable level of mobility during the day, resulting in increased opportunity for an independent life (Helsedirektoratet, 2017). Regardless of age, PA can be joyful, social and beneficial, and increase life expectancy (Lohne-Seiler & Torstveit, 2012). However, the population has in the past decades become less active. A reduced daily activity level due to an industrialized and technological society is mainly to blame for the development as sedentary work-behavior and public transport leads to an inactive lifestyle (Lohne-Seiler & Torstveit, 2012).

WHO defines older adults to be the age of 65 + (WHO, 2011). Common reported health issues among older adults is difficulties dealing with daily basic activities, mobility muscle strength, and balance (Swedish National Institute for Public Health, 2006). I addition, one of the challenges related to an older population is the decline in cognitive function, as ageing being the biggest risk factor for cognitive impairment (Cohen, Verghese, & Zwerling, 2016). 47 million people are living with dementia worldwide, and with the demographical changes the world are facing, these numbers are expected to double (United Nations, 2015). Cognitive impairment is a public health issue to the extent that it can lead to less quality of life and fewer active years, and lead to walking problems and social setting issues for the older adults (Cohen et al., 2016). Decline in cognition for older adults will also affect their caregivers as it can be physically and psychically demanding being caregivers for people with dementia. It can also lower the caregivers health and quality of life (Livingston et al., 2017). It is important to understand these issues, and find health promotion strategies facing the challenges with a continuously growing older population.

The main aims of this article is firstly to look at different approaches to health and healthy aging and discuss how to approach health promotion for older adults. Secondly, the

article looks at PA as a possible factor that can decrease the risk of physical and psychical age related challenges, especially the association to cognitive function. A theoretical description of health, health promotion and healthy aging will be given, in addition to a description of PA and cognitive function.

# 2.0 Theoretical background

#### 2.1 Demographical changes - the population is growing older

The world is facing a demographic transition in population structure and are going from a society where women give birth to many children, where few of them grow up, to a society where women are having fewer children, but most of them grow up. At the same time the population live longer (Halvorsen, 2013). Due to the increase of life expectancy and the decline in fertility rate the population is continuously growing older (Rossini & Marra, 2014; Swedish National Institute for Public Health, 2006). This is an ongoing process in almost every country in the world, however the different countries are in different parts in the transition. Europe is now reaching the end of the transition with a birth rate of 2,1 or less (Halvorsen, 2013) and is particularly exposed to the changing structure as a result from the large amount of people born after World War II (StatisticsNorway, 2014). There is expected a four-fold increase of people between 80-89 years old before the end of this century and the life expectancy for Norwegian men is expected to rise from today's 79.6 to 91.3 by the year 2100. For Norwegian women is it expected to rise from 83.5 to 92 years old in the same period (StatisticsNorway, 2014). By 2050, 21.1 % of the world's population will be over 60 years old (United Nations, 2015).

The predominance of older people will eventually create a challenge for the society as a whole as there will be fever people of working age to support the elderly in retirement (Rossini & Marra, 2014). As the population grows older, there will be an epidemiological change where there is expected a decrease in infectious diseases, but an increase in chronic diseases, which eventually will be one of the biggest challenges for the health care systems the next 25 years (Halvorsen, 2013).

For the society to be able to face these challenges, there will be important to increase the knowledge about health promotion among older people. By increasing their health and quality of life in later life stages, they will be able to live independently in their own homes, which will have a beneficial effect for both the older adults themselves and on the rest of the society considering health care and costly impacts (Swedish National Institute for Public Health, 2006).

#### 2.2 Definitions of health and health promotion

When talking about health and health promotion, there is different perceptions of what lies in the terms. A commonly used definition to explain health is the one from the constitution of the World Health Organization (WHO) in 1948. The definition describes health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 2006, p. 1). This definition brought attention as no longer only physical conditions and diseases where parameters of health as understood from the biomedical model, but also mental and social well-being (Huber et al., 2011).

The aspect of mental and social wellbeing is also apparent in the bio-psycho-social model which came as a holistic alternative to the former biomedical model domination the understanding of health to the mid-20th century (Borrell-Carrio, Suchman, & Epstein, 2004). The model reach to explain the complexity in the relationship between mental and physical aspects (Borrell-Carrio et al., 2004). Health is being influenced by biological, social and psychological factors, in addition to how we live and the community surrounding us. To understand what influences health it is important to focus on health treats, in addition to what promotes and protects health. Due to its holistic approach, the bio-psycho-social model has contributed to increase the focus on the health promotion aspects, and how to avoid development of illness and reduced quality of life (Espnes & Smedslund, 2009).

In context with health promotion, health is often defined as a continuum with different degrees of health, unlike the definition from WHO were health is understood as one state of complete wellbeing. This continuum is described as a horizontal line which stretches from H+, which is the subjective feeling of good health, to H- which is the subjective feeling of poor health. All humans are somewhere on this line, and all factors improving health and creates a movement towards H+ is seen as what is called a salutogenic approach (Lindström & Eriksson, 2015). With a salutogenic approach, the focus is on those factors which will create a higher degree of health and the possibilities humans have to achieve good health (Sletteland & Donovan, 2012). The ideal behind the approach is that if people live by the salutogenic approach, the population will achieve a longer life and create a positive health behavior (Lindström & Eriksson, 2015). The model focuses on to key concepts which is "sense of coherence" (SOC) and "resistance resources". SOC can be understood from the aspect of comprehensibility, manageability and meaningfulness, and the theory is that people with strong SOC have an understandable, manageable and meaningful life. SOC is seen as a resource for people to cope with stress. Resistance resources are crucial for the development

of SOC and may include physical, cognitive or emotional features of an individual, group or community that helps prevent or combat stressors, thus preventing tension from being converted into stress (Lindström & Eriksson, 2015). The focus on the humans resistance resources and their ability to create good health rather than focusing on poor health is a central part of the model (Sletteland & Donovan, 2012). To achieve a good health in late life stages, it is important to find factors who can serve as resistance resources to the challenges associated with growing older an in that way achieve a healthy aging and strong SOC (Lindström & Eriksson, 2015).

#### 2.3 Healthy aging -a part of health promotion

Health promotion is a term which contains many aspects. Healthy aging is one of the aspect who developed in the wake of health promotion. Regarding the definition of healthy aging there is a lack of consensus, and therefore no unanimous definition of the term (Daskalopoulou et al., 2017). WHO describes healthy aging as "the process of developing and maintaining the functional ability that enables wellbeing in older age" (WHO, 2015, p. 28). With functional ability means having the capabilities to do the things you value, such as meeting basic needs, learn and make decisions, and to maintain relationship with others and the society. In functional ability, intrinsic capacities plays a part and consist of mental and physical capacities including walking, thinking, seeing and remembering. WHO also underline that healthy aging does not require being free from disease or infirmity, as the diseases might not influence their overall wellbeing (World Health Organization, 2018).

In another report from EU "Healthy aging – A challenge for Europe" healthy aging is described as "a process of optimizing opportunities for physical, social and mental health to enable older people to take an active part in society without discrimination and to enjoy an independent and good quality of life" (Swedish National Institute for Public Health, 2006, p. 16). This definition takes in focus on equity in health and an independent life of good quality.

Fuchs et al. (2013) has identified components for healthy ageing which included good quality of life, survival to a specific age, autonomy in activities of daily living, little or no chronic diseases or disabilities, high social participation, no mild cognitive disability and behavior including PA (Fuchs et al., 2013).

Even though there is no clear definition of the term healthy ageing, factors that will allow individuals to have a healthy aging both physically and mentally, are suggested. There

is an agreement that modifiable factors can decrease the risk of premature death, prevent sickness and increase quality of life, the likelihood of healthy aging will increase (Daskalopoulou et al., 2017). Healthy aging is often affected by a unhealthy lifestyle with inactivity, smoking and alcohol as some of the greatest threats. A systematic review found that in studies done on the association between PA and different approaches to healthy ageing that those participating in PA had increased odds of a healthy aging compared to those being inactive (Daskalopoulou et al., 2017). The authors concluded that interventions to increase the chance for a healthy aging therefore should include PA.

#### 2.4 Physical Activity (PA) and sedentary behavior

The most popular and cited definition of PA came in 1985 by Caspersen and colleagues. They defined PA as "any bodily movement, produced by skeletal muscles, that requires energy expenditure" (Caspersen, Powell, & Christenson, 1985, p. 126). This definition is commonly used in context with health enhancing PA (Strath et al., 2013). PA can be divided into two different categories: Structural or incidental. Structural PA is often referred to as "exercise", and the activity is planned and undertaken to promote health benefits. Incidental PA is when the PA is unplanned and consist of daily activities (Strath et al., 2013). PA is a result from increased energy expenditure due to an increase in intensity level of the PA, and are commonly measured in metabolic equivalent (MET), kilocalories or time spent in different PA intensity categories (Strath et al., 2013). PA can occur in different dimensions and different domains and Strath et al. (2013) suggested that PA could be divided into four different dimensions being frequency, intensity, duration and type, and four different domains being leisure-time related, domestic, transport related and occupation related (Strath et al., 2013). Health enhancing PA may occur in all of these four domains and all dimensions.

Sedentary behavior: There is no standardized definition of sedentary behavior. There are however some definition explaining the term. One of the definition used is sedentary behavior being activities equivalent to intensity  $\leq 1.5$  METS. Another frequently used definition is based on the same intensity in addition to characterizing sedentary behavior as any waking behavior with energy expenditure  $\leq 1.5$  METS while in a sitting or reclining posture (Gibbs, Hergenroeder, Katzmarzyk, Lee, & Jakicic, 2015). Sedentary behavior can also be defined by counts per minute (CPM) <100, which is an intensity measure used in conjunction with accelerometers (Freedson, Melanson, & Sirard, 1998; Troiano et al., 2008).

**PA recommendations:** The Norwegian recommendations for PA and sedentary behavior for elderly over 65 years is based upon the recommendations from WHO being 150 minutes per week with moderate intensity, 75 minutes of vigorous intensity or a combination of these two. It is also recommended to do muscle strengthening training two days a week and minimize the sedentary behavior (WHO, 2011). According to a Norwegian study conducted in 2009 only 20 % of the elderly is achieving the PA-recommendations. The objectively measured activity level was also declining significantly as the age increased and the oldest group of 80-85 years had 50% lower level of activity compared to the youngest group of 65-69 years (Lohne-Seiler & Torstveit, 2012)

Assessment of PA: Empirical evidence supports that PA has beneficial effects on people's health and wellbeing (Helsedirektoratet, 2017), but there is still challenges associated to employing a valid and reliable measure of PA (Sylvia, Bernstein, Hubbard, Keating, & Anderson, 2014). To understand the relations between PA and health, and determining the effect of a PA intervention it is important to find the method suitable to the intervention, as well as finding a method which can be to minimal discomfort for the subject. The method needs to be able to measure PA over periods long enough to be representative for the normal daily life and be applicable to larger population (van Schooten et al., 2015).

The different methods used to measure PA can be divided into two different groups: objective and subjective methods (van Schooten et al., 2015). *Objective methods* include doubly labeled water, heart rate monitors, and motion sensors such as accelerometers (Trost & O'Neil, 2014). *Subjective measures* include self-reported information like diaries self and, questionnaires, in addition to interviews and behavioral observations (Sylvia et al., 2014).

**Health related benefits of PA in older adults:** Regular PA, is according to epidemiological studies, beneficial to the health of the older adults, and promotes health by being associated with higher degree of self-efficacy, quality of life, and reduces physical and psychical age related challenges. PA is also seen as preventive against chronic diseases and functional deficits that creates limitations in every-day life (Fuchs et al., 2013). Older adults staying active seems to have several years more without chronic diseases compared to their counterparts being physical inactive, suggesting that inactivity plays a bigger part in the development of chronic diseases compared to the biological aging process itself (Helsedirektoratet, 2017). Increased cardiorespiratory fitness which is the ability of circulatory, respiratory, and muscular systems to supply oxygen during sustained PA (Lee, Artero, Sui, & Blair, 2010) can prevent cardiovascular disease, and strength training leads to

an increase in muscle mass and muscle strength, which all results in better physical abilities (Pedersen & Saltin, 2015). Further, PA affects bone mass and balance, coordination and movement, and due to that, decreases risk of falling accidents and fractures (Helsedirektoratet, 2017). PA also seems to be positively associated with mental factors and quality of life for elderly, especially considering depression, dementia and cognitive impairment (Helsedirektoratet, 2017). Regarding depression PA is shown to have beneficial effects both as a preventive strategy, but also as s treatment strategy (Belvederi Murri et al., 2015; Dinas, Koutedakis, & Flouris, 2011; Mammen & Faulkner, 2013). Studies have further shown possible associations between PA and cognitive functions such as memory, concentration, attention and reaction time (Helsedirektoratet, 2017; Sofi et al., 2011). PA is also shown to contribute to enhancing SOC in older adults, which give them better resistance to stress and increased quality of life (Monma, Takeda, & Okura, 2017). PA generally decreases with time and age, and it is important to keep the activity level for the older adults on a sufficient level so they can achieve a healthy aging (Fuchs et al., 2013).

#### **2.5 Cognitive function**

Cognitive function is a term used for domains that has a rough correspondence with cerebral localizations. The domains are often divided into 5 different groups which is; learning and memory, language, visuo-spatiel, executive and pshycomotorich function (Knopman & Petersen, 2014). Cognition is a definition that includes all stages of cerebral function, representing the spectrum from high order cerebral function to Alzheimer's' disease. Aging is the biggest risk factor for cognitive decline (Cohen et al., 2016). Some cognitive declines are considered normal and a part of the healthy aging, but some of the changes are related to neurodegenerative diseases such as dementia and Alzheimer's Disease. Before reaching the stage of AD or other types of dementia, it is normal to reach the stage called mild cognitive impairment (MCI) (Kirk-Sanchez & McGough, 2014).

**Mild Cognitive Impairment (MCI)**: The clinical state between normal cognitive function and dementia is called mild cognitive impairment (MCI) (Nasreddine et al., 2005). MCI is diagnosed by decline in cognition from previous tests, or from screening tools adapted to measure cognitive decline, but at the stage of MCI there is still possible to employ compensatory mechanisms to maintain basic functions and function independently or nearly so in daily life (Knopman & Petersen, 2014; Nasreddine et al., 2005). To be able to make a

MCI diagnosis, only one of the five different domains needs to be impaired, with memory often being the earliest established cognitive decline (Knopman & Petersen, 2014). MCI is now considered a diagnosable state, often connected to early set Alzheimer's Disease (AD), and MCI is therefore associated with significantly higher risk for worsening and for further progression to dementia and AD (Knopman & Petersen, 2014; Nasreddine et al., 2005). This results in a stage where daily activities are impeded due to the decline in function (Cohen et al., 2016). An estimation of prevalence of cognitive impairment, including MCI, but not yet dementia, is estimated to be at 22 %. 12% of these cases are expected to progress to AD or other types of dementia annually (Kirk-Sanchez & McGough, 2014). Accurate diagnosis of MCI and treatment will become more important as the populations grows older (Nasreddine et al., 2005). Both prevention and treatment focusing on staying physically, socially and mentally active have grown to become more important the last years (Knopman & Petersen, 2014; Livingston et al., 2017).

There are some predictors for optimal aging and modifiable risk factors regarding MCI and AD. Factors as smoking, diabetes, vascular diseases, too high or too low BMI, low education and inactivity are listed as risk factor considering MCI and dementia. Also psychological factors such as stress and depression are associated with increased risk of dementia (Xu et al., 2015). High levels of stress is associated with increased risk of amnestic MCI (aMCI) which primarily affects memory function, and stress is associated with 30 % increased risk of development of aMCI (Katz et al., 2016). Depression is also a psychological factor which commonly occurs in association with MCI, and recent evidence suggests that depression has a negatively effect on the progression from MCI to dementia as it makes the progression go faster (Ismail et al., 2017; John, Patel, Rusted, Richards, & Gaysina, 2018). Effective interventions targeting stress and depression through PA and good social support is seen as protective to MCI (Goveas et al., 2016; Xu et al., 2015). So for reduction in development of dementia, Goveas et al. (2016) recommend to prioritize prevention and to address sociodemographic differences. Further the authors suggest an increased focus on mental health and reduction of depressive symptoms, interventions regarding vascular disease and diabetes, and interventions regarding PA, cognitive and psychosocial functioning (Goveas et al., 2016).

Assessment of Cognitive Function: To avoid risk of complications it is important to diagnose MCI and dementia at an early stage, but the diagnosis is commonly overlooked in health care with a range from 25-90% (Tsoi, Chan, Hirai, Wong, & Kwok, 2015). There are

numbers of different screening tests which are quick and useful customized to assess cognitive conditions (Trzepacz, Hochstetler, Wang, Walker, & Saykin, 2015; Tsoi et al., 2015). The Mini Mental State Examination (MMSE) is the most frequently used test by physicians for general cognitive evaluation, but other screening tests such as Mini-Cog test, the Addenbrooke's Cognitive Examination–Revised (ACE-R) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) also show comparable diagnostic performance (Tsoi et al., 2015). However, there has been difficulties detecting MCI and early dementia with the MMSE (Nasreddine et al., 2005). As a result, the Montreal Cognitive Assessment Test (MoCA) test was developed to screen patients with subjective feelings of cognitive decline that scored in the normal rage of MMSE. The MoCA test is a screening tool able to distinguish cognitively intact older people from the ones with MCI (Nasreddine et al., 2005) and is considered the best screening tool for detecting early MCI (Trzepacz et al., 2015; Tsoi et al., 2015).

## 3.0 Empirical findings on the association between PA and CF

#### 3.1 Potential mechanisms in the association between PA and cognitive function

Aging leads to alterations in brain structure and function, which eventually leads to cognitive changes. The decline in cognition is well documented as a normal consequence of aging, and these changes are called age-related cognitive changes. There are however some cognitive changes that are related to neurodegenerative diseases such as dementia, called disease-related cognitive changes (Kirk-Sanchez & McGough, 2014).

I the third decade of life, the brain beings atrophy resulting in changes in different parts of the brain. Executive functions such as decline in attention-switching, daily living activities and slower response time, rely on the frontal cortex of the brain. As a result from normal aging, the frontal cortex loses volume and function, resulting in loss of executive function (Jernigan et al., 2001). In the case of MCI and AD which is neurodegenerative diseases, the brain atrophy is shown trough functional magnetic resonance imaging (fMRI) to have more profound effect seen on the hippocampus (Dickerson et al., 2004; Dickerson & Sperling, 2008).

PA might be preventive to cognitive decline both indirectly through reduction of cardiovascular risk factors and directly through shared pathways (Cohen et al., 2016). Indirectly, higher levels of cardiovascular fitness are related to less age-related volume loss in frontal lobe (important for planning and multi-tasking), parietal and temporal lobes who contains the hippocampus (extremely important for memory function), in addition to increased neuro activity and increased cerebral blood flow (Kirk-Sanchez & McGough, 2014). It is shown trough a study with magnetic resonance imaging (MRI), a noninvasive technique that produces computerized images of the brain, and trough reviews of PA interventions that PA change the structure and function in the same brain region vulnerable to age and disease-related atrophy, suggesting that brain health could be enhanced by PA (Colcombe et al., 2006; K. i. Erickson, Gildengers, A.G., & Butters, M.A., 2012).

Animal studies done on the association between PA and cognitive function show compelling evidence for PA being able to promote neuroplasticity in the brain as running and exercise leads to increased growth factors, a healthier and larger hippocampus, and hippocampal neurogenesis in the mice (Ahlskog, Geda, Graff-Radford, & Petersen, 2011; Cotman & Berchtold, 2007). This is supported by cross-sectional and intervention studies using MRI in humans who found that higher levels of PA resulted in increased release of protective neurothrophins such as brain-derived neurotopich factors (BDNF), and larger hippocampal volume bilaterally, with a percentage of 2 % which is equivalent to reverse agerelated loss in volume by 1-2 years (K. I. Erickson et al., 2009; K. I. Erickson et al., 2011). The increased hippocampal volume as result from PA is also supported by the findings of ten Brinke et al. (2015) after a PA intervention using MRI as evidence (ten Brinke et al., 2015) Further studies done to investigate BDNF also confirm the finding of Erickson et al (2011) regarding increased release of BDNF due to PA. In addition, studies show same results as the animal studies did, finding increased level of nerve growth factor (IGF-1) as a result from PA, which promotes nerve growth in some brain regions including hippocampus (Cassilhas et al., 2007; Seifert et al., 2010).

#### **3.2 Different type of PA and cognitive function**

The empirical studies on the association between PA and cognitive function, uses different study-designs, different measures of PA and different definitions resulting in different findings.

**Observational studies:** When looking at observational studies there is evidence that higher levels of PA have a protective benefit against cognitive impairment. A prospective study done by Stubbs et al .(2017) over 22 months, reported positive association between moderate-to-vigorous PA (MVPA) and cognition (Stubbs, Chen, Chang, Sun, & Ku, 2017). This finding is supported by a cross-sectional study were the highest PA tertile performed significantly better than those in the lowest PA tertile on the cognitive screening (Brown et al., 2012). The Nurses Health Study in women (n=18766) investigated the association over a 2 year period, finding that higher levels of PA were associated with better cognitive function and a decreased risk for developing cognitive decline and dementia. The activity in this study also included easy PA such as walking (Weuve et al., 2004). There have also been longitudinal studies suggesting there is a dosage effect of PA on brain health, one of them being a study done by van Gelder et al. (2004) were the study based the findings on activity dose during a period of 10 years (van Gelder, 2004). The authors found that a decrease in intensity of PA of at least half a standard deviation was associated with a 3.6 times stronger cognitive decline than maintaining the same level of intensity (van Gelder, 2004). There have also been longitudinal studies looking at variety of exercise, and the Doetinchem study done by Angewaren et al. (2010) for a period of 5 years provided evidence that different PA

activities is beneficial to cognitive function, but intensity rather than duration of time spent in PA was associated with decreased risk of cognitive decline (Angevaren, Vanhees, Nooyens, Wendel-Vos, & Verschuren, 2010).

Other evidence suggest that any frequency of moderate exercise is associated with reduces risk of MCI when performed in mid-or late life (Geda, 2010). Middleton et al. (2010) also did a cross-sectional study on 9344 women at 65+ suggesting women who were active in any point in life, but especially as teenagers had reduced risk for cognitive impairment later in life (Middleton, Barnes, Lui, & Yaffe, 2010). Unlike the studies above, The John Hopkins Precursors study who is a 30-year cohort study, did not find any association suggesting that midlife PA was associated with cognitive health in later life. There were however some positive associated with better cognition in 2008, but higher level of PA in 2006 was associated with better cognition in 2008 (Gross et al., 2017).

Aerobic exercise intervention studies: Several exercise trails investigating the effect of PA on cognitive impairment and dementia have included older adults. Lautenschlager et al. (2008) did a 24 weeks long randomized controlled trial (RCT) with 170 older adults with cognitive complaints and at risk for further development to dementia and AD. They were instructed to do 50 min with MVPA 3 times a week, which corresponds to PA recommendations, for 6 months. Those already achieving the recommendations were instructed to do an extra session a 50 min MVPA. 18 month follow up showed only a modest improvement in cognition (Lautenschlager et al., 2008). Another study also done with 54 older adults at risk for dementia showed an active lifestyle to be more beneficial than a training intervention after a 10 week PA intervention and lifestyle mapping. The results showed no effect on cognition after a 3 month follow up after the intervention. However, the study only had a 10 week intervention, which might be too little to give any effect (Kuster et al., 2016).

Some PA intervention studies done on older adults already in state of dementia has shown promising results regarding delay in further progression. A RCT with 191 institutionalized participants doing 15 min cycling daily for 15 months showed a slight improvement in some cognitive domains especially memory function, compared to those not included in the PA intervention who had a statistical significant decline during the same period (Cancela, Ayan, Varela, & Seijo, 2016). Middleton et al. (2012) did a RCT with 126 participants with cognitive complaints. They were randomized into a 12-week study with 60

min of activity 3 days a week. The intervention group showed improvements in physical performance which again was associated with improvements in executive function. This might indicate that some of the cognitive improvements are due to the intervention, however the association is not strong (L. Middleton, Santos-Modesit, W., Poelke, G., Yaffe, K., & Barnes, D., 2012). This is supported by a study done by Linde & Alfermann (2014) who after their trial with 70 healthy older adults only could refer to limited effect only on concentration after the PA intervention (Linde, 2014).

**Resistance exercise interventions:** Regarding resistance exercise the empirical evidence is limited. There are however some studies investigating the effect resistance training has on cognitive function. van de Rest et al. (2014) did a 24-week long randomized controlled trial (RCT) with 127 participants with resistance-type exercise program consisting of two sessions per week. They found that resistance exercise training was beneficial for attention and working memory, but did not show any results for other cognitive domains (van de Rest et al., 2014). Best et al. (2015) also did a RCT with 155 women doing 52 weeks of resistance training twice a week or balance and toning twice a week. They were tested at baseline, 1 year follow up and 2 year follow up. The study found improvement in executive function and memory at 2 year follow up and suggested that resistance training might have a long-term effect on cognition (Best, Chiu, Liang Hsu, Nagamatsu, & Liu-Ambrose, 2015). A third study based on a 24-week long intervention with 62 men divided the participants into 3 groups: control, moderate intensity resistance training and high intensity resistance training. The study showed increased improvements in several cognitive domains when participating in both moderate and high intensity exercise groups (Cassilhas et al., 2007). A fourth study based on a 12-month long intervention for women found improved performance on test of executive function when participation in resistance training one to two times a week. The improvements did not show up after 6 months, meaning duration might have an impact on the effect (Liu-Ambrose, Nagamatsu, Voss, Khan, & Handy, 2012).

**Multicomponent exercise interventions:** A study done by Lui-Ambrose et al. (2008) found that strengthening and balance training formed to reduce falls, also showed a significantly improvement in executive functions (Liu-Ambrose et al., 2008). A 9 weeks RCT conducted by Bossers et al. (2015) divided 109 participants diagnosed with dementia into three groups; control, aerobic exercise, and aerobic exercise and resistance training. The training consisted of 36 sessions a 30 minutes. The combination training was shown to be most effective in slowing cognitive decline in patients with dementia (Bossers, 2015). Also a

study enrolling 1260 participants in a RCT, where the intervention group did a multidomain intervention consisting of diet, exercise, cognitive training and vascular risk monitoring, showed that multidomain intervention could improve or maintain cognitive functioning in atrisk elderly people from the general population (Ngandu et al., 2015). However, a study done by Sink et al. (2015) investigating how moderate-intensity PA program with different activities had an effect on cognition compared to a health education program, showed no improvements in cognitive function (Sink et al., 2015). A similar finding was detected in the recent RCT done by Lamb et al. (2018) who investigated the effect of aerobic exercise and strength exercise training for 494 participants already in state of dementia. After four months of exercise and a 12 month follow up, the study concluded with no association between aerobic and strength training and delay in further progression from mild dementia to a more serious form of dementia (Lamb et al., 2018).

Meta-analysis and reviews on the association: There has been done several meta analyses on the association between PA and cognitive function. A meta-analysis of 15 prospective studies (n=33816) done by Sofi et al. (2010) on nondemented subject suggested that all levels of PA had a significant and consistent protection against development of cognitive decline (Sofi et al., 2011). Another meta-analysis including 18 RCT's (n=1604) done by Groot et al. (2016) suggested a positive effect of PA on cognitive function, and that PA interventions positively influence cognitive function in people with dementia (Groot et al., 2016). A third meta-analysis including five RCT's (n=2878) done by Suoto-Barreto et al. (2017) did however contradict the first two meta-analyses' and concluded with evidence being limited and with no significant effect of exercise reducing the risk of development of cognitive decline (Barreto, Demougeot, Vellas, & Rolland, 2017). A recent meta-analyse done by Song et al. (2018) based the result on 11 studies, showed that aerobic exercise had beneficial effect on global cognition. However, the effect PA had on domain specific cognitive function were not clear (Song, Yu, Li, & Lei, 2018). A Cochrane review from 2015 looking at aerobic exercise to improve cognitive function in older, healthy adults, concluded however with no evidence found from aerobic exercise in any cognitive domain (Young, Angevaren, Rusted, & Tabet, 2015).

Larger reviews done on the association is also conflicting. Öhman et al. (2014) did a review of 22 trials that reported some positive effects of PA on cognition for persons living with MCI. Cognitive domains affected of PA was global cognition, meaning verbal fluency and visuospatial ability, in addition to executive functions, attention and delayed recall. The

review did however not find any effect of PA for those with dementia (Ohman, Savikko, Strandberg, & Pitkala, 2014). Cui et al .(2018) concludes with a positive effect from PA interventions studies suggesting PA could delay further onset from MCI to AD. They also suggests, unlike Öhman et al. (2014) , that PA could serve as a cost-effective nonpharmacological treatment solution to Alzheimer's disease as it slows down the rapid impairment (Cui, Lin, Sheng, Zhang, & Cui, 2018). Guiney & Machado (2013) found in their review that aerobic exercise could improve some specific cognitive domains, but recommended further research regarding aerobic exercise and cognitive function (Guiney & Machado, 2013). Brasure et al. (2018) also did a review consisting of 32 studies investigating the effectiveness of PA interventions on cognitive decline. The review concludes that the evidence of any effect PA have on cognitive function is largely insufficient (Brasure et al., 2018).

### 4.0 Discussion

The first aim of this article was to look at different approaches to health, health promotion and healthy aging and discuss how to approach health for older adults. The second aim was to look at physical activity as a resistance resource for cognitive impairment and dementia.

The demographical change is inevitable, and the population is getting older. If not making the health and healthy aging a priority in the health care systems, the society might end up with problems affecting all aspects of the 21<sup>st</sup> century society as the whole welfare system will be overloaded. This will affect the economics of the country and eventually the rest of the population. The challenge needs to be handled in fields of diagnostic, therapeutic, rehabilitative, but most important preventive (Ricciardi, Specchia, & Marino, 2014). This to avoid the onset or worsening of chronic degenerative diseases. Getting old and live as long as possible is considered a goal and a privilege in the western countries, but is it a privilege if the last years of life are without quality? Living long lives gives opportunities to further discover and live fully lives also after retirement, but to be able to get the opportunities that arise from living longer lives, heavily depends on health (WHO, 2015). As we strive to get as old as possible and find ways to add extra years to our lives, it is important to also strive after factors helping us to resist and delay diseases and achieve the everyday quality of life making the extra years worth living (Ricciardi et al., 2014).

#### 4.1 Health promotion in older people

When the focus is on the older adults and health promotion, it is important to choose a proper health approach. The commonly used definition for health from WHO might not be the right approach considering the older adults, because good health by definition will most likely be unachievable. The definition has been criticized due to the use of the word "complete" wellbeing (Huber et al., 2011) stating that people living with long term diseases or health issues not are able to reach good health, which applies for many older adults. The aging population and the increase in chronic diseases leads to the older adults often being hampered by chronic diseases or difficulties as a result from normal aging. It does however not mean that perceived good health is unachievable for the older adults bothered with different health

issues. The definitions from WHO however, declares people with different chronic diseases or disabilities as definitively ill (Huber et al., 2011).

When the bio-psyko-model was appearing, it provided an understanding that health and wellbeing also were more than just the absence of physical and psychical illness. On one side the model resulted in increased focus on the health promotion aspects, which unlike the definition from WHO also gave the older adults struggling with health issues the opportunity to perceived good health by definition. The model underlined that health is being influenced by different factors and even though some are struggling with diseases, there is a possibility to enhance other factors affecting the health which might result in a better quality of life. On the other side the model made the health term a much more complex theme, making it somehow more difficult to understand and cope with. Anyhow, the model resulted in increased focus on health promotion, and in the context of health and aging it is important to have the health promotion approach to health, and this model helped focus on how to decrease the risk of developing diseases, and improve health from the state you are.

As a result from the increased focus on health promotion, the term healthy aging developed. The different perception of the term does however, as earlier mentioned, result in lack of consensus. WHO points out with their definition that absence of disease not is necessary to achieve a healthy aging and that healthy aging can be fostered through the shared goal of maximising functional ability (World Healht Organization, 2018). Even though the older adults have disabilities or diseases, health promotion work can be done to build and maintain their intrinsic capacity and in that way give them the resources needed to engage in activities. SNIPH (2006) also have the similar approach to healthy aging as they want to optimize the older adult's ability to participate in the society without discrimination, and live an independent and good life (Swedish National Institute for Public Health, 2006). The definition is inclusive and can affect elderly in all health situations. Fuchs et al. (2013) tried to identify factors important for healthy aging and develop a model in the work for standardization of the term (Fuchs et al., 2013). The model can however be criticized for having to little room for sickness and disabilities as one factor for healthy aging is among others "little or no chronic diseases" which in relation to older adults will apply to a small and selected group of people.

When considering healthy aging in a health promotion aspect, WHO (2015) and SNIPH (2006) might have more realistic approach to the term unlike Fuchs et al. (2013) which might have a little to optimistic approach to healthy aging. The overall goal is not to
achieve complete absence from disease or illness, but to find resistance resources which can help each individual to climb on the health continuum and improve quality of life. Interestingly, according to the findings earlier mentioned from Daskalopoulou et al. (2017), PA seems to play a big part in healthy aging, regardless of which definition used (Daskalopoulou et al., 2017).

#### 4.2 Physical activity as a health promotion factor for cognitive function

PA is shown to give different general health benefits, and maybe that is why the focus on PA as treatment for cognitive impairment also has increased. There are several factors protecting and helping against cognitive impairment, dementia and AD (Xu et al., 2015). However, PA is the factor receiving the most focus lately. This may be due to the fact that the risk of development of some of the other factors that are seen as a threat against cognitive such as depression and stress, also are weakened by PA (Pedersen & Saltin, 2015) which makes PA a good overall strategy. Depression is as earlier mentioned shown to have a negatively effect on MCI by resulting in a higher rate of progression from MCI to dementia (Ismail et al., 2017). PA has shown to be a factor that both prevent and treat depression, which makes PA a factor that can protect against the increased risk of a faster progression from MCI to dementia for those affected by depression. Further, there is evidence that PA has beneficial effect on SOC. Better SOC is associated with reducing stress or increasing ability to cope with stress. This is beneficial as stress is seen as a risk for development of aMCI. The evidence that PA has an effect on the brain is also compelling, as it has been shown that those parts of the brain and the reactions that are influenced by PA, being larger hippocampus, nerve generation and increase in growth hormones, also are important for cognitive function (K. I. Erickson et al., 2009; Seifert et al., 2010; ten Brinke et al., 2015).

Even though PA seems to be a reasonable resource to maintain cognitive function and to prevent cognitive decline, the empirical findings seems to be equivocal. The observational studies based on cross-sectional and longitudinal studies have found consistent and compelling evidence saying PA is beneficial to prevent decline in cognitive function and the findings is supported by a Lancet study done by Livingston et al. (2017) who pointed out PA as beneficial considering increased brain cognitive reserve, reduced brain inflammation and reduced brain damage (Livingston et al., 2017). The studies seem however to disagree at

some level regarding type, intensity, frequency and duration, and whether activity during midlife is associated with later cognitive benefits or not.

For the aerobic exercise interventions studies, there still remains questions about the effect. For the studies and RCT's done on the association the findings have been weaker and less successful than expected compared to the findings from the observational, longitudinal studies. Some of the interventional studies have shown positive effect of exercise on cognition (Kuster et al., 2016; Lautenschlager et al., 2008), however the studies are often small in selection of participants, and the associations between PA and cognition are often weak an limited to certain cognitive areas. There are also conflicting findings regarding what type and dose of activity is being most beneficial, as some of the studies highlights an activity lifestyle as preventive (Kuster et al., 2016), others highlights high intensity training as effective (Colcombe et al., 2006). The RCT's range from no change in cognition to moderate changes in some specific areas of cognitive functions in older adults in risk of developing MCI. The studies also showed some evidence of PA delaying further onset from MCI to dementia. There are however different study design and population characteristics used in these studies which might explain some of the equivocal results. In addition, it is used different exercise parameters which also could affect the association.

The focus on further investigation on the association between resistance exercise and cognitive function has increased the resent years. Studies investigating the association have found evidence supporting that resistance training could have an effect on cognitive function (Best et al., 2015; van de Rest et al., 2014), but there is also some disagreement regarding the effect of the training. There is also differences regarding duration of the interventions, as some claims an effect after 6 months (van de Rest et al., 2014) and others don't (Liu-Ambrose et al., 2012) even though the amount of sessions in the two studies were the same. Some of these trends were also seen in the aerobic exercise intervention studies. It seems like a duration for 6-12months is required in several studies before any change is discovered. A reason for this might be that physical function have been to poor and needs to be worked up on a certain level before further increasing the activity level to the point where its beneficial for cognition. Especially if the intensity required for beneficial effects is MVPA.

As for multicomponent exercise interventions more evidence is needed to conclude with how the training is affecting cognition. Even though some studies have had some positive outcomes for multicomponent exercise being both preventive for in-risk patients and for slowing down progression of cognitive decline (Bossers, 2015; Ngandu et al., 2015), there

is also evidence who do not support the association. These finding are saying that multicomponent exercise including aerobic exercise and strength training do not have an effect on improving cognition or delaying further progression (Lamb et al., 2018; Sink et al., 2015). This type of exercise might however be protective against other threats against cognitive decline, such as depression, meaning the type of intervention might be indirectly associated with improvements in cognition (Kirk-Sanchez & McGough, 2014).

The meta-analyses are also equivocal as the results are ranging from significant protective effect against decline in cognition (Groot et al., 2016; Sofi et al., 2011) to no overall evidence that PA is beneficial, or at best limited to specific cognitive domains (Barreto et al., 2017; Brasure et al., 2018). The meta-analyses do however correspond with earlier findings stating the interventions need to be over longer periods of time to provide any effect. There is also disagreement within the meta-analysis whether there is an effect of PA for those already in the state of dementia. It does however appears to be stronger evidence suggesting PA is delaying or protection against MCI and dementia rather than improve cognition in cognitively healthy persons or persons already diagnosed with dementia (Young et al., 2015). Based on that, it will be important to face the challenges regarding cognitive decline before symptoms develops, or in very early state of MCI. PA might however have other beneficial effects on persons in state of dementia considering physical performance and function, behaviour, and mood (Livingston et al., 2017; Telenius, Engedal, & Bergland, 2015), which indirectly might delay further progress of the disease especially considering depression (Barreto Pde, Demougeot, Pillard, Lapeyre-Mestre, & Rolland, 2015; Livingston et al., 2017).

## 4.3 Methodological considerations

Even though longitudinal studies have reported compelling evidence of positive effect of PA on cognitive function, there is still RCT's who are the most convincing evidence in regard to causality (Livingston et al., 2017). One of the reasons for conflicting results might be the methodological challenges connected to intervention studies as earlier mentioned. The studies vary in design, in definition of cognition such as improvement in cognitive function, prevention or delay of MCI, prevention or delay of dementia diagnoses. In addition, they differentiate in how PA is defined, especially regarding type of PA and cut-offs in degree of intensity, in addition to varying how long the study is running and how PA is measured.

Even though the correlation between objective and self-reported measures of PA varies, there is shown to be a moderate correlation between questionnaire and accelerometer-accessed PA (Sabia et al., 2014). However, different methods of PA measurement will most likely give varying results between studies and might be some of the reason for why the results vary between observational and interventional studies. The measure used on cognition might also create different results as there are challenges associated to the MMSE regarding the ability to detect MCI (Saczynski et al., 2015; Trzepacz et al., 2015). The MoCA test has a greater sensitivity in regard to detecting MCI unlike MMSE (Nasreddine et al., 2005).

# **5.0** Conclusion

In conclusion, regarding older adults, choosing a proper health approach is necessary to assure that older adults achieve and perceive good health. For healthy aging and good quality of life, health promoting strategies needs to be developed, and risk factors and resistance resources needs to be identified. According to some literature, PA might serve as a resistance resource that prevents and delay cognitive impairment and the decrease of quality of life.

The evidence regarding the association between PA and cognitive function is anyhow equivocal and it does seem like more research is needed to further investigate which cognitive domains are affected of the training. Empirical findings, especially based on longitudinal studies support the association where PA serve as a protective factor to cognitive decline, but the interventional studies are not compelling. Some of the conflicting evidence in the studies might come as a result from methodological differences in the studies. The meta-analyses suggest that more research is needed to further investigate the association, especially in regard to which type and dose of the PA is most beneficial.

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# **ARTICLE 2**

# Objectively measured physical activity and mild cognitive impairment in older adults

## Abstract:

**Background:** Demographical changes are leading to an older population, where health promotion strategies will be important to maintain sustainable societies. Cognitive health is a major factor in ensuring the quality of life of older adults and preserving their independence. Some of the literature support that physical activity (PA) is associated with cognitive function, but the evidence regarding the association is somehow equivocal. Therefore, the aims of this study were to:1) investigate the association between achievement of PA recommendations and development of mild cognitive impairment in older adults (MCI), and 2) investigate the association between objectively measured PA level and development of mild cognitive impairment.

Methods and measurement: 701 participants (48.5% women) with an average age  $\pm$ (SD) 72.3 $\pm$ 1.9 years and with complete data were included in this prospective study. Physical activity was objectively measured by use of Actigraph accelerometer for 7 consecutive days. Counts per minute (CPM) over 2020 were considered moderate-to-vigorous physical activity. Cognition was measured by the use of Montreal Cognitive Assessment Test where MCI $\leq$ 21 points. Logistic regression was used as analytic method and the results are presented as odds ratio (OR), with a 95% confidence interval (CI).

**Results:** Of the 701 participants, 32,4% met the PA recommendations and 11.6% had MCI. The mulitvariable regression analyses showed no significant difference in those achieving and those not achieving PA recommendations. By contrast, those with the lowest quartile of CPM had a significantly higher risk of developing MCI compared to the highest quartile of counts per minute (OR2.28, 95%CI: 1.10-4.71, p=0.026).

**Conclusion:** The majority of the participants in this selection did not meet the weekly PA recommendations. Though, not meeting the PA recommendations did not result in increased odds of developing MCI. However, the fact that the lowest quartile CPM had statistically significantly higher odds of developing MCI, nevertheless indicates that PA is associated with cognitive function in older adults.

Keywords: Cognition function, Exercise, Training, Healthy Aging

**Abbreviations**: PA – Physical activity, VPA -Vigorous Physical Activity, MVPA -Moderate-Vigorous Physical Activity, LPA- Light Physical activity, MCI-Mild Cognitive Impairment, CF-Cognitive Function, AD-Alzheimer's Disease, RCT-Randomized Controlled Studies, CPM - Counts per minute.

# **1.0 Introduction**

The world is experiencing a demographic change which eventually will result in an older population. The world is in different parts in the transition, but Europe is particularly exposed to the change as the countries are close to reaching the end of the transition resulting in the older adults being in plural (Halvorsen, 2013). There is expected a four-fold increase of people between 80-90 years old before the end of this century and by 2050, 21.2% of the world's population will be over 60 years old (StatisticsNorway, 2014). The aging will lead to an economic impact of the health care systems and can be potentially overwhelming, especially considering age-related disorders such as cognitive decline often resulting in dementia and Alzheimer's Disease (AD) (Carvalho, Rea, Parimon, & Cusack, 2014). This development is a public health issue due to the threat against a healthy aging and older adults independency and quality of life. There will therefore be important to prioritize resistance resources against the threat of cognitive decline.

Physical activity (PA) is a well-known resistance resource for different health issues, especially chronic diseases (Pedersen & Saltin, 2015). It is therefore recommended to maintain an active lifestyle as a precondition and as a treatment for different health issues (Helsedirektoratet, 2017; WHO, 2011). Based on this, the Norwegian government recommends 150 minutes per week with moderate activity in bouts of 10 minutes, 75 minutes of vigorous activity in bouts of 10 minutes or a combination of both for older adults over 65.

Lately, there has been an increase in the interest on the association between PA and cognitive function. The association has been subject of research the last years and the literature is expanding. Yet, there are still questions regarding the association between PA and cognitive function not yet to be answered. There are studies supporting that PA delays the onset of cognitive impairment and further development to dementia and AD (Angevaren, Vanhees, Nooyens, Wendel-Vos, & Verschuren, 2010; Barnes, Yaffe, Satariano, & Tager, 2003; Tierney, Moineddin, Morra, Manson, & Blake, 2010), and exercise interventions is supporting the findings that PA is beneficial to cognitive function in older adults (Kuster et al., 2016; Lautenschlager et al., 2008; Tamura et al., 2015; Vaughan et al., 2014; Vidoni et al., 2015) . However, recent studies suggesting insufficient evidence regarding the association, one of them being a Cochrane review published in 2015 concluding with lack of evidence to support the association based on randomized controlled trials done in recent years (Brasure et al., 2018; Young, Angevaren, Rusted, & Tabet, 2015). .

WHO's global recommendations on PA for health was developed with the overall aim to provide guidance to prevent non-communicable diseases. Now, WHO also promotes the PA recommendations as beneficial to cognitive decline (WHO, 2011), making the association between PA recommendations and development of MCI an even more interesting research topic. There is also an ongoing discussion whether intensity rather than duration of the PA has the most effect on the cognition. There are studies showing an effect using high intensity exercise rather than longer moderate exercise (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Brown et al., 2012), but there is also some evidence that focuses on amount of PA rather than the intensity (Lautenschlager et al., 2008). The answer to this question is also interesting regarding which of the recommendations of 150 minutes of Moderate-to-vigorous PA(MVPA) or 75 minutes of vigorous PA (VPA) to follow for maximum effect against cognitive decline. However, previous studies are largely based on self-reported PA assessment, rather that objectively measured activity causing a larger change for bias (Zhu et al., 2017). Therefore, there is an interest in expanding the literature on the association between PA and cognitive function, using objectively measured PA.

The purpose of this study was to investigate the association between objectively measured PA and cognitive impairment in older adults.

The study is based on following two research questions:

- 1. Is not meeting the current recommendations for PA associated with an increased risk of developing MCI?
- 2. Is there any association between activity level and risk of developing mild cognitive impairment in older adults?

# 2.0 Method

The data for this paper was provided by the Generation 100 study, which is a phase IIb clinical trial. Students writing their master thesis gets access to Generation 100 data by participating in the data collection. This also gives great insight for further writing and processing of the data. I was invited to participated in the fifth and last data collection of cognitive function in the period from September 2017 to February 2018. The present study is however using data from baseline and 3 years testing.

#### **2.1 Generation 100 – Design and intervention**

The Generation 100 study is aiming to investigate the effect of exercise training on morbidity and mortality in the elderly and is conducted at St. Olav's Hospital in Trondheim. With 190 464 residents at January 2018, Trondheim is the third most populated city in Norway (SSB, 2017). All men and women with permanent address in the city of Trondheim, born in the period 1936-1942 were invited to participate in the study in 2012/2013, resulting in 6966 invitations. All possible participants were identified through the National Population Register, and they received an invitation by letter, in addition to a health-related questionnaire and a response sheet with a consent form. The individuals were encouraged to return the documents regardless of further participation in the study resulting in 3212 responds, of which 1790 consented to participate (Stensvold et al., 2015). After exclusion of some of the participants, 1567 participants, 777 men (72,5±2,1 years) and 790 women (72,5±2,1 years) enrolled in the Generation 100 study (Stensvold et al., 2015).

**Design and intervention**: The participants were randomized 1:1 into a training group or a control group. Further, the participants in the exercise group were randomized to a moderate-intensity or high-intensity group. The high-intensity training group is given instructions to complete two weekly 40 min long interval workouts with 4 minutes working periods at the intensity of 85-95% of peak heart rate with 3 minutes' active breaks between the periods at 60-70% of peak heart rate. They can also participate in a supervised spinning session every sixth week to ensure that they are exercising in the right intensity. The moderate-intensity training group is asked to complete an exercise in moderate intensity twice a week with an intensity corresponding to 70% of peak heart rate. Both high-intensity and moderate-intensity groups are using the Borg-scale as guidance for exercise intensity. The

control group is instructed to follow the current recommendations for PA given by the Norwegian government (Stensvold et al., 2015).

Inclusion/Exclusion criteria: Men and women born between 1 January 1936 and 31. December 1942, who were able to complete the exercise program were included in the Generation 100 study. Those with illness or disabilities that prohibit exercise, uncontrolled hypertension, dementia, cancer that made participation impossible, and chronic communicable infectious diseases were excluded. Also individuals with different heart conditions as symptomatic valvular, hypertrophic cardiomyopathy, unstable angina, primary pulmonary hypertension, heart failure or severe arrhythmia were excluded in addition to those who already participated in conflicting studies (Stensvold et al., 2015).

#### 2.2 Study sample

The present study is using Generation 100-data. The objectively measures PA data was retrieved at baseline before randomization. Data for cognitive function is taken from the 3 year-testing. However, for this study, of the total 1567 participants in the Generation 100 study, participants who participated at baseline and also at the 3-years testing were included (n=702). Participants with missing data on PA, cognitive function or confounding variables used in the study were excluded (n=865). A total amount of 702 participants (362 men and 340 women) was included in this study sample.

## 2.3 Variables and measures

**Independent variable - Objectively measured PA**: Objectively measured PA is assessed by the use of SenseWear Armband activity monitor (BodyMedia 7, Pttsburgh, Pennsylvania, USA) or by Actigraph (GT3X, Manufacturing Technology Inc, Florida, USA). SenseWear Armband activity monitor is a validated, portable device used on the upper right arm (Farooqi, Slinde, Haglin, & Sandstrom, 2013) Actigraph GT3X, which was used on the majority of the participants, is a widely used accelerometer and often used in large-scale studies such as Generation 100 (Zisko et al., 2015). The device is a lightweight solid-state accelerometer placed with a waist band right above the hip, measuring acceleration in one axis (Santos-Lozano et al., 2013). The acceleration measured by the devices is converted into "counts" per unit time. The counts are increasing as the accelerations increase, meaning higher the counts, higher the intensity of the activity. The counts are therefore reflecting the intensity of the subjects PA during a period and should not be confused with steps per minute (Santos-Lozano et al., 2013). The counts are specified over a user specified interval of time called an "epoch" which in this study was set to a 10-second interval (Zisko, 2017).

The participants wore the accelerometer for seven consecutive days at baseline after clinical testing and randomization, but before intervention start, both during day and night, except when in contact with water (Stensvold et al., 2015). Intervals of at least 60 consecutive minutes with zero counts, with an allowance of up to two minutes of counts greater than zero was defined as non-wear time and excluded from the analysis. Days with wear-time <10 hours and participants with days <4 were also excluded from the study.

Achieved recommendations Moderate-to-vigorous- activity (MVPA) bouts: The variable "achieved recommendations MVPA bouts" was created as a dichotomous variable based on whether the participants did or did not achieve public PA recommendations of 150 minutes of moderate to vigorous activity a week in 10 minutes' bouts. During the 10 minutes' bouts there was allowed a drop of counts under 2020 for up to two minutes (Troiano et al., 2008). If the activity dropped for over two minutes, the activity was excluded from the total amount of MVPA. As this variable were based upon the participant's average day, persons who spent over 21.4 minutes in bouts of MVPA each day during 7 days were estimated to reach the weekly PA recommendations. The groups which achieved the recommendations were used as the reference group in the analyses.

**Quartile Counts per minute**: The outcome of PA is reported in a one-axis count per minute (CPM) variable which is a commonly used measurement for analyzing overall PA (Santos-Lozano et al., 2012). The variable "Quartile CPM" were checked for skewness, kurtosis and outliers. The skewness level of 0.932 indicates a small positive skewness resulting in a score clustered slightly to the left at the low values. The kurtosis value was 1.284 indicating a rather peaked model, clustered in the center. Outliers is defined as values that extend far beyond the rest of the range, and it is recommended to remove extreme outliers who can affect the results (Pallant, 2010). The values for CPM in this study ranged from 59 – 650 CPM. Due to an extreme score (CPM of 990), one value was considered an outlier and removed from the selection resulting in the mean of CPM changing from 259,9 to 253,5. The one-axis variable was divided into quartiles for this thesis, given 4 equal groups with 25% of the sample, resulting in 175 or 176 participants in each group, stretching from the lowest measured intensity level group to the highest measured intensity level group. Quartile 1 represented the 25% of the participants with the lowest level of activity, and quartile 4

represented the participants with highest level of activity. Quartile 4 was used as the reference group in the analyses.

**Dependent variable – Mild Cognitive Impairment (MCI):** Cognitive function was measured by the use of a screening tool called Montreal Cognitive Assessment (MoCA) which is a validated screening tool covering eight cognitive domains. The screening tool is validated in different languages including Norwegian which is used in previous studies in addition to Generation 100 (Ihle-Hansen et al., 2017). The details of the MoCA test as described by Nasreddine et al. (2005):

Visuospatial abilities were assessed using a trail making task (1point), a clock-drawing task (3 points,) and a three-dimensional cube copy (1 point). Language was assessed in three different tasks. First by the use of a three-item naming task. The participant was asked to name the three animals (lion, camel, rhinoceros) and the task gave maximum 3 points. Secondly, language was assessed with repetition of two syntactically complex sentences which gave maximum 2 points. Finally, language was assessed trough a phonemic fluency task (1 point). Short term memory recall was measured by asking the participants to repeat five nouns two times as a learning trial. The task involves a delayed recall after approximately 5 minutes were the participants is asked to repeat the five nouns. This task gave maximum 5 points. Attention, concentration and working memory is tested. In the first part, the participants were asked to repeat digits forward and backwards (2 point), in the second part to complete a sustained attention task by target detection using tapping (1 point), and in the third part to complete a serial subtraction task starting at 100 and subtracting 7 each time (1 point). Abstraction was assessed by the use of a two-item verbal abstraction task which gave maximum 2 points. Orientation to time, date and space was evaluated at the end and gave maximum 6 points (Nasreddine et al., 2005).

The MoCA test gives a maximum score of 30 points. This study operates with a cut-off of MCI at  $\leq 21$  points (Freitas, Simoes, Alves, & Santana, 2013) resulting in a dichotomous variable of cognitive function were the group with a MoCA score  $\leq 21$  points were considered to have MCI and the other group not.

**Control Variables:** The selection of control variables for this study were based upon former research and literature (Stubbs, Chen, Chang, Sun, & Ku, 2017; Xu et al., 2015; Zhu et al., 2015). Sociodemographic variables included were age, gender, education and living conditions. Living conditions meaning if the participants were living alone or together with someone. Questionnaires originated from the Generation 100 study were used to gather

information about education and living conditions. The education variable consisted of seven response options and on the basis if these seven options the participants were divided into three groups: low, medium and high education. Low consisting of primary school, medium consisting of education above primary school and up to 2 years of college/university, and high consisting of  $\geq$ 3 years of college/university. The question about living conditions had three response options: "living alone", "living with spouse" and "living with others". This variable was in this study merged into a dichotomous variable with "living alone" or "living together with someone". Marital status is also a known control variable in the association but was excluded in this study due to a correlation with living conditions at a level of -.952 and a sig.level at p<0.01. A correlation above 0.9 might be problematic as the variables are measuring the same and with a level close to 1.0 multicollinearity might be a problem (Ringdal, 2013).

Other values included in the study was body mass index (BMI), smoking habits, monthly alcohol consumption, insomnia, longstanding illness and depression. BMI was calculated by dividing body weight in kg by height in m square, expressed in kg/m<sup>2</sup> and included as a continuous variable. Smoking, alcohol consumption, insomnia and longstanding illness and depression were measured by the use of questionnaires. Smoking had four response options: never, former, daily and sometimes. The variable was in this study divided into three groups (never, former, and current smoker (daily and sometimes)). The alcohol variable was measured in cl per two weeks. The continuous alcohol variable was in this study included as a quartile.

Insomnia was based upon four questions: (1) "How often during the last 3 months have you had difficulty falling asleep at night?", (2) "How often during the last 3 months have you woken up repeatedly during the night?", (3) "How often during the last 3 months have you woken too early and couldn't get back to sleep?" and (4) "How often during the last 3 months have you felt sleepy during the day". All four questions had the same three response options being "never/seldom", "sometimes" and "several times a week". However, it might be criticized to have this variable as a dichotomous (no problems/insomnia), as those not qualifying for insomnia still might have sleeping problems affecting the cognitive function (Gildner, Liebert, Kowal, Chatterji, & Snodgrass, 2014). Based on this, the variable was divided into 3 categories: No sleeping problems, sleeping problems and insomnia. The category called "sleeping problems" including those who answered "several times a week" on at least one of the fours questions, but did not meet all criteria for being diagnosed with

insomnia. If they answered "several times a week" for at least one of questions 1–3 and "several times a week" for question 4 they were classified with insomnia (Skarpsno, Nilsen, Sand, Hagen, & Mork, 2018). According to DSM-V criteria these four questions gives the information needed to diagnose insomnia (American Psyciatric Association, 2013). However, the classification used in the current study is a proxy of an insomnia diagnosis.

Longstanding illness was measured with one question from the questionnaire "Do you have any longstanding (at least 1 year) illnesses or injuries of physical or mental nature that decreases function in daily life" with response options "yes or no", and included as a dichotomous variable.

Depression was included as a dichotomous variable and measured by the use of the depression score in the Norwegian translation of the Hospital, Anxiety and Depression Scale (HADS-D) which is a self-administered validated questionnaire consisting of seven items. Each questions had tree alternative scores reaching from 0 (nor present) to 3 (highly present). The questionnaire has focus on the reduced pleasure response aspect of depression. Data from participants who completed >5 items were included (ie multiplied by 7/5, 7/6 for those with two or one missing response respectively). A cut-off threshold for the dichotomous variable was set at  $\geq$ 8 which has established reasonable screening properties in identifying major depressive disorders (Bjelland et al., 2009).

## **2.4 Statistics**

**Descriptive Statistics:** Differences in demographic variables across "quartile CPM" and "achieved PA recommendations bouts" were tested respectively by significance tests as chi-square and t-test. Chi-square is used in the analysis of the associations between two categorical variables in the population on the base of the cross-tabulations. The t-test is used when differences in mean is being investigated (Ringdal, 2013). Means and standard deviations (SD) for the continuous variables were computed using descriptive statistics.

**Multivariable analyses:** The main objective of the study was to do a predictive analysis to explore the association between one ordinal independent variable (PA) and one dependent binary variable (MCI). Based on this, a binary logistic regression was chosen as analytic method. This analytic method was chosen both to investigate the association between 1. achieved PA recommendations at baseline and the development of MCI and 2. CPM at baseline and the development of MCI. As the study also takes confounders into consideration,

multiple logistic regression analysis` were done (Field, 2009). The statistical analysis was performed using the software program SPSS Statistics, version 25.0.

Four models were constructed from the data, were model 1 was adjusted for age and gender, model 2 was adjusted for the variables in model 1 in addition to sociodemographic variables as education and living conditions, model 3 was adjusted for variables in model 2 in addition to BMI, smoking and alcohol habits, and model 4 was adjusted for model 3 in addition to insomnia, depression and longstanding illness.

The variables education, smoking, and drinking was included and adjusted for by the use of dummy-variables. All variables in the model was included as categorical except from age and BMI. To assess if there were any dose-relationship between CPM quartiles and risk of developing MCI the four CPM quartiles were added as an ordinal variable in the regression analyses. If the results are a statistical significant p-value, the test suggest there is a dose-response relationship.

Results from significance test done on the descriptive is presented as p-values. The result from the multiple regression analysis are presented as odds ratio, OR, with a 95% confidence interval (C95%CI), and p-value. Odds can be described as the probability of an event occurring divided by the probability of the event not occurring, and the odds ratio the ratio of an event occurring in one group compared to another. An example of this might be the odds for developing MCI with sedentary behavior being 2, and the odds of developing MCI without sedentary behavior being, 05, the odds ratio is 2/0.5 = 4 meaning the odds for developing MCI is 4 times higher with a sedentary behavior. If the odds ratio ends up being 1, it would indicate equal odds in both groups (Field, 2009). A confidence interval is a way of entering the error margin of a measurement or calculation on the statistics and says something about the range of values surrounding the statistic, that are believed to contain with a certain probability of 95%, the true value of statistic. A broader confidence interval indicates greater uncertainty than a small one (Field, 2009). A CI including 1 indicates that the association is not statistical significant. A statistical significant value (p-value) is used to determine the statistical significance of the result. With a low p-value the probability to draw the wrong conclusion is smaller. The probability is to be as small as possible and a frequently used level to distinguish between significant or not is a significant level on 0.05 meaning a probability on less then 5 percent. This level is often referred to as p<0.05 (Ringdal, 2013)

**Preconditions:** Variables used in the study were checked for skewness, kurtosis and outliers. To make sure the regression analyzes were reliable, they were tested with Omnibus

Tests of Model Coefficient which is a "goodness of fit" test. It was also done a Hosmer and Lemeshow test which is the most reliable test of model fit available in SPSS. In addition, the values from Cox & Snell R Square ant the Nagelkerke R Square was investigated to provide an indication of the amount of variation in the dependent variable explained by the model. All preconditions for both logistic regressions were met.

## 2.5 Ethics

All participants were given sufficient information about the study, and signed a consent form at the beginning of the Generation 100 study. All participants with previous disease history or test result indicating that participation in the study was unsafe were excluded. All participants were able to withdraw throughout the study. All data collected is treated with confidentiality and test results are saved in files without affiliation to personal identification (Stensvold et al., 2015). The participants who scored  $\leq$ 19 at the MoCA test received a letter after the test day explaining the score was below average, and they were encouraged to consult with their doctor. The cut-off at 19 was set from the Generation 100 study, as they are operating with a milder cut-off than the present study.

The Generation 100 is approved by the Regional Ethical Committee (REK) in Health Region IV (REK 2012/381 B), and this particularly study was considered and approved REK as a part of an ongoing PhD-project using the same data (REK 2016/2229 B) (See appendix 1).

# **3.0 Results**

## **3.1 Descriptive results**

Among the 701 participants, 51.5% were men and 11.6% had MCI. The mean (±SD) was  $72.3 \pm 1.9$  years, and 76.9% of the participants were living with someone. 53.9% of the participants had education exceeding primary school and up to two years of university, and 38.4% of the participants had college or university education >3 years which means the group is highly educated. 3.6% were diagnosed with depression and 32.1% reported sleeping problems of which 4.7% were diagnosed with insomnia.

In Table 1, demographics, characteristics and cognitive function are displayed according to achievement of PA recommendations. Of the 701 participants, 32.4% achieves the PA recommendations. The number of men and women achieving the recommendations are approximately equal. Of those achieving the recommendations, 10.6% had MCI, 73.1% was living with someone, 38.3% were highly educated, and only 2.6% had a depression diagnosis. Those achieving the recommendations spent in mean more time in vigorous activity (mean 3.6min) compared to those not achieving the recommendations (mean 0.7min) The participants achieving the PA recommendations had also a significantly (p<0.001) lower BMI with a mean ( $\pm$ SD) of 24.6  $\pm$  3.2 compared to the other group having a mean of 26.2  $\pm$ 3.5. There were also a statistical significantly difference between the groups considering longstanding illness, where the number of those reporting longstanding illness were higher in the group not achieving the PA recommendations (p<0.05).

| Variable       | Not achieved PA | Achieved PA     | Total      |
|----------------|-----------------|-----------------|------------|
| n(%)           | recommendations | recommendations |            |
| MCI            | 57 (12.0)       | 24 (10.6)       | 81 (11.6)  |
| Age, mean (SD) | 72.4 (2.0)      | 72.1 (1.7)      | 72.3 (1.9) |
| Gender         |                 |                 |            |
| Male           | 247 (52.1)      | 114 (50.2)      | 361 (51.5) |
| Female         | 227 (47.9)      | 113 (49.8)      | 340 (48.5) |
| Living sit.    |                 |                 |            |
| Alone          | 101 (21.3)      | 61 (26.9)       | 162 (23.1) |
| Spouse         | 373 (78.7)      | 166 (73.1)      | 539 (76.9) |
| Education      |                 |                 |            |
| Low            | 37 (7.8)        | 17 (7.5)        | 54 (7.7)   |
| Medium         | 255 (53.8)      | 123 (54.2)      | 378 (53.9) |
| High           | 182 (38.4)      | 87 (38.3)       | 269 (38.4) |
| BMI, mean (SD) | 26.1 (3.5)      | 24.6 (3.2)      | 25.6 (3.5) |
| Depression     | 19 (4.0)        | 6 (2.6)         | 25.6 (3.5) |
| (HADS-D≥8)     |                 |                 |            |
| Longstanding   | 205 (43.3)      | 78 (34.4)       | 283 (40.4) |
| illness        |                 |                 |            |
| Insomnia       |                 |                 |            |
| No             | 320 (67.5)      | 156 (68.7)      | 476 (67.9) |
| Sleep prob     | 130 (27.4)      | 62 (27.3)       | 192 (27.4) |
| Insomnia       | 24 (5.1)        | 9 (4.0)         | 33 (4.7)   |
| Time spent in  |                 |                 |            |
| VPA, minutes   |                 |                 |            |
| per week       | 0-12.0          | 0-41.0          |            |
| Min-Max        | 0.7 (1.68)      | 3.6 (6.83)      |            |
| Mean (SD)      |                 |                 |            |

Table 1. Characteristics of Participants by whether they achieved PA recommendations or not (N=701)

In Table 2, demographics, characteristics and cognitive function are displayed according to quartiles of CPM. Quartile 3 had the highest amount of MCI cases with 14.8% of the participants. Quartile 4 had the fewest cases of depression and insomnia, and the lowest mean of BMI. Time spent in vigorous activity was generally low with quartile 4 at the highest mean time with 4.4 minutes. 40.4% of the participants struggled with longstanding illness, but the highest quartile CPM had significantly fewer cases of longstanding illness compared to the other groups (p<0.001).

| 100 1      |  |  | <b>C</b>   | I Utal   |
|------------|--|--|--|--|
| <=188,4    | 188,5-244,9  | 245.0-309,1  | 309,2 +  |  |
| 24 (13.6)  | 17 (9.8)   | 26 (14.8)  | 14 (8.0)   | 81 (11,6)  |
| 72.3 (2.0) | 72.45 (2.0)  | 72.20 (1,9)  | 72.1 (1,7)   | 72.3 (1.9)   |
|            |  |  |  |  |
|            |  |  |  |  |
| 91 (51.7)  | 90 (51.7)  | 86 (48.9)  | 94 (53.7)  | 361(51.5)  |
| 85(48.3)   | 84 (48.3)  | 90 (51.1)  | 81 (46.3)  | 340(48.5)  |
|            |  |  |  |  |
| 42 (23.9)  | 32 (18.4)  | 43 (24.4)  | 45 (25.7)  | 162 (23,1)   |
| 134 (76.1) | 142 (81.6)   | 133 (75.6)   | 130 (74.3)   | 539 (76.9)   |
|            |  |  |  |  |
| 16 (9.0)   | 17 (9.7)   | 8 (4.6)  | 13 (7.4)   | 54 (7.7)   |
| 102 (58.0) | 96 (55.2)  | 94 (53.4)  | 86 (49.1)  | 378 (53.9)   |
| 58 (33.0)  | 61 (35.1)  | 74 (42.0)  | 76 (43.5)  | 269 (38.4)   |
| 27.0 (4.0) | 25.5 (3.2)   | 25.2 (3.0)   | 24.5 (3.0)   | 25.6 (3.5)   |
|            |  |  |  |  |
| 8 (4.5)    | 6 (3.5)  | 8 (4.6)  | 3 (1.7)  | 25.6 (3.5)   |
| 87 (49.4)  | 68 (39.0)  | 77 (43.6)  | 51 (29.1)  | 283 (40.4)   |
|            |  |  |  |  |
| 115 (65.4) | 118 (67.8)   | 114 (64.8)   | 129 (73.7)   | 476 (67.9)   |
| 49 (27.8)  | 44 (25.3)  | 55 (31.3)  | 44 (25.1)  | 192 (27.4)   |
| 12 (6.8)   | 12 (6.9)   | 7(3.9)   | 2 (1.2)  | 33 (4.7)   |
|            |  |  |  |  |
| 0-34.9     | 0-38.4   | 0-59 7   | 1 6-103  |  |
| 5 12(6 48) | 12 1(8 6)  | 18 4(12.8)   | 33 8(20 2)   |  |
| 5.12(0.10) | 12.1(0.0)  | 10.1(12.0)   | 55.0(20.2)   |  |
|            |  |  |  |  |
| 0-4.62     | 0-16.1   | 0-19.5   | 0-41.0   |  |
| 0.2 (0.45) | 1.9 (2.1)  | 2.4 (2.5)  | 4.4 (7.45)   |  |
| ~ /        |  |  | · · · ·  |  |
|            | $\begin{array}{r} \hline & 24 & (13.6) \\ \hline & 24 & (13.6) \\ \hline & 72.3 & (2.0) \\ \hline & 91 & (51.7) \\ & 85(48.3) \\ \hline & 42 & (23.9) \\ \hline & 134 & (76.1) \\ \hline & 16 & (9.0) \\ \hline & 102 & (58.0) \\ \hline & 58 & (33.0) \\ \hline & 27.0 & (4.0) \\ \hline & 8 & (4.5) \\ \hline & 87 & (49.4) \\ \hline & 115 & (65.4) \\ \hline & 49 & (27.8) \\ \hline & 12 & (6.8) \\ \hline & 0-34.9 \\ \hline & 5.12(6.48) \\ \hline & 0-4.62 \\ \hline & 0.2 & (0.45) \\ \hline \end{array}$ | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ | $\begin{array}{c c c c c c c c c c c c c c c c c c c $ |

Table 2. Characteristics of Participants by Quartile of CPM (N=710).

## **3.2 Logistic regression**

**PA recommendations and MCI:** The results from the regression analysis on the association between PA recommendations and MCI are shown in Table 3. An unadjusted logistic regression model for the association between MCI and achievement of PA recommendations showed no significant result (data not shown). To furthermore investigate the association four adjusted logistic regression models were conducted (Table 3). When adjusted for age and gender (model 1), education and living conditions (model 2), smoke/ alcohol habits and BMI (model 3), and insomnia, depression and longstanding illness (model 4) no statistical significant associations were discovered.

| Variable             | Achieved recom. <sup>e</sup> | Not achieved recom. |
|----------------------|------------------------------|---------------------|
| Model 1 <sup>a</sup> | Ref.                         | 1.13 (0.68-1.88)    |
| OR (95%C.I.)         |                              | p=0.637             |
| Model 2 <sup>b</sup> | Ref.                         | 1.14 (0.68-1.92)    |
| OR (95%C.I.)         |                              | p=0.618             |
| Model 3 <sup>c</sup> | Ref.                         | 1.21 (0.71-2.06)    |
| OR (95%C.I.)         |                              | p=0.492             |
| Model 4 <sup>d</sup> | Ref.                         | 1.12 (0.65-1.91)    |
| OR (95%C.I.)         |                              | p=0.693             |

Table 3. Risk of developing MCI by not achieving PA recommendations (N=701).

<sup>a</sup> Model 1: adjusted for age and gender.

<sup>b</sup> Model 2: adjusted for model 1 and education and living conditions

<sup>c</sup> Model 3: adjusted for model 2 +BMI and smoking and alcohol habits,

<sup>d</sup> Model 4: adjusted for model 3 + insomnia, depression and longstanding illness

<sup>e</sup> Denote achieved recommendations as an activity level above 150 minutes a week in 10 minutes' bouts' in moderate to vigorous activity

**CPM and MCI:** The unadjusted model (not showed in the table) for the association between PA and MCI showed a significantly higher risk of developing MCI being in the lowest CPM quartile group. However, the significance level was small, and the CI-range was large, meaning the association was weak. The results from the regression analysis on the association between CPM and MCI are shown in Table 4.

The association did not remain significant after the model being adjusted for age and gender only (model 1). However, after adjusting for education and living conditions, the p-value was back to being statistical significant with p=0.037, OR:2.12 and with a 95%CI of 1.05-4.30.

The relationship remained significant after adjustment for smoking and alcohol habits and BMI, and even strengthen the association (p=0.027, OR=2.24, 95%CI:1.10-4.56). In model 4 when adjusted for age, gender, education, living conditions, smoke and alcohol habits, BMI, insomnia, depression and longstanding illness the results showed a statistical significant association between PA and MCI being that, compared with the highest CPM quartile, the lowest CPM quartile had a significantly higher risk of developing MCI (p=0.026, OR:2.28, 95% CI:1.10-4.71). The test for linear trend showed no dose-response relationship between CPM level and risk of developing MCI (p=0.460).

An interesting finding in this logistic regression was the level of OR in quartile 3. The level is showing a higher risk of developing MCI compared to quartile 2 with a level of OR:1.78 after full adjustment, compared to quartile 2 which are showing a level of OR:1.14.

| Variable             | Qrt<br>4 <sup>e</sup> | Quartile 3       | Quartile 2       | Quartile 1       |
|----------------------|-----------------------|------------------|------------------|------------------|
| Model 1 <sup>a</sup> | Ref.                  | 1.79 (0.89-3.60) | 1.21 (0,58-2,55) | 1.99 (1.00-3.95) |
| OR (95%C.I.)         |                       | p=0.100          | p=0.609          | p=0.051          |
| Model 2 <sup>b</sup> | Ref.                  | 1.62 (0.79-3.30) | 1.10 (0.51-2.35) | 2.12 (1.05-4.30) |
| OR (95%C.I.)         |                       | p=0.188          | p=0.812          | p=0.037          |
| Model 3 <sup>c</sup> | Ref.                  | 1.86 (0.89-3.88) | 1.18 (0.55-2.55) | 2.24 (1.10-4.56) |
| OR (95%C.I.)         |                       | p=0.100          | p=0.670          | p=0.027          |
| Model 4 <sup>d</sup> | Ref.                  | 1.78 (0.84-3.78) | 1.14 (0.52-2.48) | 2.28 (1.10-4.71) |
| OR (95%C.I.)         |                       | p=0.133          | p=0.745          | p=0.026          |
| Test for linear      |                       | p=0.460          |                  |                  |
| trend                |                       | No dose-         |                  |                  |
|                      |                       | response         |                  |                  |
|                      |                       | relationship     |                  |                  |

Table 4. Risk for MCI by quartiles of CPM (N=701).

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<sup>a</sup> Model 1: adjusted for age and gender <sup>b</sup> Model 2: adjusted for model 1 and education and living conditions <sup>c</sup> Model 3: adjusted for model 2 +BMI and smoking and alcohol habits, <sup>d</sup> Model 4: adjusted for model 3 + insomnia, depression and longstanding illness

<sup>e</sup> Denote the quartiles of the proportion of total accelerometer war time in CPM. Quartile 1:

CPM<=188,4, Quartile 2:188,5-244,9, Quartile 3:245.0-309,1, Quartile 4: >=309,2.

## 4.0 Discussion

The main goal of this study was to investigate the association between objectively measured PA and mild cognitive impairment in older adults. The study looks at this association by firstly investigate the association between government PA recommendations at baseline and the development of MCI three years later, and secondly to investigate in the relationship between PA measured as quartiles of CPM at baseline and risk of MCI three years later.

Compared to those achieving the weekly PA recommendations there were no statistical significant increased risk for MCI among those who did not meet these PA recommendations. The study did however demonstrate a statistical significant relationship between PA and cognitive impairment by showing that the participants in the lowest CPM quartile, meaning the participants with the lowest PA intensity level, was at significant higher risk of developing MCI.

## 4.1 PA recommendations and MCI

The first research question focused on the association between MVPA recommendations and cognitive impairment. The results showed that 32.4% of the participants reached the PA recommendations in this present study. A study done by Zisko et al (2017) on the Generation 100 participants on baseline data showed similar findings as 37.9% of the participants reached the PA recommendations (Zisko et al., 2017). The amount reaching the recommendations in Zisko et al. (2017) is however slightly higher which might be due to the selection in the study being lager (n=1219) which might cause some differences. In addition, Zisko et al. (2015) was using Freedson cut-points of MVPA thresholds (1952-5724 cpm) which is lower than the Troiano cut-points (2020 – 5998 cpm) used in the present study (Freedson, Melanson, & Sirard, 1998; Troiano et al., 2008). This might explain the small different in achievement of PA recommendations.

Not achieving the PA recommendations had an odds ratio of OR: 1.12, with an CI: (0.65-1.91) and a p-value of 0.693 which indicates no significant increased risk of developing MCI by not reaching the PA recommendations. This finding is supported by a study done by Sabia et al. (2017) which followed the participants during 15 years without being able to promote achievement of PA recommendations as preventive for cognitive decline (Sabia et al., 2017). There are however other studies that contradict these findings, claiming there is an

association between PA recommendations and MCI. A study done by Vancampfort et al (2017) showed a significant association between PA achievements not met and MCI (Vancampfort et al., 2017), and a study done by Zhu et al. (2015) reported that amount of MVPA associated with lower prevalence of cognitive impairment was consistent with meeting PA guidelines (Zhu et al., 2015). The study of Vancampfort et al. (2017) relied on subjectively measured PA which might have been a limitation of the study, but the study of Zhu et al. (2015) used objectively measured PA which can be compared to this study. However, both studies were cross-sectional which might have been a limitation.

One of the reasons why the results contradicts might be that a very small amount of the participants in the present study spent time in vigorous activity, which means that of the 150 min MVPA, most of the time were spent in MPA. Another reason for inconsistencies might be related to how the variable is made. The variable is dichotomous and by having only two groups it creates room for big differences in average activity level. MVPA bouts-participants with cero activity and those right below the limit of 21.4 would with this threshold be in the same group. The same goes for the participants right above the limit who is considered equal to those spending over 60 minutes in MVPA every day.

Measured in bouts, activity should be 10 minutes coherent, meaning 2 min drops in the activity will lead to the activity not being counted. This is according to recommendations (WHO, 2011). However, this implies that a participant who are performing a high intensity interval session of 4x4 minutes, but with a drop of counts under 2020 for 2 minutes in the resting minutes, will lose the registration of the 4x4 interval. This might lead to big differences in time in MVPA based whether they are able to maintain high enough counts during the breaks. The association of PA recommendations and MCI therefore needs further investigation, especially with focus on the recommendations of 75 minutes a week in vigorous PA. It would also be interesting to investigate the real effect of bouts measurement of exercise. By using bouts, a lot of time spent in MVPA is excluded from the study and it would be interesting to see if the benefits from bouts exercise actually have big enough effect making it legit to exclude all the MVPA data not being in 10 minutes' bouts.

There were however some significant differences between the two groups when looking at health benefits, as the group achieving the recommendation had significantly lower BMI and longstanding illnesses. This suggest even if not having an association with MCI, there are important health benefits from following the PA recommendations. However,
regarding longstanding illnesses the diseases might also be a reason for not being able to achieve the recommendations.

## 4.2 CPM and MCI

The significant association between lowest quartile CPM and risk of MCI suggests that PA is beneficial in terms of decreasing the risk of developing MCI. Very light PA and sedentary behavior leads to significant increased risk to develop MCI. This finding corresponds with a selection of previous studies, both prospective and cross-sectional studies, exploring the association between sedentary behavior and cognitive function showing more sedentary behavior being significantly associated with lower cognitive scores and the studies recommend to promote PA in the aging group (Edwards & Loprinzi, 2017; Steinberg et al., 2015). The association is also supported by Falck et al. (2017) which reported interesting findings saying that increased level of PA and lower sedentary behavior were associated with better cognitive function in participants without MCI, and that participants with MCI had significantly more time spent in sedentary behavior (Falck et al., 2017). The study was however cross-sectional, which might have been a limitation. There are conflicting results were some studies show no strong association between sedentary behavior and MCI, but this might be a result of activities done in sedentary behavior which compensates for lack of activity, being computer work or crosswords which works as cognitive practice (Hamer & Stamatakis, 2014; Kesse-Guyot et al., 2012). The association can be further investigated by changing the focus from sedentary behavior to PA.

# 4.3 Subjectively vs Objectively measured PA

By suggesting that sedentary behavior and very light PA is risk factors for MCI, it can be argued that all activity above very light activity is beneficial to the protection of MCI. Several studies using self-reported measures on PA reports similar findings. A study done by Sanchez-Lopez et al (2018) showed similar finding corresponding with our findings when demonstrating that high levels of incidental PA were associated with better scores on cognitive tests (Sanchez-Lopez et al., 2018). Also Kuster et al (2016) reported that an active lifestyle was beneficial to cognitive decline (Kuster et al., 2016). These studies with selfreported PA can however be compromised by over-reporting of activity level and recall bias. By looking specific on studies using objectively measured PA, the basis for comparison to our study can be more reliable. There are several studies using objectively measured PA that also suggest that active individuals may be less likely to develop MCI regardless of the intensity of the activity. Stubbs et al. (2017) conducted a longitudinal study over 2 years on older adults at mean age 74.5 years where the results showed that objective light PA (LPA) offered a protective effect from future decline in cognition when measured independently from the intensity level above LPA which is MVPA. The data did however also document that MVPA had a protective effect as well, which in reality means a protective effect from all activity levels which corresponds well to the present study showing that only those having the lowest activity level measured as CPM were at increased risk of developing MCI. The age of the participants in the Stubbs' study is also comparable to the present study. However, Stubbs et al. (2017) only had 274 participants which is less than the present study (Stubbs et al., 2017). A study done by Buchman et al. (2012) in a period over 4 years with 716 participants used Actigraph accelerometer for measurement of PA and different test to measure cognitive function. Their findings indicated that daily PA level were associated with level and rate of change in cognition, and more importantly a clear association between higher level of total daily PA and reduces risk of Alzheimer's Disease. Based on this the study it should be encouraged to increase daily activity level even in very old individuals (Buchman et al., 2012). This study is also comparable to the present study as both uses Actigraph accelerometer for PA measurement, the amount of participants is approximately equal, and the study is conducted on the same age group. This hypothesis is supported by several other studies including a meta-analysis conducted by Sofi et al. (2011)(Sofi et al., 2011; Tamura et al., 2015; Tierney et al., 2010; Won et al., 2014).

## 4.4 Intensity-discussion

There is an ongoing discussion whether intensity or amount of activity is most important considering decreasing the risk of developing MCI. Several studies have suggested that high intensity rather that amount of exercise is most important for the preservations of cognitive function (Angevaren et al., 2008; Brown et al., 2012; Zhu et al., 2017). The answer to the first research question did not support any difference between the groups when considering both moderate and vigorous intensity. When looking at vigorous activity alone, the group achieving the PA recommendations spent in average more time in vigorous activity than the group not achieving the recommendations. This indicates that lack of vigorous physical activity (VPA) among those not meeting the PA guidelines did not increase the risk of developing MCI. However, the time the participants spent in vigorous activity was very limited and was at average 0.7 minutes for the group not achieving the recommendations and 3.6 minutes for those achieving the recommendations which might be too little time to draw any conclusion on whether VPA is affecting or not.

The other research question looked at quartiles of CPM and MCI, and suggested that the participants in the lowest quartile CPM had an increased risk of developing MCI. However, the mean CPM does not say how long the participants spent in sedentary time, LPA, MVPA and VPA. When looking at the amount spent in VPA in each quartile, the time increases in line with the mean CPM in the quartiles meaning the group who had the highest average CPM, also had the highest amount of time spent in VPA. When looking at all quartiles together, quartile 1 have considerably lower time in VPA compared to the other groups, and opposite to what the first research question indicated, this might suggest that VPA does affect the association. However, the same limitations apply for this association as for the first research question, because the total time spent in VPA is considered too low to conclude on the specific effect that VPA have on the association.

# 4.5 Sedentary behavior

There is also another interesting factor which might affect the association but not taken into consideration in this article. As the activity measured is a mean of the day, there is not pointed out the time spent in sedentary behavior. The intensity of the activity might not be the only factor affecting the association, but also the amount spent in sedentary time each day. The pattern of the activity meaning for example if the participants spend 20 minutes in vigorous and 10 hours in sedentary time each day or 120 minutes in light to moderate and only 4 hours in sedentary, might affect the association. Maybe is reduction in sedentary time just as important as time spend in each intensity zone. This would be an interesting topic for further research.

## 4.6 Absolute vs relative cut offs

It should also be discussed whether the cut-points of MVPA and VPA might be too high for older adults to reach. This absolute goals are the same to younger adults and fit individuals, which can lead to a misreading of older adults' activity level. Several of the older adults are not capable to reach the absolute moderate/vigorous thresholds due to a decline in maximal oxygen uptake (VO2max) which might result in underestimation of PA levels among the elderly (Aspvik et al., 2016). Zisko et al (2015) investigated the possibilities of

using new relative intensity ambulatory thresholds for elderlies in connection to the Generation 100 study and established some new relative cut-offs for MVPA (Zisko et al., 2015). There might be beneficial to use relative cut-offs in further research, so the level of activity is adjusted for older adults.

### 4.7 Dose-response

There are studies suggesting there might be dose-response association between PA and cognitive function (Vidoni et al., 2015) and a study done by Lopprinzi et al. (2017) showed an inverted U-shaped dose-response association between the two factors (Loprinzi, Edwards, Crush, Ikuta, & Del Arco, 2017). The present study did however not find a dose-response association between PA measured in CPM in quartiles and MCI. Interestingly, the odds ratio is actually higher in quartile 3 with an OR of 1.78. compared to quartile 2 which has OR of 1.14 which suggest a tendency to increased risk of developing MCI in quartile 3 compared to quartile 2. These findings are however not significant and has quite broad confidence intervals. The no dose-response association is supported by a twin prospective cohort study done by Iso-Markku et al. (2016) following 3050 participants reaching over 25 years where no dose-response association between PA and MCI were found.

# 4.8 Methodological discussion

It can be discussed were to set the cut-off regarding the MoCA test and also which cut-off thresholds to use for MVPA. For the present study it was used a MoCA cut-off at  $\leq 21$  indicating MCI. The cut-off for  $\leq 21$  was chosen based on a former validations study (Freitas et al., 2013).

When it comes to MVPA and chosen cut-off from accelerometer data there exists different definitions on the literature. This study is using cut-off points from Troiano, which is commonly used (Troiano et al., 2008)This cut-off is however stricter and harder to achieve than with the use of Freedson which is used by Zisko et al. (2017). Both cut-offs are commonly used in research, however if the present study had access to bouts Freedson MVPA it might have been more correct to use that measure, as it is slightly less strict considering the study is focusing on older adults. As earlier mentioned, using relative threshold for older adults as many of them are not able to reach the absolute thresholds as Freedson and Troiano needs more attention in research. Relative thresholds were not used in the present study as the basis for comparison to other study became smaller, but the use of relative threshold might however be the most correct thing to use in further research.

As mentioned earlier in the study, the way the MVPA bouts variable is used as a dichotomous variable will result in people being in non-activity and people who fell right below the limit of recommendations ends up in the same group which might make it hard to determine effect. When it comes to the CPM variable it is the mean activity level who is described, and not the amount of time spent in different intensity zones which means the person can be in LPA all day, spend most of the day sedentary with small bouts of MVPA, or spend a lot of time in MPA which makes it hard to say something about the effect of the different intensity zones.

## 4.9 Strengths and limitations of the study

One of the strengths of this study was the use of objective measure of PA to investigate the association between cognitive function and PA on an older population. This gives reliable measures of the activity levels and detailed activity data. The study used the MoCA-test for cognitive screening which also can be considered a strength as the test has excellent sensitivity for discovering MCI and mild AD (Nasreddine et al., 2005). In addition, the analyze was adjusted for a wide range of different potential confounders, which strengthens the reliability of the result (Buchman et al., 2012). The selection was equally represented of men and women, from different parts of the city and with different sociodemographic status. The study also aimed to investigate the association between cognitive function and PA recommendations, where the amount of previous studies is limited.

Limitations for this study is firstly the use of one axis accelerometer data who do not capture upper body movements, in addition to using two different accelerometers which may have caused uneven results in the measurement of CPM. It should also be mentioned that the confidence interval was a bit broad for the significant found between CPM and MCI which might weaken the validity of the result. The study is also using absolute cut points of MVPA, which used on older adults might be set to high. In the selection, the participants spent little time in vigorous activity, resulting in an insufficient foundation to base the association of MCI and VPA on. The participants who volunteered to this study, might represent the healthiest part of the population, in addition to a relatively high education level which might not be representative of older adults. The PA recommendations were also based upon MVPA

bouts, meaning only 10 minutes' bouts of MVPA were taken into consideration. This might have affected the distribution between the two groups and further affected the result.

There was no measurement of cognition at baseline which might lead to reversed causality meaning MCI was already developed resulting in a lower activity level.

# **5.0** Conclusion

In the present study the result suggests that older people who did not meet the PA recommendations at baseline had no increased risk of developing MCI three years later. The study did however reveal a significant relationship between PA and development of cognitive impairment by showing that the participants in the lowest quartile of mean CPM per day at baseline was at significant higher risk of developing MCI compared to their counterparts in the highest intensity quartiles of CPM. This indicates that PA is associated with the development of MCI, but CPM data used in this study does not give the information necessary to describe the variation of PA intensity during the week and which dosage of PA is being most beneficial against cognitive decline.

For further investigation, it would also be interesting to look at the association between sedentary behavior and cognitive impairment. It would also be interesting to focus on the PA recommendations of 75 minutes of VPA per week to see if achievement of those recommendations could result in benefits against development of MCI that the 150 minutes of MVPA per week recommendations could not. As the results of today are conflicting, more research is needed to determine which intensity level of PA is most beneficial against development of MCI.

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# Appendix A: Approval by the Regional Committees for Medical Research Ethichs



| Region:     | Saksbehandler:          | Telefon: | Vår dato:     | Vår referanse:                  |
|-------------|-------------------------|----------|---------------|---------------------------------|
| REK sør-øst | Harsha Gajjar Mikkelsen | 22845513 | 05.10.2017    | 2016/2229 REK sør-øst B         |
|             |                         |          | Deres dato:   | Deres referanse:                |
|             |                         |          | 22.09.2017    |                                 |
|             |                         |          | Vår referanse | må oppgis ved alle henvendelser |

Linda Ernstsen Norges teknisk-naturvitenskapelige universitet

# 2016/2229 Mental helse, kognitiv funksjon, og demens: Utgjør kondisjon en forskjell?

Forskningsansvarlig: Norges teknisk-naturvitenskapelige universitet Prosjektleder: Linda Ernstsen

Vi viser til søknad om prosjektendring datert 22.09.2017 for ovennevnte forskningsprosjekt. Søknaden er behandlet av sekretariatet i REK sør-øst på delegert fullmakt fra REK sør-øst B, med hjemmel i helseforskningsloven § 11.

# Prosjektleders prosjektbeskrivelse

"Forskningsprosjektet har som mål å undersøke sammenhengen mellom mental helse, kondisjon, kognitiv funksjon og demens hos middelaldrende og eldre. I lys av eldrebølgen, vil resultatene fra dette prosjektet kunne bidra med viktig kunnskap som kan brukes til bedre forebygging og behandling av mental sykdom og kognitiv svikt, noe som kan ha en betydelig økonomisk fordel for samfunnet. Det vil bli brukt longitudinelle data fra Helse og hukommelse i Nord-Trøndelag, HUNT - et samarbeidsprosjekt der hovedmålet er å innhente helsedata for beboere med kognitiv svikt og demens, samt Generasjon 100-studien - en randomisert kontrollert klinisk studie hvor hovedmålet er å studere effekten av 5 års trening på sykelighet og levetid hos eldre. I begge studiene er det samlet inn informasjon for estimering av kondisjon (objektivt målt kondisjon i Generasjon100 studien), mental helse, og kognitiv funksjon. I Helse og hukommelse er det i tillegg informasjon om demensprevalens."

# Endringen innebærer

Nye prosjektmedarbeidere i studien er Masterstudent Siri Bjerkan og Masterstudent Unni Ekeberg Horten, NTNU.

# Vurdering

Sekretariatet i REK har vurdert den omsøkte endringen, og har ingen forskningsetiske innvendinger til endringene slik de er beskrevet i skjema for prosjektendring.

# Vedtak

Søknad om prosjektendring godkjennes med hjemmel i helseforskningsloven § 11, annet ledd.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, endringssøknad, oppdatert protokoll og de bestemmelser som følger av helseforskningsloven med forskrifter.

# Klageadgang

Du kan klage på komiteens vedtak, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sørøst B.

Besøksadresse: Telefon: 22845511Gullhaugveien 1-3, 0484 Oslo E-post: post@helseforskning.etikkom.no

Web: http://helseforskning.etikkom.no/

All post og e-post som inngår i saksbehandlingen, bes adressert til REK sør-øst og ikke til enkelte personer

Kindly address all mail and e-mails to the Regional Ethics Committee, REK sør-øst, not to individual staff

Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst B, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn med korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no. Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Knut W. Ruyter avdelingsdirektør REK sør-øst

# Kopi til:

- Dekan Solrun Johanne Valen, Norges teknisk-naturvitenskapelige universitet

Harsha Gajjar Mikkelsen Seniorkonsulent

# Appendix B – Montreal Cognitive Assessment (MoCA)

#### Norsk Versjon 7.1

**MONTREAL COGNITIVE ASSESSMENT (MOCA)** 



| Spørreskiema 1  |               |
|---|---------------|
| 1. Kjønn: Kvinne Mann   | 2. Fødselsår: |
| 3. Høyde: cm  | 4. Vekt: kg   |
| Utdanning   |               |
| <ol> <li>Hva er din høyeste utdanning?</li> <li>Folkeskole</li> </ol> |               |
| Realskole     Yrkesskole  |               |
| Handelsskole  |               |
| Gymnas     Høgskole eller universitet, mind                           | fre enn 3 år  |
| Hagekole eller universitet mer  | enn 3 år      |

# Appendix C – Questionnaire 1 from Generation 100

6. Hvem bor du sammen med? (Sett ett eller flere kryss)

Ingen Ektefelle/samboer Andre personer

#### Mosjon og fysisk aktivitet

Med mosjon mener vi at du for eksempel går tur, går på ski, svømmer eller driver trening/idrett. Fysisk aktivitet omfatter både fysisk aktivitet i hverdagen, planlagte aktiviteter og trening.

7. Hvor ofte driver du mosjon? (Ta et gjennomsnitt)

Aldri

Sjeldnere enn en gang i uka

En gang i uka

2-3 ganger i uka

Omtrent hver dag

 Dersom du driver slik mosjon, så ofte som en eller flere ganger i uka; hvor hardt mosjonerer du? (Ta et gjennomsnitt)

Tar det rolig uten å bli andpusten eller svett

Tar det så hardt at jeg blir andpusten og svett

Tar meg nesten helt ut



| <ul> <li>9. Hvor lenge holder du på hver gang? (Ta et gjennomsnitt)</li> <li>Mindre enn 15 minutter 15-29 minutter 30 minutter - 1 time Mer enn 1 time</li> <li>10. Har du vanligvis minst 30 minutter fysisk aktivitet daglig? Ja Nei</li> </ul> |  |
|---|--|
| Mindre enn 15 minutter 15-29 minutter 30 minutter – 1 time Mer enn 1 time   |  |
| 10. Har du vanligvis minst 30 minutter fysisk aktivitet daglig?   |  |
|   |  |
| 11. Hvis du aldri eller sjelden er fysisk aktiv. Hva er det som hindrer deg:<br>Dårlig helse/funksjonsnedsettelse   |  |
| Tilgjengelighet av passende aktiviteter   |  |
| Avstand til turområder  |  |
| Tilrettelegging av turområder   |  |
| Utrygghet   |  |
| L Ikke interessert  |  |
| Annet   |  |
| 12. Omtrent hvor mange timer sitter du i ro på en vanlig hverdag?   |  |
| Helse og dagligliv  |  |
| 13. Hvordan er helsa di nå? 🗌 Dårlig 🔄 Ikke helt god 🗌 God 🗌 Svært god  |  |
| 14. Røyker du?  |  |
| Nei, jeg har aldri røykt  |  |
| Nei, jeg har sluttet å røyke  |  |
| Ja, sigaretter av og til (fest/ferie, ikke daglig)  |  |
| Ja, sigarer/sigarillos/pipe av og til   |  |
| Ja, sigaretter daglig   |  |
| ☐ Ja, sigarer/sigarillos/pipe daglig  |  |
| 15 Bruker du, eller har du brukt snus?  |  |
| Ja, men jeg har sluttet   |  |
| □ Ja, av og til   |  |
| 🗌 Ja, daglig  |  |
| <ol> <li>Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av 2 uker?<br/>(Regn ikke med lettøl) (Sett 0 hvis du ikke drikker alkohol)</li> </ol>   |  |
| Antall glass: ØI: Vin: Brennevin:   |  |
| 17. Bruker du medisin mot høyt blodtrykk?   |  |
| Ja Nei, men jeg har brukt Nei, har aldri brukt  |  |
| 24605   |  |

18. Klarer du selv, uten hjelp av andre, i det daglige å:

| Gå innendørs i samme etasje?  | 🗌 Ja          |        | Nei       |         |          |  |
|---|---------------|--------|-----------|---------|----------|--|
| Gå på toalettet?  | Ja            |        | Nei       |         |          |  |
| Vaske deg på kroppen?   | Ja            |        | Nei       |         |          |  |
| Bade eller dusje?   | Ja            |        | Nei       |         |          |  |
| Kle på og av deg?   | Ja            |        | Nei       |         |          |  |
| Legge deg og stå opp?   | Ja            |        | Nei       |         |          |  |
| Spise selv?   | 🗌 Ja          |        | Nei       |         |          |  |
| Lage varm mat?  | 🗌 Ja          |        | Nei       |         |          |  |
| Gjøre lett husarbeid (f.eks oppvask)?   | Ja            |        | Nei       |         |          |  |
| Gjøre tyngre husarbeid (f.eks gulvvask)?  | 🗌 Ja          |        | Nei       |         |          |  |
| Vaske klær?   | 🗌 Ja          |        | Nei       |         |          |  |
| Gjøre innkjøp?  | 🗌 Ja          |        | Nei       |         |          |  |
| Betale regninger?   | 🗌 Ja          |        | Nei       |         |          |  |
| Ta medisiner?   | 🗌 Ja          |        | Nei       |         |          |  |
| Komme deg ut?   | 🗌 Ja          |        | Nei       |         |          |  |
| Ta bussen?  | 🗌 Ja          |        | Nei       |         |          |  |
| 19. Har du i løpet av de siste 12 månede  | r hatt:       |        |           |         |          |  |
| Anfall med pipende eller tung pust  |               | 🗌 Ja   | 🗌 Nei     |         |          |  |
| Daglig hoste i perioder   |               | 🗌 Ja   | Nei Nei   |         |          |  |
| Høysnue eller neseallergi   |               | 🗌 Ja   | Nei       |         |          |  |
| Smerter og/eller stivhet i muskler og ledd,<br>har vart i minst 3 måneder sammenhenge | , som<br>ende | 🗌 Ja   | Nei       |         |          |  |
| 20. Hvor mange ganger har du i løpet av   | de sist       | e 12 m | åneder væ | rt hos: |          |  |
| Fastlege / alimennlege  |               |        | ganger    |         |          |  |
| Annen legespesialist utenfor sykehus  |               |        | ganger    |         |          |  |
| Kiropraktor   |               |        | ganger    |         |          |  |
| Homøopat, akupunktur, soneterapeut,   | andlar        |        | ganger    |         | 24605    |  |
| nanuspalegger eller annen alternativ ben  | andier        |        |           |         | <b>1</b> |  |
|   |               |        |           |         |          |  |

Nr  21. Har du, eller har du noen gang hatt, noen av disse sykdommene / plagene: (Sett ett kryss pr. linje) Hvis ja, hvor gammel var du første gang?

Nr

| Takk for at du tok dog ti                 | d til å eve | aro od spara | målene |
|---|-------------|--------------|--------|
| Glaukom (grønn stær, høyt trykk i øyet)   | Ja          | Nei          | år     |
| Katarakt (grå stær)                       | 🗌 Ja        | 🗌 Nei        | år     |
| Høyt stoffskifte (hypertyreose)           | Ja          | Nei          | år     |
| Lavt stoffskifte (hypotyreose)            | Ja          | Nei          | år     |
| Psykiske plager som du har søkt hjelp for | 🗌 Ja        | 🗌 Nei        | år     |
| Slitasjegikt (artrose)                    | Ja          | Nei          | år     |
| Fibromyalgi                               | 🗌 Ja        | Nei          | år     |
| Beinskjørhet (osteoporose)                | 🗌 Ja        | Nei          | år     |
| Sarkoidose                                | 🗌 Ja        | Nei          | år     |
| Bechterews sykdom                         | 🗌 Ja        | Nei          | år     |
| Leddgikt (reumatoid artritt)              | 🗌 Ja        | Nei          | år     |
| Epilepsi                                  | 🗌 Ja        | Nei          | år     |
| Kreftsykdom                               | 🗌 Ja        | 🗌 Nei        | år     |
| Eksem på hendene                          | 🗌 Ja        | Nei          | år     |
| Psoriasis                                 | 🗌 Ja        | Nei          | år     |
| Diabetes (sukkersyke)                     | 🗌 Ja        | Nei          | år     |
| Kronisk bronkitt, emfysem, KOLS           | Ja          | 🗌 Nei        | år     |
| Astma                                     | 🗌 Ja        | Nei Nei      | år     |
| Nyresykdom                                | Ja          | Nei          | år     |
| Hjerneslag/hjerneblødning                 | Ja          | Nei          | år     |
| Annen hjertesykdom                        | Ja          | Nei          | år     |
| Atrieflimmer                              | Ja          | Nei          | år     |
| Hjertesvikt                               | Ja          | Nei          | år     |
| Angina pectoris (hjertekrampe)            | Ja          | Nei          | år     |
| Hjerteinfarkt                             | Ja          | Nei          | år     |

Takk for at du tok deg tid til å svare på spørsmålene, og husk å sende inn svarene dine!



|   | GENERASJ  |                               | Pr                              | iD-nr:         |        |
|---|---|-------------------------------|---------------------------------|----------------|--------|
|   | Spørreskjema 2  |                               |                                 |                |        |
|   | 1. Kjønn: Kvinne Mann   |                               |                                 |                |        |
|   | Helse og dagligliv  |                               |                                 |                |        |
|   | <ol> <li>Har du noen langvarig (<u>minst 1 år</u>) sykdo<br/>eller psykisk art som nedsetter dine funk</li> </ol> | om, skade ei<br>sjoner i ditt | ller lidelse av<br>daglige liv? | v fysisk 🔲 Ja  | Nei    |
|   | Hvis ja:<br>Hvor mye vil du si at dine funksjoner er r  | nedsatt?                      |                                 |                |        |
|   |   | Litt<br>nedsatt               | Middels<br>nedsatt              | Mye<br>nedsatt |        |
|   | Er bevegelseshemmet   |                               |                                 |                |        |
|   | Har nedsatt syn   |                               |                                 |                |        |
|   | Har nedsatt hørsel  |                               |                                 |                |        |
|   | Hemmet pga. kroppslig sykdom  |                               |                                 |                |        |
|   | Hemmet pga. psykisk sykdom  |                               |                                 |                |        |
|   | 3. Har du vært plaget av hodepine det siste   | aret? 🔲                       | Ja 🗌 Nei                        |                |        |
|   | Hvis ja: Hva slags hodepine? Migrer   | ne 🗌 An                       | nen hodepin                     | e              |        |
|   | 4. Har du vært plaget med smerter eller ub<br>Ja, mye Ja, litt Nei, aldri   | ehag fra ma                   | gen de siste                    | 12 måneder?    |        |
|   | Medisiner   |                               |                                 |                |        |
|   | 5. Hvor mange reseptbelagte medikamen   | ter bruker d                  | tu totalt?                      | medika         | menter |
|   | Sykdommer og skader   |                               |                                 |                |        |
|   | <ol> <li>Har du noen gang de <u>siste 5 år</u> brukt me<br/>kronisk bronkitt, emfysem eller KOLS?</li> </ol>      | disiner for a                 | stma, 🗌                         | ]Ja ∏Nei       |        |
|   | 7. Har lege sagt at du har hjerteflimmer (atr   | ieflimmer)?                   |                                 | ]Ja ∏Nei       |        |
| - |   |                               |                                 | ,              | 49805  |

| Prosjektnr: |  |  |  |
|-------------|--|--|--|
|-------------|--|--|--|

8. Har du noen gang hatt:

| 4   |  |  |  |  |  |
|---|--|--|--|--|--|
| 4   |  |  |  |  |  |
| 1   |  |  |  |  |  |
| 4   |  |  |  |  |  |
| r?  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
| Vet ikke  |  |  |  |  |  |
|   |  |  |  |  |  |
|   |  |  |  |  |  |
| 10. Har du smerter i det ene eller i begge beina när du går? 🗌 Ja 🛛 🗌 Nei |  |  |  |  |  |
| Hvis ja: Hvor gjør det mest vondt? 🗌 Fot 📄 Legg 🔤 Lår 🔛 Hofte             |  |  |  |  |  |
| Etter hvilken distanse begynner smertene? Ca 50 m Ca 200 m Mer enn 500 m  |  |  |  |  |  |
|   |  |  |  |  |  |
| 🗌 Nei   |  |  |  |  |  |
| 49805   |  |  |  |  |  |
|   |  |  |  |  |  |

Prosjektnr:

| 11. Har du smerter i beina når du er i ro? |   |     | 🗌 Nei   |
|--|---|-----|---------|
| Hvis ja:                                   | Er smertene verst når du ligger i senga?  | Ja  | 🗌 Nei   |
|  | Får du mindre vondt når beinet ligger lavt,<br>f.eks. om beinet henger utfor sengekanten? | □Ja | Nei     |
|  | Har du hatt smertene i beina sammenhengende<br>i.mer.enn 14 dager?                        | Ja  | Nei     |
| 12. Har du b                               | rukt smertestillende medisin pga. smerter i beina?  | Ja  | Nei Nei |
| 13. Har du s                               | år på tå, fot eller ankel som ikke vil gro?   | Ja  | 🗌 Nei   |
| 14. Kan du s                               | sitte i minst 1 time uten å få smerter i bena?  | Ja  | 🗌 Nei   |

Mosjon og fysisk aktivitet Med mosjon mener vi at du f.eks. går tur, går på ski, svømmer eller driver trening/idrett.

15. På en skala fra 6-20, hvor hard er aktivitetene du vanligvis utfører når du mosjonerer / trener? (Ta et gjennomsnitt av den siste uka) (sett ett kryss)

| 6                       |
|-------------------------|
| 7 - Meget, meget lett   |
| 8                       |
| 9 - Meget lett          |
| 10                      |
| 11 - Ganske lett        |
| 12                      |
| 13 - Litt anstrengende  |
| 14                      |
| 15 - Anstrengende       |
| 16                      |
| 17 - Meget anstrengende |
| 18                      |
| 19 - Svært anstrengende |
| 20                      |
|                         |



| Prosjektnr: |  |  |  |  |
|-------------|--|--|--|--|
|-------------|--|--|--|--|

## 16. Hvor ofte gjør du følgende?

|                           | Aldri | Sjelden | 1-3 dager | 1 dag i<br>uken | 2-3 dager | 4-6 dager | Daglig |
|---------------------------|-------|---------|-----------|-----------------|-----------|-----------|--------|
| Går som transport         |       |         |           |                 |           |           |        |
| Går tur på vei og gangsti |       |         |           |                 |           |           |        |
| Går tur i naturen         |       |         |           |                 |           |           |        |
| Sykler                    |       |         |           |                 |           |           |        |
| Trener i idrettslag       |       |         |           |                 |           |           |        |

17. Hvor ofte benytter du deg av følgende anlegg?

|                    | Aldri | Sjelden | 1-3 dager | 1 dag i<br>uken | 2-3 dager | 4-6 dager | Daglig |
|--------------------|-------|---------|-----------|-----------------|-----------|-----------|--------|
| Gang-Sykkelsti     |       |         |           |                 |           |           |        |
| Oppmerket turløype |       |         |           |                 |           |           |        |
| Lysløype / skispor |       |         |           |                 |           |           |        |
| Svømmebasseng      |       |         |           |                 |           |           |        |
| Idrettshall        |       |         |           |                 |           |           |        |
| Treningssenter     |       |         |           |                 |           |           |        |
| Andre typer anlegg |       |         |           |                 |           |           |        |

## 18. Når du er fysisk aktiv. Hvor stor betydning har det at du kan:

| Være sammen med andre       | Ingen<br>betydning | Litt<br>betydning | Stor<br>betydning | Svært stor<br>betydning |  |
|-----------------------------|--------------------|-------------------|-------------------|-------------------------|--|
| Være alene                  |                    |                   |                   |                         |  |
| Bruke nærmiljøet der du bor |                    |                   |                   |                         |  |
| Være inne                   |                    |                   |                   |                         |  |
| Være ute                    |                    |                   |                   |                         |  |
| Bruke og oppleve naturen    |                    |                   |                   |                         |  |
| Føle deg trygg              |                    |                   |                   |                         |  |
|                             |                    |                   |                   |                         |  |

|  |   |          | Prosjektnr:   |  |
|--|---|----------|---------------|--|
| <ol> <li>Hvor langt er det fra der<br/>naturområde der du kan</li> </ol> | du bor til en park<br>være fysisk aktiv | eller et |               |  |
| Mindre enn 300 m   | 300m-1 km                               | 1-5km    | 🗌 Mer enn 5km |  |

#### Mosjon tidligere i livet

20. Hvor ofte drev du mosjon da du var 20 år gammel? (Ta et gjennomsnitt)

Aldri

Sjeldnere enn en gang i uka

🗌 En gang i uka

2-3 ganger i uka

Omtrent hver dag

 Dersom du drev mosjon să ofte som en gang i uka som 20-ăring; hvor hardt mosjonerte du? (Ta et gjennomsnitt)

Tok det rolig uten å bli andpusten eller svett

- Tok det så hardt at jeg ble andpusten og svett.
- Tok meg nesten helt ut

22. Hvor ofte drev du mosjon da du var 40 år gammel? (Ta et gjennomsnitt)

Aldri

Sjeldnere enn en gang i uka

En gang i uka

2-3 ganger i uka

Omtrent hver dag

 Dersom du drev mosjon să ofte som en gang i uka som 40-ăring; hvor hardt mosjonerte du? (Ta et gjennomsnitt)

Tok det rolig uten å bli andpusten eller svett.

Tok det så hardt at jeg ble andpusten og svett.

Tok meg nesten helt ut



#### Holdninger til fysisk aktivitet

Fysisk aktivitet omfatter både fysisk aktivitet i hverdagen, planlagte aktiviteter og trening.

 Har vennene dine/bekjente/familiemediemmer utenfor husstanden: (Sett ett kryss for hver påstand)

|   | Aldri   | Sjelde | n No    | en få | Ofte  | Veldig | Passer |
|---|---------|--------|---------|-------|-------|--------|--------|
| Foreslått at dere skulle drive fysisk<br>aktivitet sammen                                   |         |        | ga      |       |       |        |        |
| Oppmuntret deg til å være fysisk aktiv  | - 🗆     |        |         |       |       |        |        |
| Gitt deg hjelpsomme påminnelser om<br>fysisk aktivitet som: "Skal du mosjonere<br>i kveld?" |         |        |         |       |       |        |        |
| Forandret planene sine slik at dere<br>kunne drive fysisk aktivitet sammen                  |         |        |         |       |       |        |        |
| Sagt at fysisk aktivitet vil være bra<br>for helsen din                                     |         |        |         |       |       |        |        |
| Snakket om hvor godt de liker å være<br>fysisk aktive                                       |         |        |         |       |       |        |        |
| 25. Omtrent hvor lang tid vil det ta deg a<br>(Sett ett kryss for hver linie)               | å gå hj | emmef  | ra til: |       |       |        |        |
| (000 00 00 00 00 00 00 00 00 00 00 00 00  |         | 1-5    | 6-10    | 11-20 | 21-30 | > 30   | Vet    |
| Butikk for dagligvarer  |         |        |         |       |       |        |        |
| Et friområde/park/turvei  |         |        |         |       |       |        |        |
| Helsestudio/treningssenter/svømmehall<br>idrettshall/utendørs idrettsanlegg                 | V       |        |         |       |       |        |        |
| Skog/mark/fjell   |         |        |         |       |       |        |        |



| l | Prosjektnr:  |
|---|--|
|   | Arbeid   |
|   | 26. Har du tidligere hatt inntektsgivende arbeid? Ja Nei   |
|   | Hvis ja:<br>I hvilket år hadde du sist betalt arbeid?  |
|   | Hva var navnet på hovedyrket ditt (yrkestittel)?   |
|   | Hvordan vil du beskrive arbeidet ditt? (Sett ett kryss)  For det meste stillesittende arbeid (f.eks skrivebordsarbeid, montering) Arbeid som krever at du går mye (f.eks ekspeditørarbeid, lett industriarbeid, undervisning) Arbeid hvor du går og løfter mye (f.eks postbud, pleier, bygningsarbeid) Tungt kroppsarbeid (f.eks skogsarbeid, tungt jordbruksarbeid, tungt bygningsarbeid) |
|   | Arbeidet du i en fulltidsstilling eller deltidsstilling i hovedyrket ditt?  Fulltidsstilling  Deltidsstilling  |
|   | Hadde du skiftarbeid, nattarbeid eller gikk vakter?  |
|   | Boligforhold og venner   |
|   | 27. Er det kjæledyr i boligen?<br>Nei Ja, katt Ja, hund Ja, andre pelsdyr / fugl   |
|   | 28. Har du venner som kan gi deg hjelp når du trenger det? 🗌 Ja 🛛 Nei  |
|   | 29. Har du venner som du kan snakke fortrolig med? 🔲 Ja 🗌 Nei  |
|   | Hvordan føler du deg?<br>Her kommer noen utsagn om hvordan du føler deg. For hvert spørsmål setter du kryss for<br>ett av de fire svarene som best beskriver dine følelser den siste uken. Ikke tenk for lenge<br>på svaret - de spontane svarene er best.   |
|   | 30. Jeg føler meg nervøs og urolig 🗌 Nei 🔹 Litt 📄 En god del 🔄 Svært mye   |
|   | 31. Jeg gleder meg fortsatt over ting slik jeg pleide før<br>Avgjort like mye Ikke fullt så mye Bare lite grann Ikke i det hele tatt   |
|   | 32. Jeg har en urofølelse som om noe forferdelig vil skje  |
|   | Ja, og noe svært ille Litt, bekymrer meg lite  |
|   | □ Ja, ikke så veldig ille □ Ikke i det hele tatt   |
|   |  |
|   | 49805  |

| Prosjektnr:   |
|---|
| 33. Jeg kan le og se det morsomme i situasjoner   |
| Like mye nå som før Avgjort ikke som før  |
| Ikke like mye nå som før  |
| 34. Jeg har hodet fullt av bekymringer<br>Veldig ofte Ganske ofte Av og til En gang i blant   |
| 35. Jeg er i godt humør<br>□ Aldri □ Noen ganger □ Ganske ofte □ For det meste  |
| 36. Jeg kan sitte i fred og ro og kjenne meg avslappet.<br>☐ Ja, helt klart ☐ Vanligvis ☐ likke så ofte ☐ likke i det hele tatt           |
| 37. Jeg føler meg som om alt går langsommere<br>Nesten hele tiden Svært ofte Fra tid til annen Ikke i det hele tatt                       |
| 38. Jeg føler meg urolig som om jeg har sommerfugler i magen<br>☐ Ikke i det hele tatt ☐ Fra tid til annen ☐ Ganske ofte ☐ Svært ofte     |
| 39. Jeg bryr meg ikke lenger om hvordan jeg ser ut<br>Ja, har sluttet å bry meg Kan hende ikke nok<br>Ikke som jeg burde Bryr meg som før |
| 40. Jeg er rastløs som om jeg stadig må være aktiv<br>Uten tvil svært mye Ganske mye Ikke så veldig mye Ikke i det hele tatt              |
| 41. Jeg ser med glede fram til hendelser og ting  |
| Like mye som før Avgjort mindre enn før   |
| Heller mindre enn før   |
| 42. Jeg kan plutselig få en følelse av panikk   |
| Uten tvil svært ofte Ganske ofte Ikke så veldig ofte Ikke i det hele tatt   |
| 43. Jeg kan glede meg over gode bøker, radio/TV   |
| Ofte Fra tid til annen Ikke så ofte Svært sjelden   |
|   |



\_\_\_\_

|  |   |                 | Prosjektnr:       |          |  |  |
|--|---|-----------------|-------------------|----------|--|--|
| Alvorlige livshendelser sis  | te 12 måneder                           |                 |                   |          |  |  |
| 44. Har det vært dødsfall i na<br>(barn, ektefelle/samboer,  | ær familie?<br>, søsken eller foreidr   | ja [<br>e)      | Nei               |          |  |  |
| 45. Har du vært i overhenger<br>katastrofe, voldssituasjor   | nde livsfare pga. alvo<br>n eller krig? | orlig ulykke,   | □Ja □Nei          |          |  |  |
| 46. Har du hatt samlivsbrudd i ekteskap eller i lengre samboerforhold?   |   |                 |                   |          |  |  |
| <ul> <li>47. Hvis du har svart ja på ett eller flere av spørsmål 44, 45 eller 46;</li> <li>i hvilken grad har du hatt reaksjoner på dette de siste 7 dager?</li> <li>Ikke i det hele tatt</li> <li>Litt</li> <li>I moderat grad</li> <li>I høy grad</li> </ul> |   |                 |                   |          |  |  |
| Kultur /livssyn  |   |                 |                   |          |  |  |
| <ol> <li>Hvor mange ganger har du i løpet av de siste 6 måneder vært på / i:<br/>(Sett ett kryss pr. linje)</li> </ol>   |   |                 |                   |          |  |  |
| Museum, kunstutstilling  | Mer enn 3 gimnd                         | 1-3 g/mnd       | 1-6 g siste 6 mno | Aldri    |  |  |
| Konsert, teater, kino  |   |                 |                   |          |  |  |
| Kirke, bedehus   |   |                 |                   |          |  |  |
| Idrettsarrangement   |   |                 |                   |          |  |  |
| 49. Hvilket livssyn vil du si lig<br>Kristent livssyn<br>Humanetisk livssyn<br>Ateistisk livssyn<br>Annet livssyn, hva   | iger nærmest opp til                    | ditt eget? (Se  | ett ett kryss)    |          |  |  |
| Vekt   |   |                 |                   |          |  |  |
| 50. Er du fornøyd med vekta  | dinå? 🗌 Ja 🗌                            | ] Nei, for lett | Nei, for tung     | 1        |  |  |
| 51. Er din kroppsvekt minst 2  | 2 kg lavere nå enn fo                   | r 1 år siden?   | 🗌 Ja 🗌 Nei        |          |  |  |
| Hvis ja: Hva er grunnen  | til dette? 🗌 Slanking                   | ) Sykdo         | m / stress        | /et ikke |  |  |
|  |   |                 |                   |          |  |  |



|   | Prosjektnr:  |
|---|--|
| T | obakk  |
| 5 | 2. Røykte noen av de voksne innendørs da du vokste opp? Ja Nei   |
|   | Hvis du aldri har røykt eller brukt snus, gå til spørsmål 56.  |
| 5 | 3. Svar på dette hvis du nå røyker daglig eller tidligere har røykt daglig:  |
| ŀ | Ivor mange sigaretter røyker eller røykte du vanligvis daglig? sigaretter pr. dag  |
| F | ivor gammel var du da du begynte å røyke daglig?   |
| ŀ | lvis du tidligere har røykt daglig, hvor gammel var du da du sluttet?  |
| 5 | 4. Svar på dette hvis du røyker eller har røykt av og til, men ikke daglig:  |
| ŀ | Ivor mange sigaretter røyker eller røykte du vanligvis i måneden? sigaretter pr. mnd   |
| F | ivor gammel var du da du begynte å røyke <u>av og til?</u> år gammel   |
| ŀ | ivis du tidligere har røykt av og til, hvor gammel var du da du sluttet?   |
| 5 | <ul> <li>5. Bruker du, eller har du brukt, snus?</li> <li>Nei, aldri Ja, men jeg har sluttet Ja, av og til Ja, daglig<br/>(Hvis du aldri har brukt snus, hopp til spørsmål 56)</li> <li>Hvis ja:<br/>Hvor gammel var du da du begynte med snus? ar gammel</li> <li>Hvor mange esker snus bruker/brukte du <u>pr. måned</u>? esker snus pr. mnd.</li> </ul> |
| ŀ | Alkoholbruk  |
| 5 | 6. Har du drukket alkohol i løpet av de siste 4 uker?  |
|   | Hvis ja:<br>Har du drukket så mye at du har kjent deg sterkt beruset (full)?   |
|   | Luver Luta, i-ziganger Luta, siganger eiler mer  |
| 5 | 7. Hvor ofte drikker du <u>5 glass eller mer</u> av øl, vin eller brennevin ved samme anledning?           Aldri         Månedlig         Ukentlig         Daglig  |



#### Søvn

| <ol> <li>Hvor ofte har det hendt i løp</li> </ol> | pet av de | siste 3 | måneder at du | 17 |
|---|-----------|---------|---------------|----|
|---|-----------|---------|---------------|----|

| Snorker høyt og sjenerende?                | Aldri / sjelden | Av og til | Flere ggr / uka |
|--|-----------------|-----------|-----------------|
| Får pustestopp når du sover?               |                 |           |                 |
| Har vanskelig for å sovne om kvelden?      |                 |           |                 |
| Våkner gjentatte ganger om natta?          |                 |           |                 |
| Våkner for tidlig og får ikke sove igjen?  |                 |           |                 |
| Kjenner deg søvnig om dagen?               |                 |           |                 |
| Har plagsom nattesvette?                   |                 |           |                 |
| Våkner med hodepine?                       |                 |           |                 |
| Får ubehag, kribling eller mauring i bein? |                 |           |                 |

#### Utmattelse

| 59. Siste uke har jeg følt at  | unnin |  |  |    |  |
|--|-------|--|--|----|--|
| Jeg har lett for å bli utmattet  |       |  |  | Ω" |  |
| Utmattelse nedsetter min fysiske<br>funksjonsevne  |       |  |  |    |  |
| Utmattelse skaper ofte problemer for meg   |       |  |  |    |  |
| Utmattelse fører til at jeg har dårlig fysisk<br>utholdenhet over lengre tid             |       |  |  |    |  |
| Utmattelse virker negativt inn på mine gjøremål<br>og forpliktelser                      |       |  |  |    |  |
| Utmattelse er ett av mine tre mest plagsomme<br>symptomer                                |       |  |  |    |  |
| Utmattelse virker negativt inn på mitt arbeid,<br>min familie og mitt øvrige sosiale liv |       |  |  |    |  |
| Mitt pågangsmot blir dårligere når jeg er utmatte  |       |  |  |    |  |
| Jeg blir fort utmattet ved anstrengelser   |       |  |  |    |  |
|  |       |  |  | R  |  |

| Prosjektnr:   |
|---|
| Hukommelse  |
| 60. Har du god hukommelse? 🗍 Ja 📄 Nei   |
| 61. Synes du hukommelsen din er därligere nå enn for 20-30 år siden? 🔲 Ja 🛛 🗌 Nei |
| Svimmelhet  |
| 62. Hvor ofte føler du deg svimmel?<br>Aldri Sjelden Av og til Ofte Hele tiden    |
| Fall  |
| 63. Hvor mange ganger har du falt i løpet av det siste året?                      |
| 64. Har du oppsøkt lege på grunn av skade etter fall det siste året? 🗌 Ja 🗌 Nei   |
| Til kvinner   |
| 65. Har du noen gang vært gravid? 🗌 Ja 🗌 Nei                                      |
| Hvis ja:<br>Hvor mange barn har du født?  |
|   |
|   |

Takk for at du tok deg tid til å svare på spørsmålene!

