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Physical activity and exercise - The Generation 100 study

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Physical activity and exercise among older adults - The Generation 100 study

Thesis for the Degree of Philosophiae Doctor

Trondheim, June 2016

Norwegian University of Science and Technology Faculty of Medicine Department of Circulation and Medical Imaging



NTNU

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SAMMENDRAG

De fleste land i verden vil fram mot år 2050 oppleve en demografisk endring, der andelen eldre personer vil øke sterkt. Denne demografiske endringen er forventet å øke helserelaterte kostnader, både fra et samfunnsøkonomisk perspektiv og for den enkelte. Fysisk aktivitet har vist seg å være en nøkkelfaktor for forebygging av livsstilsrelaterte sykdommer, men det er mindre forskning på fysisk aktivitet blant eldre enn i resten av befolkningen. I tillegg så finnes det få langvarige, randomiserte treningsstudier med friske eldre.

Avhandlingen bygger på tre forskningsartikler. Artikkel 1 hadde som mål å beskrive design, metode og initiering av en randomisert kontrollert studie, Generasjon 100, som evaluerer effekten av langvarig trening på helse, levealder og fysisk aktivitetsnivå hos eldre. Artikkel 2 hadde som mål å beskrive det fysiske aktivitetsnivået blant eldre voksne, ved hjelp av både relative- og absolutte intensitetsgrenser for akselerometer. Artikkel 3 hadde som mål å øke kunnskapen om bakgrunnsfaktorer som er assosiert med akselerometer-målt fysisk aktivitet blant eldre.

Generasjon 100 er beskrevet i detalj i artikkel 1. Den startet opp i år 2012 og vil pågå fram til 2018. Studien inkluderte 1567 personer i alderen 70-77 år, alle bosatt i Trondheim kommune. Deltakerne gjennomgikk undersøkelser, deriblant måling av fysisk aktivitetsnivå og kondisjon (maksimalt oksygenopptak). De fylte også ut spørreskjema. Undersøkelsene gjentas etter 1-, 3- og 5 år av studien. Deltakerne ble tilfeldig trukket ut til en kontrollgruppe eller til en gruppe som trener utholdenhet med enten moderat- eller høy intensitet, to ganger per uke.

Resultatene fra artikkel 2 viste at aktivitetsnivået blant 1219 norske eldre var høyere enn i andre land, men svært likt som i en norsk nasjonal kartlegging fra 2008-2009. Kvinner hadde et høyere totalt aktivitetsnivå, og brukte mer tid i høyere relative intensiteter, sammenlignet med menn. Totalt aktivitetsnivå og tid i nær-maksimal intensitet avtok med økende alder. Eldre personer med god kondisjon var mer fysisk aktive enn de med lav- og middels kondisjon. Vi fant at relative intensitetsgrenser, justert for kjønn og kondisjon, resulterte i at en høyere andel (79 %) eldre oppfylte myndighetenes anbefalinger for fysisk aktivitet, sammenlignet med bruk av en tradisjonell absolutt intensitetsgrense (29 %).

Resultatene fra artikkel 3 viste at 9 av 14 bakgrunnsfaktorer var med og forklarte 27 % av variansen i totalt aktivitetsnivå blant 850 eldre. Aktivitetsnivået var assosiert med demografiske, miljømessige og biologiske faktorer. Kondisjon, kjønn og årstid var faktorene som sterkest assosierte med totalt fysisk aktivitetsnivå. Studien er, så langt vi vet, den største studien av bakgrunnsfaktorer for fysisk aktivitet blant eldre som har kombinert akselerometermålinger og direkte målt maksimalt oksygenopptak.

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SUMMARY

Most countries in the world will by the year 2050 experience a large demographic change, leading to an increase in the proportion of older adults. This is expected to increase health related costs, both societally and individually. Physical activity is shown to be a key factor in the prevention of lifestyle-related diseases, but there is less research on physical activity among older adults compared to the general population. In addition, there are few long-term, randomised exercise intervention studies among healthy older adults.

This thesis is based on three research papers. Paper 1 aimed to describe the design, methodology and initiation of a randomised controlled trial entitled the Generation 100 study, evaluating the effect of long-term exercise training on health, longevity and physical activity levels among older adults. Paper 2 aimed to describe physical activity levels in older adults, using both relative- and absolute intensity accelerometer thresholds. Paper 3 aimed to increase the knowledge about the background factors associated with accelerometer-measured physical activity in older adults.

The Generation 100 is outlined in detail in paper 1. It began in 2012 and will continue until 2018. The study included 1,567 people aged 70-77 years, residing in the municipality of Trondheim, Norway. Participants underwent examinations, including measurement of physical activity and cardiorespiratory fitness (maximal oxygen uptake). They also filled out questionnaires. Participants are followed-up at 1-, 3- and 5 years of the study. Participants were randomly assigned to a control group or to either a moderate- or high intensity endurance exercise group required to train two times per week.

The results from paper 2 showed that the activity level in 1219 Norwegian older adults was higher than in other countries, but very similar to a Norwegian national survey from 2008-2009. Females had a higher overall activity, and spent more time in higher relative intensities, compared to males. Overall activity and time in the near-max relative intensity decreased with age. Older adults with higher levels of cardiorespiratory fitness were also more active than those with low- and medium cardiorespiratory fitness. We found that the use of relative intensity thresholds, adjusted for gender and fitness, resulted in higher proportions (79%) of older adults meeting physical activity recommendations, compared to the use of a traditional absolute intensity threshold (29%).

The results from paper 3 showed that 9 out of 14 background factors explained 27% of the variance in overall physical activity among 850 older adults. Activity level was associated with demographic, environmental and biological factors. Cardiorespiratory fitness, gender and season were the factors most strongly associated with overall activity. The study was, to our knowledge, the largest study of background factors for physical activity among older adults that has combined accelerometry and directly measured maximal oxygen uptake.

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Cardiac Exercise Research Group

Department of Circulation and Medical Imaging, Faculty of Medicine, NTNU Supervisor: Professor Ulrik Wisløff. Co-supervisor: Researcher Dorthe Stensvold Funding source: The Liaison Committee between the Central Norway Regional Health Authority (RHA) and the Norwegian University of Science and Technology (NTNU), and the K.G. Jebsen Foundation

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Furthermore, I would like to thank all the fantastic people who have contributed to the data collections in the Generation 100 study. This includes all the master students and medical students, the nurses at the Clinical Research Facility, St. Olavs University Hospital, the engineers at the Department of Circulation and Medical Imaging, as well as the PhD candidates, medical doctors and others involved in the study.

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person in the group, I highly appreciate working here, and I think that this group has the best possible work environment! A special thanks goes to my office colleagues during these years, both for inspiring me to work even harder and for the pleasant coffee breaks and talks.

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Trondheim, March 2016

LIST OF PAPERS

This thesis is based on the following original research papers, referred to in the text as paper I, paper II and paper III:

Paper I

Stensvold D, **Viken H**, Rognmo Ø, Skogvoll E, Steinshamn S, Vatten LJ, Coombes JS, Anderssen SA, Magnussen J, Ingebrigtsen JE, Fiatarone Singh MA, Langhammer A, Støylen A, Helbostad JL, Wisløff U. (2015) A randomised controlled study of the long-term effects of exercise training on mortality in elderly people: study protocol for the Generation 100 study. *BMJ Open* 2015;5(2).

Paper II

Aspvik NP*, **Viken H***, Zisko N, Ingebrigtsen JE, Wisløff U, Stensvold D. (2016) Physical activity among older adults (70-77yrs) – and consequences of different methodological approaches: The Generation 100 study. *Submitted*. *Shared first authorship.

Paper III

Viken H*, Aspvik NP*, Ingebrigtsen JE, Zisko N, Wisløff U, Stensvold D. (2015) Correlates of objectively measured physical activity among Norwegian older adults: The Generation 100 study. *Journal of Aging and Physical Activity. Accepted for publication.* *Shared first authorship.

ABBREVIATIONS

ACSM:	American College of Sports Medicine
AHA:	American Heart Association
BMI:	Body mass index
CPM:	Counts per minute
CRF:	Cardiorespiratory fitness
CVD:	Cardiovascular disease
HIIT:	High intensity interval training
HR:	Heart rate
HR _{max} :	Maximal heart rate
HR _{peak} :	Peak heart rate
HUNT:	The Nord-Trøndelag Health Study
Kan1:	The Physical Activity among Adults and Older People Study
MCT:	Continuous moderate intensity training
MPA:	Moderate intensity physical activity
MVPA:	Moderate-to-vigorous physical activity
PA:	Physical activity
RCT:	Randomised controlled trial
SD:	Standard deviation
VO _{2max} :	Maximal oxygen uptake
VO _{2peak} :	Peak oxygen uptake
VPA:	Vigorous intensity physical activity
WHO:	World Health Organization

DEFINITIONS

Cardiorespiratory fitness:

The maximal ability of the circulatory and respiratory systems to supply fuel during dynamical work involving large muscle mass, and to eliminate fatigue products after supplying fuel.

Exercise:

A subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.

Physical activity:

Any bodily movement produced by skeletal muscles that results in energy expenditure.

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INTRODUCTION

Background

In the near future most countries in the world, including Norway, will be facing a historically unprecedented population ageing [1]. According to the World Health Organization (WHO) and the United Nations (UN) we will have a higher proportion of older adults (\geq 65 years of age) than children by the year 2050, and more people at older old age (\geq 85 years of age) than ever before [2, 3]. The demographic changes towards an older population are predicted to result in more health related costs, both individually and societally [1, 4, 5]. An increasingly larger part of these costs are predicted to be caused by non-communicative diseases (NCD) related to lifestyle and behaviour [2].

Many of the health-related challenges associated with an ageing population depend on health behaviour and policy [1, 6]. The UN recently listed physical activity (PA) as one of the key factors for combating NCDs [7]. PA is important for health, and reduces the risk of more than 20 major diseases, such as cardiovascular disease (CVD), stroke, obesity and type 2 diabetes, as well as risk of premature death [8-11]. Research on PA levels in populations of older adults is sparse when compared to studies on children, adolescents and younger adults [12, 13]. Strategies on how older adults can become more physically active are important, as this may improve health and increase self-reliance [14-17].

The present thesis focuses on PA among older adults, including recommendations, PA levels, background factors associated with PA, and methods for PA assessment.

Physical activity and health

PA has always been a natural part of human behaviour and considered important for health since ancient times [18]. Health is a complex and broad term that is difficult to define precisely [19]. A broad definition is a human condition with physical, social, and psychological dimensions, varying between positive and negative health [20, 21]. The importance of PA for health was described in detail 2000 years ago by the Greek physicians Herodicus, Hippocrates and Galen; the first printed book devoted entirely to exercise was published in 1553 [20]. In 1846, the vigorous PA of agricultural workers was thought to reduce CVD mortality, compared to sedentary workers [22].

Physical inactivity is recognised as the fourth leading cause of death worldwide, preceded only by smoking, hypertension, and high blood glucose levels [23, 24]. Regular PA increases life expectancy by influencing the development of chronic disease [25]. Older adults, who are physically active, have lower risk of all-cause mortality, CVD, hypertension, stroke, type 2 diabetes, colon-, and breast cancer compared to inactive individuals [9, 26]. Furthermore, there is growing evidence that PA can be used for the prevention, management and treatment of many chronic diseases and conditions [25, 27]. For older adults, not only maintaining their PA levels, but also initiating PA at older age, is associated with better functioning and lower mortality risk [28, 29]. This supports the encouragement of PA even among the oldest populations [29]. Despite this evidence, the existing literature has demonstrated that older age groups are less active than younger adults, and less active than the recommendations given by health authorities [30].

The increase in chronic diseases associated with unhealthy lifestyles has led to a new research field within the discipline of epidemiology, called PA epidemiology [31]. PA epidemiology is a research field that began in the 1950s that utilises sophisticated analysis methods. Dr. Jeremy Morris and colleagues found differences in occupational PA levels between bus drivers and conductors, which were related to differences in risk of developing coronary heart disease [32-34]. The work of Morris et al. was followed by Dr. Ralph Paffenbarger Jr., who initiated two pioneering epidemiological studies that examined the relationship between PA and CVD: the College Alumni Health Study and the San Francisco Longshoremen Study [22, 35, 36]. These studies were well-controlled with comprehensive examinations, and the large population samples have resulted in extensive longitudinal data regarding PA and CVD, and widely cited publications [22]. PA epidemiology broadly entails two steps. The first part is to examine the relation between PA and health from a variety of perspectives. The second part is to study the distribution and determinants of PA behaviour, knowledge used to prevent and control disease, and promote health [31]. PA epidemiology often tries to specify the dose-response relationship [37] between PA and a defined health outcome (e.g. risk factor, disease, or quality of life) [19]. An important limitation of the research within the field of PA and health is that most studies have used self-reported measures of PA [38, 39].

Physical activity, exercise and cardiorespiratory fitness

Physical activity

PA is defined as 'any bodily movement produced by skeletal muscles that result in energy expenditure' [40]. This means that the term PA is very broad, and something that everyone needs to perform to sustain life. PA can be categorised in several ways, and the simplest categorisation divides PA into three parts: while sleeping, at work, and during leisure time [40]. PA results in an increase in energy expenditure (EE) above resting levels, and the rate of EE is directly linked to the intensity of the PA performed [41]. The most common way to quantify EE for a given activity is in kilocalories (kcal), kilojoules or metabolic equivalents (METs) [42]. One MET is defined as the amount of oxygen consumed while sitting at rest and is approximately equal to 3.5 millilitres of oxygen per kilogram of body mass per minute, or 1 kcal per kilogram of body weight per hour [43, 44].

The *mode* of PA can be a specific type of activity performed, but mode can also be defined by the physiological and biomechanical demands (e.g. aerobic vs. anaerobic PA, strength or balance training) [41, 45]. In this thesis, aerobic types of PA will be the focus. The PA guidelines for Americans provide examples of specific types of aerobic PA suited for older adults, such as walking, dancing, swimming, jogging, bicycle riding or gardening [46]. Walking is the most common type of PA among older adults [47]. The American College of Sports Medicine (ACSM) has published a Compendium of Physical Activities with a code system, used to quantify the EE of hundreds of types of PA among adults [44].

The dimensions *frequency*, *duration* and *intensity* are used to quantify the total patterns of PA. Frequency is the number of times an activity is performed, and is expressed in sessions or bouts (often ≥ 10 min in length) per day or per week [41]. Duration is the length of time an activity is performed, and is generally expressed in minutes [45, 46]. PA intensity refers to the amount of work being performed, or the magnitude of the effort required to perform an activity [9]. Intensity can be expressed either in absolute or relative terms [45, 46]. Absolute intensity is determined by the external work being performed, while relative intensity takes into account the cardiorespiratory fitness (CRF) of the individual [41]. For aerobic activity, absolute intensity is typically expressed as EE (i.e. oxygen consumption, kcals or METs), speed or physiologic response (i.e. heart rate; HR) [46]. Relative intensity is often expressed as a percentage of maximal/peak oxygen uptake (VO_{2max}/VO_{2peak}), maximal/peak heart rate (HR_{max}/HR_{peak}), or heart rate reserve. Alternatively it can be expressed as a subjective level of perceived effort, for example on a Borg rating of perceived exertion (RPE) scale of 0 to 10, or 6 to 20 [46]. The total *volume* of PA is determined by an interaction between the three components frequency, duration, and intensity [45, 46]. The volume of PA may be quantified into the following units: kcal, MET-minutes or MET-hours [19]. The ACSM coding scheme can help in calculating PA volume, since PA is classified by rate of EE, estimated in MET-minutes, MET-hours, kcal, or kcal per kilogram body weight [48].

Exercise

Exercise is related to PA, but viewed more narrowly as 'a subset of PA that is planned, structured, and repetitive and has as a final or intermediate objective the improvement or maintenance of physical fitness' [31, 40]. In other words, exercise could be referred to as 'intentional PA for improving health and fitness' [42]. The terms exercise and exercise training are frequently used interchangeably [46]. Exercise that primarily uses the aerobic energy systems is effective for improving CRF [9].

Cardiorespiratory fitness

Maximal exercise capacity is often measured as CRF. CRF refers to 'the maximal ability of the circulatory and respiratory systems to supply fuel during dynamic work involving large muscle mass, and to eliminate fatigue products after supplying fuel' [40, 42]. CRF can be measured by a number of parameters, including resting HR, lactate level or HR at submaximal exercise level, VO₂ at ventilatory threshold, time to exhaustion etc. [9]. However, the most common way of quantifying CRF is usually through measured or estimated VO_{2max} [46]. CRF is one of the health-related components of physical fitness [19]. A higher level of CRF is associated with a lower risk of poor health, and adults and older adults with better CRF or who increase their CRF have a lower risk of CVD and all-cause mortality [42, 49-51]. Among patients referred for exercise testing for clinical reasons, VO_{2peak} (in METs) has been shown to be a more powerful predictor of all-cause mortality than other established risk factors [52]. CRF normally declines at a nonlinear rate and the decline accelerates with advancing age particularly when regular exercise is absent [42, 53]. For example, Fleg et al. found a decline of more than 20% per decade after the age of 70 years [54]. Conversely, it has been found that every 1 mL kg^{-1} . \min^{-1} increase in VO_{2peak} reduces the risk of death by 15% in CVD patients [55]. Exercise training leading to an increased CRF can slow or reverse the functional decline, e.g. a 6 mL·kg⁻¹ \cdot min⁻¹ increase may reduce the biological age by more than 10 years [56]. The degree of increase in CRF from exercise training will depend on the intensity, frequency, and duration of each exercise session, in addition to the length of the training period, and the initial CRF level [57, 58].

Recommendations for older adults

PA recommendations were first published in 1975 by the ACSM, entitled *Guidelines for Graded Exercise Testing and Exercise Prescription* [59]. Public health recommendations for PA are based on research regarding PA and health, and are therefore regularly updated according to continuous development in this research field [9]. For this reason the PA guidelines for adults changed in 1995 from only recommending vigorous intensity PA (VPA) to also including moderate intensity PA (MPA) [59, 60]. Specific PA recommendations for older adults were first published in 2007 by the ACSM and the American Heart Association (AHA) [61]. More recent guidelines have been published by the US Department of Health and Human Services (2008), the WHO (2010), and the Norwegian Directorate of Health (2014) [45, 46, 62]. The WHO recommendations from 2010 were the first global PA guidelines [24].

Large epidemiologic studies have estimated the volume of PA needed to achieve specific health benefits to be approximately 1000 kcal·wk⁻¹ of MPA, and that this is associated with lower rates of CVD and premature mortality [42]. This corresponds to approximately 750 MET·min·wk⁻¹ or 150 minutes per week of moderate intensity PA [63]. This 1000 kcal·wk⁻¹ volume of PA can be accumulated through a combination of PA types of varying intensities [9]. The current PA recommendations for older adults are very similar to the recommendations for younger adults, and states that the recommended amount of aerobic exercise is 150 minutes of MPA, or 75 minutes of VPA, or a combination of these two expending an equivalent amount of energy [45, 61].

Recommendations for older adults differ from the guidelines for younger adults by stating that the intensity of aerobic activity should take into account the older adult's aerobic fitness level [61]. According to the WHO, for individuals with low physical fitness, the absolute intensity and amount of PA needed to achieve many health benefits are lower than for individuals with higher PA and fitness levels [45]. Thus, older adults can meet the guidelines by doing MPA or VPA in relative intensity, or a combination of both [46]. This is particularly important for older adults with formerly sedentary lifestyles who are starting up with PA [45]. In absolute terms, moderate intensity refers to PA performed at 3.0–5.9 METs, while vigorous intensity refers to

PA at 6.0 METs or above [61]. On a relative Borg RPE scale of 6-20, MPA is usually 11-12 and VPA 13-16 [41, 45].

The PA guidelines state that there are only two intensity zones recommended for maintenance and improvement of health: MPA and VPA [45]. Therefore, light intensity activities are not included in the PA recommendations. Nevertheless, light intensity PA is becoming more relevant in research, particularly as both global inactivity and the proportions of older adults are increasing [37, 64]. Furthermore, older adults seem to spend a greater portion of their day in absolute light intensities (measured in METs and minutes in absolute accelerometer intensity zones) compared to younger adults [65, 66]. While the extent to which light intensity PA in absolute terms contributes to health among older adults is less understood, some studies indicate that there is a positive association [67, 68].

Levels of physical activity among older adults

The proportions of older adults meeting PA guidelines, based on accelerometry, vary between 5.8% (UK), 6.3% (USA) and 13.1% (Canada) [17, 69, 70]. Data from the Attitude Behavior and Change Study and the National Health and Nutrition Examination Survey, showed that Swedish and US populations aged 60-75 years accumulated 16 and 6 minutes per day of moderate-to-vigorous PA (MVPA) within 10-min bouts, respectively [71]. Large accelerometer studies have shown that overall PA declines with age [70, 72]. Despite this trend, it is not clear how patterns of PA, such as the amount of bouts of 10 min or longer of MVPA change with age [73]. Most studies have found older adult males to be more physically active than females [74].

In Norway, the largest study of PA among older adults assessed by accelerometry has been the national cross-sectional survey of PA, entitled the Physical Activity among Adults and Older People Study (Kan1) [75]. A total of 560 participants above 65 years had valid accelerometer data, monitored with the Actigraph GT1M accelerometer [13, 75]. From the Kan1 data Lohne-Seiler et al. examined compliance with the previous Norwegian PA recommendations, and found that 19.9% of the 70-74 year group and 14.8% of the 75-79 year group met the recommendations [13]. Therefore, compared to older adults in other western countries Norwegian older adults seem to be more active. Furthermore, Hansen et al. showed that overall PA, steps per day and time spent in lower intensity PA decreased from the 20-64 year group to the 65-85 year group in Kan1, while time in sedentary behaviour increased [76]. The current

Norwegian recommendations (150 min of MVPA per week) have changed from the previous recommendations (30 min of MVPA per day) applied in those studies, and it is generally important to understand how changes in guidelines may affect measures of PA levels [70]. Additionally, it is unclear whether the total decline in PA among older adults reflects a change from MVPA to more PA of lower intensities [17]. The Kan1 was followed up by the Kan2 study, with data collections during the years 2014-2015. When applying the new PA recommendations, 32% of the participants above 65 years met the recommendations, an increase from the 25% in Kan1 (years 2008-2009). Furthermore, this age group accumulated 18 minutes per day of MVPA within 10-min bouts, and the mean number of steps per day was 6989 [77].

Correlates of physical activity among older adults

To understand how best to promote PA at the population level, and to design effective PA interventions among older adults, we need to understand what background factors are associated with different levels of PA [78, 79]. Knowledge about PA correlates are therefore needed to effectively promote an active lifestyle [80]. The amount of research into correlates and determinants has increased in the past two decades, but this has mostly focused on background factors among children, adolescents and younger adults [81-83]. There are virtually an infinite number of PA correlates, but some commonly explored are demographic, biological and environmental factors [83, 84]. Using evidence-based information about PA correlates in the planning of public health interventions, may lead to more effective programmes, as factors known to contribute to inactivity can be targeted [81].

<u>Demographic correlates</u> include factors such as gender, age, education and work. Among older adults, males have been found to be more physically active than females; either measured as total PA, frequency of PA or proportions meeting PA recommendations [47, 74, 85-88]. Gender differences from objectively measured PA have shown smaller differences than self-reported PA [74]. Age has repeatedly shown an inverse relation with PA level [74, 86, 89-91]. Older age groups are often divided into younger and older old, often compared to younger adults, and seldom divided into narrow age bands of older age groups [74]. Education level is reported as having a positive association with PA [87, 92, 93], but there are also studies showing no such association [81, 91, 94]. Retirees from sedentary jobs have shown increased PA levels, while retirees from physically strenuous jobs have shown decreased total PA [95, 96].

<u>Biological correlates</u> include factors such as body composition (e.g. body mass index; BMI), CRF and health status, which can be both self-reported or medically assessed. A number of studies have shown an inverse association between BMI and PA [87, 92, 97]. There is not a clear consensus regarding the association between CRF (measured as VO_{2max} or VO_{2peak}) and PA [98-100]. Health variables like presence of chronic conditions or multimorbidity are negatively associated with PA [87, 92]. More specifically, heart diseases have been negatively associated with PA level [47]. One study, however, reported heart arrhythmia, myocardial infarction and bypass surgery to be positively associated with PA level [101]. A generally sedentary population among the healthy participants, and high compliance to a rehabilitation program involving PA among heart disease patients, probably explained this observation.

Environmental correlates can be divided into factors related to social environment and physical environment. Among social environment correlates, living situation has demonstrated mixed evidence of associations with PA among older adults. Some studies [87, 92] reported that being unmarried or living alone was associated with higher PA level, and one report that living together and also being married were associated with higher PA [47], while others reported no association with PA [81, 88, 91], or different outcomes for men and women [94]. Social support from friends or family was significantly related to PA (walking) in two studies [85, 102], but not in another [103]. Physical environment does not show a clear relationship with PA. For example walking or cycling facilities have shown mixed evidence of association with total volume of objective PA [85, 104, 105]. In total there has been a limited number of studies on physical environment and objective PA among older adults [105]. Seasonal variance and climatic conditions (e.g. time of the year, temperature and daylight length) have been shown to be associated with objective PA level among older adults in several studies [90, 106, 107], with people becoming more active in the warmer periods. The same has also been found for selfreported levels of PA [108]. Correlates of self-reported PA among older adults have been identified previously [82], but very few studies have used objective PA assessment to examine the associations, especially in large population samples of older adults in Scandinavia [103].

Physical activity and exercise assessment

PA and exercise can be monitored and quantified in several ways, depending on size of the study sample, level of precision or type of outcome variables needed, degree of economic and human costs, and other practical factors, which need to be taken into consideration [37, 41]. Among older adults, measurement of PA has additional challenges, for example related to

reduced cognition and disability [109]. Methods that have been developed for younger adult populations may therefore be inappropriate for older adults [89, 110]. In terms of economy, as a rule the economic cost of an assessment method is inversely proportional to its accuracy. For example, self-reported measures are the least expensive, but also the least accurate. Contrary to this, calorimetric assessment is a highly accurate but expensive method of measuring PA [111]. There is also a historical dimension as the possibilities for assessment of PA have changed during the last decades, in addition to a change in target groups, from individuals or small groups to larger populations [37].

PA and exercise intensity are typically assessed using both subjective and objective methods. Objective methods most often measure physiological responses, such as HR, oxygen uptake, blood lactate level, or body temperature [37, 112]. Subjective methods, e.g. the Borg RPE scale, primarily assess intensity through a person's perception towards the muscular- or respiratory systems, such as fatigue, dyspnoea, discomfort or pain [112].

Self-reported measures of PA have traditionally been the common way of quantifying PA in large population studies [74]. These methods have obvious strengths, but also important weaknesses related to the precision of the measurements, especially among older adults [30, 109, 113]. Factors like fluctuations in health status, problems with memory and cognition, and the fact that older adults tend to engage most frequently in light to moderate intensity PA, makes self-report techniques less feasible for this age group [110, 113]. Due to technological developments, objective methods have become more common as an alternative to self-report [64].

In the following section, different assessment methods are presented and evaluated in terms of advantages, disadvantages and best-suited purpose (Figure 1). The first four methods (doubly-labelled water, direct- and indirect calorimetry and observation of PA) could be categorised as criterion methods with a high degree of validity, but best suited for laboratory use or small-scale studies [114, 115]. The last four methods (self-reported PA, objective PA, HR monitoring and Borg RPE scale) are frequently used to quantify PA and exercise. All four methods have been used in the Generation 100 study [116], during examinations and during the intervention period. Assessment of PA and exercise partly overlap, but what distinguishes them most clearly is the time dimension derived from the definition of the two terms [40]. PA is therefore normally

monitored continuously for days or weeks, while exercise assessment is more related to monitoring single exercise sessions.

Doubly-labelled water and calorimetry

The metabolism of doubly-labelled water (DLW) is a very accurate method for determining carbon dioxide output, and is often considered the most valid measure of free-living PA or EE [37, 117]. A dose of DLW is ingested and the elimination of the isotopes deuterium (²H) and oxygen-18 (¹⁸O) from the body is tracked by analysing biological samples, most commonly urine [115, 118]. The DLW technique estimates PA under free-living conditions for 1-3 weeks, is suitable for most populations and inflicts only moderate burden on subjects [41, 117]. DLW is highly reliable and can be used to validate other methods such as questionnaires and accelerometers, but expensive and not very feasible in clinical studies or in larger field studies [37, 115, 119]. Another disadvantage is that DLW cannot provide information about frequency, duration and intensity [114].

Direct calorimetry measures total body heat production within a prolonged time frame [37]. This is the gold standard for PA assessment and other methods should ideally be validated against this method [115]. Disadvantages are the need for expensive equipment and large metabolic chambers, and the long measurement periods [37]. Direct calorimetry is not practical or accurate for exercise assessment under free-living conditions, and cannot provide information about metabolites [114]. Indirect calorimetry measures the ventilatory volume, overall oxygen consumption and carbon dioxide production during PA [41]. The method is a valid estimation in laboratory and field settings for short time periods and provides a reliable measure of EE [37]. Indirect calorimetry is expensive, and difficult to use for longer periods under free-living conditions [114].

Observation of physical activity

One of the earliest methods to assess PA was the direct observation by experienced observers [115]. Direct observation of PA patterns is considered a reliable method, and historically it has been used to study occupational PA and team sports [37]. Trained observers collect contextual information and evaluate different behaviours, allowing for detailed accounts of type, duration and intensity of PA [110, 114]. Observation is, due to large human and economic costs, not very well suited to epidemiological studies of PA or exercise in large populations [37, 114].

Self-reported physical activity

In public health investigations of PA the traditional way of collecting PA data has been through the use of self-reported assessment methods [120]. The most typical way of self-reporting PA in epidemiological studies is the use of questionnaires [74, 121]. The two most commonly used standardised questionnaire instruments are the International Physical Activity Questionnaire (IPAQ, developed in 1997) and the Global Physical Activity Questionnaire (GPAQ, developed in 2001), which are comparable in terms of reliability and validity [122]. Quantifying PA through questionnaires has major advantages and disadvantages. They are cost-effective, easily distributed to large groups, and they can collect information across many dimensions of PA, i.e. patterns of PA can be identified [110, 114]. On the other hand, these are subjective reports. This means that they are also susceptible to over-estimation, and can be influenced by social desirability, recall bias and cultural difference bias [12, 30]. Most PA questionnaires are developed for younger adults, meaning that they are less suited or even inappropriate for assessment among older adults [109, 111, 114]. A few questionnaires have therefore been specifically developed for older adult populations, such as the Modified Baecke Questionnaire, the Zutphen Physical Activity Questionnaire, the Yale Physical Activity Survey, the Physical Activity Survey for the Elderly and the IPAQ modified for the elderly [111, 123].

Heart rate monitoring

A widely used physiological predictor of oxygen consumption in PA research is HR monitoring [31]. HR monitoring is a feasible approach because of the relatively linear relationship between HR and EE (i.e. oxygen consumption) during steady-state exercise, from 50% of VO_{2max} to near peak effort [37, 124]. HR monitoring provides information about frequency, intensity and duration of exercise [119]. It is also suitable for most populations and can be used in water. The method is relatively inexpensive and provides quick data processing and analysis [114]. A disadvantage is that HR monitoring is best suited to assess time spent in exercise of moderate and vigorous intensity [111, 118]. In rest and during low and extremely high intensity, the relationship between HR and EE can potentially be confounded by factors other than energy demands (e.g. caffeine, stress, smoking, body position) [114, 115]. Also, in order for this method to be accurate there is a need to establish individual HR-VO₂ relationships [118], which is expensive and time-consuming. Therefore, HR monitoring may be of limited use in assessing total PA, if a large percentage of the day is spent in low intensities [124]. In addition, HR across the entire intensity scale can be affected by internal and external factors, such as gender, age,

genetics, body composition, metabolism, medicine, temperature, and time of day [111, 114, 124].

Borg rating of perceived exertion scale

The Borg RPE scale is a commonly used method for subjective intensity assessment during exercise and testing [125]. The RPE scale was designed by Borg as a proxy indicator of exercise intensity [112]. The most commonly used versions of the scale are denoted by the numbers 0-10 or 6–20, with a proportional relation between increased RPE and the scale number [99, 126]. Instead of measuring physiological responses, the RPE scale includes information from various sources, i.e. from the working muscles and joints, and the cardiovascular and respiratory functions [112]. The RPE scale is well correlated with HR (r = 0.80-0.90) [125].

Accelerometry

Questionnaires have until recently been the most common approach in PA epidemiology [37]. Recent technological improvements have made objective measures of PA possible, primarily through the use of accelerometers [64, 120]. Accelerometers are devices that measure body movements in terms of acceleration, which then can be used to estimate the intensity of PA [16]. Accelerometers are able to monitor frequency, intensity and duration of PA, and take into account the relationship between movement and time [114]. Accelerometers register many dimensions of PA, and can give outcome measures like steps, estimation of EE, total counts, counts per minute (CPM), time spent doing PA (distributed in intensity zones), and activity patterns [31, 127]. Most accelerometers are piezoelectric sensors that detect acceleration in one to three orthogonal planes [31, 113].

Known advantages of accelerometers are that they have been extensively validated against DLW under free-living conditions, they are small in size and suitable for use across all age groups and for extended time periods [118, 128]. Accelerometer assessment makes it possible to monitor activity for longer periods without depending on the memory of the participants [129]. For example, accelerometers are feasible for indicating time spent in different intensity zones, particularly lower intensities, which are often imprecisely recalled despite being the dominant intensity among older adults [66, 73]. Accelerometers are known to underestimate the EE of some types of PA, such as cycling, uphill walking or carrying extra weight [31], while overestimating EE from downhill walking [130, 131]. Additional disadvantages are that they give no information regarding type of PA, and accelerometers are relatively expensive [114].

Although the prices of accelerometers have been reduced, the cost of devices suitable for PA research are still high, and this makes them less suitable for really large population studies [120].

The raw data produced from most accelerometers are counts, which is the product of the amplitude and frequency of the accelerations. Importantly, the algorithmic conversion of the raw acceleration signal into counts varies between monitor brands, and is therefore not directly comparable [111, 124]. Furthermore, uniaxial assessment is the most common, while triaxial accelerometers have the theoretical advantage of measuring a wider range of body movements [37]. Recommendations for PA are expressed in terms of time spent above intensity thresholds. Therefore, accelerometry is most useful for surveillance of adherence to guidelines if the raw counts can be translated into time spent in MVPA [132].

Since the early 2000s, accelerometers have become more accessible for use in PA research, and the increasing number of scientific publications reflects this trend [133, 134]. There have however been relatively few studies using accelerometers to measure PA in older populations [12, 129]. In addition to the lack of information regarding older adults, there is a need for accelerometer studies with populations other than the US population [12, 121]. The use of an accelerometer intensity threshold or cut point is a systematic way to analyse large amounts of PA data in public health research [31]. Interestingly, the general practice has been to apply the same absolute intensity thresholds for MVPA across all populations, and this could be highly problematic when monitoring PA behaviour among older adults [12, 135]. These cut points have been developed using small samples of younger adults and there is a great deal of uncertainty about whether these cut points should be applied to various population groups, e.g. older adults [65].

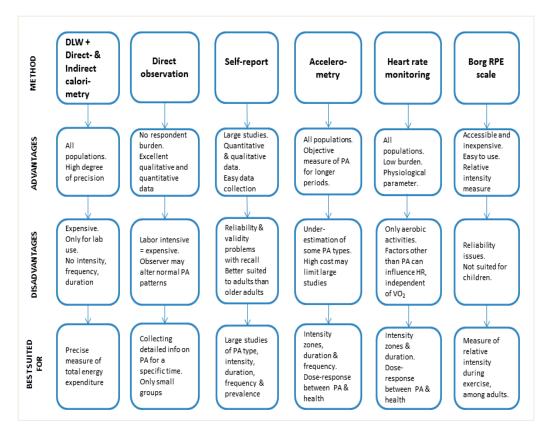


Figure 1: Methods for assessment of physical activity and exercise. Abbreviations: DLW, doubly-labelled water; PA, physical activity; RPE, rating of perceived exertion.

AIMS OF THE THESIS

The ageing population raises important questions regarding modifiable factors that can contribute to a successful ageing process, where older adults can live independent lives with low rates of disease and dysfunction. There is a need for large randomised controlled studies that can test the long-term effects of exercise training on disability, quality of life, disease and longevity in larger populations. Furthermore, population levels of PA participation among older adults are suspected to be low, and an improved understanding of why some older adults are active and others are not, is needed.

The purpose and specific aims of the thesis were:

- To develop design and methodology, and initiate a randomised controlled trial beyond the state of the art that evaluates the effect of long-term exercise training on health, longevity and physical activity level in older adults (**Paper I**).
- To describe the physical activity level in a population sample of older adults, using both relative and absolute accelerometer thresholds (**Paper II**).
- To increase the knowledge about physical activity correlates in a population sample of older adults (**Paper III**).

Based on former research we hypothesised that the PA levels among Norwegian older adults would be higher compared to other countries, and that males would be more active than females. Furthermore, we hypothesised that relative intensity thresholds, adjusted for gender and CRF, would result in a higher proportion of older adults meeting the PA recommendations, compared to the traditional use of absolute intensity accelerometer thresholds. Moreover, we hypothesised that the use of triaxial assessment would result in a higher number of minutes conceded in 10-min bouts of MVPA, compared to the uniaxial assessment. Finally, we hypothesised that objectively measured overall PA would be associated with demographic, environmental and biological correlates.

MATERIALS AND METHODS

Generation 100

All three papers presented in this thesis were based on the ongoing randomised controlled trial (RCT), entitled the Generation 100 (Paper I). The Generation 100 is a unique study with a primary aim of examining whether exercise has an effect on morbidity and mortality in an older population. The study is unique because of the combination of a large sample size of older adults, that an entire age specific population in a defined geographical area was invited, the wide spectrum of measurements performed, and because of the long intervention period of five years. This means that the study has great potential to answer important questions regarding PA, exercise and health, and in a longer period than most former studies have examined.



Figure 2: Map of Europe with Trondheim, Norway marked.

Trial site in Trondheim, Norway

The study is performed in the city of Trondheim, which is the third-most populous municipality in Norway, with a total population of 184,960 inhabitants, on 1 January 2015. The population of persons aged 65 years and above was 25,411 (14,130 females, 11,281 males), in January 2015 [136]. The municipality is geographically located in the middle of Norway

(63°26'N/10°24'E) (Figure 2). Trondheim has a typical Scandinavian climate with long winters and large differences in hours of daylight between summer and winter.

Rationale for the studies

Paper I describes the idea and background for the Generation 100 study, and offers insight into the details like time schedules, examinations, randomisation and exercise interventions. The rationale behind paper I had a clear focus on physiological or medical dimensions, and the efficacy of exercise. Since this is an ongoing RCT the future analyses examining the relationship between exercise, PA and health outcome were outlined in paper I. The scientific part of the project focused on PA among older adults, using objective measurements of PA and social science variables from questionnaires.

The candidate has been central in all stages of the study, from the planning, design and initiation of the study to the 3-year examination, performed in 2015-2016. The planning of the Generation 100 study started in January 2012 and lasted until the study started in August 2012. The planning included development of the study design, with formal approvals obtained from the Regional Committee for Medical Research Ethics and the Norwegian Tax Administration for access to the National Population Registry. In addition, license approvals for legal use of various measurement instruments were obtained from the licensees. The planning also included a myriad of meetings and development of necessary study documents and web resources, such as invitation letter, consent form, questionnaires, case report form for the clinical examinations, information circulars regarding the exercise interventions, protocol for use of accelerometers and training diaries in paper- and web versions. In addition, the planning had to solve logistical challenges related to research staff, location of examinations and exercise training sessions, printing and distribution of 6966 invitations, as well as telephone booking of individualised examination appointments for all participants. Furthermore, the candidate had to participate full-time in the data collections at three time points (baseline, one- and three year testing), in addition to contributing substantially to data processing and quality control before the statistical analyses could take place. During the baseline data collection, the candidate had the primary responsibility of coordinating the project, including oversight of 10 employees and 1,567 study participants. The PhD project has therefore resulted in invaluable practical experience with both planning and implementation of large data collections and administration of randomised controlled trials. Given this background, the inclusion of paper I, the Generation 100 study protocol, in this thesis was considered highly relevant.

The rationale behind paper II was to give a comprehensive description of the PA levels among older adults across age, gender and CRF. Furthermore, we wanted to quantify how many older adults in our population sample were meeting the health authorities' recommendations for PA, using different methodological approaches. Traditionally, PA has almost exclusively been monitored based on absolute criteria developed from population samples of younger adults. Therefore, we analysed time spent in PA intensity zones, time in bouts of MVPA and proportions meeting PA recommendations using relative intensity thresholds adjusted for gender and population CRF in the Generation 100 [131]. For reasons of comparison, time in bouts of MVPA and proportions meeting the guidelines were also analysed with an absolute cut point commonly used in large population studies [72]. Further reason for the distribution in intensity zones in paper II was that PA has typically been captured in unidimensional terms, for example time engaged in either MVPA or sedentary activity, instead of creating more comprehensive PA profiles [137].

In paper III we examined how different background factors (correlates) were associated with overall PA among older adult participants. This paper had a clear social science perspective, investigating the relation between the individual and its environment. In this paper, we included one outcome measure, overall PA, but several modifiable and non-modifiable background factors from the participants` life course.

Study design (papers I-III)

Paper I was the study protocol for the Generation 100 study, which is a phase IIb RCT with a 5-year duration, which started in August 2012 and will run until June 2018. The study protocol included scientific background and thorough descriptions of all examinations performed. This is the largest randomised controlled study examining the long-term effects of exercise on morbidity and mortality in older adults. Furthermore, this study provides the largest data on CRF, PA level and functionality among older adults in Norway. The participants were examined before randomisation, and were or will be examined at follow-up after 1, 3 and 5 years (Figure 3). Participants can also be followed-up by linking to health registries and death registries until the year 2035.

Though the Generation 100 is more of an exercise intervention, the study could be compared to the classification of PA interventions for older adults by van der Bij et al. [138]. Their categories were the following: home-based interventions; group-based interventions and educational

interventions [138]. In the Generation 100, all participants received information about their individual results at all examinations to give them an update on their health status. At baseline they also received detailed information about their prescribed exercise intervention: frequency, duration, intensity and examples of exercise sessions. Moreover, the Generation 100 has an RCT design, controlled as closely as possible by four examinations in 5 years and by offering weekly, supervised exercise training tailored to their exercise protocol. Additionally, due to the long follow-up time, detailed exercise prescriptions were given to the participants enabling them to also exercise at home.

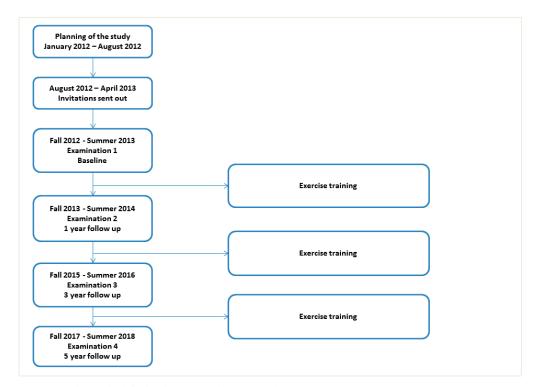


Figure 3: Time schedule for the Generation 100 study, 2012 - 2018.

The studies described in paper II and paper III were both cross-sectional studies, based on baseline data collected in the Generation 100 study. In medical terms cross-sectional data are snapshots of the population status regarding disease and exposure [139]. At baseline, all study participants underwent thorough clinical examinations. Through questionnaires they reported their current health status, as well as current and past factors that could have influenced their health status. These types of studies are also called prevalence studies because the prevalence

of a certain outcome is compared between individuals and groups with different types of exposures [139, 140]. Cross-sectional information is considered a good proxy measure for longitudinal data, when these types of data are not available [139]. The aim of paper II was to describe the PA level among older adults, while the aim of paper III was to increase the knowledge about PA correlates in older adults. In both papers II and III PA was assessed using the Actigraph GT3X+ accelerometer.

Participants - papers I-III

All men and women born from 1 January 1936 to 31 December 1942, with a permanent address in the municipality of Trondheim (6966 people, 3721 women) were invited to participate. Potential participants were identified through the National Population Registry, after approval from the formal owner of the register, the Norwegian Tax Administration. Invitations were sent by mail in batches with similar postal codes, from August 2012 until April 2013. We wanted to include participants clearly in the age category of older adults, meaning 65 years and older [2]. Furthermore, as the study is quite time consuming, with regards to testing and training, we needed to be sure that most of the participants were retired from work and hence available for testing and exercise during the day. In Norway the formal retirement age is 67 years, and after the age of 70 years employees normally cannot demand to keep their work position [141]. As a result of this very few inhabitants (7% for the years 2012-2014) have a permanent full time job position after the age of 70 [142]. In addition, large variability in function makes older adults a heterogeneous population in terms of health status and function [25, 143]. Approximately 25% of the heterogeneity is predicted to be genetically determined, while the rest is strongly affected by lifestyle, disease and exposure to health risks across the life course [143]. Against this background, and the aim of following participants in health registries and death registries within a reasonable time span, the age group 70-77 years was found suitable for the project. The first block of invitations was sent to older adults born in years 1938-42 (70-74 years), but after 3-4 months of randomisation the response/inclusion rates were too low. The steering committee of the Generation 100 therefore decided to apply to the ethical committee to also invite inhabitants born during the years 1936-1937. One RCT reported that telephone contact significantly increased recruitment rates to a PA study in older adults, compared to an invitation letter only [144]. This procedure would however not be realistic in the Generation 100, with 6966 individuals to contact.

Individuals who responded with an interest to participate were contacted by telephone for an extra control check of their eligibility, and agreement about time point for baseline examinations. The inclusion period, including examinations, screening for eligibility and randomisation of participants started in August 2012 and ended in July 2013. The criteria for exclusion are presented in Figure 4.

Exclusion criteria

- Illness or disabilities that preclude exercise or hinder completion of the study
- Uncontrolled hypertension;
- Symptomatic valvular, hypertrophic cardiomyopathy, unstable angina, primary pulmonary hypertension, heart failure or severe arrhythmia
- Diagnosed dementia
- Cancer that makes participation impossible or exercise contraindicated (Considered individually, in consultation with physician)
- · Chronic communicable infectious diseases
- Test results indicating that study participation is unsafe
- Participation in other studies conflicting with participation in the Generation 100

Figure 4: Exclusion criteria for the Generation 100 study (Paper I).

Out of the invited population, 1790 were interested in participating, 1422 responded with a decline to participate, and 3754 did not respond to the invitation. Among those interested, 174 individuals withdrew before or during the examinations, and 49 were excluded due to health reasons during examinations (Figure 5). Therefore, paper I included 1567 participants, 777 men $(72.5\pm2.1 \text{ years})$ and 790 women $(72.5\pm2.1 \text{ years})$. Detailed participant characteristics for papers I-III are presented in Table 1.

Paper II included a sample of 1219 older adults aged 70-77, all included in the Generation 100 main study. Out of the 1567 randomised participants, 320 individuals were either measured with a SenseWear activity monitor or lacked valid Actigraph data. Included participants were therefore those included in the main Generation 100 study and with valid Actigraph accelerometer data (n= 1247) (Figure 5). The criteria for valid Actigraph data will be thoroughly described in a later section of the methods.

Paper III included a sample of 850 older adults aged 70-77, all randomised to the Generation 100 main study. These participants were those with valid data from Actigraph accelerometer measures (including season of assessment), measures of CRF (VO_{2peak}) and BMI, and self-reported questionnaire data (that included education level, PA history, physically demanding work, social support for PA, living situation, perceived importance of using the neighbourhood when performing PA, perceived importance of being outdoors when performing PA and heart disease) (Figure 5).

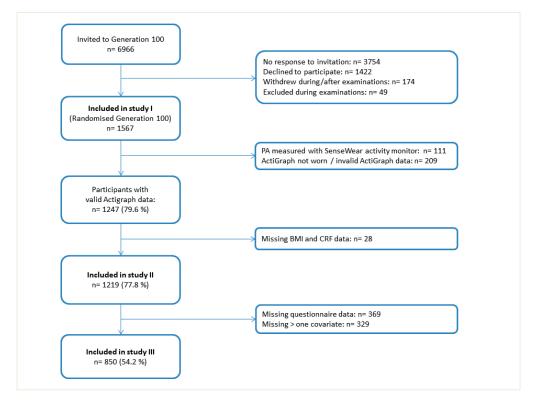


Figure 5: Flowchart for included participants, paper I-III. Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness; PA, physical activity.

Randomisation and exercise interventions

The participants were randomised to an exercise intervention or to a control group after examination. The randomisation programme was web-based and developed by the Unit for Applied Clinical Research (ntnu.edu/dmf/akf). Participants were stratified by gender and marital status and randomised 1:1 to an exercise training group or to a control group. The exercise training groups were further randomised 1:1 to continuous moderate intensity training (MCT) or high-intensity interval training (HIIT).

Exercise training groups

The HIIT group was ascribed two exercise sessions a week with 10-minute warm-up followed by 4x4 min intervals at 85-95% of HR_{max}, or minimum 16 on the Borg RPE scale. The MCT group was ascribed two weekly exercise sessions of 50-minute continuous activity at 70% of HR_{max}, or approximately 13 on the Borg RPE scale. Normally, participants in intervention studies should be blinded, but this would not be appropriate for this kind of study, as it is impossible to blind participants to exercise interventions [145]. Participants in the exercise training groups were therefore given both oral and written information regarding their intervention, described in detail in paper I.

The form of exercise training most commonly prescribed by clinicians is MCT [146, 147]. MCT is typically performed for 20-60 minutes at an intensity of 65-75% of HR_{max}/HR_{peak} [42]. The MCT exercise form is consistent with current PA recommendations of 150 min per week of MPA [146]. Nevertheless, recent research on HIIT has demonstrated more benefit from this than the MCT exercise form in several health parameters [148]. In addition, two frequently cited reasons for not exercising is a perceived lack of time and lack of enjoyment, and HIIT has shown promising results in this regard [79, 149, 150]. Elite athletes have used HIIT for many decades, but the ability of HIIT to improve health outcomes in non-athletes has received interest more recently [151]. A well-studied HIIT exercise protocol is the 4x4 model, which consists of bouts of high intensity exercise lasting approximately 4 minutes, at an intensity of 85–95% of HR_{max}/HR_{peak}, with periods of approximately 3 min rest or active recovery in between [151, 152]. HIIT is recognised as a time-efficient and effective exercise form with superior improvements in CRF compared to the traditional MCT exercise, both among healthy individuals and CVD patients [149, 152-154]. Furthermore, exercise of vigorous intensity results in lower risk of major chronic disease and induces greater cardiovascular benefits than exercise of moderate intensity [155-157].

What is more uncertain regarding the HIIT exercise form are the long-term physiological health effects, the long-term effects on adherence to exercise protocols, and the feasibility of HIIT as a public health initiative [79, 158]. Most HIIT studies have had shorter exercise intervention periods, relatively small participant samples of younger adults, and participants being closely followed in laboratory settings. Larger and longer studies under free-living conditions are therefore needed to confirm and extend earlier findings [28], and the feasibility among older adults needs to be examined. Lack of time and lack of enjoyment are two common barriers to

regular exercise [147, 150]. In a short-term perspective, HIIT was perceived to be more enjoyable than MCT, both among adult males and among patient groups [149, 159]. Bartlett et al. therefore hypothesised that HIIT might be an effective strategy to increase long-term exercise adherence [149]. This has been debated in relation to public health programmes, with arguments that HIIT has high efficacy but low effectiveness [79]. Efficacy is related to the, often short-term, effects of exercise training on physiological dimensions in controlled settings, while effectiveness relates to how interventions work in natural settings where long-term behaviour change might be more challenging for older adults [26, 160].

Control group

PA intervention studies have displayed different practices regarding the treatment of control groups: from no-contact control groups, control groups receiving non-exercise related health advice, to control groups that have been given advice or written information about PA [145]. Ideally, we would like to compare the intervention group to a non-exercise group. However, to incorporate a treatment condition that does not promote PA for a time period of 5 years would be unethical [161]. The control group in the Generation 100 was therefore informed orally about current (per 2012) national PA recommendations, defined by the Norwegian health authorities, more specifically 30 minutes of MPA every day [162]. Additionally, they were given a written document describing the guidelines, and stating that this intensity corresponds to 12-13 on the Borg RPE scale, alternatively 55-70% of HR_{max}. The Norwegian PA guidelines are publicly available through the health authorities and could therefore be considered 'usual care' [15]. The control group in our study was given information about their results from examinations in the same way as participants randomised to the two intervention arms. Participants in the control group were told that they would be contacted for new examinations after one, three and five years. Between examinations they received information letters regarding the status of the project, at Christmas time and at summer time. They were also invited to annual information meetings, where preliminary results were presented and they could ask questions about the study. This type of design, where the controls are not restricted from exercise, means an absence of a 'no treatment' control group. This can potentially preclude a comparative evaluation of outcome changes in individuals who were advised to make no changes in their PA [163]. On the other hand, since a sedentary lifestyle is known to increase the risk of several diseases, we considered it unethical not to provide the control group with advice of how to exercise, especially with such a long intervention period of 5 years. Thus, the significant difference

between the control group and exercise groups is that the exercise interventions are offered as supervised exercise training.

Measures

Physical activity

The triaxial Actigraph GT3X+ accelerometer (Actigraph, Pensacola, Florida, USA actigraphcorp.com) was used to measure PA in paper II and paper III. The ActiGraph accelerometer is commonly used for PA research [12]. The GT3X+ monitor is compact (4.6 cm \times 3.3 cm \times 1.5 cm), lightweight (19 g), and has a lithium ion rechargeable battery [164, 165]. Acceleration is the change in velocity over time and usually expressed in terms of multiples of gravitational force (9.8 m/s^2) [31]. The Actigraph filters the data to only detect movements within defined frequencies (0.25-2.5 Hz), to detect human body movement while rejecting acceleration outside the given frequency (i.e. vibration) [65, 164]. The acceleration data are sampled by a 12 bit analogue to digital converter at rates ranging from 30 Hz to 100 Hz, and stored in units of gravity inside the monitor [165]. Acceleration is converted into activity counts which are the product of the amplitude and frequency of the acceleration, and hence the counts increase linearly with the magnitude of the acceleration [111]. The activity counts reflect the intensity of bodily movement, thus the more activity a person does, the greater the number of counts recorded by the accelerometer [65]. The counts have no biological meaning and were converted to more useful units, often related to intensity, through calibration studies [118, 164]. Uniaxial PA data have been the most commonly used form of PA data [64]. Technological progress has made triaxial assessments possible, which should increase the sensitivity to detect smaller body movements [166]. The triaxial accelerometer records time varying accelerations on three axes, more specifically the vertical (Y), anteroposterior/horizontal front-back (X) and the mediolateral/horizontal right–left axis (Z) [131]. The triaxial data therefore results in more comprehensive PA assessments compared to uniaxial data that records acceleration along the vertical axis alone [118]. In paper II we used both uniaxial and triaxial PA data, while in paper III we used only triaxial PA data. Each sample was summed over an interval called an 'epoch'. The first accelerometer studies almost exclusively used 1-minute sampling intervals. However, with greater memory capacities, the epoch length has declined [167]. The epochs in paper II and paper III were set to 10-second intervals. The issue of epoch length has not been systematically examined either among younger or older adults [110, 168]. The use of a shorter sampling interval, or epoch, might reduce the misclassification errors of PA estimates, especially in populations with shorter PA bouts and under free-living conditions [169].

Therefore, it seems reasonable that shorter epoch lengths will give more accurate PA estimates in population studies of older adults, than longer epoch lengths [110].

PA data from accelerometers were collected after the clinical examinations and randomisation. Face-to-face distribution of accelerometers has been suggested as the best procedure to ensure correct use, and was implemented as a strategy to promote compliance with the monitoring protocol [168]. Furthermore, studies comparing different placement options indicate small but significant differences for hip and back placements, as well as for different locations on the hip area [168]. Our participants were individually given oral and visual instructions of how to use the monitors, and received a written procedure for correct use of the monitor. Participants were shown how to place the monitors, with the elastic belt around their waist and the monitor placed on the right hip. The participants were asked to take the monitors off only when in contact with water. After using the monitors for 7 days, the participants could either return the devices when attending an exercise session organised by Generation 100, or they could be returned by mail to the study centre, in a prepaid and addressed envelope.

Descriptive PA data from accelerometers included in papers II and III were total wear time, CPM (uniaxial and triaxial), steps per day, time in relative (adjusted for gender and population CRF) intensity zones and proportions (%) of participants meeting PA recommendations. The time distribution in intensity zones were calculated from triaxial PA data, using relative intensity cut points. Percentages meeting PA recommendations were calculated from both uniaxial PA data with absolute intensity cut points and from uniaxial and triaxial PA data with relative intensity cut points. The relative intensity cut points were developed from the Generation 100 population sample [131]. With an age group consisting of mainly retired participants, the dimensions PA at work and leisure time PA were not distinguished. Due to the use of a time filter that excluded wear time between midnight and 6:00 a.m. in paper II and paper III, PA at sleep was not a relevant dimension.

Cardiorespiratory fitness

Direct measurement of VO_{2max} or VO_{2peak} is considered to be the gold standard for CRF [57, 170]. The testing of VO_{2peak} was performed at the core facility NeXt Move, Norwegian University of Science and Technology, St Olavs University Hospital (ntnu.edu/dmf/nextmove). Oxygen uptake assessments were made during walking or running on the treadmill, or during cycling on a stationary bike. Cycling was used by the participants (3.1%) who were not able to

walk on a treadmill due to reduced functionality or leg pain. The test started with 10 minutes at a chosen warm-up speed. Approximately every two minutes either the incline of the treadmill was increased by 2% or the speed was increased by 1 km/h. The protocol ended when participants were no longer able to carry a workload due to exhaustion or until all the criteria for VO_{2max} were reached. The most accepted criterion for achievement of VO_{2max} is a plateau in VO₂ as the work rate continues to increase [170]. Oxygen uptake and HR were measured continuously during the work period. After the test, participants were asked to evaluate the degree of exertion on the Borg RPE scale (6-20). Because we also included participants that did not attain the requirements of a maximal test, the term VO_{2peak} was used. The term VO_{2peak} is often used to include data from participants not reaching the criteria for a maximal test. VO_{2peak} is the highest rate of oxygen consumption observed during an exhaustive exercise test [9]. VO_{2peak} was measured as the mean of the three highest successive 10-s VO₂ measurements. All participants with previous heart disease were tested under ECG monitoring with a medical doctor present, and the American College of Cardiology/AHA guidelines for exercise testing of patients with known CVD were followed [171].

Questionnaire data

Questionnaire data were collected during two surveys, the Generation 100 Q1 and Q2 (see appendix). The Gen100-Q1 form was distributed to participants together with the invitation letter by mail, and returned to the study centre in a prepaid and addressed envelope. The Gen100-Q2 form was handed out on the first day, and returned on the second day, during the baseline testing at the clinical facilities, St Olavs University Hospital. The data from the questionnaires included information on demographics, PA history, social- and physical environment and heart disease (Paper III), as well as frequency of PA types (Paper II). The correlates of PA were included as independent variables in the statistical model in paper III. The Generation 100 questionnaires were mainly based on the questionnaires from the third wave of The Nord-Trøndelag Health Study (The HUNT3); the HUNT3-Q1 for all participants of both genders aged 20 years and older, and the HUNT3-Q2 with additional sections for men and women 70 years and above. In addition, we included relevant PA questions from the Kan1 study, a nationwide survey of PA in the adult Norwegian population [75].

The questionnaire data were quality control checked both during the scanning process and manually in the final statistical data files used for analyses. During the scanning process the study personnel corrected misinterpretations made by the scanning machine. The original paper

versions of the forms were used to check the final data files for missing data, outliers and double checked questions. Treatment of double checked questions followed a predetermined procedure, by selecting the mean value, rounding up or deleting the answer – depending on the question. All questions demanding participants to write either letters or numbers were quality control checked manually to avoid misinterpretation during scanning of the questionnaire forms.

Clinical data

Clinical data relevant for papers II and III of this thesis included measures of body height, body weight, BMI and VO_{2peak}. The measurements of height, weight and BMI were performed at the Clinical Research Facility, St Olavs University Hospital. In addition, the Generation 100 main study included the following measurements: resting HR, blood pressure, blood samples, body composition, pulmonary function, gait speed and balance, grip strength, leg strength, cognitive function, as well as several measures from the cardiopulmonary exercise testing, including HR_{max} and HR one minute after testing. Clinical measures were initially performed all on one day, but were for logistical reasons split into two examination days, after four months of examination. The first day consisted of examinations in a resting state and the second day comprised the physical/physiological tests. Height was measured to the nearest millimetre with a mechanical telescopic measuring stadiometer with large measuring range (Seca 222, Hamburg, Germany). Body composition, including weight, was measured using bioelectrical impedance (Inbody 720, BIOSPACE, Seoul, Korea). BMI was calculated as body weight (kg) divided by the squared value of height (m) (kg/m²).

The clinical data were collected by trained study personnel, written down in a paper version of a case report form, and entered into a web based case report form (WebCRF). The WebCRF used in the Generation 100 study was developed by the Unit for Applied Clinical Research (see above). Clinical data were checked by manually comparing the original paper case report form and the WebCRF. Furthermore, the clinical data were checked statistically for errors and outliers in the electronic data files used for the statistical analyses.

Physical activity data processing and reduction (Papers II-III)

The knowledge on how to reduce and process PA data has not yet reached the same level as the accelerometer technology per se. Practices and standards have been proposed, but no consensus regarding universal guidelines has been reached [64, 172]. Procedures for quality control

checking and data summary methods are limited, and development of this might advance the use of monitors in large-scale studies and enhance comparability between studies [173]. Though there is a lack of consensus, for comparability in future research it is important with transparent research protocols and strategies for reduction of PA data prior to statistical analyses [119, 174].

PA accelerometer data used in papers II and III were processed with the Actilife software version 6.11.5 (Actigraph, Pensacola, Florida, USA) before statistical analysis of data. Non-wear time was excluded from the analysis and defined, similarly to most studies, as intervals of at least 60 consecutive minutes with zero counts, with allowance of 1-2 minutes with counts greater than zero [12]. The Actilife software labels this as the Troiano filter. Data were considered valid if participants had at least 4 days of at least 600 min·d⁻¹ (10 hours·d⁻¹) recorded, which is the most common wear time validation and refers to the waking day protocol [12]. A time filter was used the same way as in former (including Norwegian) studies, so that all PA data collected between midnight and 6:00 a.m. was excluded from the analysis [13, 76]. The use of a time filter was preferred to reflect PA during the day, instead of an alternative 24 hour wearing protocol that would have to account for the sleep at night.

Participants were instructed to use the monitor for one week, but a number of participants wore the monitor for more than the maximum 7 days. Extra days beyond the 7 days of monitoring were therefore manually deleted for those participants. For single cases of overlapping days of monitoring (i.e. two Mondays) a standard procedure was followed where the Monday with the longest wear time was selected for further analyses. In cases of two overlapping days or more (i.e. 9 days with two Mondays and two Tuesdays), a discretionary assessment was used to select the 7 days with the longest wear time. This should preferably be continuous days within one week, and consist of both weekdays and weekend days. These procedures are normally not described in research papers, but our procedures were developed specifically for this project to ensure that the seven days with the longest wear time were included in the analyses. A maximum monitor wear time of seven days was the most common in former studies of PA among older adults [12].

Statistical analyses

Paper I

The descriptive statistics in paper I were reported as means (SD) or proportions (%). Statistical tests performed in paper I were independent samples t-test, where a P-value < 0.05 was required

to declare statistically significant differences. The statistical analyses for the descriptive characteristics in paper I were performed with PASW Statistics for Windows version 21 (IBM Corporation, Somers, NY, USA). The calculations of sample size and precision (including expected width of the confidence intervals) for different mortality rates in the exercise group were performed with Stata Statistical Software version 12 (StataCorp LP, College Station, TX, USA). The primary analysis after 5 years will be to test whether there is a difference between the control- and intervention groups in all-cause mortality and new onset of disease. Furthermore, we want to analyse the effect of five years of different exercise intensities on overall PA level and risk factor profile, functionality and cognitive function.

Paper II

All statistical analyses in paper II were performed with PASW Statistics for Windows version 21. No formal sample size calculation was performed but all available participants with valid data (n = 1219) were included in the study. The sample characteristics in paper II were presented as means (SD) or proportions (%). The assumption of normality needs to be checked for many statistical procedures because their validity depends on it [175]. Finding that almost half of the PA outcome variables showed non-normal distributions when using conventional normality tests (histogram, P-plot and the Shapiro-Wilk test) made us consider performing nonparametric statistical tests (e.g. the Mann-Whitney U test and the Kruskal-Wallis test) [140]. However, the large sample size (n = 1219) was considered a strong argument for using parametric tests [175]. The one-way ANOVA test with Bonferroni adjustments, and the independent samples t-test, was used to study the association between PA (CPM, steps, intensity zones and MVPA), age groups, genders and CRF groups. The t-test was performed to compare means for significant differences between two groups, while the one-way ANOVA test was used to compare means for significant differences among three or more groups. The Pearson chi square test was used to analyse associations between categorical data (proportions (%) meeting absolute and relative PA recommendations across age, gender and CRF). A P-value < 0.05 was required to declare statistical significance. In addition, P-values < 0.001 were reported. Non-significant associations were reported with exact P-values.

Paper III

The statistical analyses in paper III were all performed using PASW statistics version 21. No formal sample size calculation was performed but all available participants with valid data (n = 850) were included in the study. The independent samples t-test and the one-way ANOVA tests

were performed for the descriptive data of the participants. Hierarchical regression was used to analyse the explained variance in PA, both for the total model and individually for the fourteen included independent variables (Table 2, paper III). Regression was the preferred method of analysis, since there was more than one independent variable, and we wanted to look at the relationship between each of the independent variables and the dependent variable, after taking into account and controlling for the remaining independent variables.

Hierarchical regression was used to see changes in the explained variance when entering the different groups of correlates, whether the groups were statistically significant and the strength of association for the respective correlate groups. The demographic correlates and PA history were entered as block 1, environmental correlates were entered as block 2 and biological correlates were entered as block 3. The measure of explained variance was given by the multiple correlation squared (R^2) and the R^2 change, which measures the total association between the outcome variable and all the predictor variables [140]. In addition to the R^2 value the hierarchical regression model also reported the unstandardized beta coefficients (standard error of the mean; SE) and the individual contribution of each correlate to the explained variance; the semi-partial correlation squared (partial r^2). The partial r^2 provides a measure of association between two variables while controlling for the effects of one or more additional covariates [140]. A P-value < 0.05 was required to declare statistical significance. In addition, P-values < 0.01 and < 0.001 were indicated for the partial r^2 values. Non-significant correlates were indicated with a partial r^2 value of 0.000. An important advantage with multivariable regression models is that several confounding variables can be controlled simultaneously [139].

Literature search

All searches for relevant literature were performed in PubMed and Web of Science databases. The literature review of relevant data from original research has primarily focused on studies with population samples of older adults. PA recommendations for older adults suggest that in most cases and for healthy individuals, the guidelines will apply to individuals aged 65 years or older [45, 46]. Consistent with this logic, the majority of the literature citations in this thesis were from studies involving predominantly healthy, free-living participants aged 65 years and older.

Ethics

The Generation 100 main study was approved by the Regional Committee for Medical Research Ethics, Norway (REK 2012/381 B). The Generation 100 was registered in a clinical trials registry in August 2012 (ClinicalTrials.gov, Identifier: NCT01666340). All participants gave their written informed consent, and the study conformed to the declaration of Helsinki. The studies presented in papers II and III in this thesis have been approved by the Regional Committee for Medical Research (REK 2013/1903 B).

RESULTS

The results chapter summarises the main results from the three papers included in the thesis. Furthermore, new tables and figures are presented to supplement the results presented in the papers.

Participant characteristics

Participant characteristics for papers I (n = 1567), II (n = 1219) and III (n = 850) are presented in Table 1. The National Population Register was used as a basis for recruitment. Baseline data for height, weight, BMI and CRF were clinically measured, while data for heart disease, education and living situation were self-reported.

Variable	Paper I		Paper II		Paper III	
N	1567	SD	1219	SD	850	SD
Females (%)	50.4%		51.2%		47.6%	
Age (years)	72.8	2.2	72.8	2.2	72.4	1.9
Height (cm)	170.1	8.8	170.0	8.6	170.6	8.6
Weight (kg)	75.5	13.4	75.0	13.2	74.7	12.4
BMI (kg/m^2)	26.0	3.6	25.9	3.5	25.6	3.3
CRF (ml/kg/min)	28.7	6.5	28.9	6.5	29.6	6.5
Heart disease (%)	11.7%		10.7%		12.1%	
High education (%)	50.6%		49.3%		54.0%	
Living alone (%)	25.1%		24.8%		23.9%	

Table 1. Participant characteristics for papers I-III.

Data are presented as mean \pm SD or proportions (%). Abbreviations: BMI, body mass index; CRF, cardiorespiratory fitness (measured as peak oxygen uptake; mL/kg/min); High education, college or university education.

In total, 6966 inhabitants (53% females) were invited to participate, and 1567 (50% females) were included. In addition, we obtained questionnaire data from 1361 individuals who declined to participate. Males and females included in the study were one year younger (P < 0.01) than those not willing to participate. More participants (50% vs. 32%, P < 0.01) had high education, while fewer participants reported poor health (13% vs. 34%, P < 0.01), heart diseases and diabetes (P < 0.01), and fewer were current smokers (9% vs. 12%, P < 0.01) compared to those

not participating. There were no differences in cancer and mental health problems. More participants reported moderate levels of PA (69% vs. 58%, P < 0.01), while more non-participants reported low (16% vs. 9%, P < 0.01) and high (26% vs. 22%, P < 0.05) levels of PA (Paper I).

Physical activity levels (Paper II)

Data for accelerometer CPM, steps per day, total number of minutes in relative (determined by population gender and percent of VO_{2max}) intensity zones, and proportions meeting PA recommendations are presented in Figures 6-13. In this section, participants were categorised into the following levels of CRF: low level of CRF (males <27.0 mL·kg⁻¹·min⁻¹; females <23.6 mL·kg⁻¹·min⁻¹), medium level of CRF (males 27.0-35.6 mL·kg⁻¹·min⁻¹; females 23.6-29.8 mL·kg⁻¹·min⁻¹) and high level of CRF (males >35.6 mL·kg⁻¹·min⁻¹; females >29.8 mL·kg⁻¹·min⁻¹).

Uniaxial and triaxial counts per minute

Mean CPM values for all participants were 251 and 503 using uniaxial and triaxial PA assessment, respectively. Uniaxial CPM were similar between genders, whereas females (518 CPM) obtained a higher triaxial CPM than males (485 CPM, P < 0.001) (Paper II). Compared to those having a medium level of CRF, individuals with a high level of CRF had 19.5% and 14.2% higher (P < 0.001) CPM values assessed by uniaxial and triaxial recordings, respectively. Similarly, compared with those having a low level of CRF, individuals with a medium level of CRF had 23.0% and 17.2% higher (P < 0.001) uniaxial CPM and triaxial CPM, respectively (Figure 6).

Females with low levels of CRF had higher triaxial CPM than males with low levels of CRF (P < 0.001), and females with medium levels of CRF had higher triaxial CPM than males with medium levels of CRF (P < 0.05). There were no gender differences in triaxial CPM among participants with high levels of CRF. There were no gender differences in uniaxial CPM within the different levels of CRF (low, medium or high, Figure 6).

Participants aged 70-71 years had 11% (262 vs. 236 CPM, P = 0.005) and 8% (517 vs. 478 CPM, P = 0.011) higher uniaxial CPM and triaxial CPM than those aged 76-77 years, respectively. Females aged 70-71 years had 10% higher triaxial CPM than males aged 70-71

years (543 vs. 492, P = 0.015), whereas there were no gender differences in triaxial CPM among those aged 72-75 and 76-77 years. There were no gender differences in uniaxial CPM within the age groups (Figure 7).

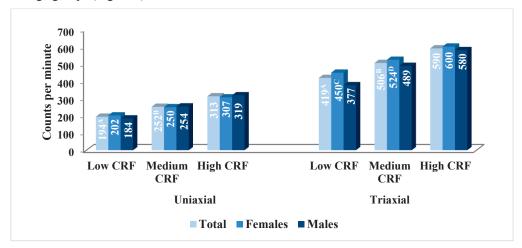


Figure 6: Counts per minute distributed across cardiorespiratory fitness and gender, for uniaxial and triaxial data assessment. ^ASignificantly (P < 0.001) different from the medium CRF and high CRF. ^BSignificantly (P < 0.001) different from the high CRF. ^CSignificantly (P < 0.001) different from the male low CRF. ^DSignificantly (P < 0.05) different from the male medium CRF . CRF groups: Males low <27.0 mL·kg⁻¹·min⁻¹, Females low <23.6 mL·kg⁻¹·min⁻¹, Males medium 27.0-35.6 mL·kg⁻¹·min⁻¹, Females medium 23.6-29.8 mL·kg⁻¹·min⁻¹, Males high >35.6 mL·kg⁻¹·min⁻¹, Females high >29.8 mL·kg⁻¹·min⁻¹. CRF, cardiorespiratory fitness.

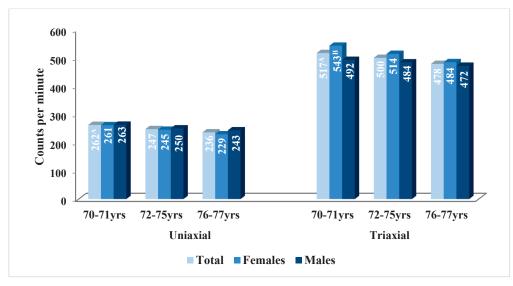


Figure 7: Counts per minute distributed across age groups and gender, for uniaxial and triaxial data assessment. ^ASignificantly (P < 0.05) different from the 76-77 year age group. ^BSignificantly (P < 0.05) different from the male 70-71 year age group.

Steps

Participants with high levels of CRF accumulated on average 1350 more steps per day than participants with medium level CRF, and 2847 more steps than participants with low levels of CRF (P < 0.001). There were no gender differences in steps per day within the different levels of CRF (low, medium or high, Figure 8). Furthermore, there were no age differences in steps per day. In addition, there were no gender differences in steps per day within the age groups (70-71, 72-75 or 76-77 years) (Figure 9).

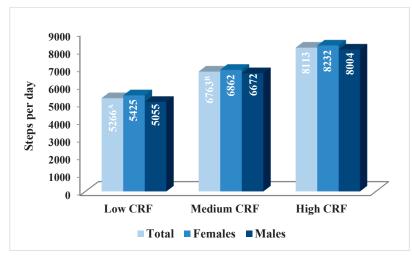


Figure 8: Total number of steps per day distributed across cardiorespiratory fitness groups and gender. ^ASignificantly (P < 0.001) different from the medium CRF and high CRF. ^BSignificantly (P < 0.001) different from the high CRF. CRF groups: Males low <27.0 mL·kg⁻¹·min⁻¹, Females low <23.6 mL·kg⁻¹·min⁻¹, Males medium 27.0-35.6 mL·kg⁻¹·min⁻¹, Females medium 23.6-29.8 mL·kg⁻¹·min⁻¹, Males high >35.6 mL·kg⁻¹·min⁻¹, Females high >29.8 mL·kg⁻¹·min⁻¹. CRF, cardiorespiratory fitness.

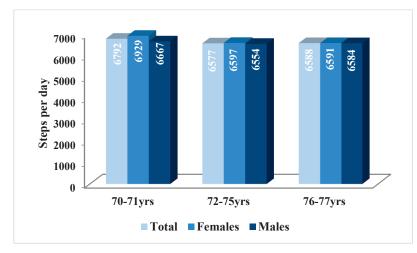


Figure 9: Total number of steps per day distributed across age groups and gender.

Minutes in relative intensity zones

Participants with high levels of CRF accumulated more minutes in the relative moderate- (46-63 VO_{2max} %) and vigorous (64-90 VO_{2max} %) intensities than those with medium- and low levels of CRF (P < 0.001). For the relative near max- (\geq 91 VO_{2max} %) and MVPA (\geq 46 VO_{2max} %) intensities, participants with high levels of CRF obtained more minutes than those with medium- and low levels of CRF (P < 0.001), and those with medium levels of CRF obtained more minutes than those with low levels of CRF (P < 0.001) (Figure 10).

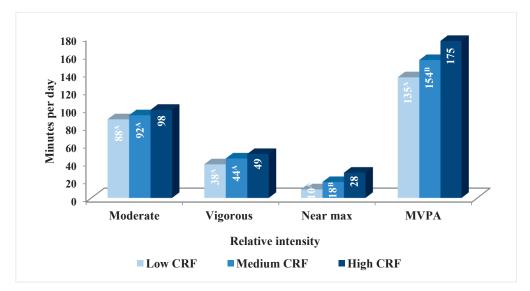


Figure 10: Total minutes of physical activity performed in moderate, vigorous and near max relative intensities, distributed across cardiorespiratory fitness groups. ^ASignificantly (P < 0.001) different from the high CRF. ^BSignificantly (P < 0.001) different from the low CRF and high CRF. Relative intensity zones: Moderate (46-63 VO_{2max} %), Vigorous (64-90 VO_{2max} %), Near max (\geq 91 VO_{2max} %), MVPA (\geq 46 VO_{2max} %). CRF groups: Males low <27.0 mL·kg⁻¹·min⁻¹, Females low <23.6 mL·kg⁻¹·min⁻¹, Males medium 27.0-35.6 mL·kg⁻¹·min⁻¹, Females medium 23.6-29.8 mL·kg⁻¹·min⁻¹, Males high >35.6 mL·kg⁻¹·min⁻¹. CRF, cardiorespiratory fitness; MVPA, moderate-to-vigorous physical activity.

Females accumulated more minutes in the relative moderate- (P < 0.001), vigorous- (P < 0.001), near max- (P = 0.004) and MVPA (P < 0.001) intensities than the males. Total number of minutes in relative MVPA was 57% higher for females than for males (Figure 11). Participants aged 70-71 years accumulated 30% more minutes in the relative near max intensity than those aged 76-77 years (P = 0.001). There were no age differences in total minutes of relative moderate-, vigorous- or MVPA intensities (Paper II).

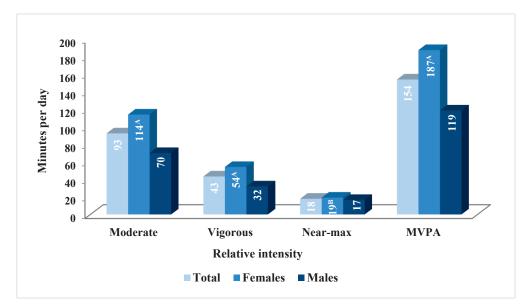


Figure 11: Total minutes of physical activity performed in moderate, vigorous and near max relative intensities, distributed across gender. ^ASignificantly (P < 0.001) different from the males. ^BSignificantly (P < 0.05) different from the males. Relative intensity zones: Moderate (46-63 VO_{2max} %), Vigorous (64-90 VO_{2max} %), Near max (\geq 91 VO_{2max} %), MVPA (\geq 46 VO_{2max} %). MVPA, moderate-to-vigorous physical activity.

Proportions meeting PA recommendations

Higher proportions (%) of participants with high levels of CRF met the PA recommendations, than among participants with a medium- and low level of CRF (P < 0.001). This association was found for uniaxial absolute-, uniaxial relative- and triaxial relative MVPA thresholds (Figure 12). In total, higher proportions met the PA recommendations using relative- (triaxial 71%, uniaxial 79%) than absolute (29%) intensity thresholds, and higher proportions met the recommendation using uniaxial- (79%) than triaxial (71%) relative PA assessment (Paper II).

More females than males met the PA recommendation using the uniaxial- (8% points difference) and triaxial (18% points difference) relative MVPA accelerometer thresholds (P = 0.001), while there was no gender difference for the uniaxial absolute threshold (Figure 13). There were no age differences in proportions meeting PA recommendations, either for absolute uniaxial, relative uniaxial, or relative triaxial intensity thresholds (Paper II).

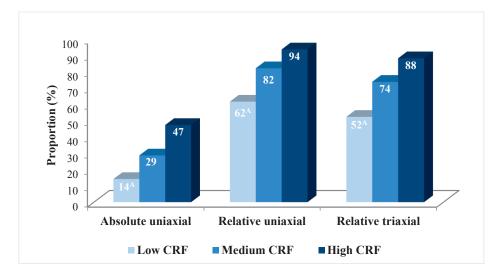


Figure 12: Proportions (%) meeting physical activity recommendations, distributed across cardiorespiratory fitness for absolute uniaxial, relative uniaxial and relative triaxial data assessment. ^ASignificant (P < 0.001) difference between the CRF groups. Absolute uniaxial; ≥ 2020 CPM, relative uniaxial; males ≥ 267 CPM, females ≥ 213 CPM and relative triaxial; males ≥ 1653 CPM, females ≥ 1077 CPM. CRF groups: Males low <27.0 mL·kg⁻¹·min⁻¹, Females low <23.6 mL·kg⁻¹·min⁻¹, Males medium 27.0-35.6 mL·kg⁻¹·min⁻¹, Females medium 23.6-29.8 mL·kg⁻¹·min⁻¹, Males high >35.6 mL·kg⁻¹·min⁻¹, Females high >29.8 mL·kg⁻¹·min⁻¹. CRF, cardiorespiratory fitness.

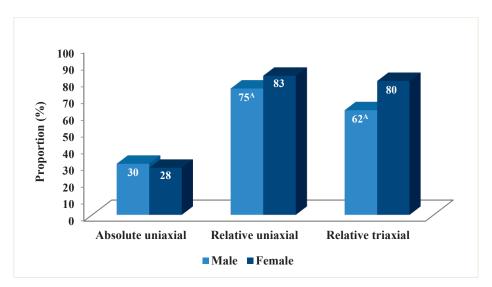


Figure 13: Proportions (%) meeting physical activity recommendations, distributed across gender for absolute uniaxial, relative uniaxial and relative triaxial data assessment. ^ASignificantly (P < 0.001) different from the females. Absolute uniaxial; ≥ 2020 CPM, relative uniaxial; males ≥ 267 CPM, females ≥ 213 CPM, and relative triaxial; males ≥ 1653 CPM, females ≥ 1077 CPM.

Physical activity correlates (Paper III)

After including all 14 PA correlates, the total explained variance in overall PA (measured as triaxial CPM) was 27.1% (P \leq 0.001). Among the demographic correlates, gender had the strongest explanatory power, explaining 3.9% of the variance in PA. Age, PA at 40 years old and the interaction effect between education and gender explained 0.8%, 0.8% and 0.6% of the variance, respectively. Among the environmental correlates, season and outdoor importance for PA were the only significant correlates, explaining 2.7% and 0.4% of the variance in PA, respectively. All of the biological correlates (CRF, BMI and heart disease) individually contributed to increase the explanatory power of the model. CRF was the correlate most strongly associated with overall PA, contributing to 10.1% of the explained variance (P \leq 0.001) (Figure 14).

The five PA correlates, physically demanding work, education (both genders), living situation, social support and neighbourhood importance for PA, were also included in the hierarchical regression model. None of these correlates contributed significantly to increase the explained variance (partial $r^2 = 0.000$) (Paper III).

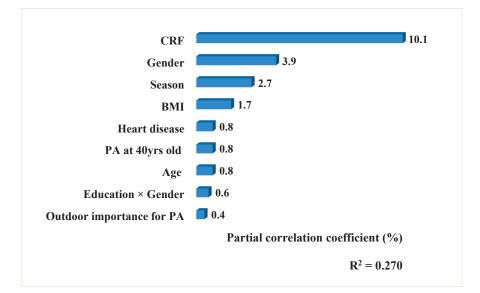


Figure 14: Correlates of overall physical activity in the Generation 100. Total explained variance (R^2): 0.270 ($P \le 0.001$). BMI, body mass index; CRF, cardiorespiratory fitness; PA, physical activity.

DISCUSSION

This thesis presents the study protocol and data on PA in older adults, aged 70-77 years. The first part of the discussion reflects on the initiation of the Generation 100 study and large exercise training interventions among older adults. The second part discusses the main results from paper II and paper III. The last part discusses PA assessment, strengths and limitations across the studies, as well as suggestions for future research.

The Generation 100 study

Design and methodology

Epidemiological studies have shown that exercise is associated with a lower risk of type 2 diabetes [176], hypertension [177], dementia [178], breast cancer [179], colon cancer [180] and premature death [9]. However, there are some limitations with epidemiological designs as the data cannot determine the cause and effect between exercise and health [139], and the literature lacks large RCTs that can examine the effect of exercise on successful ageing [21, 59]. Generation 100 is the first long-term RCT study examining the effects of exercise on morbidity and mortality among older adults. Human ageing will often, even without disease, lead to a decline in most physiological parameters such as CRF [25, 53]. Furthermore, ageing is associated with increased risk for several chronic diseases. For example, 23% of the total global burden of disease is attributable to people 60 years and older, comorbidity affects around 2 out of 3 people aged 65 years and above, and 85% of all deaths from CVD occur at age 65 years and above [5, 125]. The population ageing is expected to result in an even higher future prevalence of chronic diseases, and increased societal challenges related to economy and health care systems [1]. Existing data indicate that exercise and PA may be important factors to promote successful ageing [21, 181-183]. Generation 100 will in the coming years give important information about the cause and effect relationship between exercise and PA and health among older adults.

Generation 100 is the first RCT to evaluate the long-term effects of HIIT and MCT among older adults. There is evidence indicating that HIIT can be an effective alternative to traditional exercise training to benefit various health outcomes [79, 184]. For example, HIIT is an effective way of increasing CRF, both among healthy younger adults and patients with cardiometabolic diseases [152, 153]. However, older adults tend to be excluded from RCTs [5, 151] and few RCTs have evaluated the effect of HIIT among healthy older adults [147]. Molmen-Hansen et al. demonstrated that short term HIIT improved diastolic and systolic function, both at rest and

during exercise [185]. However, this study lasted for only 12 weeks and included 16 healthy, sedentary older adults. This could indicate a beneficial long-term effect of HIIT also among older adults 65 years and above. The optimal exercise intensity, frequency and duration is still unclear among older adults [186].

A more holistic approach towards health among older adults has been called for, with comprehensive health assessments as an aim [5]. It has been suggested that health outcomes among older adults should incorporate measures of functioning, together with measures of physiological risk [4]. This holistic perspective was taken into consideration when stating the aims and designing the Generation 100 study, by providing the opportunity to evaluate the effect of exercise training on social participation, physical function, cognitive function, CVD, oxygen uptake, PA levels, pulmonary function, muscle strength, gait speed and characteristics, medications, falls and fall-related injuries, dementia, depression, fatigue, rate of hospitalisation, use of healthcare services and overall morbidity. This wide approach corresponds well with the previously published multidimensional health definition [20, 21]. In addition to the effect on morbidity and mortality, the Generation 100 will provide the largest data on fitness and PA level in older adults in Norway.

Recruitment and participation

In Generation 100, 22.5% of the invited population was included in the main study. In general, it is difficult to define an acceptable participation rate, since this could be attributed to factors like age, exclusion criteria, study design and respondent burden. The two largest health surveys in Norway until now, looking at PA levels and CRF, were the Kan1 and HUNT 3. Despite differences in design, these studies are therefore interesting to compare to Generation 100. The Kan1 study had a total (aged 20-85 years) participation rate of 32%, with the highest participation rate among those with higher education. In Kan1, 628 (aged 66 years and above, 50% females) older adult participants were measured with Actigraph accelerometers [75]. The HUNT3 main study had a 54% total (aged 20 years and above) participation rate, with 59% and 50% participation rates for females and males, respectively. Participants were resident in both urban (65%) and rural (35%) municipalities [187]. Noteworthy, in contrast to Generation 100 and Kan1, the HUNT3 fitness study had the following exclusion criteria: CVD, cancer, obstructive lung disease and blood pressure medication [188]. In the HUNT3 study only 269 participants (51% females) aged 70 years and above measured their CRF directly on a treadmill, whereas these participants self-reported their PA levels through questionnaires [188].

Importantly, both the Kan1 an HUNT3 had epidemiological designs collecting cross-sectional data, where participation lasted only 1-2 days. Thus, the individual participant burden in Generation 100 will be much higher, as it includes an exercise intervention.

At this early stage of the Generation 100 study, it is difficult to quantify the adherence rates, since the trial is still ongoing. The literature also lacks clear conclusions regarding how to maintain older adults in evidence-based PA programmes [145, 186]. Previously, large longterm exercise interventions with RCT design have shown low degrees of adherence. The Heart Failure and A Controlled Trial Investigating Outcomes of Exercise Training (HF-action) study examined exercise training and all-cause mortality or all-cause hospitalization in 2331 (59 years, 28% females) heart failure patients [189, 190]. After 1 year they experienced a 38% full adherence rate, while an additional 14% were partial adherers [190]. The Lifestyle Interventions and Independence for Elders (LIFE) study included older adults with physical limitations, to test the effect of a PA program on risk of major mobility disability [191]. The 1635 participants (79 years, 67% females) in LIFE attended 63% of scheduled exercise sessions during 2.6 years, after excluding absence due to medical reasons [192]. In Generation 100 we have consciously implemented specific measures to increase the adherence. Participants were asked to fill out training diaries after each session and return these on a monthly basis to the research unit. Furthermore, we offer supervised exercise sessions twice a week with either walking/running or bike spinning. In the winter period we also organize indoor exercise sessions. Despite a large population sample, we have four examinations in five years, where participants receive individual feedback on health- and fitness status. Participants receive newsletters and are invited to annual information meetings. We are also implementing a procedure of sending text messages to remind participants about exercising. Based on preliminary data, 87% of the randomised participants were still formally participating after 1 year of the RCT.

Physical activity levels (Paper II)

Paper II gave a comprehensive picture of the PA levels of older adults in Norway. Previous studies of the proportions meeting PA guidelines have mainly been based on self-reported PA [17]. Studies have shown that self-reported PA often overestimates PA levels [76, 193]. Therefore, we wanted to utilise an accelerometer to quantify PA levels. The objective PA levels of our population sample are discussed in the following sections.

Relative intensity

Despite the fact that PA is an important component in the prevention and management of many chronic diseases associated with ageing, PA levels tend to decline with age [194]. Many studies have found that low percentages of older adults meet the recommendations of 30 minutes with MVPA, e.g. in the US and UK [17, 72]. Given the growing proportion of older adults, low levels of PA represent a potential future public health problem [194]. One reason for the low amounts of MVPA in former studies may be that the intensity thresholds were not adjusted for CRF, despite this being included in the recommendations [195]. As the CRF normally decreases with age, many older adults need to perform PA of lower absolute intensity, but similar in relative intensity, than those with higher levels of CRF [45]. Relative intensity should also be taken into account when monitoring PA, but despite the strong empirical arguments for presenting PA data relative to fitness absolute intensity is still the most common way to express the data [109, 196]. Furthermore, it seems like there is no preferred intensity threshold to define MVPA in older adults, and recent studies have therefore used many different thresholds [12, 197]. In line with this, Evenson et al. showed that MVPA estimates vary among older adults depending on the intensity threshold chosen, and suggested more research to identify the appropriate method of setting accelerometer cut points for MVPA in older adults [198]. Individualised cut points are not always feasible, and age specific cut points may therefore be an appropriate compromise [12]. In addition, the optimal cut points for objective PA and health outcomes are not yet established and these may be different from the cut points commonly used today [76]. The use of relative intensity PA thresholds, developed for our sample of older adults, has therefore been an attempt to develop this field of research. Despite this focus, absolute thresholds still have some advantages for use in large population studies; i.e. data are more easily accessible and the data are more easily comparable across different populations.

In contrast to most literature, we observed that females accumulated more minutes of relative MVPA than males [74]. This finding was in line with the observed gender difference for triaxial CPM, meaning that females were more active, both measured as overall PA and related to the recommended health beneficial PA. The results could be related to different sample characteristics in favour of females. However, females actually had higher proportions with low levels of CRF, and lower proportions with higher education, compared to males. In addition, there was no difference in total age between genders. One explanation could be a higher proportion of males than females with heart disease, which was associated with reduced overall PA in paper III. Recently published papers have reported both total minutes of MVPA and

MVPA accumulated within bouts [199, 200]. In our study, males obtained 64% of the relative MVPA of the females, for both total minutes of MVPA and bout-accumulated MVPA. This could indicate that even though females were more active than males, they had similar patterns in regard to distribution of PA obtained from exercise sessions and from sporadic PA of at least moderate intensity. Interestingly, there was no age difference in relative MVPA, neither in total minutes nor accumulated in 10-min bouts.

For all participants in our study, total minutes in relative MVPA per day was 3.5 times higher (154 vs. 44 minutes) compared to the relative MVPA accumulated within 10-min bouts. The analyses of bout-accumulated MVPA were done because PA guidelines state that the recommended 150 minutes per week should be performed in episodes of at least 10 minutes [46]. Interestingly, when analysing our data in 10-min bouts, individuals with low levels of CRF accumulated on average 51% less time in MVPA than individuals with high levels of CRF. On the contrary, obtained independent of bouts, those with low levels of CRF achieved 23% less time in MVPA compared to those with high levels of CRF. This finding clearly illustrates how the use of strict physical activity quantification criteria (MVPA performed in 10-min bouts) can underestimate total PA time accumulated in levels beneficial for health. When processing MVPA in bouts, we used a standard procedure that defined bouts as 10 or more consecutive minutes above the relevant threshold, with allowance for interruptions of 1 or 2 minutes below threshold, referred to as a modified 10-min bout [72]. Time in MVPA bouts was therefore terminated after 3 minutes below the given threshold. An older adult might perform HIIT exercise with 4x4 minute work periods (at 85-95% of HR_{peak}), with 3 minute resting periods (at 60-70% of HR_{peak}) in between [151]. Hence, the procedure for data processing means that none of the 4 minute working periods of HIIT will count as recommended PA, since the older adults' PA intensity in the resting periods will drop below an absolute MVPA threshold for more than the acceptable 1-2 min. Nevertheless, this is a very common way of processing objective PA data to quantify proportions meeting PA recommendation. In addition to the fact that PA may be misclassified as not being accumulated within 10-min bouts, the possible health benefits associated with MVPA of less than 10 minutes duration are less known, and this should be explored [129].

Recommended levels of physical activity

In paper II we found that 29-79% of the participants met the PA recommendation, depending on the applied methodology for PA assessment. Thus, compared to former studies showing 613% [17, 69, 70], we found much higher proportions meeting PA recommendations. Paper I showed that many (16%) older adults with low PA levels declined to participate in the Generation 100 study, perhaps due to disease or reduced motivation. However, this was more than balanced by an even higher proportion (26%) of highly active people who declined to participate. Importantly, our population sample volunteered to be part of an exercise intervention study. The participants could have been either fairly active at baseline or sedentary individuals highly motivated to change their lifestyle [145]. However, when comparing our data to the Norwegian cross-sectional Kan1 study, using identical criteria in terms of PA recommendations and the same absolute intensity accelerometer threshold, we found that the real differences in PA levels were small, with approximately 20% meeting the PA recommendation in both population samples (Paper II) [13]. Therefore, it is extremely important to be aware of the way PA is monitored and analysed, as different methods (and interpretations) will give very different results. The proportions meeting PA recommendations increased enormously when utilising relative intensity thresholds [131] instead of an absolute threshold [72]. Interestingly, the uniaxial assessment resulted in higher proportions (79% vs. 71%) meeting PA recommendations, than the triaxial assessment. Since the triaxial assessment captures more complex movements than the uniaxial, one could expect this assessment method to reward participants more for the same body movements. However, our results indicated that this was more than equalised by the use of proportionally higher accelerometer thresholds. There were no age differences in proportions meeting PA recommendation, for any of the three measurement methods.

Counts per minute

The mean uniaxial CPM value (251 CPM) for the participants (70-77 years) in our study ranked between the Kan1 age groups 70-74 years (301 CPM) and 75-79 years (237 CPM) [13]. The youngest, and most active, age group (70-71 years) in Generation 100 actually had lower CPM (261 CPM) than those aged 70-74 years in the Kan1. This indicates that the PA level of our sample was not biased by recruitment to an exercise intervention. In contrast, compared to PA studies from other countries, such as Germany [97], UK [201] and US [198] populations, the Generation 100 sample had a higher level of overall PA. Furthermore, there was a positive association between level of CRF and CPM, for both uniaxial and triaxial assessments, and CRF was most strongly associated with CPM in paper III. Females with low- and medium levels of CRF had a higher CPM than the males with similar levels of CRF, using the triaxial PA assessment of CPM. This gender difference was an interesting finding since most former studies

have found no gender differences [13] or males to be the most active [72, 74]. Contrary to the triaxial assessment, the uniaxial assessment revealed no gender difference in CPM. This could indicate that males and females have different movement patterns, for example related to gait patterns or an unequal distribution of vertical and horizontal movements, which will be captured differently by the uniaxial and triaxial assessments. Age has repeatedly been negatively associated with PA levels, but this difference has often been found between older adults and much younger adults (e.g. 20-65 years) [72, 103]. The observed age difference in CPM between the youngest and oldest age group in our study was interesting since this illustrates a decline in PA levels among older adults, even in a population sample with small age differences. The age difference for both uniaxial and triaxial CPM was interesting, since no age difference was found for either uniaxial- or triaxial relative MVPA. This could be explained by the fact that an accelerometer count is more of an absolute measure, whereas the relative MVPA was adjusted for gender and population CRF.

Steps

The mean number of steps per day for all Generation 100 participants was 6652 steps. This was similar to a population-based study of older adults in UK (6443 steps) [202], while much higher than a US population (3987 steps) [203]. It has been suggested that people should achieve 10,000 steps per day, but the use of steps in public health promotion has been debated [118, 204]. The scepticism towards the 10,000 steps is supported in more recent reviews of associations between step and health outcomes, finding thresholds of 7100-8000 steps per day, depending on populations and health outcomes examined [205, 206]. Interestingly, when looking at the analysed sub-groups across CRF, gender and age, only the males and females with the highest levels of CRF exceeded even the lowest recommendation of 7100 steps per day. Furthermore, the mean number of steps per day was positively associated with level of CRF. Interestingly, in contrast to the results from assessment of CPM, there were no age- or gender differences in steps per day. Though CPM and steps could be considered the least 'manipulated' outcomes from accelerometers and these two outcomes have formerly been highly correlated [202], our results indicate that they could capture somewhat different dimensions of PA.

An important limitation with counting steps per day is that assessment of steps neglect intensity and bouts of PA, which are necessary to monitor adherence to recommendations based on MVPA. It has in fact been found that PA recommendations can be met by doing 3-4,000 steps per day, as long as the intensity is sufficiently high [205], while you can also take 10,000 steps per day and not meet the PA recommendation [204]. Though this was not analysed in our paper, a measure of steps per minute, which is more related to intensity than just total number of steps per day, could potentially be an outcome better associated with PA recommendations [205, 207].

Physical activity types

According to Pedišić and Bauman, a technical shortcoming with accelerometers is that they do not capture all types of activities [120]. For example, accelerometers do not capture the full energy cost of cycling, resistance exercise, walking on stairs or uphill, and walking while carrying extra weight, because acceleration patterns do not change in these types of PA [31]. In addition, most accelerometers need to be taken off when performing activities in water [120, 121]. Nevertheless, it is often assumed that the contribution of these activities to the overall PA is small [124]. In paper II, approximately 25% of our sample reported to be cycling weekly, 35% exercised at a fitness centre, and 18% females and 7% males reported attending a swimming pool, weekly. These numbers indicate that some amounts of PA were underestimated in our results. At the same time, approximately 80% reported performing recreational walking, more than 70% used walking as a form of transport and almost 60% were hiking in nature, on a weekly basis. Other studies have also found similar results with walking as clearly the most common type of PA among older adults [47, 203]. Furthermore, we found that more males than females used ski tracks and cycling regularly, while more females performed recreational walking on road/pathways (Paper II). Contrary to our results, a study from Iceland found that more males used swimming as an exercise form than females, and the total proportion who reported swimming regularly was also higher in Iceland than in our study [195].

Correlates of objective physical activity (Paper III)

Data from our study showed that CRF had the strongest association with PA, as this correlate alone explained 10% of the variance. This finding and the other results in paper III are unique since CRF was used as a correlate of objective PA in a large sample of older adults in Norway. Jackson et al. found CRF to be positively associated with self-reported PA, across the whole adult life span [53]. Novak et al. found more fit individuals to be more active, but contrary to our study they wanted to avoid potential training effects by analysing data for overall PA only from adults who did not exercise regularly [100]. Most studies have analysed the association between PA and CRF the other way, by examining how much of the variance in CRF can be

explained by PA, and found low to moderate correlations across gender and age groups [98, 99, 208, 209]. Therefore, the cause and effect-relationship is difficult to determine, i.e. whether a higher level of CRF will result in higher levels of PA, or if higher levels of PA will result in increased CRF level. The finding regarding CRF and PA was also in line with paper II, where the categorised CRF was positively associated with overall PA, steps per day and minutes in MVPA.

The variables included in paper III explained 27% of the variance in overall PA. The choice of correlates included in paper III was partly based on earlier reviews describing relevant correlates with varying associations with PA [82, 83, 210], and partly based on the available data from the Generation 100 study. Some of the studies that have described correlates are more than ten years old making it important to look for possible changes in time trends. Although several reviews have focused on factors associated with PA behaviour, only a few have focused specifically on older adults of both genders [211]. Interestingly, we identified that among the environmental correlates, neither living situation, social support nor importance of neighbourhood for PA contributed to explain the variance in PA. Furthermore, heart disease was associated with PA, but ranked only a shared 5th out of 9 correlates in terms of explaining the variance in overall PA. Interestingly, education was only associated with PA among males in our study. Although not known in Generation 100, this may be explained by older adult females taking responsibility for the majority of routine housework, even after retirement [212]. However, one limitation with hip worn accelerometers is their inability to account for nonambulatory activities [164]. Hence, an unknown proportion of the housework would not be counted as PA. Reasons for the conflicting findings in former research regarding education and PA in older adults could be methodological differences, i.e. self-reported vs. objective PA and different outcome measures of PA and education [87, 93]. Although the variables gender and age are non-modifiable factors, the findings that they were associated with PA should be used to target health promotion especially in males and amongst the oldest individuals [213]. Hence, it will be important to customize interventions for males and older populations so that they can succeed in increasing and maintaining their PA levels.

We found that those who perceived it as important to be outdoors during PA were more active than those who did not. It is generally important to understand PA patterns by location, since this may help in the design of PA interventions among older adults [214]. Kerr et al. suggested that future studies could be improved by objective measures of both PA and outdoor time, e.g.

accelerometers, GPS devices or body-worn cameras to capture images of location [214]. Furthermore, warmer season was positively associated with overall PA, in line with most studies of PA and seasonal factors, such as weather and temperature [90, 106, 107]. In contrast to our results, Badland et al. found no association between PA levels and seasonality, but this study was performed in Perth, Australia with a stable, temperate climate. The authors suggested that PA research should consider weather patterns at the specific study location to assess the potential importance of seasonality [215]. For our study it was considered relevant to include seasonality, since the mean temperature in Trondheim normally varies between 13.0° Celsius in July and -3.0° Celsius in January, while the amount of precipitation is higher in July than in January [216]. The mean temperatures for January 2013 and July 2013 were -3.8° Celsius and 14.2° Celsius, respectively [217]. This must be considered small deviations from the normal mean temperatures, indicating that our results were obtained under normal climatic conditions for this geographical area. In addition, the total time of daylight varies significantly between spring/summer and fall/winter months. A Swedish study by Hagstromer et al. concluded that in a northern population, studies assessing PA was not greatly affected by seasonality [218]. This is interesting as Sweden and Norway are neighbouring countries, on the same latitude and hence with a similar climate and amount of daylight. The discrepancy could be explained by the younger age group included in the Swedish study (45 years).

In our study we examined the background factors associated with PA, and this term needs to be distinguished from determinants that are factors with a causal relationship to PA [82]. Longitudinal observational studies and experimental data could identify determinants that have strong causal effects on PA, while correlates are cross-sectional data that are associated with PA [81]. This means that the relationship between PA and these factors may be bidirectional. [213]. Hopefully data from the Generation 100 (after 5 years of intervention) will help address whether PA influences the correlates or the correlates influences the PA.

Information from these types of studies is useful for practitioners to be aware of the most important factors that influence PA, and hence target PA interventions for these sub-groups [213]. Furthermore, increasing the understanding of the factors that influence PA behaviour in older adults is important for the development of effective intervention strategies [47, 194].

Physical activity assessment

The Generation 100 study has provided a unique opportunity to investigate accelerometer data to describe PA among older adults in a Scandinavian country. First, what levels of PA measured in both absolute and relative intensity are achieved? Second, to what extent do older adults meet current health recommendations for PA? Thirdly, what background factors are associated with overall PA? Accelerometry provides valuable data for answering these types of questions, and assessment of intensity and background factors for PA can help PA promotion among older adults [89].

After years of experimenting with different methods, it is still difficult to make accurate field assessments of PA [37]. Accelerometers could have widespread practical application if equipment costs continue to fall [30]. Nevertheless, the increased use of accelerometry in PA epidemiology and the use of objective measures of PA in this thesis should not be perceived as an understanding that self-reported measures are outdated. Accelerometer data alone do not provide sufficient information for a PA surveillance system, hence the two methods should rather continue as a complementary way of understanding different dimensions of PA [120, 219]. Self-reported data are easily accessible since they require no equipment, and are often used in large health surveys. For example, a recent WHO review of PA surveillance in the EU member states showed that almost all national and international surveys were based on various subjective measures [122]. Furthermore, the International Prevalence Study on Physical Activity with results from 20 countries also used self-reported measures [220]. Therefore, it seems clear that for comprehensive assessment of PA in large-scale population surveillance, self-report measures are still required [120]. Combinations of different PA data will result in more comprehensive assessments and understanding of more dimensions of PA.

Strengths and limitations

The Generation 100 study is unique because of its large sample size and because of the length of the intervention period. Despite this, one should be careful to generalize our results to the whole older adult population of Norway. In paper I we saw that included participants were healthier than those who did not want to participate. However, we included both healthy and unhealthy (heart disease, cancer, diabetes) participants and aimed to include the general elderly population in Trondheim. Interestingly, it also seemed like the most active people did not want to participate, since a higher proportion of those who declined to participate reported high levels of PA. Moreover, though we wanted to include the general population, we also needed to

specify exclusion criteria taking into account the safety dimension of study participation. As a result, this study did not include participants who could not follow our exercise programme due to safety concerns.

In papers II and III the method used for assessment of PA was accelerometry. There are both advantages and challenges of using PA data from objective assessments, especially because this is a relatively new research field where development of methods is not yet completed [121, 127]. For example, PA may be underestimated and there are potential problems with monitor placement when monitoring for many days [119]. Despite these potential weaknesses, Westerterp evaluated the quality of five methods for PA assessment, and accelerometers were ranked first, clearly ahead of behavioural observation, DLW, HR monitoring and questionnaires [166].

One of the strengths with papers II and III was the high amount of wear time. Ageing effects on physical and cognitive health may potentially limit the ability of an older adult to be compliant with an accelerometer protocol [113]. The quality of accelerometer data will be affected by individuals forgetting to wear the device, or not knowing how to properly attach the device in the recommended position [129]. A significant amount of accelerometer wear time is typically defined with a criterion of at least 4 days with 10 hours wear time [12]. In papers II and III the mean wear time was 16 hours, out of the maximum 18 hours when using the defined time filter. Regarding valid days, 92% of the participants wore the accelerometer for at least 6 days. Previous studies have found that 3 days of monitoring of accelerometer data are needed to accurately predict PA levels in older adults [221], and a mean wear time of 11.2 hours per day [121]. These numbers indicate that the wear time for the analysed sample in Generation 100 must be considered highly acceptable.

It is important to note that PA was assessed after inclusion and randomisation had taken place, and hence after exercise training was prescribed. However, the participants were monitored before they had attended the first supervised exercise session, which marked the start of the intervention period. In addition, participants were instructed to live as normal as possible for the assessment period.

In addition to the correlates included in paper III there are other potential correlates of PA, such as psychological factors, major life events, socioeconomic position, macro-economic environments and biological factors like genetics and evolutionary physiology [81, 222-227]. During the planning of Generation 100 there was a balance between competing research interests, and we had to give priority to those correlates that we found most relevant. Therefore, we included relevant correlates available in the Generation 100 data collection.

Future research

Evidence-based approaches are recommended to increase the effectiveness of public health practice and to achieve objectives for population health levels [228]. The Generation 100 study could contribute to relate exercise and PA to health outcomes among older adults. The literature also lacks knowledge concerning whether exercise and/or PA will result in increased 'healthspan'. Moreover, for such a long time period as 5 years one could assume that HIIT and MCT might not be mutually exclusive, neither for older adults. Therefore, from both physical-and mental health perspectives it could be equally important to determine the ideal combination of these two exercise regimes. In addition, the long-term health effects of different types of exercise (aerobic-, resistance-, and balance training) should also be examined. One important aspect that should be examined from a large, long-lasting RCT study like Generation 100 are the effects on participation and dropout rates, and adherence to prescribed exercise training. In this regard, using qualitative research like interviewing would be highly useful to gain a deeper understanding of the mechanisms behind this.

To extend the work in paper II, it would be useful to look at how feasible different PA intensity cut points are to predict health outcomes. It would also be interesting to test the reliability of relative intensity cut points under free-living conditions. In addition, it would be beneficial to create individual PA profiles, e.g. by using a combination of both accelerometer data and self-reported data, and connect these to health outcomes. Furthermore, though accelerometry was used in these studies it is important to mention that there is a rapid progress in the development of equipment for PA surveillance. For example, assessment of HR every second of a year could very soon be realistic.

The study of background factors for PA, presented in paper III, had a cross-sectional design. One should aim to have follow-up data when possible, to be able to infer causality between background factors and PA, using the term determinants instead of correlates. The Generation 100 will have these kinds of data available within a couple of years, making it important to follow up the results from paper III. Additionally, besides the ideas presented regarding use of Generation 100 data, the literature lacks an updated review of a broad range of correlates of objectively measured PA among older adults.

CONCLUSIONS

This thesis has presented and discussed three papers that focus on PA and exercise in an elderly population. Older adults are a population group partly neglected in PA and exercise research, and the research presented here is an important step to increase the knowledge in this field.

Paper I has described the design, methodology and initiation of an RCT study beyond the state of the art. The Generation 100 study will give new knowledge as to whether exercise has an impact on morbidity and mortality among older adults, and whether exercise training has an impact on PA and several major health issues that affect the older adult population. Related to the population ageing, our data will hopefully contribute to a better understanding of successful ageing, and serve as an example of how to implement large health initiatives in the future.

In paper II 29% of the older adults met the PA recommendation, when analysed with an absolute intensity threshold, and this appears to be a higher proportion than in comparable countries. As hypothesized, we found that relative intensity thresholds resulted in higher proportions of older adults meeting PA recommendations, compared to the use of an absolute intensity accelerometer threshold. Overall PA and time in near max relative intensity declined with age. Furthermore, females had a higher overall PA and spent more time in higher relative intensities compared to males. Individuals with higher levels of CRF had higher levels of PA, than those with low- and medium levels of CRF. Surprisingly, uniaxial PA assessment resulted in more minutes spent in 10-min bouts of MVPA compared to triaxial PA assessment. Paper II clearly illustrated the consequences of using different methodological approaches in PA surveillance among older adults.

In paper III the demographic, environmental and biological correlates explained 27.0% of the variance in PA among older adults. CRF was the correlate that was most strongly associated with PA, with gender and season as the second and third most important correlates, respectively. This was, to our knowledge, the largest study of PA correlates in older adults that has combined objectively measured PA and CRF and our findings should be used to design future health interventions.

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Paper I

Stensvold D, **Viken H**, Rognmo Ø, Skogvoll E, Steinshamn S, Vatten LJ, Coombes JS, Anderssen SA, Magnussen J, Ingebrigtsen JE, Fiatarone Singh MA, Langhammer A, Støylen A, Helbostad JL, Wisløff U. (2015) A randomised controlled study of the long-term effects of exercise training on mortality in elderly people: study protocol for the Generation 100 study. *BMJ Open* 2015;5(2).

BMJ Open A randomised controlled study of the long-term effects of exercise training on mortality in elderly people: study protocol for the Generation 100 study

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ABSTRACT

Introduction: Epidemiological studies suggest that

exercise has a tremendous preventative effect on

100 is a randomised, controlled study where the

Trondheim, Norway, were invited to participate.

individuals (790 women) were included and

primary aim is to evaluate the effects of 5 years of

morbidity and premature death, but these findings

need to be confirmed by randomised trials. Generation

exercise training on mortality in an elderly population.

Methods and analysis: All men and women born in

the years 1936-1942 (n=6966), who were residents of

Between August 2012 and June 2013, a total of 1567

randomised to either 5 years of two weekly sessions of

moderate-intensity training (50 min of continuous work at \sim 70% of peak heart rate), or to a control group that

followed physical activity advice according to national

recommendations. Clinical examinations, physical tests

high-intensity training (10 min warm-up followed by

4×4 min intervals at ~90% of peak heart rate) or,

and questionnaires will be administered to all

health registries until year 2035.

participants at baseline, and after 1, 3 and 5 years.

Participants will also be followed up by linking to

Ethics and dissemination: The study has been conducted according to the SPIRIT statement. All

participants signed a written consent form, and the study has been approved by the Regional Committee

for Medical Research Ethics, Norway. Projects such as

this are warranted in the literature, and we expect that

data from this study will result in numerous papers

published in world-leading clinical journals; we will

also present the results at international and national

Trial registration number: Clinical trial gov

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conferences

NCT01666340.

BACKGROUND

Owing to worldwide increasing longevity, the world population is rapidly ageing. It has

Strengths and limitations of this study

- This study is the first randomised controlled trial to evaluate the effect of exercise training on morbidity and mortality in an elderly population.
- If proven beneficial, exercise as medicine is an inexpensive, accessible and available treatment with few negative side effects, for the evergrowing ageing population.
- The study is unique due to the large sample size included and because of the long intervention period (5 years).
- Unfortunately, this study did not include participants who could not follow our exercise programme due to safety concerns or disability.

been estimated that the proportion of people aged 60 years and older will double from about 11% in 2000 to 22% in 2050, and the age group 65 years and older will, for first time, outnumber children under the age of 5 by 2017.¹ In Norway, life expectancy in women and men is predicted to increase by 10 years from 83 and 79 years, respectively, over the next 80 years.² Future demands for healthcare services depend on illness and disability in the older population. Active ageing is a term used by WHO to describe "the process of optimizing opportunities for health, participation and security, in order to enhance quality of life and wellbeing as people age", and includes delay of senescence and compression of morbidity and mortality.3 With societal expectances of an increasing older population, interventions that compress years with disability alongside increased life expectancy are warranted.⁴ The ageing process is characterised by functional and physiological changes, and includes a decline in activity,⁵ mobility,⁶

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maximal oxygen uptake (VO_{2max})⁷ and muscle mass.⁸ In addition, the risk of most diseases, including type 2 dia-betes,⁹ pulmonary diseases,¹⁰ cardiovascular diseases,¹¹ cancer,¹² and mental disorders such as depression and dementia,¹³ all increases with age.^{14 15} Physical activity and social engagement have been emphasised as important pathways to improve and maintain health in the elderly.16 17 It has been shown that older people who report being inactive reach a disability threshold (defined as needing help from another person to carry out several daily-life activities) 14 years earlier than those who report being highly active.¹⁸ Importantly, becoming physically active even in older age seems to provide health benefits.¹⁹ Randomised, controlled trials have shown that regular exercise training increases fitness²⁰ ²¹ and reduces several of the traditional risk factors for cardiovascular disease.^{22 2^3} It has also been shown that high-intensity exercise training has the potential to induce larger increases in VO_{2max} and cardiovascular function than low-intensity or moderate-intensity training in healthy individuals, $2^{0-22-24}$ as well as in people with metabolic syndrome²³ and in those with hypertension, and in patients with heart failure,²⁵ intermittent claudication²⁶ and coronary artery disease.^{27 28} However, reducing traditional risk factors for disease does not necessarily result in longer survival as it has been shown, exemplified by pharmacological interventions, that initial improvements in surrogate markers are not able to show corresponding effects on major end points.^{29 30} Multiple epidemiological studies have suggested that physical activity is associated with a reduced risk of premature death $^{31-35}$ and that poor physical fitness is a strong predictor of mortality.^{36–38} Even a small difference in fitness appears to make a substantial impact on survival.³⁹ Furthermore, epidemiological studies have suggested that physical activity is associated with lower risk for developing diabetes,⁴⁰ hypertension,⁴¹ depression,⁴² dementia,⁴³ breast cancer,⁴⁴ colon cancer⁴⁵ and of accidental falls.⁴⁶

Although many reports suggest that high physical activity and fitness may have favourable health effects, there is a possibility that the level of physical activity is strongly correlated with a person's state of health, and may not be the cause of it. Thus, there is a need for large randomised controlled studies that can test the long-term effects of exercise training on social participation, disability, disease and survival in the general population. The Generation 100 study will be the first large controlled randomised clinical trial where the primary aim is to study effects of exercise training on total mortality in an elderly population. The present paper describes the design and significance of the Generation 100 study.

AIMS

Primary aim of Generation 100

► To determine the effects of regular exercise training over a 5-year period on overall mortality in elderly people (70–76 years of age).

Secondary aims of Generation 100

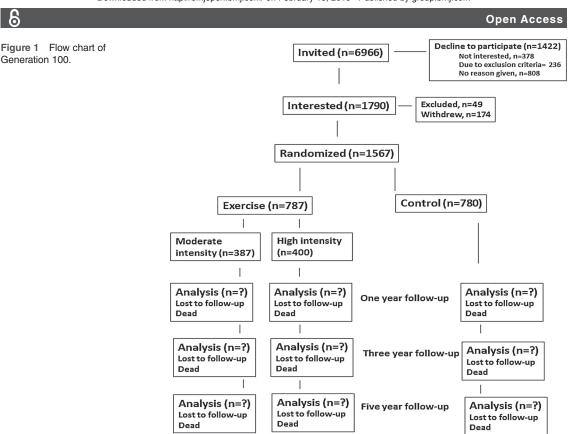
- ► To evaluate the effect of exercise training over a 3-year and 5-year period on social participation, physical function, cognitive function and overall morbidity (new diagnosis and worsening of disease status).
- ▶ To evaluate the effect of high-intensity versus moderate-intensity training over a 3-year and 5-year period on traditional risk factors for cardiovascular disease, maximal oxygen uptake, physical activity level, pulmonary function, muscle strength, gait speed and characteristics, need for prescription medications, falls and fall-related injuries, dementia, depression, fatigue, rate of hospitalisation, and cost and use of healthcare services (general physician, nursing homes and home care).
- To increase the knowledge regarding genetic predisposition for fitness (VO_{2max}) and cardiovascular diseases in order to facilitate prevention strategies before symptoms appear. We also intend to identify potential therapeutic targets by searching for blood-borne factors induced by training, using transcriptomics (messenger RNAs and microRNAs) and proteomics arrays.

METHODS

Design

This is a phase IIb clinical trial, where the participants are stratified by sex and marital status and randomised 1:1 into an exercise training group or to a control group (figure 1). The exercise training group was further randomised 1:1 into moderate-intensity or high-intensity training. Inclusion started August 2012 and ended in June 2013. The study will run until June 2018. The participants are tested at baseline (before randomisation) and at follow-up after 1, 3 and 5 years. The Unit for Applied Clinical Research at the Norwegian University of Science and Technology developed the randomisation procedure to ensure impartial assignments. After randomisation, participants received verbal and written information about their intervention. Participant data can be linked to the following registries until 2035: Cause of Death Registry, Statistics Norway, Norwegian Patient Register (NPR), National Injury Registry, Cancer Registry of Norway, Norwegian Myocardial Infarction Registry, National Population Register, GERICA (use of municipal care services) and the Norwegian Prescription Database. Generation 100 was registered in a clinical trials registry in August 2012 (ClinicalTrials.gov, Identifier: NCT01666340). All protocol modification must be approved by the Regional Committee for Medical Research Ethics, Norway. Participants are given a project-specific code. This project code is used during all analyses of the data. The procedures for data entry, coding and storage have been developed in close collaboration with the Norwegian Data Inspectorate and the Regional Committee for Medical Research Ethics, Norway. The participants gave informed, written consent to the main study and to receive invitations to

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substudies. Participation in the main study is not influenced by willingness to participate in substudies. All substudies must have approval from the Regional Committee for Medical Research Ethics, and studies will not involve interventions that are in conflict with the main study.

Settings and participants

This study is conducted in Trondheim, the third-most populous municipality in Norway, with a population of 176 348 1 January 2012.⁴⁷ Healthcare is provided predominantly by a public system, financed through general taxes, with no or nominal charge.48 All men and women born from 1 January in 1936 to 31 December in 1942, with a permanent address in the municipality of Trondheim (6966 people, 3721 women) were invited to participate (figure 1). Potential participants were identified through the National Population Register. An invitation letter consisting of an informational brochure about the study, a health-related questionnaire and a response sheet with a consent form was sent to potential participants. All individuals were asked to return the response sheet with the consent form and the questionnaire independent of willingness to meet at baseline examinations. Inclusion and exclusion criteria are given in box 1. In total, 46% (3212) responded, 1422 were not

interested while 1790 consented to participate. Of the 1790 people who initially said they were interested, 49 persons were excluded, and 174 actively withdrew or did not show up for testing. Thus, 1567 people, 777 men (72.5±2.1 years) and 790 women (72.5±2.1 years) were included (figure 1). Sample characteristics, based on the questionnaire (see online supplementary file 1) sent out with the invitation letter are shown in table 1. The portion of sedentary behaviour is lower in the participants included in our study compared with those who did not participate. Interestingly, 26% of those who did not want to participate reported to be highly active (almost every day), while the corresponding number among the participants was 22%. In the nonparticipating group, 32% reported to have higher education (college/university), which is the same percentage as for those who are 67 years and older in the general Norwegian population.⁴⁷ In the participating group, 50% reported to have higher education. In total, 87% of the included participants and 66% in the nonparticipating group reported to have good health. Thus, the participants in our study are more active, have higher education and better health compared with the non-participating group. In Trondheim, the death rate among those 68-72 years of age was 1.3% in 2010, and among those 70-74 years old, 1.7%. In Norway, the age

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Box 1 Inclusion and exclusion criteria

Inclusion criteria

- Born during 1936, 1937, 1938, 1939, 1940, 1941 or 1942.
- Able to complete the exercise programme (determined by the researchers).

Exclusion criteria

- Illness or disabilities that preclude exercise or hinder completion of the study.
- Uncontrolled hypertension.
- Symptomatic valvular, hypertrophic cardiomyopathy, unstable angina, primary pulmonary hypertension, heart failure or severe arrhythmia.
- Diagnosed dementia.
- Cancer that makes participation impossible or exercise contraindicated. Considered individually, in consultation with physician.
- Chronic communicable infectious diseases.
- Test results indicating that study participation is unsafe.
- Participation in other studies conflicting with participation in Generation 100.

of retirement is 67 years, thus we wanted to include people shortly after their working career ended. Initially, people born between 1938 and 1942 (inclusive) were invited. However, acceptance was lower than expected and fewer than 1500 participants were enrolled in the study. Therefore, in order to increase the sample size according to power calculations (see below), we additionally included those born in 1936 and 1937.

Ethics

The risk of exercise is considered very small; however, the risk of complications/death is higher during and immediately following training/testing.⁴⁹ Nevertheless, the health benefits from exercise training are sufficiently high and are considered less harmful than inactivity. The control group will not have access to supervised exercise training. However, they will be advised to follow current national guidelines for physical activity and will not take part in guided training. This reflects the 'treatment' currently offered to the public. Providing sufficient clear information is a high priority, so that participants feel that they know what consenting entails.

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Examinations

Figure 2 shows the physical test battery and examinations performed at baseline after 1, 3 and 5 years in all groups. All test personnel were blinded for intervention. Briefly, four different questionnaires are used in this study: Questionnaire 1 was sent out together with the invitation letter, thus those who wanted to participate and those who did not want to participate were both asked to fill out this questionnaire 2 consisted of more detailed questions. Questionnaire 2 consisted of more detailed questions about specific aspects of health, lifestyle, social environment and family medical history. The short form health survey SF-8 (1-week recall version) is used to describe quality of life and chronic pain (Q3). The questions from Q1, Q2 and Q3 have

	Included	Not participating	p Values
Number of participants	1567	1361	
Age (years)	72	73	<0.01
Height (cm)	172 (9)	171 (9)	< 0.05
Weight (kg)	75 (13)	76 (14)	NS
College/university education (%) (SD)	50	32	<0.01
Current smoker (%)	9	12	< 0.01
Self-reported health (%)			< 0.01
Poor	13	34	
Good	87	66	
Self-reported diseases (%)			
Myocardial infarction	5	11	<0.01
Angina pectoris	3	7	< 0.01
Heart failure	0.7	3	<0.01
Atrial fibrillation	6	12	< 0.01
Diabetes mellitus	5	11	< 0.01
Cancer	16	19	NS
Mental health problems	9	11	NS
Living condition, percentage of participants			< 0.05
Per cent living alone	25	29	
Per cent living with others	75	71	
PA, percentage of participants			
Low	9	16	<0.01
Moderate	69	58	<0.01
High	22	26	< 0.05

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Figure 2 Time points of assessments and the outcome variables measured.

		Open Access
2013/2014	2015/2016	2017/2018
One year follow-up	Three years follow-up	Five years follow- up
Examination 2	Examination 3	Examination 4
Blood sample	Blood sample	Blood sample
Blood pressure	Blood pressure	Blood pressure
Resting heart rate	Resting heart rate	Resting heart rate
Weight, height and	Weight, height and	Weight, height and
waistline measurements	waistline measurements	waistline measurements
Body composition	Body composition	Body composition
Questionnaire 2,3,4	Questionnaire 2,3,4	Questionnaire 2,3,4
Walking test	Walking test	Walking test
Grip strength test	Grip strength test	Grip strength test
Leg strength test	Leg strength test	Leg strength test
Maximal oxygen uptake	Maximal oxygen uptake	Maximal oxygen uptake
Maximal heart rate	Maximal heart rate	Maximal heart rate
Heart rate 1 minute	Heart rate 1 minute	Heart rate 1 minute
after testing	after testing	after testing
Physical activity level	Physical activity level	Physical activity level
Pulmonary function	Pulmonary function	Pulmonary function
Cognitive screening	Cognitive screening	Cognitive screening
	One year follow-up Examination 2 Blood sample Blood pressure Resting heart rate Weight, height and waistline measurements Body composition Questionnaire 2,3,4 Walking test Grip strength test Leg strength test Leg strength test Maximal oxygen uptake Maximal heart rate Heart rate 1 minute after testing Physical activity level Pulmonary function	One year follow-up Three years follow-up Examination 2 Examination 3 Blood sample Blood sample Blood pressure Blood pressure Resting heart rate Resting heart rate Weight, height and Weight, height and waistline measurements Body composition Bdv composition Body composition Questionnaire 2,3,4 Questionnaire 2,3,4 Walking test Grip strength test Leg strength test Leg strength test Maximal oxygen uptake Maximal oxygen uptake Maximal heart rate Heart rate 1 minute after testing after testing Physical activity level Physical activity level Pulmonary function Pulmonary function

many of the same questions that have been used in the Nord-Trøndelag Health Study (HUNT). 50-52 In addition, the participants are also asked to fill out a diet form (Q4). Only those who were included in the study fill out questionnaire Q2-Q4. Blood samples are obtained from an arm vein. Serum triglycerides, glucose, high-density lipoprotein, total cholesterol, C reactive protein, glycosylated haemoglobin (HbA1c) and c-peptide are measured immediately using standard procedures at St Olavs Hospital, Trondheim, Norway, Serum and EDTA-treated plasma are centrifuged at 3000 rpm for 10 min at 20°C. Aliquots are stored at -80°C, in case new blood markers will be analysed later. In addition, full blood from EDTA is taken and stored (at Regional Biobank) at -80° C for later DNA analysis. Blood pressure is taken in fasting state at rest and immediately after exercise testing. Testing of VO_{2max} is performed on a treadmill identical to that used in previous studies in our group,²⁵ and participants with previous heart diseases are tested under ECG monitoring, and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for exercise testing of patients with known cardiovascular disease is followed.⁵³ Body composition and weight are measured using bioelectrical impedance (Inbody 720, BIOSPACE, Seoul, Korea). Gait characteristics are measured by the GAITRite electronic gait mat (CIR Systems Inc, Havertown, Pennsylvania, USA).54 Grip and leg strength were measured by the JAMAR Hydraulic Hand Dynamometer (Lafayette Instrument Company, USA) and a leg press machine (FCM 5540 Leg Press Rehab Standard, Helsinki University of Research, HUR, Finland), respectively. Objectively measured physical activity is assessed by SenseWear Armband activity monitor (BodyMedia 7, Pittsburgh, Pennsylvania, USA) or by Actigraph (GT3X, Manufacturing Technology Inc, Florida, USA). After the clinical test at the hospital, all participants are given either SenseWear or Actigraph monitor. The participants are instructed to wear it for 7 days continuously (24 h), except when in contact with water (shower/bath/swim). The lung function tests are performed with the Sensormedics Vmax22 Encore (CareFusion, San Diego, California, USA) in accordance Thoracic Society/European the American with Respiratory Society (ATS/ERS) recommendations. Cognitive function and brain structure were tested using a combination of questionnaires57 and MRI of the brain using 3 T with 32 channel head coil and the following protocol: three-dimensional T1-weighted ADNI, Flair, T2 and SWI volumes, and diffusion tensor imaging. Novel genetic biomarkers(serum, plasma, DNA, RNA) will be analysed using high-throughput OMICS technology (genotyping or exome sequencing, DNA methylation, RNA sequencing, microRNA screening, mass spectrometrybased proteomics and MR metabolomics) using validated methods established at Norwegian University of Science Technology's Genomics, Proteomics and and Metabolomics Core Facilities. Health economic analysis will be calculated as the sum of hospital cost (inpatient, day care and outpatient care), use of general physician and primary healthcare (rehabilitation, nursing homes, home care, etc).

Sample size and statistics

Overall mortality was selected as the primary outcome for the sample size calculation. For this purpose, the exercise intervention groups (moderate and high intensity) will be pooled and compared with the control group. Epidemiological studies have reported a 50% lower death rate after 14–16 years of follow-up in people who are active compared with those who are inactive.^{34 58} In Trondheim (2010), 2% of the population between 70 and 77 years old died, and the expected mortality rate after 5 years will be approximately 10%. With a power of 90%, about 600 participants are needed in each group to detect a 50% reduction in mortality (ie, from 10% to 5%). We aimed to include 1500 participants to allow for up to 20% of dropouts. It is unknown, however, whether exercise has an effect on mortality. We therefore focus



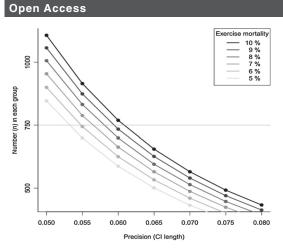


Figure 3 Sample size and precision (expected width of the CI) for different mortality rates in the exercise group. The chosen number (750 in each group) is shown as a horizontal light grey line.

on the precision of the estimated absolute mortality group difference in terms of the expected width of the resulting CI for the true difference. With 750 participants in each group, the expected 95% CI width will be between 0.05 and 0.06 depending on the observed mortality in the intervention group (figure 3). We think this precision is acceptable and emphasise that it does not depend on whether the result is statistically significant or not. The comparisons of change between the groups will be made by the intention-to-treat principle. Thus, data will be analysed according to the group that participants are assigned to, regardless of possible crossover and/or adherence to the intervention. In addition, we will perform a per protocol analysis, based on adherence to the intervention. The analysis will be made based on whether participants have followed the prescribed intervention or not. Non-adherence will be defined as having performed less than 50% of the prescribed training sessions over the 5 years. Survival and morbidity analysis will be carried out by performing χ^2 and log-rank tests. Cox regression analyses will be used to compute HRs of all-cause mortality and onset of new diseases between the groups. The precision of the estimates will be assessed by 95% CIs. All statistical tests will be two-sided.

Interventions

High-intensity training

Participants randomised to high-intensity training are asked to complete two weekly \sim 40 min long workouts. The participants are instructed to use a Borg 6–20 scale (rating of perceived exertion) as guidance for exercise intensity.⁵⁹ They are supervised to perform a light 10 min warm-up, followed by 4 min working periods (intervals) interspersed by 3 min active breaks. The intensity during the intervals should be 85–95% of peak

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heart rate, corresponding to approximately 16 on the Borg scale.^{59 60} Breaks consist of working at an intensity corresponding to ~12 on the Borg scale (60–70% of peak heart rate). Every sixth week the participants meet for a supervised spinning session (ergometer cycling) where they exercise with a heart rate monitor, to ensure that they exercise at the recommended intensity, as described above. In addition, organised training is offered twice per week in different walking areas around Trondheim. Attendance to these activities is voluntary, and participants may choose to perform their exercise training individually. The activity type performed will vary between seasons of the year and includes indoor and outdoor activities such as: walking/running, cross-country skiing and aerobics.

Moderate-intensity training

To obtain isocaloric exercise, participants randomised to moderate-intensity training are asked to complete 50 min of continuous moderate-intensity exercise corresponding to 70% of peak heart rate ('talking pace') twice a week.^{27 61} The participants are instructed to use the Borg scale as guidance for exercise intensity, and the exercise intensity should be perceived as approximately 13 on the Borg scale.^{59 60} The protocol regarding frequency and type of exercise was the same as for the high-intensity group.

Control group

The control group will be instructed to follow current recommendations for physical activity in Norway,⁶² meaning 30 min of moderate-level physical activity every day. No further supervision is given.

Adherence

Different strategies are used to improve and evaluate adherence to exercise training. Participants in the exercise groups are asked to fill in exercise logs immediately after each exercise session and send all the logs to the research centre either in prepaid envelopes monthly, or to use internet-based forms following each exercise session.⁶³ The procedures for reporting were prepared after consulting the Regional Committee for Medical and Health Research Ethics and the Data Inspectorate of Norway. To increase motivation, spouses are randomised to the same intervention group. The control group reported their physical activity level once a year, using a questionnaire. All participants are invited to an information meeting once a year, and newsletters are sent out twice a year. The participants can contact the administration of the study by phone or email, and they can find all necessary information about the study and the different interventions on the study's homepage. An adherence committee was initiated after 1 year. The committee will be responsible for implementing measures that increase adherence in the exercise groups, such as arranging different activity events.

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Organisation

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The steering committee of Generation 100 has developed the study protocol and is responsible for data collection, management, publications and the final data set. All major scientific and ethical questions will be resolved by majority vote. The committee is responsible for finding solutions to unforeseen questions/problems that arise in the course of the study. In addition, a Safety committee, consisting of two physicians, will continuously monitor the safety of the study and the study progression. The first 300 included in the study filled out a safety report 1 month after the initiation of the study. In addition, participants fill out a safety report every year after the initiation of the training. The participants should report if there has been: no special events, worsening of disease, newly diagnosed disease, or if they have been in the hospital. In addition, participants are asked to classify the cause of the event to different diseases/incidents. Furthermore, the Norwegian population registry is checked every year to uncover unreported mortality. Five times during the study, the safety committee will evaluate if there are any differences in the number of events between the groups (1 month, 1 year, 2 year, 3 year and 4 year), and continuously evaluate if it is ethically justifiable to let the study continue. Adverse advents during training and testing will be reported to the safety department at the university. The study has one physician (medical director), who will take care of those participants suffering from harm related to participation in the study.

Dissemination

Participants will receive their test result immediately after the test. In addition, participants will be invited to an annual meeting where general and new information will be given. Providing sufficient information to the participants is a high priority. It is anticipated that Generation 100 will garner widespread interest and media attention, and will have results in a series of articles that will be published in highly ranked international scientific journals.

DISCUSSION

To our knowledge, Generation 100 will be the first study with the primary aim of examining whether exercise has an effect on mortality in an older population. Generation 100 is unique because of the large sample size, because the entire population is invited and because of the long intervention period. The descriptive data demonstrate that a larger portion of those who were randomised reported better health, higher education and less heart disease compared with those who did not participate. However, the study consists of a diverse group of elderly people, as healthy people and people with many different diseases are both included. The heart failure-action (HF-action) study was the first large (n=2331, average age 59 years, 661 females) randomised study with the primary aim of evaluating the effect of

exercise alone on all-cause mortality and all-cause hospitalisation.65 In contrast to Generation 100, HF-action only included patients with heart failure. After adjusting for highly prognostic predictors, exercise training was associated with a significant, but modest, reduction in mortality and hospitalisation.⁶⁶ However, the intervention in that study included only 36 supervised exercise sessions, followed by home-based exercise, and, importantly, only 38% of the participants in the exercise group fully adhered to exercise after 1 year.⁶⁷ Exercise training with high intensity has previously shown to induce greater cardioprotective effect compared with moderate exercise. 22 27 47 68 To our knowledge, Generation 100 will be the first study to evaluate the long-term effect of both high-intensity training and moderate intensity on how people age. Longevity seems to be an important health goal for most western countries, and improved health, increased self-reliance and preventing diseases are highlighted as important strategies to reduce the anticipated financial burden of an ageing population. $^{1\ 15}$ Data from Generation 100 will contribute to an improved understanding and provide solutions on how to achieve active ageing. Further, our data will demonstrate if exercise can be used as a preventive intervention for disease and functional decline, and give more and healthier years to those who are systematically physically active. If proven beneficial, exercise as medicine will be a relatively cheap, accessible and available treatment, with few negative, but a large number of positive side effects that can be offered systematically to a large ageing population. The use of exercise as prevention and treatment will potentially benefit a large proportion of the population, and may give a significant economic benefit both at an individual level and from a societal perspective. In conclusion, Generation 100 will give new knowledge to whether exercise has an impact on morbidity and mortality in elderly people, and further if exercise training has an impact on several major health issues that affect the elderly population. In light of the ageing population, our data will hopefully contribute to a better understanding of ageing, and serve as an example of how to implement large health initiatives in the future.

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Paper II

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Physical activity among older adults (70-77yrs) – and consequences of different methodological approaches: The Generation 100 study

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Abstract

Background: A number of studies have documented the health benefits of physical activity (PA). Assessment of PA recommendation adherence on a population level is necessary to test the effectiveness of PA public health strategies. Traditionally, population PA recommendation adherence is measured with accelerometers utilizing absolute intensity moderate-to-vigorous PA (MVPA) thresholds which often cannot be reached by older adults, due to a decline in cardiorespiratory fitness (CRF). Due to limitations in the methodology the information needed to assess relative intensities of effort has been lacking. Thus the literature lacks studies that examine and compare relative- and absolute intensity PA among older adults. The primary aim of the current study was to present a comprehensive description of PA in a large sample of Norwegian older adults, with objectively measured CRF and PA. The secondary aim was to compare proportion of the same elderly population meeting PA recommendation with MVPA utilizing both uniaxial and triaxial relative (CRF-and-gender-population-adjusted) and Troiano (uniaxial) absolute intensity threshold.

Methods: PA was assessed for 7 days using the Actigraph GT3X+ accelerometer in 1219 older adults (624 females) aged 70-77 years. CRF was directly measured as peak oxygen uptake (VO_{2peak}). The absolute MVPA threshold selected was 2020 counts-per-minute (CPM), while the relative MVPA thresholds for uniaxial (females: 213 CPM, males 267 CPM) and triaxial (females: 1077 CPM, males: 1653 CPM) PA data were developed specifically for the Generation 100 population sample (Gender and population CRF adjusted).

Results: Females spent more time at higher relative intensities than males. Overall PA and near max intensity PA declined with age. Moderately and highly fit individuals were more physically active, compared to the unfit. Proportions meeting PA recommendations were 29%, 79% and 71% when utilizing uniaxial absolute and relative uniaxial- and triaxial MVPA, respectively.

Conclusions: This study has presented a comprehensive description of PA among older adults, with objectively measured PA. In addition, this is the first study comparing relative versus absolute intensity PA among older adults. The present study clearly illustrates the consequences of using different methodological approaches in PA surveillance (absolute/relative MVPA), among older adults.

Key words: Physical activity, older adults, PA recommendations, relative intensity, absolute intensity, MVPA, the Generation 100 study

Background

Demographic data indicate tripling of the population over the age of 60 by the year 2050 [1]. The highest burden on global health is presented by non-communicable diseases (NCDs), whose incidence increases with age [2]. Much evidence has documented health benefits of physical activity (PA), and established PA as a key preventive treatment for NCDs [3-5]. As a result older adults are recommended to undertake either absolute or relative intensity moderate-to-vigorous PA (MVPA) amounting to 150 minutes per week, preferably in 10 minute bouts [6]. To test the effectiveness of PA public health strategies requires assessment of PA recommendation adherence on a population level [7]. Since the PA recommendation is given in both absolute and relative intensity, both should be utilized when measuring adherence to PA recommendation on a population level [8, 6, 9].

Traditionally, studies examining objective PA, using accelerometers, have assessed vertical axis counts-per-minute (uniaxial CPM). Newer technology making triaxial CPM assessment available, has made it possible to measure more complex movement patterns, compared to uniaxial PA data. In addition, most studies have used uniaxial one-size-fits-all MVPA thresholds derived from validation studies in younger adults and older adolescents (ages 18 and older) utilizing absolute intensity [10-13]. Using this methodology, only 3-20% of older adults meet the absolute PA recommendation [14, 15, 10]. The effort required to perform absolute intensity moderate activity depends on the fitness level. As ageing often result in a declined cardiorespiratory fitness (CRF), absolute thresholds, could effectually underestimate relative MVPA among older adults [13, 16]. Due to limitations in the methodology the information needed to assess relative intensities of effort has been lacking [17]. It is therefore not known how many older adults meet the relative PA recommendation. To overcome this limitation we developed relative intensity thresholds specifically for our Norwegian population sample of older adults [18].

The current study presented a comprehensive description of PA in this large sample of Norwegian older adults, with objectively measured CRF and PA. Additionally, the study compared proportions of the same population of older adults meeting PA recommendation, with PA assessed using relative (CRF-and-gender-population-adjusted) and absolute intensity threshold.

Methods

Study population

The present study was a cross-sectional sub-study of a larger study entitled Generation 100 (http://www.ntnu.edu/cerg/generation100). All males and females born between years 1936 to 1942, with a permanent address in the municipality of Trondheim were invited to participate [19]. More details regarding the Generation 100 study, including criteria for eligibility and comorbidities and risk factors of this population sample, were described elsewhere [19].

The present study was approved by the Regional Committee for Medical Research (REK 2013/1903 B), and addresses baseline data from the Generation 100 study (August 2012 to June 2013). All participants gave their written informed consent, and the study was conducted in conformity with the declaration of Helsinki. Participants with incomplete/missing accelerometer data, clinical data, and questionnaire data were excluded. In total 1219 participants (78% of the Generation 100 participants), 595 (49%) males and 624 (51%) females, with an age ranging from 70-77 were included in the present study.

Measures

Assessment of PA

A triaxial Actigraph GT3X+ accelerometer (Actigraph, Pensacola, Florida, USA) was used to assess PA utilizing three axes, e.g. vertical (Y), horizontal right–left (X) and horizontal front–back axis (Z). The PA data is converted into activity counts, which reflect the intensity of bodily movement. The higher the number of counts, the more active a person [20]. Each sample was summed over a user specified interval of time called an 'epoch'. The epoch was set to a 10-s interval. The outcome variable is reported in uniaxial and triaxial counts min⁻¹ (CPM). While uniaxial CPM (vertical axis) has been the most common way of analyze overall PA data, triaxial CPM measures more complex movement patterns in all three planes of motion compared to uniaxial PA data [21, 22]. Step counts were calculated as a daily mean assessed by the accelerometer.

In addition, the registered accelerometer time was categorized in intensity zones using relative thresholds validated for this age group [18]. Minutes in different intensity zones were calculated by summing all minutes of activity above the different relative threshold. PA was categorized as low (all data below moderate), moderate, vigorous and near max intensity [23]. Furthermore, three MVPA output variables were calculated; Absolute uniaxial MVPA (MVPA≥2020 uniaxial CPM) [10]; relative uniaxial MVPA (females: 213 CPM, males: 267 CPM) and relative triaxial MVPA (females: 1077 CPM, males: 1653 CPM) [18]. Both absolute- and relative MVPA were calculated by summing all minutes in sustained bouts of at least 10 min above the corresponding moderate intensity thresholds, with allowance for one or two interruptions. Regarding fulfillment of the national PA recommendation, the bouts of MVPA were dichotomized (meeting/not meeting), using a threshold of 150 minutes per week (from now on referred to as absolute and relative PA recommendation).

The participants received the monitor the day they came in for clinical testing, and were told to wear it for 7 consecutive days. The Actilife software version 6.11.5 (Actigraph, Pensacola, Florida, USA) was used to process accelerometer data. Non-wear time was excluded from the analysis, and was defined as intervals of at least 60 consecutive minutes with zero counts, with allowance of 2 minutes with counts greater than zero [10]. All data between 6:00 a.m. and midnight were included in the analysis. Data were considered valid if the subject had at least 4 days of at least 600 min $\cdot d^{-1}$ recorded [10].

Assessment of CRF

CRF was measured as VO_{2peak} (mL·kg⁻¹·min⁻¹). Detailed protocol has been published elsewhere [19, 24]. Briefly, testing of VO_{2peak} was performed either as walking/running on a treadmill (97%) or cycling (3%) on a stationary bike. The mean of the three successively highest 10-seconds VO₂ registrations (ml/kg/min) was used as VO_{2peak}. CRF was categorized as low, medium and high [18]. The distribution of participants to CRF groups is presented in Table 1.

Other measures

The Generation 100 questionnaire Q2 was used to measure types of activities, such as walking, fitness center, cycling, swimming etc. Frequency of activity type was measured with a 7-point scale (Never, seldom, 1-3 days per month, 1 day per week, 2-3 days per week, 4-6 days per week, daily), and dichotomized into less than weekly vs. once a week or more. Gender and age were obtained from the National Population Registry. Age was calculated from month/year of birth and month/year of inclusion, and dichotomized into 3 age groups (70-71, 72-75 and 76-77 years). Detailed protocol for assessment of body weight (kg), body height (cm) and body mass index (kg/m²) (BMI) has been published elsewhere [19]. Seasonal

data were obtained from the activity data (month of assessment). Based on the Norwegian climate the season variable (season) was dichotomized into "colder" (November-March) and "warmer" (April-October) months. The colder months have high probability of snow, ice and relatively few hours of daylight.

Statistical procedures

Statistical analyses for sample characteristics, CPM- and intensity distributions were performed with PASW Statistics 21 for Windows (IBM Corporation, Somers, NY, USA). Sample characteristics are presented as means (standard deviations) and proportions (Table 1). A One-way ANOVA test (Bonferroni) and independent samples t-test were used to study the association between PA (CPM, intensity zones and MVPA), age groups, gender and CRF groups (Table 2, 3 and 4). Pearson chi square test was used to study associations between categorical data (Proportions meeting absolute and relative PA recommendations distributed by age, gender and CRF) (Table 4). A P-value < 0.05 was required to declare statistical significance.

Results

Participant characteristics

Age, height, weight, BMI, gender and CRF for the participants are presented in Table 1. Of the 1219 older adults included, 59% wore the accelerometer for 7 valid days, 33% wore it for 6 valid days, and 8% wore it for 4-5 days. The average daily wear time was 964.8 minutes (16 hours); 968 minutes for males and 962 minutes for females, respectively. PA data assessments were equally distributed between "warmer" (April-October) (48.2%) and "colder" (November-March) (51.8%) months of the year. The proportion of the different relative

intensity for men and women in total was 84.1% in low, 9.6% in moderate intensity, 4.5% in vigorous intensity and 1.8% near max. Activity levels among the participants varied widely, ranging from 40-905 and 133-1168 CPM per day for uniaxial and triaxial assessment, respectively. Steps per day ranged from 1105 to 18414 steps. Furthermore, there was a wide range in both 10 min bouts of relative uniaxial (0-372 min) and triaxial MVPA (0-286 min), and absolute MVPA (0-133 min) per day (Table 2, 3 and 4).

PA types

Walking was the most common activity among older adults. Eight out of ten reported recreational walking on the road/pathways as a primary form of activity, seven out of ten reported walking as a form of transport and six out of ten reported hiking in the nature, at least once a week (Figure 1). On a weekly basis, approximately 35% were exercising at a fitness center, 25% were cycling, 17% participated in organized sports, and 13% were swimming. More males were active in using ski tracks and cycling compared to females, while females were more active in recreational walking and swimming than males. There were no gender differences regarding sports, fitness center, marked walking trails, walking as a form of transport and hiking in nature.

PA and age

The age group 70-71yrs was found to have a significantly higher overall PA than those aged 76-77yrs, using both uniaxial and triaxial CPM (p<0.05). In contrast, the amount of daily steps didn't differ between age groups (Table 2). No significant age related differences were found between time in low, moderate and vigorous relative intensity PA, while the 70-71yrs accumulated significantly more time in near max relative intensity PA (Table 3). There were no significant differences in percent of time spent in absolute MVPA bouts (1.8%, 1.7% and

1.5% for the age groups 70-71yrs, 72-75yrs and 76-77yrs, respectively). Moreover, time in relative triaxial/uniaxial MVPA bouts amounted to 4.8%/5.8%, 4.5%/5.5% and 4.1%/5.0% for the 70-71yrs, 72-75yrs and 76-77yrs, respectively (non-significant). Moreover, the proportion of participants meeting PA recommendations showed no significant age differences, for either the relative (uniaxial and triaxial), or for the absolute MVPA thresholds. The largest differences were found between uniaxial absolute and uniaxial relative MVPA with differences of 47.9 percentage points (pp) (70-71yrs), 48.8pp (72-75yrs) and 56.7pp (76-77yrs), respectively (Table 4).

PA and gender

Females had a significantly higher overall PA than males when using triaxial CPM (p<0.001), but not when applying uniaxial CPM. In addition, the amount of daily steps did not differ between males and females (Table 2). Females spent significantly less time in the low intensity zones and more time in the higher relative intensity zones (moderate, vigorous and near max), compared to males (p<0.01) (Table 3). Moreover, females accumulated significantly more time in relative MVPA bouts (triaxial: 5.6% and uniaxial: 6%), than males (triaxial: 3.5% and uniaxial: 5%) (p<0.001). In contrast, analyzing time in absolute MVPA bouts showed no significant gender difference (1.8% for males, 1.6% for females). Higher proportions of males and females met the relative PA recommendation (uniaxial and triaxial), compared to the absolute PA recommendation. The largest differences were found between the absolute PA recommendation and the uniaxial relative PA recommendation, with differences of 45pp for males, and 55pp for females (Table 4).

PA and CRF

Participants overall PA was positively associated with CRF, both for uniaxial and triaxial CPM, and steps (p<0.001) (Table 2). Highly fit older adults spent less time in low relative intensity PA and more time in higher relative intensity zones (moderate-, vigorous- and near max), compared to unfit individuals. In addition, moderately fit older adults spent more time in vigorous and near max relative intensities than the unfit (Table 3). Moreover, the unfit participants spent less time in triaxial (3.1%) and uniaxial (4.0%) relative MVPA bouts, compared to the moderately fit (triaxial: 4.6% and uniaxial: 5.6%) and highly fit individuals (triaxial: 6.2% and uniaxial: 7.2%). Similarly, the fittest participants spent the most time in absolute MVPA (2.5%) compared to the moderately fit (1.7%) and unfit individuals (0.9%), (Table 4).

PA and season

In a preliminary analysis PA was found to be significantly higher in the warmer months, compared to the colder months. Older adults had a significantly (p<0.001) higher overall PA in warmer months compared to colder months, using both uniaxial (267 vs. 235 CPM) and triaxial (524 vs. 481 CPM) data, and steps (7040 vs. 6340). Warmer months also accumulated more minutes in absolute (19 vs. 14 min) and relative (triaxial: 52 vs. 37 min and uniaxial: 65 vs. 42 min) MVPA bouts, compared to colder months. Furthermore, the proportion meeting PA recommendation was significantly higher in warmer than in colder months both for absolute (34.2% vs. 24.2%) and relative (triaxial: 76.5 vs 66.1% and uniaxial: 86.1% vs. 72.4%). There were no seasonal differences in total registered accelerometer time (p=0.148).

Discussion

The present study found that females spent significantly more time in higher relative intensities, compared to males. Older adults' overall PA declined with age, when measured as uniaxial and triaxial CPM, while not when measured as steps. Minutes in higher relative intensities were maintained across age categories, except for time spent in near max intensity. Moderately and highly fit older adults were more physically active overall and spent more time in the higher relative intensities, than the unfit. In addition, older adults were more physically active and more likely to fulfill the PA recommendations in warmer months compared to colder months. These associations did not differ across gender, age and CRF. A major finding of the present study was that a much greater proportion of the population sample was meeting the relative compared to the absolute PA recommendation. Walking was reported as the most common type of PA among the older adults.

Standardized methods of surveillance (i.e. absolute MVPA threshold) have been called for to assess prevalence of PA and to allow for national and international comparisons [6, 7]. Most studies using accelerometry to look at proportions of the population meeting PA recommendation, have used uniaxial data and absolute MVPA thresholds [22]. In order to compare our results to the only Norwegian study with a similar population (older adults) [14], we applied the same criteria on our population sample. This includes the use of uniaxial data, former national PA guidelines (30 min of MVPA per day) and an absolute MVPA threshold (MVPA \geq 2020 CPM) [10]. By doing this we found similar results compared to Lohne-Seiler et al. [14], with approximately 20% of our population sample meeting PA recommendation. By applying the current national PA guidelines (150 min/week of MVPA) to the absolute uniaxial MVPA threshold, three out of ten older adults met the PA recommendation.

Sparling and colleagues criticized the current PA recommendation for being unrealistic, and argued that reducing sedentary time and increasing low PA, might be more realistic and pave the way to more exercise in higher intensities among older adults [25]. This critique is however based on studies utilizing absolute intensity thresholds when quantifying proportions meeting PA recommendation. When applying absolute intensity thresholds, older adults are more susceptible to not reaching the PA recommendation [16, 3], due to declining CRF [26, 27]. Importantly, the PA recommendation also acknowledge the importance of relative intensity, especially for older adults [6, 8, 28]. The present study found a large difference in the proportion of our older adults meeting PA recommendation when we applied absolute versus the relative intensity threshold, illustrating that an older adult performing relative MVPA might not reach what is commonly defined as MVPA in absolute terms, and would, as a result, be classified as not meeting the absolute intensity PA recommendation [16]. On the contrary, when the MVPA threshold is adjusted for the population CRF and gender, that same older adult might meet the relative intensity PA recommendation. This could explain the differences in the proportion of our population meeting the PA recommendation when PA is assessed in absolute versus relative intensity. Importantly, the consequences (i.e. health benefits) of meeting the PA recommendation in absolute versus relative intensity terms have yet to be determined. More research is therefore needed in this regard.

Furthermore, when relative intensity was assessed using either uniaxial or triaxial data, the proportion of the same population meeting the relative PA recommendation differed. Despite knowing that triaxial accelerometer data measures different movement patterns compared to uniaxial data [21], the same PA intensity should ideally be captured equally when using uniaxial and triaxial thresholds. The difference might be explained by the fact that the relative thresholds were developed in laboratory settings on a treadmill, while the participants` PA was assessed in free-living conditions. While walking/running on a treadmill is a very controlled form of PA externally affected by speed and inclination, free-living PA is more

complex in regard of acceleration (i.e. speed and change in direction) and surface (i.e. uphill/downhill, stairs etc.).

These differences clearly illustrate the consequences of using different methodological approaches in PA surveillance, especially among older adults [16]. Nevertheless, it is noteworthy that almost a third of our older adults still didn't meet the relative PA recommendation. The intention of using relative intensity is to adjust the criteria for meeting the PA recommendation to the actual population level of fitness. Therefore, older adults not meeting the PA recommendation, especially the relative recommendation, should be an important target for future PA interventions.

When analyzing overall PA using uniaxial CPM (and steps) there were no significant differences between males and females, which is supported by a comparable study from Norway [14]. These findings are, however, in contrast to most studies on PA among older adults, which found males to be significantly more active than females [22, 10, 16]. Interestingly, when analyzing triaxial CPM, females were found to be significantly more active than males. Moreover, females spent significantly more time in the higher relative intensities (triaxial CPM) and a higher proportion of them met relative PA recommendation compared to males. There was however no significant difference in the proportions of males and females meeting the absolute PA recommendation. This contrasts Evenson et al. [16] that found consistent absolute intensity MVPA patterns regardless of the chosen thresholds, with males always more active than females. Finding females to spend more time in relative MVPA than males, contrasts both our absolute MVPA (non-significant) and the findings of Evenson et al. [16]. It is possible that females spend time in activities susceptible to underestimation when measured suing absolute intensity MVPA, such as household chores [29, 30]. An older unfit female performing household activity at moderate-to-high relative intensity might not reach what is commonly defined as moderate-to-high absolute intensity

PA, required for meeting the absolute PA recommendation. Importantly, since females have a generally lower CRF compared to males they will be more susceptible to not meeting absolute PA recommendation [31].

Interestingly, despite a narrow age span, the overall PA was inversely associated with age, with significantly higher CPM (uniaxial and triaxial) in the 70-71yrs compared to the 76-77yrs category. This is in line with former studies on this age group [32, 14, 10]. Since steps did not differ between the age groups, the age group difference in CPM is likely to be explained by the inclusion of PA intensity. More specifically, our results suggest that the variation in CPM between age groups might be explained by the amount of time spent in near max relative intensity. This was the only relative intensity zone that decreased from the youngest (70-71yrs) to the oldest age group (76-77yrs). In addition, the proportion of our population sample meeting PA recommendation did not differ between age groups, neither in absolute nor in relative intensity terms. This finding contrasts earlier studies which found an inverse relationship between PA assessed in absolute thresholds and age. This was however found in samples with wider age spans, compared to our sample (70-77yrs).

Research examining the association between PA and CRF, has traditionally used PA as an independent variable and CRF as a dependent variable [33, 34]. Contrary to this, Novak et al. found that people with higher CRF (VO_{2max}), spent more time being active throughout the day [35]. CRF was included in the present study to contribute to a better description of PA. As expected, we found a positive association between CRF and PA, which is supported by the literature [34-36]. Unfit older adults spent less time in PA of higher relative intensities, compared to moderately fit older adults, who, again, spent less time in high relative intensity PA than highly fit older adults. The authors acknowledge that since this was a cross-sectional study, there is a potential reverse direction of effect. An older adult's high CRF might be a

result of their PA behavior. Still our results strongly indicate that CRF should be an important factor in future research and PA interventions.

Importantly, the population of older adults is a heterogenic group in terms of health parameters [37]. Despite having thresholds adjusted for the population sample CRF and gender, the thresholds are not accounting for variation in the population sample CRF (low, medium, high). In the present study, the CRF ranged from 10.1-49.9 mL·kg⁻¹·min⁻¹ for females and 12.1-52.8 mL·kg⁻¹·min⁻¹ for males. The relative thresholds will therefore still be susceptible to underestimating PA intensity in older adults with low CRF, and overestimating among those with high CRF. One important question is whether future surveillance should be standardized to allow for comparison, using absolute levels of energy expenditure, or acknowledge the importance of relative levels of effort. The Harvard Alumni Health Study found that in older men self-reported relative intensity PA was a strong predictor of coronary heart disease [27]. More research is therefore needed to examine the association health outcomes have to MVPA, measured both in absolute and relative terms.

Walking, such as recreational walking, walking as a form of transport and hiking in nature, was the most common type of PA among older adults (Figure 1), and this is supported by earlier studies [38]. Aging may result in altered gait patterns [39] and higher metabolic costs of walking (altered relative intensity of effort) [40], which can affect the outcome of MVPA. Using an absolute MVPA threshold set too high could result in an underestimation of relative MVPA during walking [16]. Our results also showed that older adults perform other outdoor activities, such as cycling and skiing. In addition, we found that older adults also perform indoor activities (i.e. fitness center, sports and swimming). Our population sample of older adults was more active in the warmer months compared to the colder months. This could be explained by the fact that "colder" months (in Norway) consist of more snow, higher prevalence of ice and relatively fewer hours of daylight. This highlights the importance of accessibility to indoor PA facilities, which would make activity more independent of these seasonal differences. Both outdoor environments and indoor facilities should be important focus areas for political decision makers and for future interventions to implement a physically active behavior among older adults.

Strengths and limitations

One strength of this study is the use of an objective measure of PA in a large sample (n=1219)of older adults. Surveillance of older adults PA is important due to current concerns regarding the population aging, and associated challenges [6, 7]. Most PA research has used selfreported forms of PA assessment (questionnaires) [11, 22], which are susceptible to overestimation, recall bias and social desirability, especially among older adults [7, 32, 22]. Assessing PA with accelerometers reduces many of the challenges related to self-reported measures [41]. Furthermore, the use of triaxial CPM is a relatively new way of assessing PA, and contributes to a more complex measure of PA. The accelerometer used in this study (Actigraph) records ambulatory activity well, but can underestimate activities such as cycling, skiing, resistance exercise, upper body movements and carrying loads [42]. The participants were also instructed not to use the accelerometer during aquatic activities. One out of ten of our participants reported to swim weekly. However, walking was the most frequent activity type reported among this sample of older adults, which is a type of activity that is well captured by accelerometers. This strengthens the generalizability of our results to similar age groups worldwide. One other strength is the direct measure of CRF by direct ergospirometry, instead of using estimated CRF values or substitute measures of CRF, which is more common in large population-based public health studies [34].

The use of a more relative assessment of PA has been called for [8, 28, 6]. Implementing relative intensity PA thresholds, specifically developed for our sample of older adults, is an attempt to develop this field of research. However, one should keep in mind that the relative thresholds don't take into account individual CRF differences in the investigated population sample. Still, absolute thresholds and thresholds adjusted for population CRF and gender are more feasible than individualized thresholds for large population studies.

Regarding external validity and generalizability, it is important to note that the analyzed sample is relatively healthy (i.e. self-reported PA and BMI) and more educated compared to the invited, but not participating, individuals [19].

Conclusions

In the present study females spent significantly more time in higher relative intensities, compared to males. Older adults' overall PA and time in near max relative intensity declined across age groups. Moderately and highly fit older adults were more physically active, compared to the unfit older adults. Furthermore, this is the first study comparing absolute and relative (adjusted for gender and population CRF) MVPA among older adults. Our results clearly illustrate the consequences of using different methodological approaches in PA surveillance (MVPA thresholds, uniaxial/triaxial PA data), especially among older adults. A major finding of the present study was that applying absolute and relative intensity thresholds, resulted in different proportions of the population sample meeting the PA recommendation. This study illustrates how PA surveillance based on absolute intensity could underestimate relative PA among older adults, especially among those with low CRF.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NPA and HV contributed equally to this work and should both be considered first authors. All authors contributed to the conception and design of the study. All authors were responsible for the collection of the Generation 100 data in corporation with colleagues at CERG NTNU, Norway. NPA and HV provided the data for analysis, undertook the data analysis, and drafted the manuscript. All authors provided critical insight and revisions to the manuscript. All authors read and approved the final version of the manuscript submitted for publication.

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	Male (n=595)	Female (n=624)
Age, yr (mean ± SD)	72.7 ± 2.2	72.9 ± 2.2
Age groups, n (%)		
70-71	217 (36.5)	204 (32.7)
72-75	267 (44.9)	305 (48.2)
76-77	111 (18.7)	115 (18.4)
Height, cm (mean ± SD)	176.9 ± 5.6	163.4 ± 5.2
Weight, kg (mean ± SD)	82.4 ± 11.4	68.0 ± 10.6
BMI (mean ± SD)	26.3 ± 3.3	25.5 ± 3.7
CRF^{a} (mean \pm SD)	31.7 ± 6.8	26.3 ± 5.1
CRF groups, n (%)		
Low ^b	145 (24.4)	201 (32.2)
Medium ^b	300 (50.4)	279 (44.7)
High ^b	150 (25.2)	144 (23.1)

Table 1: Participant characteristics.

 $\label{eq:creative} \begin{array}{l} {}^{a}\text{CRF: VO}_{2peak} \text{ measured in } mL\cdot kg^{-1}\cdot min^{-1}. \\ {}^{b}\text{CRF} \mbox{ groups; Males low } <\!\!27.0 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}, \mbox{ Females low } <\!\!23.6 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}, \mbox{ Males medium } 27.0-35.6 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}, \mbox{ Females medium } 23.6-29.8 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}, \mbox{ Males high } >\!35.6 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}, \mbox{ Females high } >\!29.8 \mbox{ mL}\cdot kg^{-1}\cdot min^{-1}. \end{array}$

1 5	57		1		
	n	CPM uniaxial ^{a,b}	CPM triaxial ^{a,b}	n	STEPS ^a
Total	1219	251.2 (3.0)	502.9 (4.6)	1139	6651.9 (73.9)
Age group					
70-71	421	262.1 (5.5) ^d	516.7 (8.3) ^d	387	6791.6 (134.8)
72-75	572	247.3 (4.2)	499.6 (6.5)	526	6576.7 (109.6)
76-77	226	235.9 (5.7)	478.1 (9.2)	226	6587.7 (143.2)
One-way ANOVA Bonferroni		P = 0.005	P = 0.011		P = 0.399
Gender					
Male	595	253.3 (4.6)	484.5 (6.6)	564	6600.6 (108.7)
Female	624	247.4 (3.7)	517.7 (6.2)	575	6702.2 (100.5)
Independent-samples T test		P = 0.312	P < 0.001		P = 0.492
CRF group					
Low ^c	346	194.4 (4.0) ^e	419.2 (6.8) ^e	328	5266.2 (114.0)
Medium ^c	579	251.9 (3.9) ^f	505.8 (6.2) ^f	541	6762.9 (97.6) ^f
High ^c	294	313.0 (6.5)	590.0 (9.3)	270	8112.8 (152.8)
One-way ANOVA Bonferroni		P < 0.001	P < 0.001		P < 0.001

Table 2: Overall physical activity, measured in CPM and steps.

^aActual means and standard error of the mean (SE) for ease of interpretation. ^bUniaxial and triaxial counts per minute ^cCRF groups; Males low <27.0 mL·kg⁻¹·min⁻¹, Females low <23.6 mL·kg⁻¹·min⁻¹, Males medium 27.0-35.6 mL·kg⁻¹·min⁻¹, Females medium 23.6-29.8 mL·kg⁻¹·min⁻¹, Males high >35.6 mL·kg⁻¹·min⁻¹, Females high >29.8 mL·kg⁻¹·min⁻¹. ^dSignificantly (P < 0.05) different from the 76 to 77-yr group. ^eSignificantly (P < 0.05) different from the medium- and high CRF group. ^fSignificantly (P < 0.05) different from high physical fitness group.

		Wear time ^a		Mi	Minutes in intensity zones ^b	es ^b	
	u		Low PA	Moderate	Vigorous	Near Max	MVPA
Total	1219	964.8 (1.9)	811.0 (2.2)	92.5 (1.0)	43.4 (0.7)	17.9 (0.5)	153.8 (1.7)
Age group							
70-71	421	968.0 (3.2)	811.3 (3.8)	91.8 (1.8)	45.0 (1.2)	$19.9(0.9)^{d}$	156.7 (3.2)
72-75	572	961.0 (2.8)	807.3 (3.4)	93.4 (1.5)	42.8 (1.0)	17.5 (0.7)	153.7 (2.5)
76-77	226	968.4 (3.9)	820.0 (4.5)	91.7 (2.2)	41.8 (1.5)	15.0 (1.0)	148.5 (3.6)
One-way ANOVA Bonferroni		P = 0.160	P = 0.118	P = 0.737	P = 0.190	P = 0.001	P = 0.263
Gender							
Male	595	968.2 (2.7)	849.7 (2.7)	70.1 (1.0)	32.0 (0.7)	16.5 (0.7)	118.6 (1.8)
Female	624	961.5 (2.6)	774.2 (2.8)	113.9 (1.3)	54.2 (1.0)	19.2 (0.7)	187.3 (2.2)
Independent-samples T test		P = 0.075	P < 0.001	P < 0.001	P < 0.001	P = 0.004	P < 0.001
CRF group							
Low ^c	346	951.0 (3.7) ^e	$816.1 (4.3)^{f}$	87.8 (1.9) ^f	37.5 (1.2) ^e	9.5 (0.5) ^e	$134.8(3.1)^{e}$
Medium ^c	579	968.2 (2.6)	$814.2(3.2)^{f}$	92.3 (1.5) ^f	$44.0(1.0)^{\mathrm{f}}$	$17.7~(0.6)^{\rm f}$	154.1 (2.5) ^f
High ^c	294	974.3 (3.8)	798.8 (4.6)	98.4 (2.1)	49.0 (1.3)	28.1 (1.1)	175.4 (3.4)
One-way ANOVA Bonferroni		P < 0.001	P = 0.018	P < 0.001	P < 0.001	P < 0.001	P < 0.001
^a Wear time; registered accelerometer time (minutes per day). Actual means and standard error of the mean (SE). ^b Minutes in intensity zones; Total registered accelerometer time distributed in intensity zones, using triaxial CPM. Actual means and standard error of the mean (SE). ^c CRF groups; Males low <27.0 mL·kg ⁻¹ ·min ⁻¹ , Females low <23.6 mL·kg ⁻¹ ·min ⁻¹ , Males medium 27.0-35.6 mL·kg ⁻¹ ·min ⁻¹ , Females medium 23.6-29.8 mL·kg ⁻¹ ·min ⁻¹ , Males high	neter time ul registere is and stan nL·kg ⁻¹ ·m r. Fenales	(minutes per day). Ac ed accelerometer time dard error of the meau in ⁻¹ , Females low <23	tual means and standard error distributed in intensity zones, n (SE). t ML-kg ⁻¹ -min ⁻¹ , Males hL-kg ⁻¹ -min ⁻¹ , Males high	0 0 1	⁴ Significantly ($P < 0.05$) different from the 76 to 77-yr group. Significantly ($P < 0.05$) different from the medium- and high CRF Significantly ($P < 0.05$) different from high physical fitness group.	Significantly ($P < 0.05$) different from the 76 to 77-yr group. Significantly ($P < 0.05$) different from the medium- and high CRF group. Significantly ($P < 0.05$) different from high physical fitness group.	-dno

Table 3: Total wear time and minutes spent in relative intensity zones, per day.

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		Uniaxial a	Uniaxial absolute threshold ^a	Uniaxial re	Uniaxial relative threshold ^b	Triaxial re	Triaxial relative threshold ^b
	u	10 min bouts of MVPA ^c	Meeting PA recommendation (%) ^d	10 min bouts of MVPA ^c	Meeting PA recommendation (%) ^d	10 min bouts of MVPA ^c	Meeting PA recommendation (%) ^d
Total	1219	16.3 (0.5)	29.0	53.5 (1.2)	79.0	43.8 (1.0)	71.1
Age group							
70-71	421	17.0 (0.9)	31.4	56.6 (2.3)	79.3	46.6 (2.0)	73.2
72-75	572	16.4 (0.7)	28.8	53.2 (1.8)	77.6	43.2 (1.5)	70.3
76-77	226	14.9 (1.1)	25.2	48.3 (2.0)	81.9	40.0 (1.9)	69.5
One-way ANOVA Bonferroni		P = 0.342	$P = 0.259^{f}$	P = 0.057	$P = 0.407^{f}$	P = 0.076	$P = 0.509^{f}$
Gender							
Male	595	17.3 (0.8)	30.3	48.8 (1.6)	75.1	33.7 (1.1)	62.2
Female	624	15.3 (0.7)	27.9	57.9 (1.8)	82.7	53.4 (1.6)	79.6
Independent-samples T test CRF group		P = 0.053	$P < 0.363^{f}$	P < 0.001	$\mathbf{P} = 0.001^{\mathrm{f}}$	P < 0.001	$\mathbf{P} = 0.001^{\mathrm{f}}$
$\mathrm{Low}^{\mathrm{e}}$	346	$8.8 (0.6)^{g}$	14.2	$38.2(1.8)^{g}$	61.6	29.3 (1.4) ^g	52.3
Medium ^e	579	16.4 (0.7) ^h	28.7	53.9 (1.7) ^h	82.0	44.2 (1.5) ^h	73.7
High ^e	294	24.9 (1.3)	47.3	70.6 (2.8)	93.5	60.0 (2.4)	88.1
One-way ANOVA Bonferroni		P < 0.001	$P < 0.001^{f}$	P < 0.001	$P < 0.001^{f}$	P < 0.001	$P < 0.001^{f}$
^a Absolute threshold applied to uniaxial counts per minute (Troiano et al. 2008) ^b Relative thresholds applied to uniaxial and triaxial counts per minute (Zisko et al. 2015) ^c MVPA, Moderate-to-vigorous PA (min ⁻ d ⁻¹), minutes conceded in 10 continuous minutes of MVPA per day, with allowance of 1-2 minutes drop. Mean and standard error of the mean.	l counts per ll and triaxia in·d ⁻¹), minu minutes dro	minute (Troiano et ul counts per minute ates conceded in 10 pp. Mean and stand	al. 2008) e (Zisko et al. 2015)) continuous minutes of ard error of the mean.	*CRF groups: Males low medium 27.0-35.6 mL·kg >35.6 mL·kg ⁻¹ ·min ⁻¹ , Fet fpearson Chi-Square test	⁶ CRF groups; Males low <27.0 mL ·kg ⁻¹ ·min ⁻¹ , Females low <23.6 mL ·kg ⁻¹ ·min ⁻¹ , Males medium 27.0-35.6 mL ·kg ⁻¹ ·min ⁻¹ , Females medium 23.6-29.8 mL ·kg ⁻¹ ·min ⁻¹ , Males high >35.6 mL ·kg ⁻¹ ·min ⁻¹ , Females high >29.8 mL ·kg ⁻¹ ·min ⁻¹ .	1 ⁻¹ , Females low <23. medium 23.6-29.8 ml L.kg ⁻¹ .min ⁻¹ .	6 mL·kg ⁻¹ ·min ⁻¹ , Males L·kg ⁻¹ ·min ⁻¹ , Males high

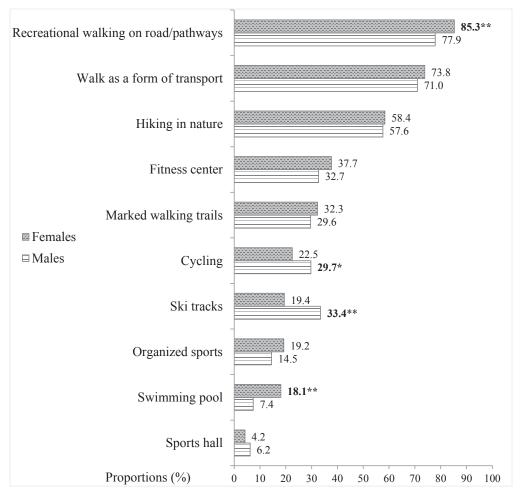


Figure 1: Types of physical activity, proportions (%) participating at least once a week. ^{**}Significantly (P < 0.01) different between genders. ^{*}Significantly (P < 0.05) different between genders.

Paper III

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Correlates of objectively measured physical activity among Norwegian older adults: The Generation 100 study

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Abstract

The aim of this study was to identify how demographics and physical activity history, environmental and biological correlates are associated with objectively measured physical activity (PA) among older adults. PA was assessed objectively in 850 older adults (70-77 years, 47.6% females) using the Actigraph GT3X+ activity monitor. Hierarchical multiple regression analysis was used to identify important PA correlates. The included correlates explained 27.0% of the variance in older adult's PA. Cardiorespiratory fitness (CRF), gender and season were the most important correlates, explaining 10.1%, 3.9% and 2.7% of the variance, respectively. PA was positively associated with CRF, females were more physically active than males and PA increased in warmer months compared with colder months. This is, to our knowledge, the largest study of PA correlates in older adults that has combined objectively measured PA and cardiorespiratory fitness. Our findings provide new knowledge of how different correlates are associated with PA.

Key words: Physical activity, older adults, correlates, Generation 100

Introduction

It is well established that physical activity (PA) is an important factor for current and future health. A moderate to high level of PA is associated with reduced risk of cardiovascular disease, cancer, diabetes, and mental health disease (Physical Activity Guidelines Advisory Committee, 2008; Taylor et al., 2004; U.S. Department of Health and Human Services, 1996). Becoming physically active even in older age has been shown beneficial for health. Older adults who report to be physically active reach a disability threshold 14 years later in life compared to those who report to be physically inactive (Hamer, Lavoie, & Bacon, 2013; Peeters, Dobson, Deeg, & Brown, 2013). The number of older adults (aged 70 or older) meeting the PA recommendation is shown to vary, i.e. 6% of Norwegian and 20% of US older adults meet the recommendation (Lohne-Seiler, Hansen, Kolle, & Anderssen, 2014; Tucker, Welk, & Beyler, 2011). To develop well designed PA interventions, a better understanding of important factors (correlates), that are associated with overall PA in older adults, is needed (A. E. Bauman et al., 2012).

PA behavior in older adults has been shown to be associated with demographical correlates such as gender and age (Kaplan, Newsom, McFarland, & Lu, 2001; McMurdo et al., 2012), education, PA history and physically demanding work (Chung, Domino, Stearns, & Popkin, 2009; Friedman et al., 2008; Pan et al., 2009), environmental correlates such as social support, living situation and season (Booth, Owen, Bauman, Clavisi, & Leslie, 2000; Palacios-Cena et al., 2011; Van Cauwenberg et al., 2011; Witham et al., 2014), and biological correlates such as body mass index (BMI) and heart disease (Chad et al., 2005; Ortlieb et al., 2014). Cardiorespiratory fitness (CRF) is also found to be associated with PA (Novak et al., 2009), with more fit people spending more time being active compared to less fit people (19). However, directly measured CRF has never been included in a large sample study of PA correlates in older adults.

The most common method to assess PA in older adults is by using a questionnaire with only very few studies utilizing objective measures of PA (Sun, Norman, & While, 2013). Self-reported PA is shown to have some limitations compared to objectively measured PA, such as susceptibility to over-estimation, recall and cultural difference bias, especially in older adults (Sallis & Saelens, 2000; Santos-Lozano et al., 2012; Washburn, 2000). Studies on objective measures of PA and its association to PA correlates in older adults are therefore needed. The aim of this study was to identify how correlates, including directly measured CRF, were associated with objectively measured PA in older adults.

Methods

Design and participants

The present study was a cross-sectional sub-study from the larger study, Generation 100 (http://www.ntnu.edu/cerg/generation100). All males and females born between years 1936 to 1942, with a permanent address in the municipality of Trondheim were invited to participate. Further details regarding eligibility were published elsewhere (Stensvold et al., 2015).

The present study was approved by the Regional Committee for Medical Research (REK 2013/1903 B), and addresses baseline data from the Generation 100 study (August 2012 to June 2013). All participants gave their written informed consent, and the study was conducted in conformity with the declaration of Helsinki. Individuals with complete and valid objectively measured PA, clinical and questionnaire data were included in the present study. A total of 850 participants, 445 (52%) males and 405 (48%) females, with an age ranging from 70-77 at baseline were included in the analysis. Descriptive characteristics of the participants are presented in Table 1.

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Measurement of physical activity

The triaxial Actigraph GT3X+ accelerometer (Actigraph, Pensacola, Florida, USA) was used to measure overall PA in this study sample of older adults. Actigraph GT3X+ is a small lightweight activity monitor that measures and records accelerations. It uses a solid state triaxial accelerometer to collect motion data on three axes; vertical (Y), horizontal right–left (X) and horizontal front-back axis (Z). The Actigraph also includes the vector summed value known as 'vector magnitude' (triaxial) (Santos-Lozano et al., 2012). Acceleration is converted into activity counts that increase linearly with the magnitude of the acceleration. The present study used triaxial data, which measures more complex movement patterns in all three planes of motion compared with vertical locomotion (uniaxial). Each sample was summed over a user specified interval of time called an 'epoch'. The epoch was set to a 10-s interval. The outcome variable was reported in minutes, more specifically, mean number of triaxial counts min⁻¹ (CPM). The activity counts reflect the intensity of bodily movement, thus the higher number of counts measured, the more active a person is (Hall, Howe, Rana, Martin, & Morey, 2013). CPM was used as an outcome variable in this study due to its robustness as it is not influenced by any external criteria (i.e. intensity threshold) other than wear time (Troiano et al., 2008). An absolute intensity threshold to determine proportions meeting PA recommendations is commonly used (Sun et al., 2013). Absolute thresholds have been criticized for neglecting relative PA intensity (Ozemek, Cochran, Strath, Byun, & Kaminsky, 2013). Additionally, the aim of the study was not to determine the proportion of our population sample that meets PA recommendation, but rather to investigate correlates of overall PA. For these reasons we found CPM to be the most suitable outcome variable.

The monitor was placed around the waist of the participants the day they came in for clinical testing, and the participants were told to wear it for 7 consecutive days (including day and night). The Actilife software version 6.11.5 (Actigraph, Pensacola, Florida, USA) was

used to analyze accelerometer data. All data between 6:00 a.m. and midnight were included in the analysis. Non-wear time, defined as intervals of at least 60 consecutive minutes with zero counts with allowance of 1-2 minutes with counts greater than zero, was excluded from the analysis. Data were considered valid if the subject had at least 4 days of at least 600 min·d⁻¹ (10 hours·d⁻¹) recorded (Troiano et al., 2008). In total, 77.8% of the participants wore the accelerometer for 7 valid days, additionally 17.9% wore it for 6 valid days, and 4.3% wore it for 4-5 days. The average daily wear time was 964.0 minutes (\approx 16 hours); 961.6 minutes for females and 966.3 minutes for males, respectively.

Demographics and activity history

Self-reported data from the Generation 100 study (questionnaires) were used to examine the following correlates: Gender, age, physical activity at the age of 40 (PA at 40), physically demanding work (during working career) and education. Gender was dummycoded (female vs. male); age was continuous (70-77); PA at 40 was an ordinal variable from a 5 point scale measuring PA frequency ("never" – "almost every day"); physically demanding work was an ordinal 4 point scale variable dichotomized into no (work that mostly involves sitting) vs. yes (work that requires much walking, lifting and heavy physical labor); and education was dichotomized into low education (not attended College or University) vs. high education (attended College or University). Interaction effects were tested for education and gender.

Environmental correlates

Environmental correlates included both social and physical environmental correlates. Social support (from family/friends/peers) and living situation were considered as social environmental correlates. Social support was measured using a 6-item scale, where the participants rated separately how often their family/friends/peers had been supportive of their PA. The response to each item was based on a 5-point scale, ranging from never to very often.

Since Cronbach's alpha was 0.881, Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) was 0.860 and Bartlett's test of sphericity was statistically significant (p<0.001), the scale had an acceptable reliability and criterion-related validity. A mean score of all constituent items was computed, with higher score indicating a greater amount of support for PA. Only participants with a response rate of 100% for the respective items were included when the mean scores were computed (no allowance for missing item). Furthermore, the participants were asked about their living situation (alone vs. not alone). Physical-environmental correlates included two items: The participant's "perceived importance of using the neighborhood to be physically active" (neighborhood importance for PA) and "perceived importance of being outdoors when they are physically active" (outdoor importance for PA). Both correlates were dichotomized (not important vs. important). Furthermore, season was included as a physical-environmental correlate. Based on the Norwegian climate, more specifically Trondheim, the season variable (months) was dichotomized into "colder" (November-March) and "warmer" (April-October) months. The colder months have high probability of snow, ice and relatively few hours of daylight.

Biological correlates

Biological correlates included heart disease, CRF (VO_{2peak}) and BMI. Heart disease was dichotomized (no presence vs. presence), where presence means that the participants have reported at least one heart disease (myocardial infarction, angina pectoris, heart failure, atrial fibrillation, or other heart disease). Testing of VO_{2peak} (mL·kg⁻¹·min⁻¹) was performed either as walking on a treadmill (97.3%) or cycling (2.7%) on a stationary bike. Participants with previous heart diseases were tested under ECG monitoring, and the American College of Cardiology/American Heart Association guidelines for exercise testing of patients with known cardiovascular disease was followed (Stensvold et al., 2015). VO_{2peak} was used to include participants that did not attain the requirements of a maximal test. A persons' VO_{2peak}

was measured as the mean of the three successively highest 10-s VO₂ registrations. Weight and height were objectively measured (clinic) to the nearest kilogram and millimeter, respectively. BMI was calculated as body weight (kg) divided by the squared value of height (m) (kg/m²). Both VO_{2peak} (CRF) and BMI were used as continuous variables in the statistical analysis.

Analysis

All statistical analyses were performed with PASW Statistics 21 for Windows (IBM Corporation, Somers, NY, USA). Descriptive data were presented as proportions/means and standard deviations (SD) (Table 1). An independent-samples t-test was used to study the association between gender and objectively assessed overall PA (CPM) and the continuous PA correlates (age, PA at 40 years, BMI, CRF, and social support). Chi square test was used to study the association between gender and the dummy-coded PA correlates (heart disease, physical demanding work, education, living situation, neighborhood importance for PA, outdoor importance for PA and season). To analyse the relationships between the outcome variables, overall PA, and the sets of potential correlates for PA, hierarchical regression was applied. The analysis was built up from consecutive blocks containing categories of correlates. This approach ensured that increases in the explained variance in overall PA between participants (multiple correlations squared and R squared change) by adding a new block, can be attributed solely to the variables in the added block. Demographics and activity history correlates were entered in block 1 as a non-modifiable reference for the following blocks. Environmental correlates, that are modifiable, were entered in block 2 together with season. The modifiable factors VO_{2peak} and BMI, in addition to heart disease, were entered as biological correlates in block 3. Preliminary analyses (normality, heteroscedasticity and collinearity) were conducted to ensure that there was no violation of the assumptions of linear regression. Unstandardized coefficients (β) and the individual contribution of each correlate to

the explained variance (semi-partial correlation squared) were reported. A p value < 0.05 was required to declare statistical significance.

Results

Descriptive data

The proportion of females and males were 48% and 52%, respectively, and mean age 72.4±2.0 years for males and 72.5±1.9 years for females (Table 1). The mean overall CPM was 507.6±158.0. Females had a significantly higher overall PA than males (524.3±151.0 and 492.4±162.3 CPM, respectively). Males had significantly higher education and BMI, CRF, and presence of heart disease compared to females. More females than males have had a physically demanding work, were living alone, and reported higher social support. Males reported greater importance of using the neighbourhood to be physically active than females. There were no significant gender differences in age, PA at 40 years, outdoor importance for PA, and season ("warmer" and "colder" months).

Hierarchical regression

Demographics and PA history included in Block 1 accounted for 5.0% of the variance in older adults' overall PA ($R^2 = 0.050$, p < 0.001) (Table 2). In Block 1 PA at 40 years and gender were the two correlates explaining most of the variance in current overall PA. When including the five environmental correlates in Block 2, the explained variance in overall PA increased to 11.2% ($R^2 = 0.112$, p < 0.001), with season (2.4%) and PA at 40 years (2.1%) having the strongest explanatory power. In Block 3 that also includes biological correlates, the explained variance increased to 27.0% ($R^2 = 0.270$, p < 0.001). Each of the biological correlates individually contributed to increase the explanatory power, with CRF being the most important correlate, contributing with 10.1% of the explained variance (p < 0.001).

Altogether, nine of the 13 correlates contributed significantly to the explained variance in older adults' overall PA. Gender had the second strongest explanatory power in the model (3.9%), where females had a higher overall PA than males. The overall PA was inversely associated with age for both genders. Those who reported higher PA frequency at the age of 40 had also a higher current objectively measured PA. Furthermore, an interaction effect was found between education and gender, where higher education was positively associated with PA for males, but not for females. Physically demanding work was not associated with overall PA. The environmental correlates have mixed association with overall PA. While social support and living situation did not associate with overall PA, both outdoors and season were positively associated with overall PA. Neighbourhood was not associated with overall PA. Those who reported presence of heart disease had a lower overall PA than those who reported no presence of heart disease. Furthermore, an increasing BMI had a negative association with overall PA, while an increasing CRF had a positive association with overall PA.

Discussion

To our knowledge, this is the largest of PA correlate studies where both PA and CRF have been measured objectively in older adults. The main finding was that CRF, measured as VO_{2peak}, had the strongest association to PA. Most research examining the relationship between PA and CRF, has used PA as an independent variable and CRF as a dependent variable. In this tradition, Aspenes et al. (Aspenes, Nauman, Nilsen, Vatten, & Wisloff, 2011) found that self-reported PA level at baseline was positively associated with CRF 23 years later, while Loe et al. (Loe, Rognmo, Saltin, & Wisloff, 2013) found a poor overall correlation (r=0.24) between self-reported PA level and oxygen uptake. In contrast to these studies we used CRF as an independent variable in our statistical analysis. Our results showed that CRF was the correlate that explained most of the variance in overall PA in older adults,

meaning that more fit older adults were more physically active than less fit older adults. The authors acknowledge that since this was a cross-sectional study, there is a potential reverse direction of effect. An older adult's high CRF might be a result of a high overall PA. Novak et al. hypothesized that since CRF is determined partially by genetics and partially by PA levels, those with high CRF will also have high PA levels. Similar to our result, they showed that more fit people spent more time being active compared with less fit people. The authors concluded that endurance capacity (measured as VO_{2max}), and not body size, was the best determinant of daily activity levels (Novak et al., 2009). This, and finding CRF to have the highest individual explanatory power in our study, suggests that older adults' overall PA would benefit from an increased CRF. High intensity training (HIT) is found to be the most efficient way of improving adults' CRF (Moholdt et al., 2012; Nes et al., 2012; Tjonna et al., 2013). It is however not clear how HIT can be implemented as a sustainable training regime in the older population. More research is therefore required on how HIT might be delivered into the community for older adults.

In our study we found body size, measured as BMI, to be inversely proportional to PA levels, which is supported by other studies (Kaplan et al., 2001; Ortlieb et al., 2014; Palacios-Cena et al., 2011). A strong inverse association between CRF and BMI has been reported previously (Radovanovic et al., 2014), which could possibly account for some of the variation in PA levels observed in lean versus obese people. Importantly, more research on this subject is needed. Furthermore, we found that older adults with heart disease had a lower PA than those without heart disease. This association is less understood in literature (Chad et al., 2005; Papadopoulou et al., 2003). Our results indicate that CRF, BMI and heart disease should all be incorporated in both future research and interventions regarding older adults' PA, especially CRF. Additionally, this study stresses the importance of CRF compared with BMI (body shape/size) when developing PA interventions.

Females in our study were significantly more active than males. This contrasts findings of earlier studies (Booth et al., 2000; Chad et al., 2005; Jefferis et al., 2014; Kaplan et al., 2001; Lohne-Seiler et al., 2014). The differences in these results and those of our study could be attributed to the methodologies utilized. Only studies by Lohne-Seiler et al. and Jefferies et al. used objectively measured PA. Both of these studies have used uniaxial data. Lohne-Seiler et al. included only 118 females and 134 males aged 70-79 and found no differences between genders in overall PA. Jefferies et al. measured moderate-to-vigorous physical activity (MVPA) and not overall PA in a larger age interval including participants from 70-93 years of age and found males to be more active than females in higher intensities (Jefferis et al., 2014). When compared to the studies utilizing self-reported data differences in results could be attributed to the recall bias associated with self-reported measures where females tend to neglect reporting low intensity activities and activities of routine nature such as household chores (Orsini, Bellocco, Bottai, Pagano, & Wolk, 2006; Washburn, 2000). Moreover, previous studies have shown that activity levels decrease with age (Kaplan et al., 2001; Lohne-Seiler et al., 2014; McMurdo et al., 2012; Sun et al., 2013). Interestingly, despite the narrow age-span in our study, higher age was associated with significantly lower PA levels. The decrease in PA level seen with increased age, even in a relatively healthy older population, does alarm the need for strategies so that people can sustain their PA level throughout life.

Studies report conflicting findings when it comes to association between education and PA in older adults. This could be due to methodological differences, i.e. self-reported PA, and different outcome measures of PA and education (Kaplan et al., 2001; Palacios-Cena et al., 2011; Pan et al., 2009). The present study found that higher education was positively associated with PA for males, but not for females. It is reasonable to assume that individuals with higher education have better prerequisites to act according to health messages promoting

PA. Lack of association between education and PA in females could be explained by females in this age group having more household activities than males, potentially constituting the majority of their daily PA. In contrast to earlier studies, our results showed no association between former physically demanding work and current PA (Chung et al., 2009). The conflicting results could be due to a difference between self-reported- versus the objectively assessed PA. More research is needed to understand if and how the total PA changes after transition into retirement (Barnett, van Sluijs, & Ogilvie, 2012). We found a positive association between PA at the age of 40 (measured by frequency of exercise) and current PA. Our result was in line with previous findings that PA early in life is positively associated with PA later in life (Friedman et al., 2008). Analyzing lifespan changes in PA are important but challenging, since major life events may affect PA behavior (e.g. health status, work situation, living situation, relationship status etc.) (Engberg et al., 2012).

Our results showed no association between older adults' PA and social support and living situation. The lack of association of PA with social support was also seen in a British study of older adults (Jefferis et al., 2014). This contrasts a recent study by Jackson et al. (Jackson, Steptoe, & Wardle, 2015) finding males and females to be strongly influenced by their partner's behavior in relation to making health behavior changes. An explanation for the conflicting result could be due to study differences, i.e. study sample with only couples (age ≥50), and their use of a self-reported measure of PA (Jackson et al., 2015). The physical environment was of greater importance for the explained variance in PA among older adults, than social environment. Season had the third strongest influence on the explained variance in overall PA. In line with previous studies, older adults were less physically active during "colder" months (November to March), than "warmer" months (April to October) (McMurdo et al., 2012; Witham et al., 2014). One explanation for this could be that "colder" months (in Trondheim, Norway) consist of more snow, higher prevalence of ice and relatively fewer

hours of daylight. Furthermore, while we found no relationship between neighborhood importance for PA and overall PA, we found outdoor importance for PA to have a positive relationship with PA. In order to stimulate older adults to be physically active, our results indicate that the outdoors should be prioritized in future public health interventions. A comprehensive study of the association between neighborhood walkability and older adults' PA, concluded that special attention should be paid to low income neighborhood residents (Van Holle et al., 2014). This field of research is less understood in this age group, and more research is required (Booth et al., 2000; Strath et al., 2012; Van Cauwenberg et al., 2011).

Additional regression analyses, including the same correlates as in table 2, showed identical associations and explained variance when using uniaxial CPM instead of triaxial CPM. Furthermore, performing the same analysis on triaxial CPM without a time filter (including data between midnight and 6:00 a.m.) resulted in identical associations as in Table 2, but had a lower explained variance (24%). Moreover, using time spent in MVPA instead of CPM, yielded similar associations but reduced the explained variance to 15% and 19%, for uniaxial MVPA (MVPA>1952 CPM) (Freedson, Melanson, & Sirard, 1998) and triaxial MVPA (MVPA>2690 CPM) (Sasaki, John, & Freedson, 2011), respectively. This suggests that our results (hierarchical linear regression analysis) seem to be independent of which PA outcome was chosen.

We are aware that our study had some limitations. The results from this study should be interpreted with an understanding that the data were from a cross-sectional study. Crosssectional studies are suggested as an efficient and empirical way of screening a large variety of potential correlates of PA. The statistical associations from cross-sectional studies do not allow causal inferences, but they can provide a basis for generating further hypotheses (A. E. Bauman et al., 2012; Adrian E. Bauman, Sallis, Dzewaltowski, & Owen, 2002). The waist worn accelerometer used in this study records ambulatory activity well, but can underestimate

activities such as cycling, skiing, resistance exercise, and upper body movements. In this sample of older adults walking was the most frequently reported activity type, and walking is known to be well captured by waist worn accelerometers. One limitation of this study was the use of self-reported single-items to determine the importance of neighborhood and outdoors for PA, and physically demanding work. All three variables were dichotomized before the statistical analyses, making them less susceptible for misinterpretation. We recognize that adding a multidimensional measure of environmental importance for PA would have strengthened the study. For example, objective measures of neighborhood walkability, sidewalk conditions etc. Furthermore, it should be noted that the present study uses a retrospective measure of PA at age 40, which makes it vulnerable for recall bias (Friedman et al., 2008).

A strength of the present study was that it included a large study sample with both males and females from an older population. This gives us the opportunity to study overall PA and its association with PA correlates, exclusively in older adults. In addition, Generation 100 is the largest Norwegian study on older adults (70-77 years) using objective assessment of PA. Earlier research has stated a need for studies on older adults which employ validated measurements of PA (Sun et al., 2013).

Another strength of our study was the inclusion of a broad range of correlates to explore the associations with overall PA. Including multiple levels and contexts, such as individual and environmental correlates, provides a better understanding of PA behavior (A. E. Bauman et al., 2012). The chosen correlates in this study explained 27% of the variance in PA, which is in accordance with other correlate studies (Hansen, Ommundsen, Holme, Kolle, & Anderssen, 2013; McMurdo et al., 2012). However, the authors acknowledge that it is difficult to compare the explained variance between studies, due to differences in both sample and analyzed variables. In addition to the correlates included, one should be aware of other

potential correlates of PA (A. E. Bauman et al., 2012; Adrian E. Bauman et al., 2002), e.g. genetics and evolutionary biology (Lightfoot, 2013). Moreover, the strongest single correlate of overall PA, CRF, was measured by direct ergospirometry instead of using estimated CRF values or substitute measures of CRF, which is more common in large population-based public health studies (Aspenes et al., 2011).

The analyzed sample was relatively healthy and more educated compared to the invited, but not participating, subjects (Stensvold et al., 2015), so any generalization regarding our findings on other populations are cautioned. Furthermore, our participants were relatively more educated and fewer of them reported physically demanding work compared to age matched data from Statistics Norway (Kristiansen, 2015; Mørk, 2011). However, our gender-related findings regarding physically demanding work were no different from those reported by Statistics Norway. Despite this, our sample consists of participants with a wide range of PA levels and CRF values. More studies of PA correlates in different populations of older adults are therefore needed to confirm our findings.

Conclusions

The complete set of correlates explained 27.0% of the variance in overall PA level in older adults. CRF was the most important correlate, explaining 10.1% of the variance, followed by gender (3.9%) and season (2.7%). Females were more physically active than males and PA decreased with increasing age for both genders. Furthermore, education was positively associated with PA for males, not for females. The correlates outdoor importance for PA and "season" were positively associated with older adults' PA. This is, to our knowledge, the largest of PA correlate studies in older adults that has combined objectively measured PA and directly measured CRF. The present study provides new knowledge of how different correlates are associated with overall PA in older adults.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

HV and NPA contributed equally to this work and should *both* be considered first authors. All authors contributed to the conception and design of the study. All authors were responsible for the collection of the Generation 100 data in corporation with colleagues at CERG NTNU, Norway. HV and NPA provided the data for analysis, undertook the data analysis, and drafted the manuscript. All authors provided critical insight, and revisions to the manuscript. All authors read and approved the final version of the manuscript submitted for publication.

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Variables	Female n 405	Male n 445	All n 850	Gender differences
СРМ	524.3±151.0	492.4±162.3	507.6.±158.0	P < 0.001
Age, yr	72.5±1.9	72.4±2.0	72.4±1.9	ns
PA at 40yrs old (0=never, 4=daily)	2.5±0.9	2.5±1.0	2.5±0.9	ns
Physical demanding work (yes %)	45.9	34.2	39.8	P < 0.001
Education (high %)	47.9	59.6	54.0	P < 0.001
Living situation (alone %)	38.3	10.8	23.9	P < 0.001
Social support (0=no support, 5=very supported)	1.6±0.8	1.5±0.8	1.5±0.8	P < 0.05
Neighbourhood importance for PA (yes %)	74.8	61.3	67.8	P < 0.001
Outdoor importance for PA (yes %)	73.8	69.7	71.6	ns
Season ("Colder months" %)	49.1	52.8	51.1	ns
Heart disease (yes %)	6.4	17.3	12.1	P < 0.001
BMI (kg/m ²)	25.2±3.5	26.0±3.0	25.6±3.3	P < 0.01
CRF	26.6±4.9	32.4±6.7	29.6±6.5	P < 0.001

Table 1: Participant characteristics

Values are means (SD) or percentage distributions Abbreviations: CPM, counts·min⁻¹; PA, physical activity; BMI, Body mass index; CRF, Cardiorespiratory fitness measured as VO_{2peak} (ml/min/kg); ns, non-significant; SD, standard deviation

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Table 2

n = 850		Block 1			Block 2			Block 3	
	β	(SE)	Partial r^2	β	(SE)	Partial r^2	β	(SE)	Partial r^2
CPM	1011.3	198.6		1058.6	201.6		838.7	199.4	
Demographics and activity history									
Gender (male)	-60.2	15.8	0.017^{***}	-49.2	15.9	0.011^{***}	-89.2	15.3	0.039^{***}
Age	-7.6	2.7	0.009**	-10.5	2.3	0.017^{***}	-6.5	2.6	0.008^{**}
PA at 40yrs old	27.3	5.9	0.025***	24.5	5.8	0.021***	13.6	5.3	0.008^{**}
Physical demanding work (yes)	-5.3	11.2	0.000	-7.5	11.0	0.000	-2.5	10.0	0.000
Education (high)	-4.6	15.5	0.000	-8.5	15.1	0.000	-15.9	13.7	0.002
Education \times Gender	43.5	22.0	0.005*	46.8	21.3	0.006*	42.2	19.4	0.006*
Environmental correlates									
Living situation (not alone)				T.T-	12.8	0.000	-8.4	11.6	0.000
Social support				5.4	6.7	0.000	6.5	6.1	0.001
Neighbourhood importance for PA (yes)				24.8	11.8	0.005*	8.4	10.8	0.001
Outdoor importance for PA (yes)				38.6	12.4	0.014^{***}	22.2	11.3	0.004^{*}
Season ("Warmer months")				25.3	5.6	0.024***	24.7	5.1	0.027***
Biological correlates									
Heart disease (yes)							-37.9	14.7	0.008^{**}
BMI							-6.1	1.6	0.017^{***}
CRF							8.9	0.9	0.101***
Explained variance (R ²)		Block 1:	0.050***		Block 2:	0.112***		Block 3:	0.270***

*ps0.05, **ps0.01, ***ps0.001 Abbreviations: *β*, unstandardized beta coefficient; SE, standard error of the mean CPM, counts min⁻¹; PA, physical activity; BMI, Body mass index (kg/m²); CRF, Cardiorespiratory fitness measured as VO_{2peak} (ml/min/kg)

Appendix 1: Generation 100 Questionnaire 1, used in paper I, II and III Appendix 2: Generation 100 Questionnaire 2, used in paper II and III

APPENDIX

GENERASJON Nr	
Spørreskjema 1	
1. Kjønn: 🗌 Kvinne 🗌 Mann 2. Fødselsår:	
3. Høyde: cm 4. Vekt: kg	
Utdanning	
 5. Hva er din høyeste utdanning? Folkeskole Realskole Yrkesskole Handelsskole Gymnas Høgskole eller universitet, mindre enn 3 år Høgskole eller universitet, mer enn 3 år 	

Boligforhold og venner

- 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
- 8. 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



	Nr
9.	Hvor lenge holder du på hver gang? (Ta et gjennomsnitt)
	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? 🗌 Ja 🛛 🗌 Nei
11	l. Hvis du aldri eller sjelden er fysisk aktiv. Hva er det som hindrer deg: ☐ Dårlig helse/funksjonsnedsettelse
	Tilgjengelighet av passende aktiviteter Avstand til turområder
	☐ Tilrettelegging av turområder
	Utrygghet
	Ikke interessert
	Annet
12	2. Omtrent hvor mange timer sitter du i ro på en vanlig hverdag?
He	else og dagligliv
13	3. Hvordan er helsa di nå? 🗌 Dårlig 🛛 Ikke helt god 🗌 God 🗌 Svært god
14	I. 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	5 Bruker du, eller har du brukt snus?
	Nei, aldri
	Ja, men jeg har sluttet
	Ja, av og til
16	☐ Ja, daglig δ. Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av 2 uker?
10	(Regn ikke med lettøl) (Sett 0 hvis du ikke drikker alkohol)
	Antall glass: ØI: Vin: Brennevin:
17	7. 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	Νε	ei
Gå på toalettet?	🗌 Ja	Νε	ei
Vaske deg på kroppen?	🗌 Ja	Νε	ei
Bade eller dusje?	🗌 Ja	Νε	ei
Kle på og av deg?	🗌 Ja	Νε	ei
Legge deg og stå opp?	🗌 Ja	Νε	ei
Spise selv?	🗌 Ja	Νε	ei
Lage varm mat?	🗌 Ja	Νε	ei
Gjøre lett husarbeid (f.eks oppvask)?	🗌 Ja	Νε	ei
Gjøre tyngre husarbeid (f.eks gulvvask)?	🗌 Ja	Νε	ei
Vaske klær?	🗌 Ja	Νε	ei
Gjøre innkjøp?	🗌 Ja	🗌 Ne	ei
Betale regninger?	🗌 Ja	🗌 Ne	ei
Ta medisiner?	🗌 Ja	🗌 Ne	ei
Komme deg ut?	🗌 Ja	🗌 Ne	ei
Ta bussen?	🗌 Ja	Νε	ei
19. Har du i løpet av de siste 12 månede	er hatt:		
Anfall med pipende eller tung pust		🗌 Ja	🗌 Nei
Daglig hoste i perioder		🗌 Ja	🗌 Nei
Høysnue eller neseallergi		🗌 Ja	🗌 Nei
Smerter og/eller stivhet i muskler og ledd har vart i minst 3 måneder sammenheng		□Ja	🗌 Nei

20. Hvor mange ganger har du i løpet av de siste 12 måneder vært hos:

Fastlege / allmennlege		ganger
Annen legespesialist utenfor sykehus		ganger
Kiropraktor		ganger
Homøopat, akupunktur, soneterapeut, håndspålegger eller annen alternativ behandler		ganger



Nr

21. Har du, eller har du noen gang hatt, no (Sett ett kryss pr. linje)			ene / plagene: mel var du første gang?
Hjerteinfarkt	Ja	🗌 Nei	år
Angina pectoris (hjertekrampe)	🗌 Ja	🗌 Nei	år
Hjertesvikt	🗌 Ja	🗌 Nei	år
Atrieflimmer	🗌 Ja	🗌 Nei	år
Annen hjertesykdom	🗌 Ja	🗌 Nei	år
Hjerneslag/hjerneblødning	Ja	🗌 Nei	år
Nyresykdom	🗌 Ja	🗌 Nei	år
Astma	🗌 Ja	🗌 Nei	år
Kronisk bronkitt, emfysem, KOLS	🗌 Ja	🗌 Nei	år
Diabetes (sukkersyke)	🗌 Ja	🗌 Nei	år
Psoriasis	🗌 Ja	🗌 Nei	år
Eksem på hendene	🗌 Ja	🗌 Nei	år
Kreftsykdom	🗌 Ja	🗌 Nei	år
Epilepsi	🗌 Ja	🗌 Nei	år
Leddgikt (reumatoid artritt)	🗌 Ja	🗌 Nei	år
Bechterews sykdom	🗌 Ja	🗌 Nei	år
Sarkoidose	🗌 Ja	🗌 Nei	år
Beinskjørhet (osteoporose)	🗌 Ja	🗌 Nei	år
Fibromyalgi	🗌 Ja	🗌 Nei	år
Slitasjegikt (artrose)	🗌 Ja	🗌 Nei	år
Psykiske plager som du har søkt hjelp for	🗌 Ja	🗌 Nei	år
Lavt stoffskifte (hypotyreose)	🗌 Ja	🗌 Nei	år
Høyt stoffskifte (hypertyreose)	🗌 Ja	🗌 Nei	år
Katarakt (grå stær)	🗌 Ja	🗌 Nei	år
Glaukom (grønn stær, høyt trykk i øyet)	🗌 Ja	🗌 Nei	år

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



Nr



Prosjektnr:			
ID-nr:			

Spørreskjema 2

1.	Kjønn:	Kvinne	🗌 Mann
----	--------	--------	--------

Helse og dagligliv

2. Har du noen langvarig (<u>minst 1 år</u>) sykdom, skade eller lidelse av fysisk I a Nei eller psykisk art som nedsetter dine funksjoner i ditt daglige liv?

Hvis ja:

Hvor mye vil du si at dine funksjoner er nedsatt?

	Litt nedsatt	Middels nedsatt	Mye 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 sist Hvis ja: Hva slags hodepine? Migre 4. Har du vært plaget med smerter eller ut Ja, mye Ja, litt Nei, aldri 	ene 🗌 An	nen hodepir	ne	
Medisiner 5. Hvor mange reseptbelagte medikame	nter bruker c	lu totalt?	medikame	enter

Sykdommer og skader

6.	Har du noen gang de <u>siste 5 år</u> brukt medisiner for astma, kronisk bronkitt, emfysem eller KOLS?	□Ja	🗌 Nei
7.	Har lege sagt at du har hjerteflimmer (atrieflimmer)?	🗌 Ja	Nei



				Pros	jektnr:		
8.	Har du noen gang hatt:			Hvis ja, h første ga	vor gammel ng?	var du	
	Lårhalsbrudd	🗌 Ja	🗌 Nei		år gammel		
	Brudd i handledd/underarm	🗌 Ja	🗌 Nei		år gammel		
	Brudd/sammenfall av ryggvirvler	🗌 Ja	🗌 Nei		år gammel		
	Nakkesleng (whiplash)	🗌 Ja	🗌 Nei		år gammel		
9.	Har du foreldre, søsken eller barn (Sett ett kryss pr. linje)	som har,	eller har hatt,	følgende	sykdommer	?	
	Hjerneslag eller hjerneblødning fø	r 60 års a	lder	🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Hjerteinfarkt før 60-årsalder			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Astma			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Allergi/høysnue/neseallergi			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Kronisk bronkitt/emfysem/KOLS			Ja	🗌 Nei	🗌 Vet ik	ke
	Kreftsykdom			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Psykiske plager			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Beinskjørhet (osteoporose)			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Nyresykdom (ikke nyresten, urinve	eisinfeksjo	on, urinlekkasj	e) 🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Diabetes (sukkersyke)			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Demens			🗌 Ja	🗌 Nei	🗌 Vet ik	ke
	Hvis ja: Var det mor som hadde d	lemens?	Ja I	Vei			
Sr	nerter i beina						
10). Har du smerter i det ene eller i be	egge beina	a når du går?	🗌 Ja	🗌 Nei		
	Hvis ja: Hvor gjør det mest vondt	? 🗌 Fot	🗌 Legg	🗌 Lår	Hofte		
	Etter hvilken distanse begynner sr	nertene?	🗌 Ca 50 m	🗌 Ca 20	00 m 🗌 Me	er enn 500	m
	Forsvinner smertene når du står s	tille ett pa	r minutter?	Ja	Nei		
	Blir smertene bedre når du bøyer	deg fremo	over eller sette	er deg neo	l? 🗌 Ja 🛛	Nei	
						49805	
					L		

Prosjektnr:

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

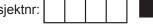
Mosjon og fysisk aktivitet

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 <u>den siste uka</u>) (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 i mnd	1 dag i uken	2-3 dager i uken	4-6 dager i uken	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 i mnd	1 dag i uken	2-3 dager i uken	4-6 dager i uken	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 betydning	Litt betydning	Stor betydning	Svært stor betydning	
Være alene					
Bruke nærmiljøet der du bor					
Være inne					
Være ute					
Bruke og oppleve naturen					
Føle deg trygg					
					4000



Prosje	ktnr:		
19. Hvor langt er det fra der du bor til en park eller et naturområde der du kan være fysisk aktiv?			
Mindre enn 300 m 300m-1 km 1-5km Mer en	n 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
- 21. Dersom du drev mosjon så ofte som en gang i uka som 20-åring; 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
- 23. Dersom du drev mosjon så ofte som en gang i uka som 40-åring; 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

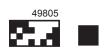
Fysisk aktivitet omfatter både fysisk aktivitet i hverdagen, planlagte aktiviteter og trening.

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

Aldri	Sjelde			Ofte	Veldig	Passer ikke
		2				
å gå hj	emme	fra til	l:			
	1-5 min					Vet ikke
/						
	a gå hj	a gå hjemme 1-5 min 	a gå hjemmefra ti 1-5 6-10 min min 	ganger ganger	ganger ganger	ganger ofte ga



Prosjektnr:	
Arbeid	
26. Har du tidligere hatt inntektsgivende arbeid?	
Hvis ja: 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, undervisnin Arbeid hvor du går og løfter mye (f.eks postbud, pleier, bygningsarbeid) Tungt kroppsarbeid (f.eks skogsarbeid, tungt jordbruksarbeid, tungt bygningsarbeid) 	ng)
Arbeidet du i en fulltidsstilling eller deltidsstilling i hovedyrket ditt?	
Hadde du skiftarbeid, nattarbeid eller gikk vakter? 🗌 Ja 🛛 🗌 Nei	
Boligforhold og venner	
27. Er det kjæledyr i boligen?	
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? Her kommer noen utsagn om hvordan du føler deg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser den siste uken. Ikke tenk for lenge 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	
 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 	



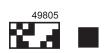
Prosjektnr:
33. Jeg kan le og se det morsomme i situasjoner
Like mye nå som før
Ikke like mye nå som før
34. Jeg har hodet fullt av bekymringer ☐ Veldig ofte ☐ Ganske ofte ☐ Av og til ☐ En gang i blant
35. Jeg er i godt humør
Aldri Noen ganger Ganske ofte For det meste
36. Jeg kan sitte i fred og ro og kjenne meg avslappet
🗌 Ja, helt klart 🛛 🗌 Vanligvis 🔛 Ikke så ofte 🗌 Ikke i det hele tatt
37. Jeg føler meg som om alt går langsommere
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
Ikke i det hele tatt Fra tid til annen Ganske ofte Svært ofte
39. Jeg bryr meg ikke lenger om hvordan jeg ser ut
☐ Ja, har sluttet å bry meg ☐ Kan hende ikke nok
Ikke som jeg burde Bryr meg som før
40. Jeg er rastløs som om jeg stadig må være aktiv
🗌 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
Heller mindre enn før Nesten ikke i hele tatt
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 <u>sis</u>	te 12 måneder				
44. Har det vært dødsfall i na (barn, ektefelle/samboer,		⊡ Ja [re)	Nei		
45. Har du vært i overhengende livsfare pga. alvorlig ulykke, 🗌 Ja 🗌 Nei katastrofe, voldssituasjon eller krig?					
46. Har du hatt samlivsbrudo	l i ekteskap eller i le	ngre samboe	rforhold? 🗌 Ja 🛛	Nei	
47. Hvis du har svart ja på e i hvilken grad har du hatt ☐ Ikke i det hele tatt		de <u>siste 7 da</u>			
Kultur /livssyn					
48. Hvor mange ganger har (Sett ett kryss pr. linje)	du i løpet av de <u>siste</u>	<u>e 6 måneder</u> v	vært på / i:		
Museum, kunstutstilling	Mer enn 3 g/mnd	1-3 g/mnd	1-6 g siste 6 mnd	Aldri	
Konsert, teater, kino					
Kirke, bedehus					
Idrettsarrangement					
49. Hvilket livssyn vil du si lig Kristent livssyn Humanetisk livssyn Ateistisk livssyn Annet livssyn, hva	ıger nærmest opp til	ditt eget? (Se	ett ett kryss)		
Vekt					
50. Er du fornøyd med vekta	dinå? 🗌 Ja 🗌] Nei, for lett	Nei, for tung		
51. Er din kroppsvekt minst 2	2 kg lavere nå enn fo	or 1 år siden?	Ja Nei		
Hvis ja: Hva er grunnen	-			t ikke	



Prosjektnr:
Tobakk
52. Røykte noen av de voksne <u>innendørs</u> da du vokste opp?
Hvis du aldri har røykt eller brukt snus, gå til spørsmål 56.
53. Svar på dette hvis du <u>nå</u> røyker daglig eller <u>tidligere</u> har røykt daglig:
Hvor mange sigaretter røyker eller røykte du vanligvis daglig? sigaretter pr. dag
Hvor gammel var du da du begynte å røyke <u>daglig</u> ? år gammel
Hvis du tidligere har røykt daglig, hvor gammel var du da du sluttet?
54. Svar på dette hvis du røyker eller har røykt av og til, men <u>ikke daglig</u> :
Hvor mange sigaretter røyker eller røykte du vanligvis i måneden? sigaretter pr. mnd
Hvor gammel var du da du begynte å røyke <u>av og til</u> ?
Hvis du tidligere har røykt av og til, hvor gammel var du da du sluttet?
55. Bruker du, eller har du brukt, snus? ☐ Nei, aldri ☐ Ja, men jeg har sluttet ☐ Ja, av og til ☐ Ja, daglig
(Hvis du aldri har brukt snus, hopp til spørsmål 56)
Hvis ja:
Hvor gammel var du da du begynte med snus?
Hvor mange esker snus bruker/brukte du <u>pr. måned</u> ? esker snus pr. mnd.
Alkoholbruk
☐ Ja ☐ Nei 56. Har du drukket alkohol i løpet av de <u>siste 4 uker</u> ?
Hvis ja: Har du drukket så mye at du har kjent deg sterkt beruset (full)? ☐ Nei ☐ Ja, 1-2 ganger ☐ Ja, 3 ganger eller mer
57. Hvor ofte drikker du <u>5 glass eller mer</u> av øl, vin eller brennevin ved samme anledning?



Prosjektnr:			
,			

Søvn

58. Hvor ofte har det hendt i løpet av de siste 3 måneder at du:

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				L	lolt opia
Jeg har lett for å bli utmattet	Helt uenig				lelt enig
Utmattelse nedsetter min fysiske funksjonsevne					
Utmattelse skaper ofte problemer for meg.					
Utmattelse fører til at jeg har dårlig fysisk utholdenhet over lengre tid					
Utmattelse virker negativt inn på mine gjør og forpliktelser	emål 🗌				
Utmattelse er ett av mine tre mest plagson symptomer	nme 🗌				
Utmattelse virker negativt inn på mitt arbei min familie og mitt øvrige sosiale liv	d, 🗌				
Mitt pågangsmot blir dårligere når jeg er ut	mattet				
Jeg blir fort utmattet ved anstrengelser					
				2	19805



Prosjektnr:
Hukommelse
60. Har du god hukommelse? 🗌 Ja 👘 Nei
61. Synes du hukommelsen din er dårligere nå enn for 20-30 år siden? 🗌 Ja 🛛 🗌 Nei
Svimmelhet
62. Hvor ofte føler du deg svimmel?
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: Hvor mange barn har du født?

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

