DISSERTATIONS IN
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Leena Hakola

Cardiorespiratory Fitness and Physical Activity in Older Adults

Publications of the University of Eastern Finland
Dissertations in Health Sciences

UNIVERSITY OF
EASTERN FINLAND

LEENA HAKOLA

Cardiorespiratory Fitness and Physical Activity in Older Adults

A Population-based Study in Men and Women

To be presented by permission of the Faculty of Health Sciences, University of Eastern Finland
for public examination in Medistudia auditorium MS302, Kuopio,
on Friday, April 10th 2015, at 12 noon

Publications of the University of Eastern Finland
Dissertations in Health Sciences
276

Foundation for Research in Health Exercise and Nutrition,
Kuopio Research Institute of Exercise Medicine
Institute of Biomedicine, Faculty of Health Sciences,
University of Eastern Finland
2015

Juvenes Print
Tampere, 2015

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University of Eastern Finland
Kuopio Campus Library
P.O.Box 1627
FI-70211 Kuopio, Finland
http://www.uef.fi/kirjasto

Cover image: Raija Törrönen

ISBN (print): 978-952-61-1730-0
ISBN (pdf): 978-952-61-1731-7
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

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Hakola, Leena
Cardiorespiratory Fitness and Physical Activity in Older Adults, A Population-based Study in Men and Women
University of Eastern Finland, Faculty of Health Sciences
Publications of the University of Eastern Finland. Dissertations in Health Sciences 276. 2015. 73 p.

ISBN (print): 978-952-61-1730-0
ISBN (pdf): 978-952-61-1731-7
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

ABSTRACT

High cardiorespiratory fitness and regular physical activity (PA) lower the risk of many chronic diseases independently of each other. To evaluate and compare cardiorespiratory fitness among older individuals, reference values for maximal oxygen consumption (VO_{2max}) in different age groups are needed. Further, to promote PA it is essential to identify individuals who have insufficient levels of PA, and to recognize moderators of effectiveness of exercise interventions at increasing and maintaining the increased PA.

The aims of this thesis were to produce reference values for cardiorespiratory fitness for older men and women; to explore correlates of low PA at baseline in a randomized controlled trial; and to determine the moderators of long-term maintenance of increased aerobic exercise during a 4-year randomized controlled trial among individuals with insufficient PA at baseline. The thesis is part of the Dose-Responses to Exercise Training (DR's EXTRA) Study, which is a 4-year randomized controlled trial on the health effects of regular physical exercise and diet in a large population sample of men and women aged 57-78 from Eastern Finland.

This study provided age- and sex-specific reference values for VO_{2max}, maximal metabolic equivalents and maximal work rate measured during cycle ergometer tests, based on 672 men and 677 women. The cross-sectional decline of VO_{2max} was about 15% per decade. A high body mass index and satisfactory or poor health were independently associated with low self-reported PA in both genders. Other independent correlates of low PA were symptoms of depression and cardiovascular disease in women. In men, other independent correlates were age, being divorced or separated, having a weak social network, having a poor diet, a health professional's suggestion to increase PA, and still being at work. The aerobic exercise intervention was effective at increasing and maintaining increased aerobic exercise in most older adults, and it was especially effective in individuals who were among the youngest in the present study, working, had symptoms of depression or were past smokers at baseline. Change in aerobic exercise showed a modest positive association with change in VO_{2max} in men but not in women.

Individuals who were near retirement or had symptoms of depression were likely to have low PA levels at baseline, but they were also most likely to maintain increased aerobic exercise long-term. Thus, these individuals could be a reasonable target for aerobic exercise interventions among older individuals, while those who did not maintain increased exercise may need more individualized interventions. Future studies are needed to find predictors of increased PA in other types of interventions and populations, as well as predictors of changes in VO_{2max} over time.

National Library of Medicine Classification: QT 256, WT 141, WE 103, WF 110
Medical Subject Headings: Exercise test; Oxygen Consumption; Reference Values; Motor Activity; Aged; Health Behavior; Randomized Controlled Trials as Topic

Hakola, Leena
Hengitys- ja verenkiertoelimistön suorituskyky ja fyysinen aktiivisuus ikääntyvillä, väestötutkimus miehillä ja naisilla
Itä-Suomen yliopisto, terveystieteiden tiedekunta
Publications of the University of Eastern Finland. Dissertations in Health Sciences 276. 2015. 73 s.

ISBN (print): 978-952-61-1730-0
ISBN (pdf): 978-952-61-1731-7
ISSN (print): 1798-5706
ISSN (pdf): 1798-5714
ISSN-L: 1798-5706

TIIVISTELMÄ

Korkea hengitys- ja verenkiertoelimistön suorituskyky sekä riittävä fyysinen aktiivisuus vähentävät toisistaan riippumatta riskiä sairastua moniin kroonisiin sairauksiin. Ikääntyvien suorituskyvyn mittaustuloksen tulkitsemiseen tarvitaan luotettavat ikäryhmäkohtaiset maksimaalisen hapenottokyvyn (VO_{2max}) viitearvot. Väestön fyysisen aktiivisuuden lisäämiseksi on tärkeää tunnistaa vähiten liikkuvat henkilöt, sekä tunnistaa tekijöitä, jotka selittävät liikunnan pitkäaikaista lisäämistä.

Tutkimuksen tavoitteena oli tuottaa hengitys- ja verenkiertoelimistön suorituskyvyn viitearvot ikääntyville miehille ja naisille. Lisäksi tavoitteena oli selvittää, mitkä tekijät olivat yhteydessä vähäiseen fyysiseen aktiivisuuteen ja mitkä tekijät selittivät pysyvää liikunnan lisäämistä nelivuotisen kestävyysliikuntaintervention aikana alkutilanteessa vain vähän liikkuvilla. Väitöstyö perustuu DR's EXTRA-tutkimukseen, joka on nelivuotinen satunnaistettu kontrolloitu tutkimus liikuntaharjoittelun ja ruokavalion vaikutuksista terveyteen. Aineisto on laaja otos itäsuomalaisia 57-78-vuotiaita miehiä ja naisia.

Väitöskirjan keskeinen tuotos on maksimaaliseen pyöräergometritestiin perustuvat sukupuolen ja iän mukaan tuotetut VO_{2max}:in, metabolisen ekvivalentin (MET), ja maksimikuorman viitearvot 672 miehellä ja 677 naisella. VO_{2max} lasku poikkileikkausasetelmassa oli noin 15 prosenttia kymmenessä vuodessa. Korkea kehon painoindeksi ja huono koettu terveys olivat yhteydessä kyselyyn perustuvaan vähäiseen fyysiseen aktiivisuuteen miehillä ja naisilla. Vähäisen fyysisen aktiivisuuden itsenäisiä korrelaatteja olivat naisilla myös depressiiviset oireet ja sydän- ja verenkiertoelimistön sairaudet, ja miehillä työssä olo, parisuhteesta eroaminen, ja elintapoihin liittyvät tekijät. Kestävyysliikuntaryhmäläiset lisäsivät liikuntaa pitkäaikaisesti 2,5 kertaa niin usein kuin vertailuryhmäläiset, ja interventio oli erityisen tehokas henkilöillä, jotka olivat tutkimusjoukon nuorimpia, työelämässä, joilla oli depressiivisiä oireita tai jotka olivat lopettaneet tupakoinnin. Liikunnan muutos oli suorassa yhteydessä VO_{2max}:n muutokseen miehillä, mutta ei naisilla.

Eläkeiän kynnyksellä olevat henkilöt sekä ne, joilla oli depressiivisiä oireita liikkuivat lähtötilanteessa muita vähemmän, mutta lisäsivät muita useammin liikuntaansa ohjausta saadessaan. Tällaiset henkilöt voisivat siis olla sopiva kohderyhmä liikuntainterventioille, kun taas henkilöt, jotka eivät lisänneet liikuntaansa, voivat hyötyä yksilöllisemmistä interventioista. Lisätutkimusta tarvitaan siitä, miten tehokkaita muun tyyppiset interventiot ovat liikunnan lisäämisessä, ketkä hyötyvät niistä eniten ja siitä mitkä tekijät selittävät VO_{2max}:in muutoksia ikääntyvillä.

National Library of Medicine Classification: QT 256, WT 141, WE 103, WF 110
Yleinen Suomalainen asiasanasto: maksimaalinen hapenotto; kuntotestit; fyysinen aktiivisuus; ikääntyneet; terveyskäyttäytyminen; kestävyysharjoittelu; satunnaistettu kontrolloitu tutkimus

Acknowledgements

This study was carried out at the Kuopio Research Institute of Exercise Medicine. I have had the pleasure to participate in the eventful and energetic phase of data collection in the Dose-Responses to Exercise Training (DR's EXTRA) Study between 2005-2009, and to finalize my thesis based on this study between 2012-2015. I would like to express my gratitude to all of the people who have contributed to this work.

First of all, I want to thank Professor Rainer Rauramaa, M.D., Ph.D., the Principal Investigator of the DR's EXTRA Study and the Principal Supervisor of my thesis, for giving me the opportunity to work in the DR's EXTRA Study. It was an excellent chance for a graduate to witness and to participate in implementation of such a gigantic study. I am grateful for the possibility to use such a great dataset in my thesis. Thank you also for introducing the international community of exercise medicine to me in several Puijo Symposia.

I want to express my warmest gratitude to my Supervisors Professor Timo Lakka, M.D., Ph.D., and Adjunct professor Kai Savonen, M.D., Ph.D. Both of you have contributed markedly to the study with your ideas in the analysis and comments on the writing. Our meetings were lively, loud and long. I truly appreciate your time and devotion in the fine-tuning of the manuscripts. I have learned a lot from our open and good-natured discussions, which sometimes turned into debates. I also want to thank you for your encouragement during the challenging times of the study.

I want to thank the Reviewers Adjunct professor Jyrki Kettunen, Ph.D. and Adjunct professor Juha Peltonen, Ph.D., for the expert comments and constructive criticism that contributed to the final improvements of my thesis. For the language revision, I warmly thank Adjunct professor Neil Cronin, Ph.D.

I sincerily thank Researchers Maija Hassinen, Ph.D. and Pirjo Komulainen, Ph.D., the co-writers in all the manuscripts of my thesis. You are the encyclopedia of DR's EXTRA Study, and I want to thank you for helping me with numerous details in my thesis. I also want to thank you for your friendly and encouraging support related to the research, as well as to all of the changes in my personal life during the last ten years. I also want to thank Doctor Hannu Litmanen, M.D. for sharing your expertise in exercise testing.

Reija Männikkö, M.Sc., and Harri Heikkilä, M.Sc., thank you for your peer-support and friendship. It has been a pleasure to work with you during the DR's EXTRA intervention and to share experiences in data collection and analyses, writing process and family life.

I have been privileged to work with an amazing team of people in the Kuopio Research Institute of Exercise Medicine. The atmosphere during the years of data collection was jovial and full of Savo dialect. I want to thank Hannele, Sirpa T, Saila, Jukka, Tuula, Eva, Kirsi A, Kirsi H, Eino, Helena, Marja-Liisa, Sari, Sirpa H, Malla, Tiina and Professor Ilkka Penttilä for the co-work and friendship. I also want to thank all the participants of the DR's EXTRA Study, with a special thanks to participants in the aerobic exercise group.

I want to thank all my friends from many settings for sharing their lives with me. Special thanks to Laura Karavirta, Ph.D., for your friendship, bicycle trips and the comments on my thesis.

Kiitos äidille ja isälle siitä, että olette aina löytäneet tekemisistäni ne hyvät puolet. Thank you to all my siblings Lotta, Piita, Veli and Jutta for being part of my family's life. Thank you Helinä, Asko and Jutta, for welcoming me into your family.

Mikko, I sincerily thank you for your love and support. You have, more than anyone, encouraged me to finish my thesis and you have been supportive of all my trips to Kuopio. Most importantly, I thank you for sharing the special family life of ours. I also thank the little ones in the family for spreading your enthusiasm, joy and love.

Finally, I thank all the funding organizations that have contributed to the present study and supported the work at the Foundation for Research in Health Exercise and Nutrition, Kuopio Research Institute of Exercise Medicine. The DR's EXTRA Study has been supported financially by Ministry of Education and Culture of Finland, Academy of Finland, The Integrated Project in FP6 of the European Commission (EXGENESIS), Kuopio University Hospital, City of Kuopio, Finnish Diabetes Association, Finnish Foundation for Cardiovascular Research, Päivikki and Sakari Sohlberg Foundation and the Social Insurance Institution of Finland. This thesis has further been funded by personal grants from Juho Vainio Foundation, the Finnish Cultural Foundation and Kuopio University Foundation.

Tampere, February 2015

Leena Hakola

List of the original publications

This dissertation is based on the following original publications:

I Hakola L, Komulainen P, Hassinen M, Savonen K, Litmanen H, Lakka TA and Rauramaa R. Cardiorespiratory fitness in aging men and women: the DR's EXTRA Study. *Scandinavian Journal of Medicine and Science in Sports 2011;21:679-687.*

II Hakola L, Hassinen M, Komulainen P, Lakka TA, Savonen K and Rauramaa R. Correlates of low physical activity levels in aging men and women: the DR's EXTRA Study. *Journal of Aging and Physical Activity 2015;23:247-255.*

III Hakola L, Savonen, K, Komulainen P, Hassinen M, Rauramaa R and Lakka TA. Moderators of maintained increase in aerobic exercise among aging men and women in a 4-year randomized controlled trial: the DR's EXTRA Study. *Journal of Physical Activity and Health.* 2015, Epub ahead of print.

Contents

Abbreviations

HDL	High-density lipoprotein
DR's EXTRA	Dose-Responses to Exercise Training
LDL	Low-density lipoprotein
MET	Metabolic equivalent (of task)
NNT	Number needed to treat
PA	Physical activity
RER	Respiratory exchange ratio
VO_{2max}	Maximal oxygen consumption
VO_{2peak}	Peak oxygen consumption

1 Introduction

Low cardiorespiratory fitness and insufficient physical activity (PA) are independent modifiable risk factors for premature morbidity and mortality (1-4). Although low cardiorespiratory fitness and insufficient PA are closely related and have similar correlates, they are separate concepts (Figure 1) (3-6). In the developed countries insufficient PA has been identified as the fourth leading risk factor for mortality after tobacco use, overweight or obesity, and elevated blood pressure (7). It is also the sixth leading risk factor for disability after tobacco use, alcohol consumption, overweight or obesity, elevated blood pressure, and high blood glucose (7). Although the health benefits of PA and good cardiorespiratory fitness are acknowledged, and regular PA is known to improve cardiorespiratory fitness, about half of all adults and older adults in Europe and Americas have insufficient levels of PA (8). In Finland (9) and in some other countries (10,11), participation in leisure-time PA has increased over the last 30 years. However, plenty of sedentary activities related to work, transportation and free time are available in modern society that enable a physically inactive lifestyle (12-14).

The growing life expectancy in Finland continuously increases the proportion of older adults (15). Cardiorespiratory fitness decreases with aging (16,17), and population-based reference values for different age groups are needed to help professionals to better evaluate an individual's fitness level and responsiveness to regular exercise training for primary and secondary prevention purposes. The promotion of good cardiorespiratory fitness and health among older adults is essential to reduce the individual and national disease burden and health care costs (18). Researchers and policymakers are worried about the polarization of PA participation, and there is concern about how to increase PA, especially among insufficiently active individuals (18-20).

There is a relatively large body of knowledge indicating that a higher socioeconomic status, better health and healthier lifestyle are associated with higher levels of PA (21). In addition, older adults tend to be physically less active than younger adults, and men tend to be more active than women (21). However, little is known about whether the correlates of PA differ between older men and women. Also, only a few studies have explored the determinants of increased PA during PA interventions (22-24). Moreover, there is no evidence about the moderators of effectiveness of exercise interventions at increasing and maintaining increased PA among older adults. Knowledge on the moderators of increased PA would help target appropriate interventions to individuals who would most likely benefit from them.

The aim of the present thesis was to produce reference values for cardiorespiratory fitness in a population sample of older men and women, and to explore correlates of low PA and moderators of increases and maintained increases in aerobic exercise among participants of a 4-year lifestyle intervention study.

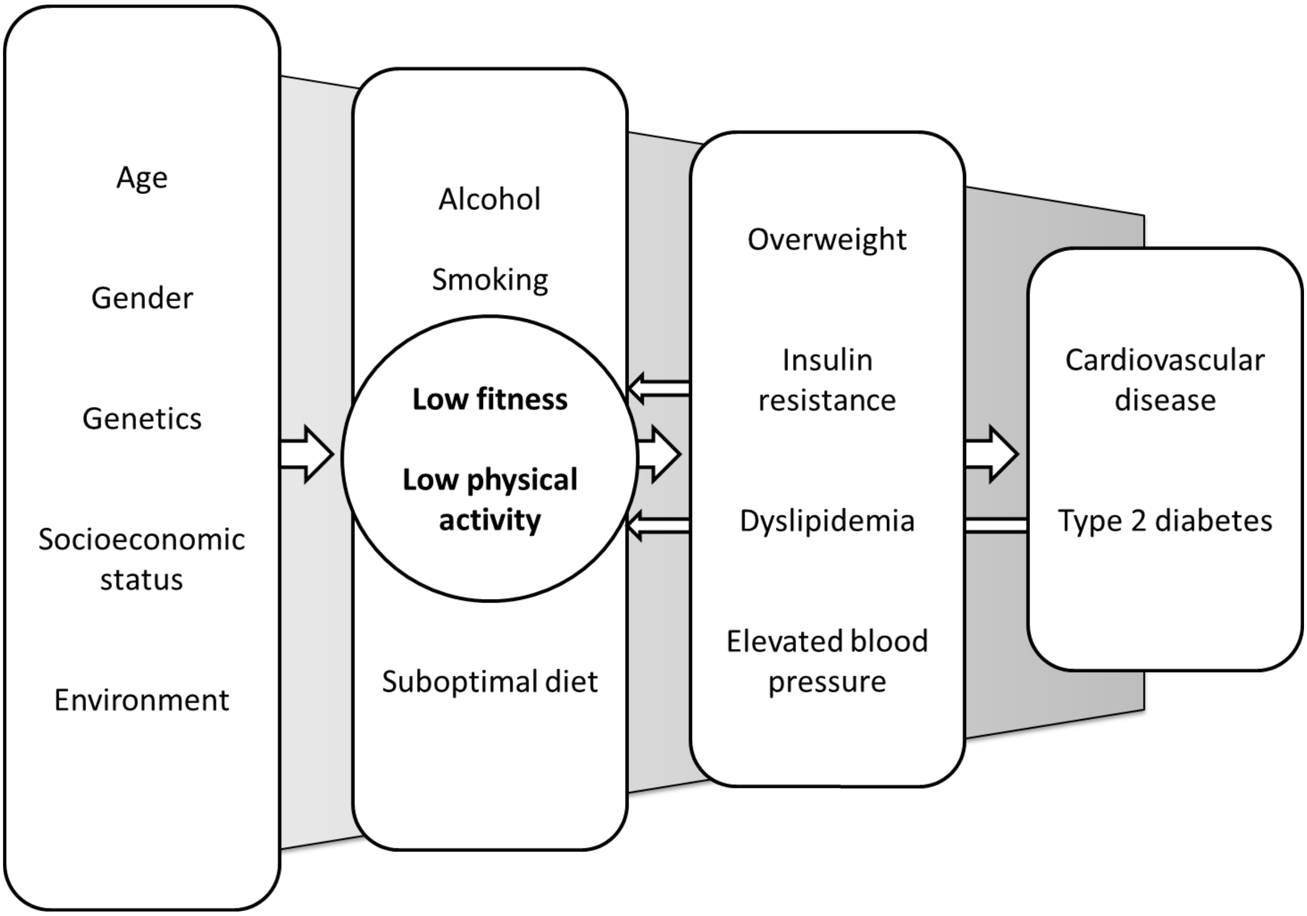

Figure 1. Principal risk factors and risks of low fitness and low physical activity

2 Review of the Literature

2.1 CARDIORESPIRATORY FITNESS

2.1.1 Definition of cardiorespiratory fitness

Cardiorespiratory fitness refers to the ability of circulatory and respiratory systems to supply oxygen to skeletal muscles, and the ability of the skeletal muscles to utilize the oxygen during prolonged moderate-to-vigorous PA (25). Cardiorespiratory fitness is closely related to aerobic exercise performance, which refers to the ability to maintain a certain velocity or power output produced by the body's large muscles for a prolonged time (26). This type of work requires increased work of both skeletal and cardiac muscles and results in increased energy expenditure (26,27). A healthy individual with excellent cardiorespiratory fitness can run, ride a bicycle or do cross-country skiing at a high pace for an hour or more, whereas an individual with poor cardiorespiratory fitness gets easily fatigued or out of breath while walking at a modest pace (25). However, aerobic performance depends not only on cardiorespiratory fitness but also on exercise economy and motivation to maintain high-intensity exercise (28).

2.1.2 Assessment of cardiorespiratory fitness

Cardiorespiratory fitness can be estimated in submaximal or maximal exercise tests and measured directly as maximal oxygen consumption (VO_{2max}) in maximal tests (25). The most commonly used exercise modes in laboratory exercise testing include pedaling on a cycle ergometer and walking or running on a treadmill (29). These exercise modes provide the opportunity to estimate work rate and to observe electrocardiogram, heart rate and other variables during the test (29). In progressive incremental protocols, the work rate on a cycle ergometer or the speed or grade of the treadmill are increased gradually every one to three minutes (29). Typical increases in the work rate on a cycle ergometer are 5 to 25 watts (W) per minute (29). The increment of the work rate can also be continuous, ramp-like (29). Other protocols include constant work rate for 5 to 30 minutes (29). Finally, there are also discontinuous protocols that include breaks between incremental exercise stages (29) and protocols with individual work rate increments (30).

Submaximal exercise tests can include constant work rate protocols, incremental tests that are stopped before exhaustion, or field tests (31-34). In submaximal tests, cardiorespiratory fitness is estimated based on the assumed linear relationship between work rate and heart rate (25,31-34). Submaximal assessments cannot take interpersonal variation in heart rate response, heart rate reserve or exercise economy into account, and include the assumption that steady-state heart rate is achieved during each work rate (25). Therefore, submaximal testing contains more sources of error than maximal exercise testing for the estimation of VO_{2max} (25). However, submaximal testing is convenient for determining heart rate and other physiological responses to submaximal work rates, and has fewer requirements for testing personnel and facilities than maximal testing (25).

In maximal tests the work rate is increased until exhaustion, and the estimation of cardiorespiratory fitness is based on maximal work rate achieved, test duration or measured oxygen consumption (25). Maximal exercise testing is safe as indicated by 0.8 major complications per 10 000 exercise tests in preventive clinic patients (35) and 1.2 major cardiac events per 10 000 exercise tests among patients with or suspected to have coronary artery disease (36). A challenge in maximal exercise testing is that it may be difficult to motivate an individual to exercise at their maximal level if they are not used to a maximal workout (25).

The VO_{2max} can be measured directly from the respiratory gases during a maximal exercise test or estimated based on work rate achieved (indirect assessment) (25). Indirect assessments cannot take interpersonal variation in movement economy into account, and therefore contain more sources of error than direct measurement of VO_{2max} (25). Protocols with smaller rather than larger increments result in better estimation of VO_{2max} (30,37).

The VO_{2max} measured during an incremental maximal exercise stress test is the gold standard for measuring cardiorespiratory fitness (29,38). The concept of VO_{2max} assumes that each individual has his or her upper limit of uptake and utilization of oxygen in energy production during exercise (38-40), and that oxygen consumption depends on cardiac output, pulmonary ventilation and perfusion, peripheral blood flow, skeletal muscle mass, and the ability of skeletal muscles to use oxygen (26,41). The idea of VO_{2max} was first originated by Hill and Lupton in 1923 (38). Maximal cardiac output (the highest amount of blood the heart can pump in liters per minute), the maximal product of heart rate and stroke volume, has been recognized as a key factor of cardiorespiratory fitness (38,40,42). Higher blood volume, higher end-diastolic filling and better left ventricular contractility contribute to larger stroke volume and therefore to higher cardiac output (43,44). Based on the Fick equation, oxygen consumption can be calculated as the product of cardiac output and arterio-venous oxygen difference (VO_2 = cardiac output × $(a\text{-}v)O_2$) (45). It has been suggested that in well-trained individuals, oxygen transport is the limiting factor of VO_{2max} while in untrained subjects mitochondrial oxidative capacity sets the limit to VO_{2max} (41). However, respiratory, circulatory and metabolic components all contribute to VO_{2max} (41). VO_{2max} is one of the most widely used measurements in exercise science (39). VO_{2max} is important in sports (46) and clinical work (47-49), and it is also widely used as an overall health predictor (1).

If the subjects are prepared, equipment calibrated and data processed appropriately, the measurement of VO_{2max} during an exercise test is precise and reproducible with a 3% to 9% difference between measurements (29). The idea of the exercise test is to reach the maximal capacity of the cardiorespiratory system, and to measure and calculate the amount of oxygen that the body is using and the amount of carbon dioxide the body is producing during maximal work (29). The expressions peak oxygen consumption (VO_{2peak}) or symptom limited VO_{2max} are often used for the highest measured oxygen consumption (50). This choice of terminology leaves out the assumption that a plateau in oxygen consumption increment is observed while work rate is still increasing (39,40). VO_{2max} can be expressed as l/min, ml/kg of body weight/min, ml/kg of lean mass/min and ml/cm of body height/min (29) or ml/kg of body weight^{b}/min, where b ranges from 0.69 to 0.89 (51).

2.1.3 Age as a determinant of cardiorespiratory fitness

The inverse association between age and cardiorespiratory fitness was first reported in a sample of 93 healthy males aged 6 to 91 in the 1930's (52). Later Åstrand presented reference values for VO_{2max} based on data from hundreds of males and females aged 5-65 (53). Shvartz and Reibold also reported reference values for VO_{2max} based on healthy untrained individuals from 62 separate studies in nine countries (17). According to these studies the highest VO_{2max} values are observed around the age of 20, after which VO_{2max} declines with age. However, the number of adults aged over 65 in these studies was limited to only a couple of individuals per study. Two recent papers review VO_{2max} in adults (54,55). One them formed a combined regression equation for age-dependent decline in VO_{2max} but stated that most equations were based mainly on younger individuals and extrapolated to the elderly (55).

A few studies in larger population samples of older adults have measured VO_{2max} directly by respiratory gas analysis before the year 2000 (56,57) and around the 2010's (58-61). In these cross-sectional studies among older adults, VO_{2max} measured during a treadmill exercise test declined by about 10% per decade (56-59) (Table 1). Two other studies in population samples of adults and older adults have shown similar declines in directly measured VO_{2max} per decade when using cycle ergometer exercise tests (60,61). Further, a similar decline was reported in middle aged Finnish men tested using a cycle ergometer (62). However, in cross-sectional studies the oldest individuals are likely to be healthy survivors, and cross-sectional studies may therefore underestimate the rate of decline in VO_{2max} (63). The results of prospective cohort studies suggest that VO_{2max} decrement accelerates with aging, at a rate of 20% to 25% per decade among individuals aged over 70, and that the rate of decline may be more rapid in men than in women (Figure 2) (16,64).

Table 1. Age-related decline in cardiorespiratory fitness in cross-sectional studies with directly measured maximal oxygen consumption in population samples including older adults. The decrement was calculated based on data provided for the age range 60-80 in each study.

	Population			**VO_{2max} at age 60-69**	**Change/ 10 years**	**Change/ 10 years**	**Change/ 10 years**
			N	**ml/kg/min**	**%**	**ml/kg/min**	**l/min**
(57)	Age: 55-86	Men	152	23	-8	-3.1	-0.3
	Canada	Women	146	20	-10	-2.5	-0.2
(56)	Age: 55-94	Men	363	28	-14	-2.6	Not
	USA, no CVD	Women	454	22	-10	-2.7	Provided
(58)	Age: 20-70+	Men	1929	39	-10	-3.7	-0.4
	Norway, healthy	Women	1881	31	-9	-3.0	-0.3
(59)[a]	Age: 20-85	Men	394	32	-7	-4.3	-0.3
	Norway, healthy	Women	365	29	-18	-3.2	-0.2

VO_{2max} = maximal oxygen consumption; CVD = cardiovascular disease [a] in this study provided age range was 60-85. The percentual change was calculated based on values given in ml/kg/min.

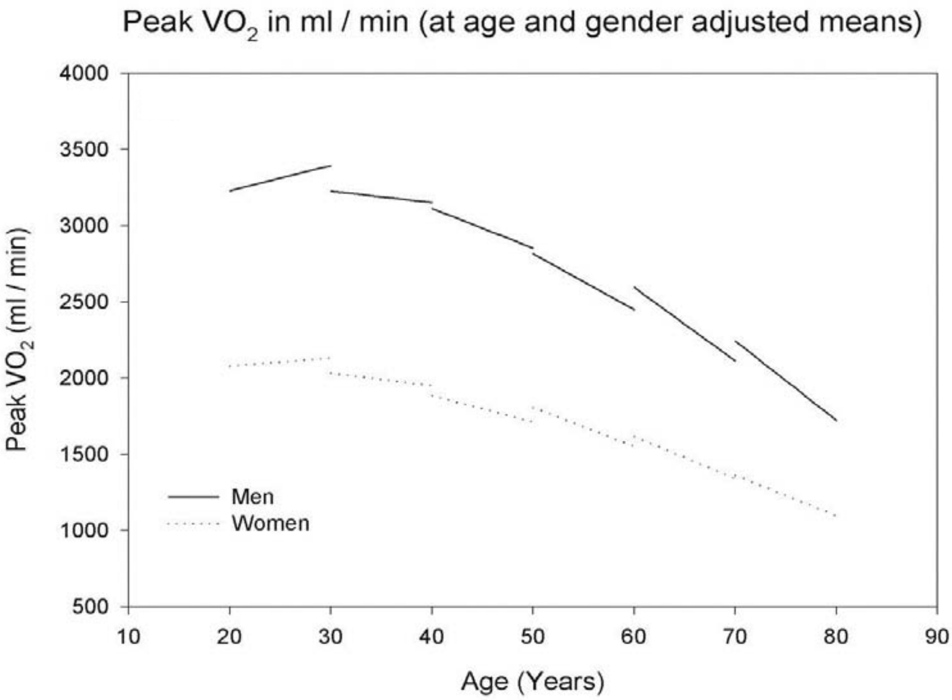

Figure 2. Predicted per-decade longitudinal change in peak oxygen consumption for age decades from the 20s through the 70s in the Baltimore Longitudinal Study of Aging (16). Adapted with permission from Lippincott Williams and Wilkins/Wolters Kluwer Health.
Peak VO_2=peak oxygen consumption

There are multiple reasons for the decline in cardiorespiratory fitness with age including biological aging, changes in lifestyle habits, the development of chronic diseases and the use of medication, or a combination of several reasons (65). Typical changes with aging are decreases in maximal heart rate, maximal stroke volume and thereby maximal cardiac output, decrease in lean body mass, increase in fat mass and possibly changes in muscle oxidative capacity (66,67). It is unknown to what extent the decrement of VO_{2max} is related to reduction of PA (especially vigorous PA), diseases, medication and aging itself in the general population. In a study of middle-aged men, PA accounted for a higher percentage of the variation in VO_{2max} in younger and healthy men, whereas other factors including central obesity and health were more important determinants in older men (62). Finally, in master athletes the change in training stimulus accounted for the majority of variation in the decline of VO_{2max} (65).

2.1.4 Other determinants of cardiorespiratory fitness

The level of cardiorespiratory fitness is strongly hereditary (68). In addition to genes, epigenetic modifications can also affect cardiorespiratory fitness (69). VO_{2max} in sedentary subjects shows a clear familial resemblance, and heritability estimates for VO_{2max}, as well as cardiac function and skeletal muscle enzymatic activities, are around 50% (68).

Women have in general 20% to 30% lower VO_{2max} than men (56-59), which is explained by the generally smaller body size and higher proportion of body fat in women (66). When VO_{2max} is expressed as l/min or ml/kg/min, women have about 30% or 20% lower values than men, respectively (56-59,66). When VO_{2max} is expressed as ml/kg muscle mass/min the gender difference often disappears (66).

Most individuals, including older adults and individuals with chronic disease, can improve their cardiorespiratory fitness and its components by exercise training (43,70-73). A meta-analysis of controlled aerobic exercise studies among older adults showed an average 16% increase in VO_{2max} compared with control groups (74). However, some individuals in the population seem to be non-responders to traditional exercise training (68,75). Increases in maximal cardiac output and arterio-venous oxygen difference have been observed among those who respond to aerobic exercise training (72). These improvements may be due to increased blood volume (44,70), increased end-diastolic filling (43), improved left ventricular contractility (43,76) and thereby increased maximal stroke volume (43,72), by increased blood flow into working muscles (77), and increased capillary density in skeletal muscles (71,73). Further, aerobic exercise training increases the ability of human skeletal muscles to use oxygen by muscle fiber type transformation from type IId/x to type IIa, facilitating mitochondrial biogenesis, increasing the amount or activity of aerobic enzymes (71,78,79) and increasing intramuscular energy reserves (80,81).

While exercise training generally increases VO_{2max}, bed rest has fast detraining effects on it and VO_{2max} has been shown to decrease about 30% during a 90-day bed rest (82). Thus, prolonged disuse of muscles leads to a deconditioned state and decreased cardiorespiratory fitness (29).

Patients with heart failure, coronary heart disease, or pulmonary diseases often have decreased cardiorespiratory fitness (29). They may have abnormal systolic and diastolic cardiac function, abnormal exercise ventilatory responses due to early onset of metabolic acidosis, abnormal ventilation-perfusion relationship due to low cardiac output, decreased lung compliance, and increased airway resistance (29). Patients with type 1 diabetes seem to have lower VO_{2max}, perhaps due to impaired regulation of peripheral circulation (83). Patients with abnormal oxygen carrying capacity (e.g. anemia), abnormal oxygen utilization (e.g. mitochondrial myopathy) or peripheral artery disease may have decreased cardiorespiratory fitness (29,84). Further, patients with musculoskeletal or neural problems may have decreased cardiorespiratory fitness due to deconditioning (29). Medications, especially those that lower heart rate, can decrease cardiorespiratory fitness by decreasing maximal heart rate and therefore maximal cardiac output (29). In addition to pathological changes and medication, deconditioning related to illness or hospitalization can decrease cardiorespiratory fitness in patients with several diseases (29).

Obese individuals often have lower cardiorespiratory fitness than normal weight individuals when oxygen consumption is scaled to body weight (29,85). This underestimates cardiorespiratory fitness and therefore scaling for ideal body weight or fat free mass is needed to interpret the test results properly (29,85). Individuals with impaired glucose regulation or type 2 diabetes have lower VO_{2max} than their age and sex matched counterparts (85). The low VO_{2max} is largely explained by the high body weight among those with abnormal glucose regulation, but the difference from VO_{2max} of healthy individuals seems to remain when VO_{2max} is expressed as l/min (85). Reduced central and especially peripheral circulatory responses during exercise may contribute to lower VO_{2max} in individuals with impaired glucose regulation (86). Body composition is an important determinant of VO_{2max} whereby higher lean mass is associated with higher, and higher fat mass with lower VO_{2max} expressed in ml/kg/min (87).

Although the conditions mentioned above usually decrease an individual's VO_{2max}, there is variability in patient's cardiorespiratory fitness that depends on the individual's previous cardiorespiratory fitness and PA level, as well as severity of diseases and presence of other diseases (29). Therefore, an individual with a chronic disease can have cardiorespiratory fitness well above or well below the average.

2.1.5 Cardiorespiratory fitness and health

There is strong evidence from prospective cohort studies that individuals with higher levels of cardiorespiratory fitness have lower risk of all-cause (1), cardiovascular (1), and cancer (88,89) mortality, and lower risk of incidence of cardiovascular events (1) including myocardial infarction or coronary revascularization procedure (90,91) and ischemic or any stroke (92), compared to those with low cardiorespiratory fitness. Prospective or intervention studies have also shown that individuals with higher cardiorespiratory fitness are less likely to gain excess weight (93), develop hypertension (94), heart failure (95), metabolic syndrome (96), and type 2 diabetes (97), and have a lower risk of becoming dependent (98) than individuals with lower fitness.

2.2 PHYSICAL ACTIVITY

2.2.1 Definition of physical activity

PA is any bodily movement produced by the contractions of skeletal muscles that increase energy expenditure above a basal level (27,99). PA can be related to occupation, leisure-time, transport or household activities (100). Structured and repetitive **exercise** (training) and **sports** participation aim to maintain or improve at least one component of fitness or performance, and are often considered as one feature of leisure-time PA (99). The frequency, intensity, duration, mode and energy expenditure of PA are meaningful variables with regards to enhancing fitness or promoting health (101).

Aerobic PA involves dynamic work of large muscle groups and results in increased energy expenditure for which the energy is produced mainly aerobically in the mitochondria (27). Brisk walking and bicycling are typical modes of aerobic PA (99). Aerobic exercise (training) refers to structured and repetitive participation in aerobic PAs that aim to improve or maintain cardiorespiratory fitness (27). **Resistance** exercise (training) or **muscle strengthening** activities aim to increase muscular strength, power or endurance and typically involve a varying number of sets and repetitions of selected movements that overload muscles with periods of rest between the sets (27). Training in a gym, calisthenics or heavy garden work are modes of muscle strengthening activities (99). **Flexibility activities**, such as stretching, aim to maintain or increase joint range of motion (99).

The categorization of PA intensity is inconsistent, both with terminology and cut-off values (Table 2). In particular, accelerometer derived PA intensity categories vary markedly (102). The most typical cut-off values and measures for sedentary behavior and PA intensities are shown in Table 2. Intensities are usually given for aerobic PAs and based on absolute values (for example 3-6 metabolic equivalents, METs) or relative values (for example percentage of maximal heart rate).

The current PA recommendations (99,103) state that adults and older adults should do at least 150 minutes of moderate intensity aerobic PA per week or at least 75 minutes of vigorous aerobic PA per week or an equivalent combination of moderate and vigorous PA. In addition, muscle strengthening and flexibility activities are recommended. For healthy adults the recommended intensity should be based on absolute level, thus at least moderate intensity PA should exceed 3 METs (99). In older adults, the intensity can be adjusted to match an individual's fitness (99,101,103). For example, older adult's maximal capacity may be 5 METs, which is lower than the given absolute lower limit of vigorous PA in adults. Thus, PA at an absolute intensity of 4.5 METs can be moderate or vigorous depending on an individual's fitness. Individuals who do not meet PA recommendations, usually concerning aerobic PA, are considered **insufficiently active** (7).

Table 2. Categorization of sedentary and physical activity intensities

	Objective measures		**Perceived exertion**	**Description**
	Absolute intensity	Relative intensity	Relative intensity	
Sedentary	1.0-1.5 METs <200 cpm	<40% HRmax <20% HRR <20% VO_2R	Scale (6-20) <8 Scale (0-10) <8	Activities such as sitting, lying down, and watching television
Light	1.6-2.9 METs 200-1999 cpm	40-54% HRmax 20-39% HRR 20-39% VO_2R	Scale (6-20) 8-11 Scale (0-10) 2-4	Easily sustainable aerobic activity without noticeable increase in breathing rate
Moderate	3.0-5.9 METs 2000-3999 cpm	55-69% HRmax 40-59% HRR 40-59% VO_2R	Scale (6-20) 12-13 Scale (0-10) 5-6	Aerobic activity comparable to brisk walking. Increase in breathing rate.
Vigorous/ Heavy/Hard	≥6.0 METs ≥4000 cpm	70-89% HRmax 60-84% HRR 60-84% VO_2R	Scale (6-20) 14-16 Scale (0-10) 7-8	Aerobic activity during which talking is difficult due to breathing.
High/ Very hard	≥9.0 METs	≥90% HRmax ≥85% HRR ≥85% VO_2R	Scale (6-20) 17-19 Scale (0-10) ≥9	An intensity that is hard to maintain for longer than about 10 minutes.

Table is based on previous publications (27,99,101,104-106). METs = metabolic equivalents of task, cpm = counts per minute measured with accelerometer, HRmax = maximal heart rate, HRR = heart rate reserve (maximal heart rate – resting heart rate), VO_2R = oxygen consumption reserve (maximal oxygen consumption – resting oxygen consumption).

2.2.2 Assessment of physical activity

There are several ways to assess PA and the purpose of assessment and available resources determine which method is used. The following methods are suitable for assessment of PA in free living humans.

PA questionnaires and interviews often include questions related to past PA in different settings and/or of different modes of PA (100,107-110). They often give data on frequency, average duration and intensity of PA sessions of which PA induced energy expenditure can be calculated (100). Self-reports are often used in large scale studies because they are inexpensive and easy to use for both subjects and researchers (100). Questionnaires and interviews can give specific information about types of PA (for example berry picking or bicycling), which cannot be observed with other current measurements (100,107). However, self-reports are prone to measurement error and bias caused by misreporting due to social desirability or recall error (100). PA questionnaires generally only have moderate validity (correlation coefficients 0.30 to 0.39) against objective measures and slightly better reliability (0.62 to 0.71) (100). Similar results have been obtained in validation studies among older adults (111). **PA logs or diaries** are forms of self-report and can have slightly higher correlations with objective measures than retrospective questionnaires (112).

Doubly labeled water technique is considered the gold standard measure of total energy expenditure in humans over measurement periods of 4 to 20 days (112). The method is based on calculating carbon dioxide production based on the disappearance rates of orally ingested stable isotopes of oxygen (^{18}O) and hydrogen (^{2}H) (113). PA induced energy expenditure can be estimated based on total and basal energy expenditure (112). Disadvantages of the double labeled water technique in PA studies include the high cost and special equipment needed for assessment, and the inability to distinguish patterns of exercise, including duration, frequency and intensity (112). In addition, an error of about 5% can occur in energy expenditure estimation if an individual's respiratory quotient is not known (112).

Motion sensors are mechanical and electronic devices that register the motion or acceleration of the body or limb (114). They can be attached to different sites of the human body or clothing (114). Pedometers are the simplest motion sensors, which count steps but cannot detect direction or intensity of the movement (114). Accelerometers can sense linear acceleration along one or several directions as well as angular motion, and therefore sense the frequency and intensity of movement (114). A common output is activity counts per defined period of time (114). Based on such counts, PA can be categorized by intensity (102) and the energy expenditure caused by PA can be calculated based on device and population specific formulas derived from validation studies (114). Individual calibration increases the accuracy. A pooled correlation coefficient for energy expenditure derived from triaxial accelerometers and doubly labeled water in seven studies was around 0.6 for both total and PA induced energy expenditure (115).

The use of **heart rate monitors** in PA measurements is based on the fairly linear increase in heart rate in relation to increase in energy expenditure of exercise, especially at higher heart rates (116-118). However, in sedentary and light intensity activities, other factors than PA such as emotions can affect heart rate (112). There is also interindividual variety in heart rate response to increased PA and energy expenditure depending on gender, genetics and fitness level (117). Individual calibration increases the accuracy of heart rate monitoring to estimate energy expenditure, but it also makes the assessment more costly (112). Heart rate monitors are not well tolerated for continuous monitoring for longer periods of time (112).

Multisensor systems combine accelerometry with other sensors that detect body reactions to PA, for example heart rate, skin temperature or global positioning system (GPS) (115,119,120). These devices have similar correlations with energy expenditure measured with doubly labeled water as triaxial accelerometers (115).

Accelerometers, multisensory devices and questionnaires can detect frequency, duration and intensity of PA, but they are more accurate in higher than lower intensity PA (100,115). Currently, new methods such as wearable electromyography shorts are being used to measure sedentary time and light PA (121).

Validation of PA measuring tools is difficult because there is no gold standard to measure PA, and different tools measure different aspects of PA over different durations (115). Although the doubly labeled water method is the gold standard for measuring long term energy expenditure, it cannot distinguish frequency, duration or intensity of PA (112). Motion sensors and self-reports have been validated against doubly labeled water, as well as other motion sensors or questionnaires (100,115). Activity monitors have also been validated against respiratory gas analysis derived energy expenditure or manual or video observation of step count (115). The often used correlation coefficient has been criticized as a suboptimal statistical method in validation studies, while Bland-Altman methods have been recommended (122).

2.2.3 Age as a determinant of physical activity

In cross-sectional studies, older individuals have been shown to have lower levels of PA than younger individuals based on self-report (11,123-130) and objective measures (106,131,132) (Table 3). In follow-up studies, higher age has been associated with lower future PA (133-135) (Table 4) or faster decline in PA (136,137). However, a study among people aged 18-60 reported that the oldest tertile increased their leisure-time PA most during the 22-year follow-up between 1981 and 2004 (138).

To conclude the results of cross-sectional and longitudinal studies concerning PA during the human life span, the level of PA usually declines in the teenage years, and remains relatively stable during adulthood until another decline in the later years of life (125,126,136,137,139,140). Aging individuals seem to particularly decrease the amount of vigorous and moderate intensity PA (125), which is likely to be due to the decline in locomotor performance (141) and prevalence of health conditions (134). A similar decline in PA with increasing age has also been observed in animal species including insects, rodents and monkeys, and therefore it is likely that the decline in PA is partly biological and partly environmental (139).

Age has shown no association with PA adherence in most intervention studies among older adults (22,142-147) (Table 5). However, oldest individuals have been less likely to increase PA during an intervention in some (22,23) but not all studies (148) (Table 6).

2.2.4 Other determinants of physical activity

A large percentage of variation in levels of human PA is explained by inheritance (68,149). Family studies have provided maximal heritability estimates ranging from 15% to 60% for total PA as well as for sedentarism, leisure-time PA, and sports participation (68). The initial evidence in human genes or regions that are associated with PA or inactivity is related to neurotransmitters, energy balance and stature and limb height (68).

In most studies, men have exhibited higher levels of PA than women (106,128-130,132,150). Younger age (127-130,132-135), higher education (127-130,135) and higher income (127,129,130) have been associated with higher levels of PA among older adults in some but not all studies (130,134,135,151,152).

The presence of health conditions or chronic diseases (11,106,129,130,132,134,135,152), overweight or obesity (11,106,130,133,134,151), symptoms of depression (106,132,134,135) or poorer perceived health (106,127-129,133,134) have been associated with lower levels of PA among older adults in cross-sectional (Table 3) and prospective studies (Table 4).

Higher social connectivity has been associated with higher levels of PA in most studies (130,150,153), while associations between PA and smoking or alcohol consumption have been inconsistent among older adults (11,106,130).

In addition to the demographic, health- and lifestyle-related correlates of PA shown in Tables 3 and 4, some psychological variables such as high self-efficacy and behavioral control have consistently been associated with higher levels of PA (106,127,132,150,153). In addition to these individual level determinants of PA (biological and psychological features of an individual) (154,155), also interpersonal (e.g. social support, cultural norms) (150,156), life event (157), environmental (e.g. built and natural environment) (153,158,159), regional and national policy (e.g. transport, health sector, education) (21,158,160), and global determinants of PA (e.g. economic development, global media) (21,161,162) have been examined. Intervention qualities (e.g. personal/group level, face-to-face/internet/phone-delivered, exercise type and exercise goals, individualized programs, theory-based) (163) can also affect PA levels. Only a few studies have simultaneously analyzed several correlates of PA in aging men and women separately (130,152), and none of them examined whether gender modifies these associations.

Table 3. Correlates of physical activity in cross-sectional studies among older adults

Correlate	Reference
Demographic correlates	
Gender	
Male gender associated with higher level of PA	(11,106,128-130,132,135,150)
No difference in PA between men and women	(106)
Age	
Younger age associated with higher level of PA	(11,106,127-130,132)
No association between age and PA	(130)
U-shaped association between age and PA	(150)
Marital status	
Married more active than others	(129,135)
No difference in PA between married and others	(130,150)
Married less active than others	(11)
Education	
Higher education associated with higher PA level	(129,130)
No association between education and PA	(11,135)
Income	
Higher income associated with higher PA	(127,129,130)
No association between income and PA	(130)
Working status	
Working (vs. not working) associated with higher PA level	(129,135)
No association between working status and PA	(150)
Health correlates	
Perceived health	
Better perceived health associated with higher level of PA	(106,127-129)
No association between perceived health and PA	(11)
Health conditions	
Health conditions associated with lower level of PA	(11,106,129,130,132,135)
Body mass index	
Higher body mass index associated with lower level of PA	(11,106,130)
Depression score	
Higher depressive score associated with lower level of PA	(106,132,135)
Lifestyle correlates	
Social connectivity	
More social contacts associated with higher level of PA	(130,150,153)
Living alone and loneliness not associated with PA	(106)
General social support not associated with PA	(127)
Participation in social activities associated with lower level of PA	(129)
Smoking	
No association between smoking status and PA	(11,106)
Current smoking associated with lower level of PA	(130)
Alcohol consumption	
Regular drinking associated with higher level of PA	(130)
Binge drinking associated with lower level of PA	(130)

PA = physical activity

Intervention studies that have explored the predictors of **adherence** to exercise prescription show that being physically active, fit, and a non-smoker, as well as having a high self-efficacy related to PA, have consistently predicted good adherence to exercise interventions among insufficiently physically active older adults (22,143,164) (Table 5).

Few **intervention studies** among older adults or patient populations including older adults have studied determinants of **PA change** (22-24) (Table 6). Results are inconsistent and vary between different populations and interventions.

There are no studies of the moderators of the effectiveness of PA interventions at increasing PA in randomized controlled trials in population samples of older individuals. One randomized controlled trial showed that only baseline PA and education modified the effectiveness of a PA intervention at increasing PA among adults (24) (Table 6). However, the participants of the randomized controlled trial were primary care patients aged 30 or over and not all of them had low levels of PA at baseline.

Table 4. Predictors of physical activity levels in follow-up studies among older adults

Correlate	Reference
Demographic correlates	
Age	
Older age associated with lower level of PA	(133-135)
Older age associated with faster decline in PA	(136,137)
Married	
No association between marital status and level of PA	(152)
Education	
Higher education associated with higher level of PA	(133,135)
No association between education and PA	(134,151,152)
Income	
No association between income and PA	(134)
Working	
Job loss associated with lower level of PA	(135)
Retirement	
Retirement associated with increased PA	(165-168)
No association between retirement and PA	(166,168)
Health correlates	
Perceived health	
Better perceived health associated with higher level of PA	(133,134)
Health conditions	
Health conditions associated with lower level of PA	(134,135,152)
No association between single health condition and PA	(152)
Body mass index	
Higher body mass index associated with lower level of PA	(133,134,151)
Higher body mass index associated with increasing PA	(134)
Depression score	
Symptoms of depression associated with lower levels of PA	(134,135)
Lifestyle correlates	
Smoking	
Smoking associated with lower level of PA	(134)
No association between smoking status and PA	(133,151)
Alcohol consumption	
No association between alcohol consumption and PA	(134,151)
PA	
Previous PA associated with later PA	(133,151,152)

PA = physical activity

2.2.5 Physical activity and health

There is strong evidence from prospective cohort studies that physically active men and women have lower all-cause mortality (2,169,170) and lower risk of developing coronary heart disease (171), ischemic and hemorrhagic stroke (172), type 2 diabetes (173), metabolic syndrome (174), colon cancer (175), breast cancer (176) and functional disability (177) than insufficiently active men and women. Regular structured PA or exercise also have favorable effects on symptoms of depression (178), cognitive function (179), blood pressure (180), body composition (181), systemic inflammation (182), muscular and aerobic fitness (74,183), mobility (184), bone mineral density (185) and prevention of falls (186).

A non-linear dose-response relationship exists between total duration of PA and most fitness and health indicators on a population level (2,169,187,188). The largest health benefits are observed when increasing PA from sedentary lifestyle to about 15 daily minutes of at least moderate intensity aerobic PA, and there are smaller additional benefits when increasing PA to the recommended 150 minutes per week and over (2,188). To increase VO_{2max} among older adults, sufficient intensity of aerobic exercise is more important than the total duration of aerobic exercise, whereby an intensity of 60-70% of VO_{2max} seems to yield optimal improvements in VO_{2max} (74). However, recent and future studies on high intensity interval training and individual training responses may change our understanding of the importance of different components of exercise for fitness and health benefits (75,189).

Table 5. Predictors of adherence to physical activity prescription or the levels of physical activity in intervention studies among older adults

	Study population	**Intervention groups**	**Outcome**	**Predictors**
(142)	Healthy men (13) & women (33) Mean age 71.3 USA	Supervised strength training 4 months	Participating in strength and endurance training 6 months after intervention	Satisfaction with exercise routine (+) Satisfaction with body image (+) Age (NS) Weight (NS) Body mass index (NS) Easy access to exercise location (NS)
(155)	Healthy, sedentary men (36) & women (67), Mean age 70.2 USA	1) Endurance + strength or 2) flexibility Pooled	Adherence % of prescription at 12 months	Social support (NS) Baseline self-efficacy (NS) Change in self-efficacy (+)
(143)	Sedentary men (50) & women (51) Mean age 67.0 USA	Aerobic exercise 4 to 8 months	Total PA in 1-year follow-up	Maximal oxygen consumption (+) Fast finger tapping (+) Anxiety (-) Age (NS) Gender (NS) Prior exercise adherence (NS) General mental health (NS) General cognitive functioning (NS)
(144)	Volunteers men (13) & women (38) Mean age 60.5 USA	Walking for financial incentive and control groups pooled	Aerobic minutes over 4-week period	Financial incentive (+) Education (-) Income (-) Working (-) Age (NS) Gender (NS)
(190)	Low to middle socioeconomic status men (304) & women (692) Age 65-67.9 Chile	Resistance training 2 times/week	Adherence ≥24 classes/year	Gender (NS) Age (NS) Depression (-) Diabetes mellitus (-) Retired (+) Body mass index (NS) Smoking(-) Prior PA (+) Social support (-) Violent crime in the neighborhood (-) Well-kept green areas (+) Impoverished households in area (-)
(145, 164)	[a]Sedentary, healthy men (42) & women (32) Mean age 56.4 [b]Men (149), women (120) Mean age 56.6	1) Moderate group-based 2) Moderate home-based 3) Low-intensity home-based pooled[a] pooled or separately[b,c]	[a]Exercise adherence relative to prescription [b]2/3 of exercise prescription	**7-12 months[a]** Smoking (-) Exercise self-efficacy (+) Self-motivation (NS) Exercise intervention intensity (NS) Perceived exertion, enjoyment and convenience of intervention (NS) **12-24 months[b,c]** Employment status (NS) Stress (-) General physical functioning (+) Social support (NS) **7-12 months[a]/12-24 months[b,c]** Separated (-)/(NS) Home-based exercise (+)/(+) Age (NS)/(NS) Gender (NS)/(NS) Ethnicity (NS) Education (NS)/(-) Income (NS) Body mass index (NS)/(-)

Table 5 continues

Table 5 continues

	Study population	**Intervention groups**	**Outcome**	**Determinants**
(191)	Urban women (46) Mean age 54.5 USA	Counseling 1 or 5 times, pooled	PA at 12 weeks	Change in exercise self-efficacy (+) Change in social support (family)(-) Change in social support (friends) (NS)
(192)	Healthy, low active women (76) Mean age 58.9 Netherlands	Endurance + strength, supervised and individual 1 year	At least moderate-intensity physical activity in 1-yr follow-up	Age <60 years, >65 years (+) PA (+) Employment (+)
(193)	Low active primary care patients men (179) & women (2) Mean age 68.7 USA	Walking, 3 groups with different number of phone call reminders, pooled	Frequency of walks in 10 month follow up	Walking companion (+) Motivational phone calls (+)
(146)	Sedentary men (35) and women (91) Mean age 66.7 USA	Supervised 1) Walking or 2) toning, 6 months, pooled	PA 5 years after intervention	Age (NS) Gender (NS) Ethnicity (NS) Marital status (NS) Education (NS) Income (NS) Positive affect 2 years after intervention (+) Exercise self-efficacy 2 years after intervention (+) Exercise intervention, walking (+)
(147)	Sedentary men (67) and women (146) with risk of mobility disability Mean age 76.5 USA	Combination of group and home-based exercises, 12 months	Adoption (1-2 months): center visits Maintenance (7-12 months): PA self-report	**Adoption/Maintenance** Age (NS)/(NS) Gender (NS)/(?) Ethnicity (NS)/(NS) Education (NS)/(NS) Body mass index (NS)/(NS) Arthritis (NS)/(NS) Heart attack/failure (NS)/(NS) Pacemaker (NS)/(+) Lung disease (-)/(NS) Physical functioning (NS)/(NS) Low energy/fatigue (NS)/(+) Pain (NS)/(NS) Symptoms of depression (NS)/(NS)
(22)	Underactive (≤2times/week & ≤2hours/week) adults ≥50 years AC: men (184) women (697) ALED: men (188) women (886) USA	AC: face-to-face orientation + 8 phone calls, 6 months; ALED: weekly group meetings 20 week intervention	Meeting general PA recommendati ons AC: 6 months ALED: 2-year follow-up after 20 week intervention	**AC/ALED** Age (-)/(NS) Gender (NS)/(NS) Race (NS)/(NS) Education (NS)/(+) Body mass index (NS)/(NS) ≥2 health conditions (NS)/(NS) Diabetes (NS)/(NS) Hypertension (NS)/(NS) Arthritis (-)/(NS) Coronary heart disease (-)/(NS) Osteoporosis (NS)/(NS) Perceived health (+)/(NS) Social support (NS)/(+) Self-efficacy (NS)/(+) Symptoms of depression (NS)/(NS) Perceived stress (NS)/(-) PA (+)/(+)

Association with outcome variable positive (+), negative (-) or non-significant (NS); intervention groups presented are those included in the analysis. PA = physical activity; AC = Active Choices program; ALED = Active Living Every Day program. [a]reference (164), [b]reference (145), [c]The results by study groups are not specified in this table, reference (145).

Table 6. Determinants of increase in physical activity in intervention studies among older adults

Study population	Intervention	Outcome	Determinants
Intervention group only			
Diabetic insufficiently active men and women (66±8 years) (23)	Personal counseling: individual exercise program 12 months, +12 months follow-up	Change in vigorous and moderate PA and walking (24 months-0 months)	**Vigorous PA/Moderate PA/Walking** Age (NS)/(NS)/(-) Education(-)/(NS)/(NS) Working status (NS)/(NS)/(NS) Body mass index (-)/(NS)/(-) Sitting (NS)/(NS)/(+), Socio-cognitive profile (NS)/(NS)/(NS) Moderate baseline PA (NS)/(-)/(NS) Vigorous baseline PA (NS)/(+)/(NS) Motivation (NS)/(NS)/(NS)
Underactive (≤2times/week & ≤2hours/week) adults ≥50 years (22)	AC: face-to-face orientation + 8 phone calls; ALED weekly group meetings 20 week intervention	Change in moderate-to-vigorous PA AC: 6 months ALED: 2-year follow-up after 20 week intervention	**AC/ALED** Age (-)/(-) Male gender (NS)/(-) Hispanic race (+)/(NS) Education (NS)/(NS) Body mass index (NS)/(+) ≥2 health conditions (NS)/(+) Diabetes (NS)/(NS) Hypertension (NS)/(NS) Arthritis (NS)/(NS) Coronary heart disease (-)/(NS) Osteoporosis (NS)/(+) Perceived health (NS)/(NS) Social support (+)/(NS) Self-efficacy (NS)/(NS) Symptoms of depression (NS)/(NS) Perceived stress (NS)/(NS) Middle 1/3 of PA (+)/(+)
Intervention and control group			
Primary care, diabetic or hypertensive >30 years (58±12) (24)	Telephone counseling 18 calls/12 months Usual care (4 newsletters/12 months)	Change ≥60 min in moderate-to-vigorous PA during 12 months	**Telephone counseling/ usual care** Age (NS)/(NS) Gender (NS)/(NS) Married (NS)/(-) Education Secondary (NS)/(+)* Retired (NS)/(+) Income (NS)/(NS) Body mass index (NS)/(+) PA (-)/(NS)*

Association to outcome variable positive (+), negative (-) or non-significant (NS); PA = physical activity; AC = Active Choices program; ALED = Active Living Every Day program. *statistically significant interaction ($p<0.05$)

Although there are clear benefits of regular PA there is also a risk of adverse events related to PA (99). The most common adverse effects are musculoskeletal injuries followed by circulatory, body temperature regulation and infection related problems (99). The risk of sudden cardiac death during exercise is low relative to the number of hours exercised (194). Although the risk is particularly increased during vigorous PA compared to rest, the overall risk of cardiac death during a given day (rest and activities combined) is lower among active than inactive individuals (194,195). The risk of adverse effects is lowest in low impact exercises performed in safe environments and by young and healthy individuals (99).

3 *Aims of the Study*

The overall purpose of the thesis was to provide information about the levels of cardiorespiratory fitness and the determinants of PA in a large population sample of older men and women. This study adds to knowledge by providing reference values of directly measured VO_{2max} from maximal cycle ergometer tests in a representative population of Finnish older adults. Further, new knowledge is provided on gender differences of correlates of low PA. Finally, this study was the first long-term randomized controlled exercise trial to explore the moderators of increases and maintained increases in aerobic exercise.

The specific aims were

1. To provide reference values of directly measured VO_{2max}, maximal METs and maximal work rate in a feasible way, and to describe the differences in VO_{2max} between healthy people and those with chronic diseases, as well as between genders (Original Study I).

2. To study the associations of variables related to demographics, health, diseases, social relations, and lifestyle with low levels of PA, and to explore whether gender modified the associations of low PA with its correlates (Original Study II).

3. To identify baseline characteristics that modify the effectiveness of aerobic exercise intervention at increasing aerobic exercise and maintaining increased aerobic exercise among older adults with low levels of PA at baseline in a 4-year randomized controlled trial (Original Study III).

4 Methods

4.1 STUDY POPULATION AND DESIGN

The subjects were participants of the Dose-Responses to Exercise Training (DR's EXTRA) Study, which is a 4-year randomized controlled trial on the effects of regular physical exercise and diet on endothelial function, atherosclerosis and cognitive function (196). The target study population was a representative random sample of 1500 men and 1500 women aged 55-74 living in the City of Kuopio, Eastern Finland in 2002. Formation of the final study population and reasons for not participating in the study are shown in Figure 3. Altogether 1479 individuals participated in baseline examinations and 69 individuals were excluded based on the study physician's evaluation due to diseases and conditions hampering safe engagement in an exercise intervention (e.g. severe cardiovascular or pulmonary diseases), participation in the long-term follow-up (e.g. malignant or other severe diseases) or co-operation (e.g. dementia, severe mental diseases or excess alcohol consumption). Participants with symptoms that needed further examination or care were advised to seek health care, or in some cases referred directly for further examinations.

Finally, 1410 individuals were randomly allocated into a reference group or one of the five intervention groups, and they formed the core group for the analyses in the subsequent studies (Figure 3). Randomization was done under the surveillance of the principal investigator, and was done in blocks of 180 subjects so that 30 subjects were randomized into each of the six study groups. The subjects were asked to choose one of the identical sealed opaque envelopes that were in a mixed order and contained the group assignment. At this time, participants were re-informed, in detail, of the study design and procedure.

Those 69 individuals who participated in the baseline assessments but were not randomized into any of the study groups were older ($p<0.001$) and less educated ($p<0.001$), had lower body height ($p=0.02$) and serum high-density lipoprotein (HDL) cholesterol ($p=0.003$), higher body weight ($p=0.05$), body mass index ($p<0.001$), plasma glucose level ($p=0.003$) and serum triglyceride level ($p=0.03$), had a greater likelihood of symptoms of depression ($p<0.001$), coronary heart disease ($p<0.001$) and stroke ($p<0.001$), and were more likely to be smokers ($p=0.003$) than the 1410 individuals randomized into one of the six study groups.

The DR's EXTRA Study is registered in the International Standard Randomised Controlled Trial Number Register (ISRCTN45977199). The study protocol was approved by the Research Ethics Committee of the Hospital District of Northern Savo. All participants gave written informed consent.

4.1.1 Study I

Study I was based on the baseline data of the 1410 randomized participants and those 1349 participants with successfully measured VO_{2max} were included. Reasons for missing VO_{2max} data in 61 individuals were that the test was performed without respiratory gas analysis (n=40), there was a technical problem (n=5), the test was submaximal (n=9) or the test was not performed due to disease (n=7). Those 61 individuals who were excluded due to missing VO_{2max} data were shorter ($p=0.04$), were more often widows ($p=0.05$), had a higher depression score ($p<0.001$), worse perceived health ($p=0.001$), and were more likely to have joint disease ($p=0.01$) compared to the 1349 individuals who were included in the study.

4.1.2 Study II

Study II was based on the baseline data of the 1410 randomized participants. After individuals with insufficient data on PA (n=5), social network and support (n=40), income (n=35), diet (n=13), labor market position (n=3), depression score (n=2), health professional's suggestion to increase PA (n=1), or more than one of these variables (n=8) were excluded, the Study II population consisted of 636 men and 667 women. The excluded 107 individuals with missing data had a higher body mass index (p=0.04), slept more (p=0.01), and had a lower VO_{2max} (p=0.02), social network score (p=0.02) and alcohol consumption (p=0.02), as well as worse perceived health (p=0.03) compared to the 1303 individuals who were included.

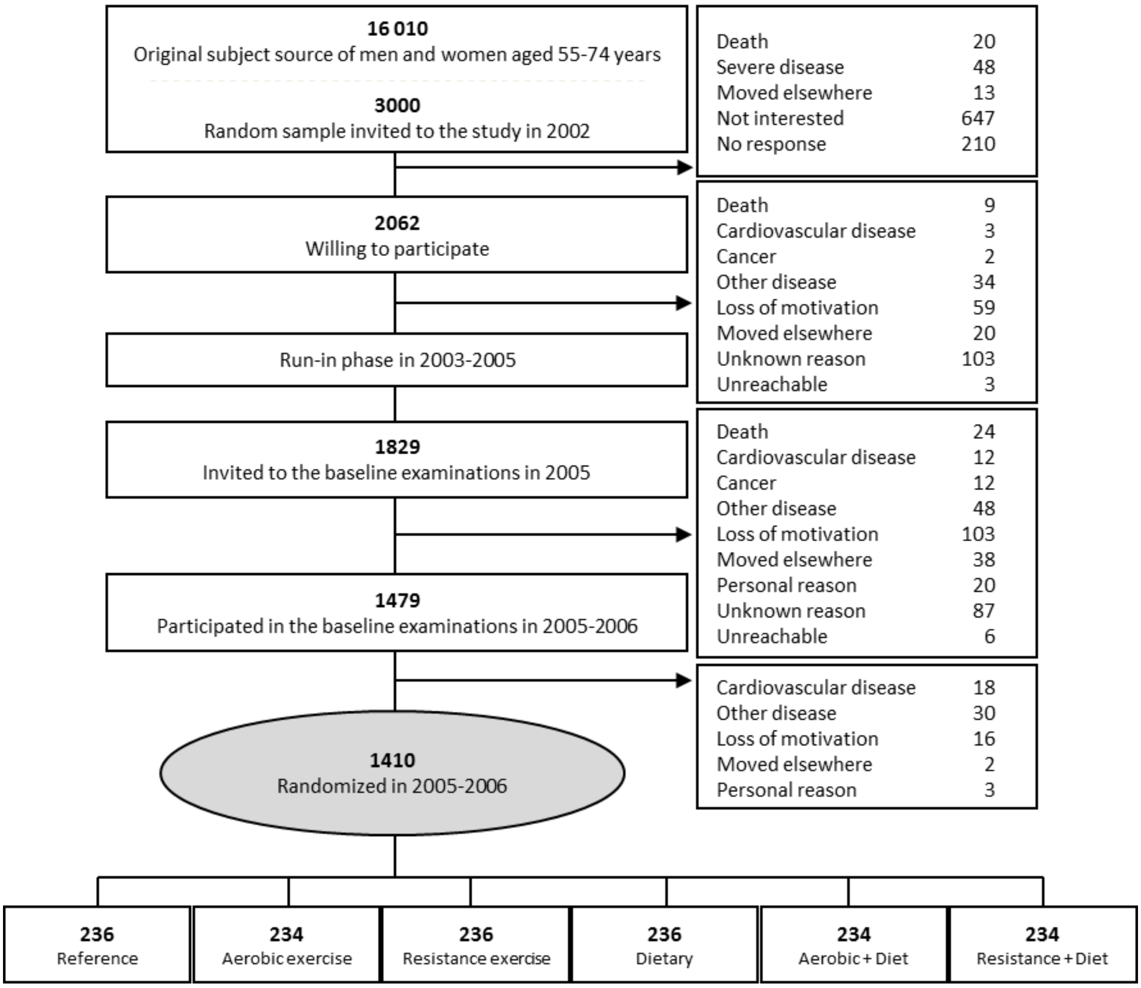

Figure 3. Flowchart of the DR's EXTRA Study recruitment and allocation into study groups

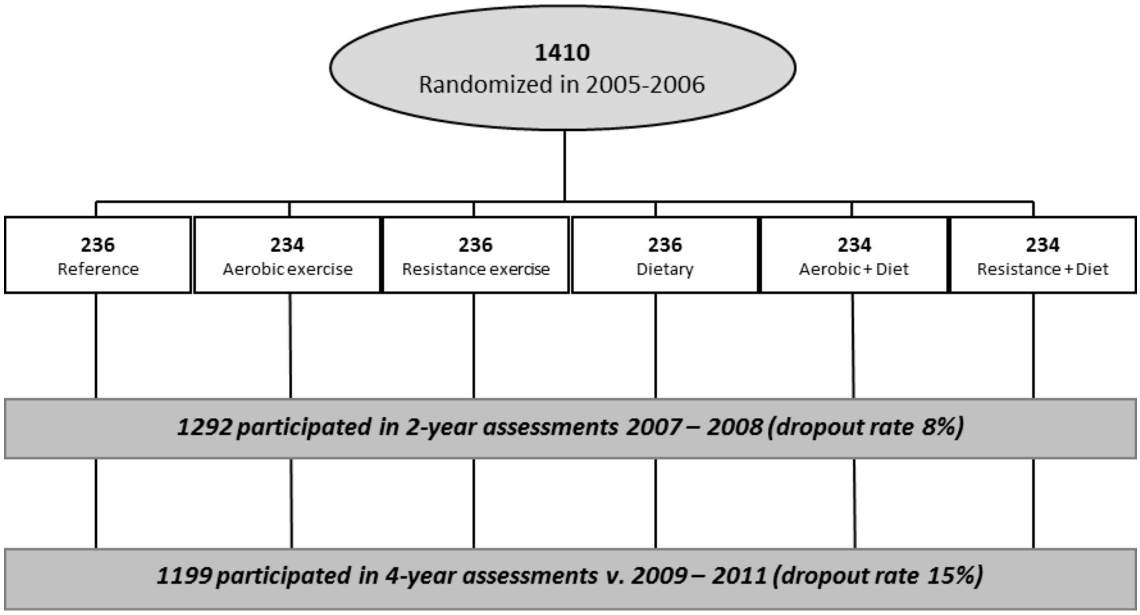

Figure 4. Dropout rates at 2-year and 4-year assessments in the DR's EXTRA Study

4.1.3 Study III

Study III was based on baseline, and 2-year and 4-year follow-up data. The 1410 randomized individuals were randomly allocated into six groups: reference group (n=236), aerobic exercise group (n=234), resistance exercise group (n=236), diet group (n=236), combined aerobic exercise and diet group (n=234), and combined resistance exercise and diet group (n=234). At the 4-year follow-up the dropout rate among all randomized participants was 15% (Figure 4). In the present study, individuals randomized into the reference group, diet group, aerobic exercise group or combined aerobic exercise and diet groups were included. For statistical analyses, reference and diet groups were combined into a control group, and aerobic exercise and combined aerobic exercise and diet groups were combined into an aerobic exercise group (Figure 5). Of the 940 individuals included, 467 (49.7%) had low aerobic exercise level (<150 minutes of moderate-to-heavy and <75 minutes of heavy aerobic exercise per week) at baseline. This selection was based on PA recommendations for aerobic PA (99). Of these 467 individuals, 69 (15%) dropped out during four years. Dropout rate was 19% in the control group and 14% in the aerobic exercise group. Dropout reasons in aerobic exercise/control groups were death (n=3/5), disease (n=12/13), relocation (n=2/0), personal (n=9/19), and unknown (n=3/3). After excluding dropouts and those with insufficient data on PA at two or four years (n=6) and baseline social support and network (n=7), income (n=8) or both (n=1), VO_{2max} (n=18) and diet (n=4), the final study sample was 354 individuals of whom 169 were in the control group and 185 in the aerobic exercise group.

Individuals with low moderate-to-heavy aerobic exercise levels who were included in the present study (n=354) were younger (p=0.003), more likely to be working (p=0.001), had a higher income (p=0.04), had better perceived health (p=0.002), had a lower likelihood of type 2 diabetes (p=0.05), had a higher social network score (p=0.006), higher VO_{2max} (p=0.01) and were less likely to have ever participated in competitive sports (p=0.04) than the individuals with low aerobic exercise levels who dropped out or had missing data.

There were further missing data for VO_{2max} at two years (n=22) and four years (n=20), resulting in a study population of 332 individuals at two years and 334 at four years in the analysis considering changes in VO_{2max}.

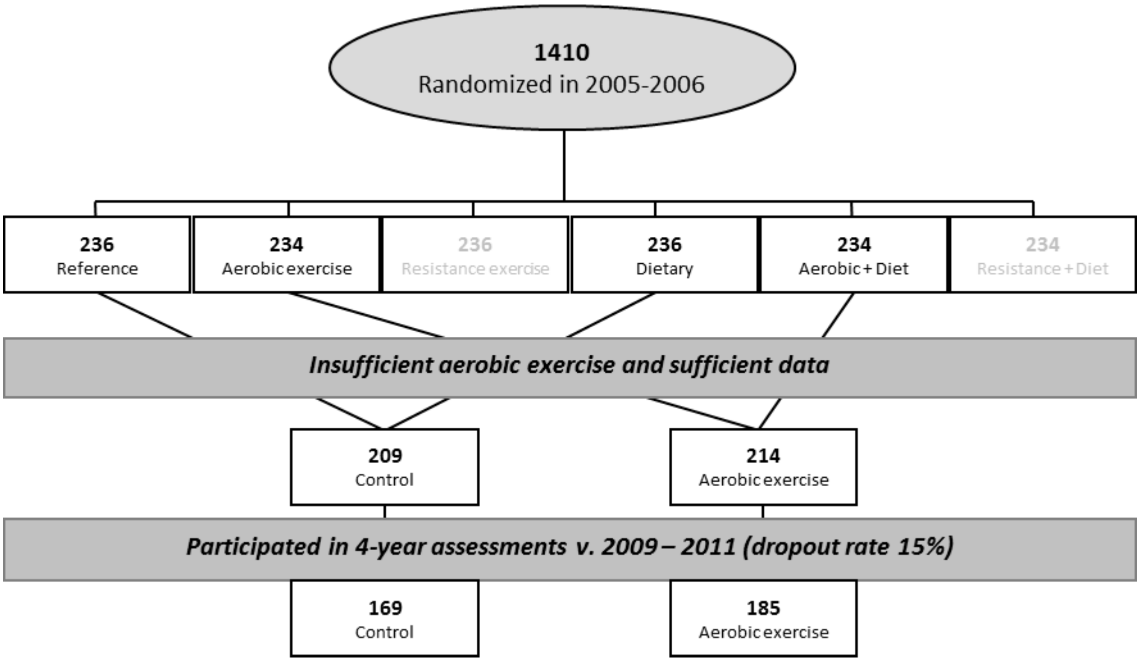

Figure 5. Formation of study population in Study III in the DR's EXTRA Study

4.1.4 Interventions (Study III)

Individuals in the aerobic exercise, diet and combined aerobic exercise and diet groups visited an exercise professional or a dietician or both and participated in exercise or diet counseling or both four times during the first six months of the intervention and biannually thereafter until the end of the 4-year intervention. The aerobic exercise program was individualized based on the preferences, health and fitness of the participants. The goal of the aerobic exercise group after progressive increase was to exercise at least five times per week with a duration of at least 60 minutes per session at an intensity corresponding to 55 to 65% of VO_{2max} measured during a maximal exercise test. At six months, individuals in the aerobic exercise group were further randomized into two groups with aerobic exercise recommendations of either 60 minutes or 90 minutes of aerobic exercise five times per week.

Exercise intensity was defined as exercise heart rate or walking speed based on data from a maximal cycle ergometer exercise test, corresponding to 55% to 65% of VO_{2max}. The participants could borrow heart rate monitors from the research group to estimate their exercise intensity. The 30-minute face-to-face counseling sessions included motivation, written exercise prescriptions including stretching tips, delivery of printed material on local exercise opportunities and checking of optional exercise logs. The intervention also included three group discussion sessions about health behavior or Nordic walking. The intervention included on average 11 personal and two group visits in the aerobic exercise and diet groups and up to 22 personal and three group visits in the combined aerobic exercise and diet group.

Diet counseling was based on the Finnish Nutrition Recommendations (197). The main goals were to substitute saturated fat with unsaturated fat and to increase the intake of fibre and antioxidants. After 6 months, the subjects were randomly allocated into the Finnish Nutrition Recommendations group or the special nutrition group. The special nutrition group was instructed, in addition to Finnish Nutrition Recommendations, to increase the intake of vegetables, fruits, berries, chicken, nuts and almonds as well as to decrease the intake of red meat. The instructions were individually tailored by the nutritionists.

The reference group was orally informed about general public health advice on PA and diet at baseline. The study visits were carried out during three separate days at baseline and at 2-year and 4-year follow-up. In addition, there was one visit for returning the questionnaires at three months for all participants.

4.1.5 Timeframe of the assessments

The present thesis is based on the baseline assessments of cardiorespiratory fitness, PA and a large range of correlates and modifiers, and on two-year and four-year assessments of cardiorespiratory fitness and PA (Table 7).

Table 7. Assessments at baseline, two years and four years utilized in the present thesis

Assessments	Baseline	Two years	Four years
Physical activity			
DR's EXTRA PA Questionnaire (moderate-to-heavy aerobic exercise)	x	x	x
DR's EXTRA PA Interview (moderate-to-vigorous PA)	x		
Maximal exercise test	x	x	x
Diet, smoking, alcohol consumption	x		
Body size	x		
Biochemical assessments and blood pressure	x		
Perceived health	x		
Diseases and medications	x		
Demographic variables	x		
Social network and social support	x		

4.2 ASSESSMENT OF CARDIORESPIRATORY FITNESS

To standardize the conditions before the exercise stress test, the subjects received written instructions to take their medications normally, and to avoid strenuous exercise for at least 24 h, heavy meals, coffee, tea and cola drinks for at least 2 h, alcohol consumption for at least 48 h and cigarette smoking for at least 4 h before the exercise test. A nurse confirmed these prerequisites and a physician interviewed and examined the subjects to evaluate contraindications. A maximal symptom-limited incremental exercise stress test was performed using an electrically braked cycle ergometer (Ergometrics 900, Ergoline, Bitz, Germany). The test started with a 3-min warm up at a work rate of 20 W and continued with 20 W increments every minute until exhaustion. The subjects were informed about the test protocol beforehand and they were verbally encouraged to reach their maximum. To standardize body movement, subjects were advised to sit all the time while pedaling and to keep both hands on the handlebars, except during blood pressure measurements when one hand was released.

Oxygen consumption and carbon dioxide production were measured directly with the breath-by-breath method using a paramagnetic and infrared analyzer for oxygen and carbon dioxide, respectively (VMax 29, SensorMedics Corporation, Yorba Linda, California, USA). VO_{2max} was defined as the mean of the three highest values of oxygen consumption measured consecutively over 20 second intervals and was expressed as l/min and ml/kg/min. Cardiorespiratory fitness was also expressed as METs whereby one MET refers to the resting metabolic rate and corresponds to oxygen consumption of 3.5 ml/kg/min. The last completed work rate was defined as the maximal work rate and was expressed as W or W/kg. The exercise test was considered maximal if the respiratory exchange ratio (RER) was ≥1.1 or if the test was terminated due to cardiovascular or pulmonary reasons, muscle fatigue or overall fatigue. Borg's scale (6–20) was used to assess perceived exertion during the test (198). Electrocardiography was recorded throughout the exercise test (Cardiosoft, GE Medical Systems, Freiburg, Germany). Blood pressure was measured from the upper arm every 2 minutes during the test with a standard mercury sphygmomanometer.

Cardiorespiratory fitness was assessed at baseline, two-year and four-year assessments (Table 7).

4.3 ASSESSMENT OF PHYSICAL ACTIVITY

Two PA measures were used in the present study (Table 7). Variable moderate-to-vigorous PA was based on DR's EXTRA PA interview (Studies I and II). Variable moderate-to-heavy aerobic exercise was based on DR's EXTRA 12-Month PA Questionnaire (Study III).

4.3.1 Studies I and II

To assess the frequencies and durations of the sessions of light, moderate and vigorous leisure-time PA during the previous month, the DR's EXTRA PA interview, modified from a previous questionnaire (199), was used. Commuting to and from work, recreational activities such as gardening or berry-picking as well as all types of sports were considered leisure-time PA. The intensity levels of PAs were written and described verbally based on the modes and pace of PA as well as the breathing and sweating levels. The subjects were first asked to choose one or more suitable PA categories based on the intensity level (no PA on weekly basis, light PA, moderate PA, vigorous PA). The subjects were then asked to choose the frequency (1, 2-3, 4-5 or ≥6 times/week) and the average duration of each session (<15, 15-30, 31-60, 61-120 or >120 minutes/session) for each PA category. The total duration at each intensity level was computed by multiplying the frequency and duration. For the frequency alternatives 2-3 and 4-5 as well as the duration alternatives 15-30, 31-60 and 61-120, the mean value was used: e.g. 2.5 times/week*22,5 minutes. The duration of moderate-to-vigorous PA was positively correlated with VO_{2max} (ml/kg/min) in men (Spearman's correlation coefficient, $r=0.35$, $p<0.001$) and in women ($r=0.34$, $p<0.001$). The duration of light PA was not correlated with VO_{2max} (ml/kg/min) in men ($r=-0.02$, $p=0.68$) or in women ($r=-0.02$, $p=0.59$).

In Study I, PA was expressed as energy expenditure in MET-hours/week. MET-values for each intensity level of PA were determined based on the means of maximal METs achieved during the exercise stress tests in 22 age- and sex-specific groups. MET-values were multiplied by duration of PA at each intensity level. The following percentages of MET-reserve were used: 35% for light, 55% for moderate and 75% for vigorous PA, resulting in the following MET ranges: light 2.5 MET to 3.6 MET, moderate 3.3 MET to 5.0 MET and vigorous 4.2 MET to 6.5 MET. The smallest values were used in women aged 77–78 and the largest values for men aged 57–58.

In Study II, the subjects were divided into those who reported moderate or vigorous PA (high PA) and those who did not report such activity (low PA) based on the definition of physical inactivity in the 2008 Physical Activity Guidelines for Americans (99). The daily number of hours of sleeping and sedentary activities, including sitting and lying down awake, to an accuracy of 0.5 hours were also recorded.

4.3.2 Study III

To assess PA the DR's EXTRA 12-Month PA Questionnaire has been modified from the Minnesota Leisure-Time PA questionnaire (200), and the Kuopio Ischemic Heart Disease Risk Factors Study Questionnaire (107) was used. The participants filled in the frequencies of different PAs for each month during the previous 12 months, and mean duration and mean intensity (1 light, 2 moderate, 3 heavy, 4 very heavy) of each PA. The study personnel checked the form. In this study following forms of aerobic exercise were included in the analyses: walking and cycling for commuting, walking, Nordic walking, jogging, running, orienteering, cross country skiing, skating, cycling, rowing, paddling, swimming, water gymnastics, golf, other ball games, downhill skiing and snowboarding, dancing, bowling, aerobics and group and home-based gymnastic exercises.

The frequency of each form of aerobic exercise (sessions/week) was multiplied by the average duration of corresponding aerobic exercise (minutes/session) resulting in the total duration of each aerobic exercise (minutes/week). The durations of the aerobic exercises with subjective intensity levels from 2 to 4 were summed to compute the total duration of moderate-to-heavy aerobic exercise. Time spent in each form of moderate-to-heavy aerobic exercise during the previous 12 months was computed by multiplying the number of sessions of the form of aerobic exercise of subjective intensity levels from 2 to 4 by the average duration of the sessions of corresponding aerobic exercise in minutes per session. The total duration of moderate-to-heavy aerobic exercise was computed by summing the times spent in each form of moderate-to-heavy aerobic exercise. The total duration of light aerobic exercise was computed by summing the times spent in the forms of aerobic exercise with a subjective intensity level of 1. The duration of moderate-to-heavy aerobic exercise was positively correlated with VO_{2max} (ml/kg/min) among participants of Study III in men (r=0.23, p=0.02) and in women (r=0.23, p=0.02). The duration of light aerobic exercise was not correlated with VO_{2max} in men (r=-0.02, p=0.77) or in women (r=-0.10, p=0.19).

A participant was defined as having low aerobic exercise if he or she reported moderate-to-heavy aerobic exercise totaling less than 150 minutes per week or heavy aerobic exercise less than 75 minutes per week based on current recommendations for aerobic PA (99). An increase in aerobic exercise was defined as an increase in moderate-to-heavy aerobic exercise of at least 60 minutes per week assessed at two years from baseline. Maintained increase in aerobic exercise was defined as an increase in moderate-to-heavy aerobic exercise of at least 60 minutes per week assessed at two years and four years from baseline. An increase in aerobic exercise of at least 60 minutes per week has previously been defined as a meaningful increase in exercise regarding health (148).

4.4 ASSESSMENT OF OTHER LIFESTYLE VARIABLES

Self-reported smoking was categorized as never (or non-smoker in Study III), past smoker and current smoker, and alcohol consumption as portions of alcohol (12 g) consumed during the past 7 days divided into approximate tertiles (0, 1-4, ≥5) in Study II and into two groups at median (0-1; >1 portions per week) in Study III. Participation in competitive sports at any time during the life span was assessed with a single question.

Food consumption and nutrient intake were assessed by a four-day food record, including three weekdays and one weekend day. Food records were given to the participants at the first study visit and were returned one week later. Recording dates were defined by the researcher and were 1) from Wednesday to Saturday, 2) from Thursday to Monday, except Sunday, or 3) from Sunday to Wednesday. The participants were given detailed written and verbal instructions. Missing information was completed when the food record was returned. These instructions were given and responses were checked by clinical nutritionists or trained nurses. The amount of food consumed was estimated by a picture booklet of portion sizes (201), using household gauges or weighing. Data from the food record were analyzed using nutrient calculation software (MicroNutrica®, The Social Insurance Institution of Finland) (202). Based on a four-day food record, a five-grade diet score (scale 0-4) was created according to the number of achieved dietary goals based on nutrition recommendations of the American Diabetes Association (203,204). The goals were 1) ≥400 grams of vegetables per day, 2) ≥2 servings of fish per week (≥30 grams per day), 3) ≥14 grams of fiber per 1000 kilocalories, and 4) ≤10% of daily energy intake from saturated fatty acids. The dietary score (0-4 goals achieved) was categorized as low (0), medium (1-2), and high (3-4 goals achieved) in Study II and as low (0-1) or high (2-4 goals achieved) to form two groups of as equal size as possible in Study III.

4.5 ASSESSMENT OF BODY SIZE

Body height (accuracy 0.1 cm) was measured using a metal scaled height meter. Body weight (accuracy 0.1 kg) was measured with a digital scale in light indoor clothing without shoes. Body mass index was calculated by dividing body weight in kilograms by the square of body height in meters. In Study II, body mass index was standardized by forming a z-score for the analysis. In Study III, the participants were categorized based on body mass index into those with a normal body weight (<25.0 kg/m^2), overweight (25.0-29.9 kg/m^2) or obesity (≥30.0 kg/m^2). Waist circumference (accuracy 0.5 cm) was measured on bare skin, midway between the bottom of the rib cage and the top of the iliac crest. Subjects stood with their feet 12 centimeters apart with their weight equally distributed on each leg. The mean of two separate measurements was used in the analyses.

4.6 ASSESSMENT OF BLOOD PRESSURE

Blood pressure in the right arm was recorded in a sitting position after a five minute rest using a mercury sphygmomanometer. The first appearance of the Korotkoff sounds (205) was recorded as the systolic blood pressure and the disappearance of the sounds was recorded as the diastolic blood pressure. Two independent consecutive measurements of systolic and diastolic blood pressure were taken, and the mean of the measurements was used.

4.7 BIOCHEMICAL MEASUREMENTS

Venous blood samples were taken without stasis into glass tubes in the morning after a 12 hour fast at the first baseline visit and the samples were analyzed daily. Hexokinase method (Thermo Clinical Labsystems Oy, Finland) was used for fasting plasma glucose analysis. Serum total cholesterol (Thermo Electron Corporation, Finland), serum HDL cholesterol (Thermo Electron Corporation, Finland) and serum triglycerides (Thermo Electron Corporation, Finland) were analyzed by enzymatic photometric methods. Serum low-density lipoprotein (LDL) cholesterol was calculated according to the Friedewald formula (206).

Oral glucose tolerance test with a 75 g glucose load was carried out in the morning after a 12 hour fast. The blood samples were taken in a fasting state and 30, 60 and 120 minutes after glucose load. Based on World Health Organization criteria (207), individuals without type 1 diabetes were classified as having impaired fasting glucose if the fasting plasma glucose was between 6.1 and 6.9 mmol/l and 2-hour glucose was <7.8 mmol/l. Impaired glucose tolerance was defined as fasting plasma glucose <7 mmol/l and 2-hour glucose between 7.9 and 11.1 mmol/l, and type 2 diabetes was defined as fasting plasma glucose ≥7 mmol/l or 2-hour glucose ≥11.1 mmol/l. Impaired glucose regulation was defined as having impaired glucose tolerance, impaired fasting glucose or both. For those individuals who did not participate in the oral glucose tolerance test, the classification into normal or impaired fasting glucose or diabetes was based on fasting plasma samples or self-reported type 2 diabetes.

4.8 DEFINITION OF METABOLIC SYNDROME

Metabolic syndrome was defined by the National Cholesterol Education Program Adult treatment panel III criteria (208). Having at least three of the following risk factors was defined as having metabolic syndrome: elevated blood pressure (≥130/85 mmHg or drug treatment), increased fasting plasma glucose (≥6.1 mmol/l), low HDL cholesterol (<1.03 mmol/l in men and <1.29 mmol/l in women, high triglycerides (≥1.7 mmol/l) and abdominal obesity (waist circumference >102 cm in men and >88 cm in women).

4.9 ASSESSMENT OF PERCEIVED HEALTH, DISEASES AND MEDICATIONS

The participants were divided into three groups of self-reported health (Excellent, pretty good; Good; Satisfactory, poor) in Study II and into two groups (Good-to-excellent; Satisfactory-to-poor) in Study III. The participants were divided into two groups for disease limiting PA (Yes; No), and the suggestion of a physician or a nurse to increase PA (Yes; No). The history of type 2 diabetes, cardiovascular disease (coronary heart disease, cerebrovascular disease, heart failure, peripheral artery disease), pulmonary disease (asthma, chronic obstructive pulmonary disease, sleep apnea, other), joint disease (osteoarthritis, rheumatoid arthritis), and cancer (breast, prostate, colorectal, ovarian, cervical, other) was assessed by a questionnaire. The number of chronic diseases was calculated by summing the prevalence of type 2 diabetes, cardiovascular disease, pulmonary disease, joint disease and cancer, and was classified as 0, 1 or ≥2 diseases (Studies II and III). In Study I metabolic syndrome, impaired glucose regulation or type 1 diabetes were also summed as a disease alternative to type 2 diabetes. The symptoms of depression were assessed with the Center for Epidemiologic Studies Depression Scale (range 0 to 35 points), and the participant was defined as having symptoms of depression if the value was ≥16 points (209). Medication was recorded in a self-administered questionnaire.

4.10 ASSESSMENT OF DEMOGRAPHIC VARIABLES

Age was calculated from date of birth at the first visit and used as continuous (Study I), standardized by forming a z-score (Study II) or categorized variable (tertiles: ≤62.1; 62.2-68.4; ≥68.5 years) in Study III. Marital status, education, working status and household income were assessed by a self-administered questionnaire at baseline. The participants were divided into three groups according to the highest level of education in Study II (Basic: elementary or comprehensive school; Vocational: vocational school, high school, upper secondary school or higher vocational diploma; University: university graduate), or into two groups based on the median number of years in education in Study III (≤10; >10 years). The participants were divided into three groups according to marital status (Married or cohabiting; Divorced or separated; Unmarried and widowed) in Study II and in two groups according to marital status (Married or cohabiting; Not married including divorced or separated, unmarried and widowed) in Study III. Regarding working status, they were divided into three groups (Working; Retired; Other including unemployed, those on job-alteration leave) in Study II or in two groups (Working; Not working) in Study III. For household income, they were dividied into three groups (<20 000; 20001-60000; >60000 €/year) in Study II and into two groups (≤40000; >40000 €/year) in Study III.

4.11 ASSESSMENT OF SOCIAL NETWORK AND SUPPORT

Social network and social support were assessed with a validated questionnaire (210,211). Social network score (0 to 17 points) was formed from questions related to rooting to the neighborhood, meeting friends and family as well as social participation, and the score was divided into tertiles (weak: 0-12; medium: 13-14; strong: 15-17 points) in Study II and in two based on the median (low ≤13; high ≥14 points) in Study III. Social support score (0 to 8 points) was formed from questions related to availability of concrete help, advice and emotional support from other people, and the score was divided into approximate tertiles (weak: 0 to 6, medium: 7, strong: 8 points) in Study II and in two based on the median (low to medium: 0 to 7 points, high: 8 points) in Study III.

4.12 STATISTICAL METHODS

All statistical analyses were performed with SPSS 15.0 (Study I) or SPSS 19.0 (Studies II and III) for Windows (SPSS Inc., Chicago, Illinois, USA). In Studies I-III, a p-value of <0.05 was considered statistically significant.

4.12.1 Study I

VO_{2max} was studied separately in men and women, in non-diseased individuals and in those with any chronic disease. Independent samples t-test, the Mann–Whitney U-test and the chi-square ($\chi 2$) test were used to study the difference in basic characteristics between men and women. Because of skewed distributions, log-transformed values were used for plasma glucose and serum triglycerides. To demonstrate the dependency of VO_{2max}, maximal METs and maximal work rate on age, linear, quadratic, cubic and exponential regression models in different groups were tested and the model with the highest adjusted R-squared (R^2) was chosen for the graphic expression. Based on these regression equations and on the variable distribution, cut-off values of the five categories of cardiorespiratory fitness in two-year age intervals in men and women were presented: very low (<2.5%), low (2.5% to 15.9%), medium (16% to 84%), high (84.1% to 97.5%) and very high (>97.5%). Two-year intervals were used because it was possible with the large dataset and because of expected differences between age groups. The percentages were based on the assumption that values were normally distributed and the given percentages accounted for one and two standard deviations from the mean. Cut-off values were mostly based on quadratic equations, except for maximal work rate in women. In this case, a linear equation was chosen due to the higher adjusted R^2. The associations between some pre-specified variables and VO_{2max} were investigated using independent samples t-test (smoker/non-smoker; β-blocker user/non-user) and linear regression analysis (waist circumference; moderate-to-vigorous PA). Univariate analysis of variance adjusted for age was used to study the difference in VO_{2max} between the non-diseased and diseased groups.

4.12.2 Study II

Independent samples t-test, the Mann-Whitney U-test, or the $\chi 2$-test were used to analyze differences in means or frequencies between individuals with low and high PA. Univariate logistic regression analysis was used to study the odds ratios (OR) and their 95% confidence intervals (95% CI) of having low PA in men and women. Forward stepwise logistic regression models including all variables used in univariate analysis were used to find the independent correlates of having low PA in men and women separately. Forward stepwise logistic regression was used to avoid potential collinearity issue related to intercorrelated variables. To study whether gender modified the associations of the correlates of PA with the odds of having low PA, interaction terms were included in the logistic regression models that included men and women. Dummy variables were used for marital status and labor market position (e.g. working vs. not working) to test the interactions because the variables were not ordinal.

4.12.3 Study III

Independent samples t-test, the Mann-Whitney U-test or the $\chi 2$-test were used to analyze differences in baseline characteristics between individuals in the aerobic exercise and control groups.

The number of participants needed to be treated with exercise counseling for one individual to maintain increased aerobic exercise was calculated corresponding to the number needed to treat (NNT) as follows: 1/|proportion of those who maintained increased aerobic exercise in the control group - proportion of those who maintained increased aerobic exercise in the aerobic exercise group|. The NNT analysis was conducted in the final study population of 354 individuals, as well as in all 467 randomized individuals, while those without 2-year or 4-year follow-up exercise data were considered to have not increased aerobic exercise. Independent samples t-test was used to analyze differences in exercise and VO_{2max} change between individuals in the aerobic exercise and control groups, and between individuals who maintained increased aerobic exercise from two to four years and those who did not. Further, to study whether two-year and four-year changes in moderate-to-heavy aerobic exercise as continuous variables were associated with two- and four-year changes in VO_{2max}, respectively, a linear regression analysis was used.

Logistic regression analyses were performed to study ORs and 95% CIs for increase in aerobic exercise assessed at two years, and for maintained increase in aerobic exercise assessed at two and four years in the aerobic exercise group compared to the control group. The same analyses were performed for different subgroups of baseline characteristics. To test whether these baseline variables modified the effectiveness of the aerobic exercise intervention, the statistical significance of interaction between the baseline characteristics and the study group in the logistic regression models were tested. The possible moderators for the effectiveness of the aerobic exercise intervention were chosen based on observed associations with PA in the literature (21).

5 Results

5.1 CHARACTERISTICS OF PARTICIPANTS

5.1.1 Study I

At baseline, men had higher VO_{2max}, maximal work rate, perceived exertion at the end of the exercise test, body weight, body height, waist circumference, diastolic blood pressure, fasting serum triglycerides, and reported more moderate-to-vigorous PA than women (Table 8). Men had lower systolic blood pressure, fasting serum total cholesterol, and fasting serum HDL cholesterol than women. Men were more likely to be smokers and had a greater likelihood of cardiovascular disease, diabetes, and pulmonary disease, but a smaller likelihood of joint disease compared to women (Table 8).

5.1.2 Study II

Altogether, 245 (39%) men and 318 (48%) women reported no moderate or vigorous PA, and were defined as having low PA (Table 9). Men and women who had low PA had a higher body weight and a lower VO_{2max}, reported more sitting and light PA, had worse perceived health, and had a higher depression score and a lower social network score than men and women with high PA. Men with low PA were more often divorced or separated and current smokers, were more likely to be suggested to increase PA by a health professional, and had a poorer diet than men with high PA. Women with low PA were older, had more chronic diseases, and consumed less alcohol than women with high PA (Table 9).

5.1.3 Study III

There were no differences in baseline characteristics between participants in the aerobic exercise and control groups (Table 10).

Table 8. Baseline characteristics of the 1349 men and women in Study I

	Men n=672	**Women n=677**	**p-value**
Age, years	66.3 (5.4)	66.5 (5.3)	0.37
Body weight, kg	83.6 (13.6)	70.5 (12.9)	<0.001
Body height, cm	173.6 (6.1)	160.0 (5.8)	<0.001
Body mass index, kg/m^2	27.7 (4.0)	27.5 (4.9)	0.47
Waist circumference, cm	99.0 (11.0)	88.6 (12.9)	<0.001
Maximal oxygen consumption, l/min	2.17 (.49)	1.45 (.31)	<0.001
Maximal oxygen consumption, ml/kg/min	26 (6)	21 (5)	<0.001
Maximal METs in exercise test	7.5 (1.8)	6.0 (1.4)	<0.001
Maximal work rate, W	179 (42)	118 (30)	<0.001
Maximal heart rate, beats per minute			
In all individuals	149.6 (21.7)	148.8 (19.7)	0.46
In 457 men and 485 women without heart-rate lowering medication[a]	157.8 (16.4)	154.6 (16.7)	0.003
Borg scale of perceived exertion[b]	18.1 (1.5)	17.7 (1.8)	<0.001
Systolic blood pressure, mmHg	145.6 (18.9)	150.1 (21.1)	<0.001
Diastolic blood pressure, mmHg	84.3 (9.4)	82.3 (9.1)	<0.001
Fasting plasma glucose, mmol/l	6.03 (1.10)	5.65 (.82)	<0.001
Fasting serum total cholesterol, mmol/l	4.88 (.93)	5.26 (.92)	<0.001
Fasting serum LDL cholesterol, mmol/l	3.17 (.85)	3.24 (.85)	0.12
Fasting serum HDL cholesterol, mmol/l	1.51 (.42)	1.86 (.48)	<0.001
Fasting serum triglycerides, mmol/l	1.39 (.76)	1.31 (.64)	0.047
Moderate-to-vigorous PA, MET-hours/week	14.1 (16.9)	8.0 (11.5)	<0.001
Daily smoker, %	8.5	5.0	0.006
Cardiovascular disease, %	28.6	18.8	<0.001
Pulmonary disease, %	25.3	18.8	0.004
Joint disease, %	53.3	64.8	<0.001
Diabetes, %	16.5	9.5	<0.001
Metabolic syndrome, %	27.7	25.0	0.26
Cancer[c], %	8.3	10.9	0.11

Data are presented as mean (standard deviation) or percentage. p-values are for differences between genders from independent samples *t*-test, Mann-Whitney U-test, or χ^2-test. MET = metabolic equivalent. [a]Users of β-blockers and digitalis were excluded. [b]Borg scale from 6 (no exertion at all) to 20 (maximal exertion). [c]Breast cancer (n=36), prostate cancer (n=28), colorectal cancer (n=7), ovarian cancer (n=2), other cancer (skin, bladder, cervical) (n=59).

Table 9. Baseline characteristics of 1303 men and women with low and high physical activity levels in Study II

	Men			**Women**		
	Low PA n=245	**High PA n=391**	**p-value**	**Low PA n=318**	**High PA n=349**	**p-value**
Age, years	66.3 (5.9)	66.2 (5.1)	0.80	67.1 (5.5)	66.0 (5.0)	0.006
Weight, kg	86.3 (14.9)	81.3 (11.7)	<0.001	72.9 (14.3)	68.8 (11.7)	<0.001
Height, cm	173.6 (6.3)	173.8 (6.1)	0.62	159.9 (6.2)	160.1 (5.6)	0.68
Body mass index, kg/m^2	28.6 (4.5)	26.9 (3.2)	<0.001	28.6 (5.6)	26.8 (4.3)	<0.001
Sleeping, hours/day	7.6 (1.2)	7.5 (1.0)	0.17	7.3 (1.2)	7.5 (1.1)	0.11
Sitting, hours/day	7.4 (2.7)	6.3 (2.4)	<0.001	7.1 (2.7)	6.2 (2.2)	<0.001
Light PA, hours/week	3.4 (1.7-4.5)	1.9 (0.8-3.8)	<0.001	3.4 (1.9-6.8)	3.4 (1.7-4.5)	<0.001
Moderate PA, hours/week	0.0 (0.0-0.0)	3.8 (1.9-6.8)	<0.001	0.0 (0.0-0.0)	3.4 (1.9-5.0)	<0.001
Vigorous PA, hours/week[a]	0.0 (0.0-0.0)	0.0 (0.0-0.0)	<0.001	0.0 (0.0-0.0)	0.0 (0.0-0.0)	<0.001
Maximal oxygen consumption, ml/kg/min (n=1249)	24 (6)	28 (6)	<0.001	19 (4)	23 (5)	<0.001
Marital status (married/divorced/unmarried/widow)[b], %	82/12/2/3	90/5/2/2	0.01	58/15/7/20	60/14/10/17	0.35
Household income (<20/20-40/41-60/>60 thousand €/year), %	20/50/20/10	16/48/25/12	0.37	32/44/16/7	30/48/16/7	0.69
Education (basic/vocational/university)[c], %	35/51/14	35/50/15	0.95	37/48/14	37/52/11	0.28
Employment (working/retired/other), %	21/74/5	15/81/3	0.08	14/82/4	15/82/3	0.88
Perceived health (excellent/pretty good/ good/ satisfactory/ poor), %	0/13/31/55/1	3/25/39/33/1	<0.001	1/16/28/49/7	3/26/38/33/0	<0.001
Type 2 diabetes, %	12	10	0.37	7	4	0.10
Cardiovascular disease, %	43	37	0.09	38	27	0.002
Pulmonary disease, %	30	23	0.06	23	17	0.04
Joint disease, %	51	47	0.28	66	55	0.005
Cancer, %	8	9	0.58	12	9	0.24
Number of diseases (0/1/2/3/4), %	20/31/32/13/2	25/35/30/8/2	0.15	17/39/29/12/3	28/42/23/7/1	0.001
Depression score (range 0-35), points	7 (3-13)	6 (3-10)	0.006	9 (5-14)	8 (4-12)	<0.001
Physician or nurse suggested increasing PA, %	53	36	<0.001	42	36	0.13
Social network score (range 0-17), points	13 (11-15)	14 (12-16)	<0.001	13 (11-15)	14 (12-15)	0.002
Social support score (range 0-8), points	7 (6-8)	8 (6-8)	0.24	8 (6-8)	8 (7-8)	0.25
Alcohol consumption, portions/week	4 (0-10)	4 (0-9)	0.38	0 (0-3)	1 (0-3)	0.05
Smoking (never/past/current), %	29/51/19	39/50/11	0.004	73/19/8	74/20/6	0.54
Diet score (0/1/2/3/4 goals), %	24/29/30/11/5	14/28/30/22/7	<0.001	15/32/24/21/8	14/22/34/20/10	0.86

Data are presented as mean (standard deviation), median (interquartile range) or percentage (%). p-values are for differences between individuals with low PA and those with high PA from independent samples *t*-test, Mann-Whitney U-test, or χ^2-test. Low PA = no moderate-to-vigorous physical activity on a weekly basis, High PA = moderate-to-vigorous physical activity on a weekly basis. [a]Vigorous PA was reported by 18% of active men and by 5% of active women. [b]Married = married or cohabiting, divorced = divorced or separated, [c]Education: basic = middle, elementary or comprehensive school; vocational = vocational school, high school, upper secondary school or higher vocational diploma; university = university graduate.

Table 10. Baseline characteristics of 354 participants with low aerobic exercise level at baseline in aerobic exercise and control groups in Study III

	Aerobic exercise group (n=185)	**Control group (n=169)**	**p-value**
Female, %	50.8	46.2	0.38
Age, years	66.1 (5.3)	65.7 (5.5)	0.60
Body weight, kg	80.8 (15.7)	78.9 (13.6)	0.21
Body height, cm	167.6 (9.8)	166.8 (8.7)	0.44
Body mass index, kg/m^2	28.7 (4.7)	28.3 (4.1)	0.36
Light aerobic exercise, minutes/week	33 (0-120)	44(12-115)	0.22
Moderate-to-heavy aerobic exercise, minutes/week	58 (22-95)	54 (16-100)	0.82
Maximal oxygen consumption, l/min	1.79 (0.5)	1.85 (0.6)	0.30
Maximal oxygen consumption, ml/kg/min	22 (5)	23 (6)	0.05
Married or cohabiting, %	78	79	0.74
Household income (>40 000 €/year), %	26	34	0.11
Working, %	20	23	0.48
Education, years	10 (8-14)	10 (8-13)	0.55
Perceived health (excellent, pretty good/good/satisfactory, poor), %	1/14/38/46/2	1/22/35/41/1	0.29
Type 2 diabetes, %	8	12	0.24
Cardiovascular disease, %	34	34	0.95
Pulmonary disease, %	23	24	0.93
Joint disease, %	60	52	0.13
Cancer, %	12	9	0.28
Number of diseases (0/1/2/3/≥4) %	17/42/29/11/2	25/33/30/10/2	0.30
Disease limiting PA, %	29	21	0.08
Symptoms of depression, %	16	14	0.58
Social network score, points	13 (12-15)	13 (12-15)	0.70
Social support score, points	8 (7-8)	8 (6-8)	0.69
Alcohol consumption, portions/week	1 (0-6)	2 (0-7)	0.17
Smoking (non-smoking/past/current), %	56/34/10	50/39/12	0.53
Diet score (0/1/2/3/4 goals), %	16/34/28/18/5	20/33/27/13/7	0.56
Participated in competitive sports ever, %	32	33	0.80

Data are presented as mean (standard deviation), median (interquartile range) or percentage (%). p-values are for differences between individuals in aerobic exercise group and those in control group from independent samples *t*-test, Mann-Whitney U-test, or χ^2-test.

5.2 CARDIORESPIRATORY FITNESS (STUDY I)

5.2.1 Cardiorespiratory fitness by age and gender

The mean VO_{2max} was 2.17 l/min (26 ml/kg/min) in men and 1.45 l/min (201 ml/kg/min) in women. Women had on average 33.2% (20.8%) lower VO_{2max} than men. The mean test duration after a 3-min warm-up was 8.1 min in men and 5.1 min in women. The mean maximal work rate was 179 W (2.19 W/kg) in men and 118 W (1.71 W/kg) in women. A Borg scale value of 17 (very heavy) indicating perceived exertion was reached by 85% of men and 79% of women. Altogether 98% of the individuals achieved the RER ≥1.1.

The VO_{2max} values of all individuals, with curves representing the cut-offs for the five categories of cardiorespiratory fitness, are presented in Figure 6 separated by gender. The VO_{2max} decline rate with age in ml/kg/min was slightly steeper among men than women in the whole study sample (p=0.18 for interaction between age and gender), but there was no gender difference in the decline rate in the non-diseased individuals (p=0.74). The VO_{2max} decline with age accelerated in the older men (Figure 6), while the decline was less steep in the older women.

Tables 11a and 11b show the cut-off values of VO_{2max}, maximal METs and maximal work rate in the five categories of cardiorespiratory fitness (very low, low, medium, high and very high) among men and women in 2-year age intervals from 57 to 78 years.

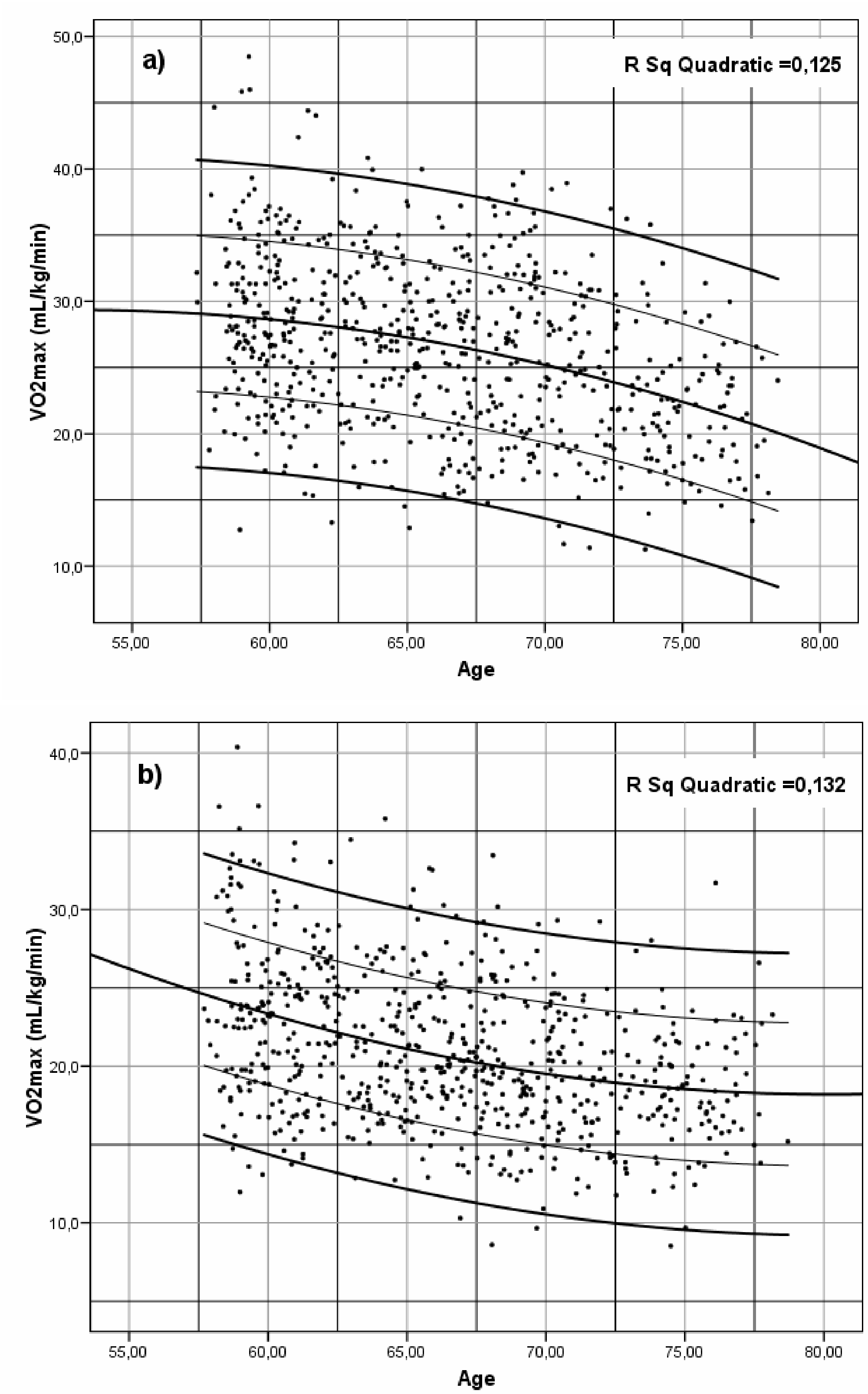

Figure 6. Maximal oxygen consumption (ml/kg/min) by age for (a) all 672 men and (b) all 677 women. Lines from the lowest to the highest represent -2 SD (2.5%), -1SD (16%), mean (50%), +1 SD (84%) and +2 SD (97.5%). SD = standard deviation, R Sq (R^2) Quadratic = proportion of explained variation in quadratic regression. VO_{2max} = maximal oxygen consumption

Table 11a. Categories of cardiorespiratory fitness expressed as maximal oxygen consumption (ml/kg/min), maximal metabolic equivalents (METs) and maximal work rate (W/kg) according to age in men. Values are based on quadratic regressions.

Men Age	**n**		**Very low**	**Low**	**Medium**	**High**	**Very high**
57-58	40	ml/kg/min	<18	18-22	23-34	35-41	>41
		MET	<5.0	5.0-6.5	6.6-9.9	10.0-11.6	>11.6
		W/kg	<1.4	1.4-1.8	1.9-2.9	3.0-3.5	>3.5
59-60	124	ml/kg/min	<17	17-22	23-34	35-40	>40
		MET	<4.9	4.9-6.4	6.5-9.8	9.9-11.5	>11.5
		W/kg	<1.4	1.4-1.8	1.9-2.8	2.9-3.5	>3.5
61-62	61	ml/kg/min	<17	17-21	22-33	34-40	>40
		MET	<4.8	4.8-6.3	6.4-9.7	9.8-11.4	>11.4
		W/kg	<1.3	1.3-1.7	1.8-2.8	2.9-3.4	>3.4
63-64	75	ml/kg/min	<16	16-21	22-33	34-39	>39
		MET	<4.6	4.6-6.2	6.3-9.5	9.6-11.2	>11.2
		W/kg	<1.3	1.3-1.7	1.8-2.7	2.8-3.4	>3.4
65-66	76	ml/kg/min	<16	16-20	21-32	33-39	>39
		MET	<4.4	4.4-5.9	6.0-9.3	9.4-11.0	>11.0
		W/kg	<1.2	1.2-1.6	1.7-2.7	2.8-3.3	>3.3
67-68	83	ml/kg/min	<15	15-19	20-31	32-38	>38
		MET	<4.2	4.2-5.7	5.8-9.1	9.2-10.8	>10.8
		W/kg	<1.1	1.1-1.5	1.6-2.7	2.8-3.2	>3.2
69-70	67	ml/kg/min	<14	14-19	20-30	31-37	>37
		MET	<4.0	4.0-5.5	5.6-8.9	9.0-10.6	>10.6
		W/kg	<1.0	1.0-1.5	1.6-2.5	2.6-3.2	>3.2
71-72	50	ml/kg/min	<13	13-18	19-29	30-36	>36
		MET	<3.7	3.7-5.2	5.3-8.6	8.7-10.3	>10.3
		W/kg	<1.0	1.0-1.4	1.5-2.4	2.5-3.0	>3.0
73-74	46	ml/kg/min	<12	12-17	18-28	29-35	>35
		MET	<3.2	3.2-4.7	4.8-8.3	8.4-10.0	>10.0
		W/kg	<0.8	0.8-1.3	1.4-2.3	2.4-3.0	>3.0
75-76	38	ml/kg/min	<10	10-15	16-27	28-33	>34
		MET	<3.0	3.0-4.5	4.6-7.9	8.0-9.6	>9.6
		W/kg	<0.7	0.7-1.2	1.3-2.1	2.2-2.8	>2.8
77-78	12	ml/kg/min	<9	9-14	15-26	27-31	>32
		MET	<2.6	2.6-4.2	4.3-7.5	7.6-9.2	>9.2
		W/kg	<0.6	0.6-1.0	1.1-2.1	2.2-2.7	>2.7

Table 11b. Categories of cardiorespiratory fitness expressed as maximal oxygen consumption (ml/kg/min), maximal metabolic equivalents (METs) and maximal work rate (W/kg) according to age in women. Values are based on quadratic (ml/kg/min and METs) or linear (W/kg) equations.

Women Age	**n**		**Very low**	**Low**	**Medium**	**High**	**Very high**
57-58	41	ml/kg/min	<16	16-19	20-28	29-34	>34
		MET	<4.5	4.5-5.6	5.7-8.3	8.4-9.6	>9.6
		W/kg	<1.2	1.2-1.5	1.6-2.4	2.5-2.9	>2.9
59-60	93	ml/kg/min	<15	15-18	19-27	28-33	>33
		MET	<4.2	4.2-5.3	5.4-7.9	8.0-9.3	>9.3
		W/kg	<1.1	1.1-1.4	1.5-2.3	2.4-2.9	>2.9
61-62	75	ml/kg/min	<14	14-17	18-26	27-32	>32
		MET	<3.9	3.9-5.1	5.2-7.7	7.8-9.0	>9.0
		W/kg	<1.0	1.0-1.4	1.5-2.3	2.4-2.8	>2.8
63-64	74	ml/kg/min	<13	13-16	17-25	26-31	>31
		MET	<3.6	3.6-4.8	4.9-7.4	7.5-8.8	>8.8
		W/kg	<0.9	0.9-1.3	1.4-2.2	2.3-2.7	>2.7
65-66	83	ml/kg/min	<12	12-15	16-25	26-30	>30
		MET	<3.4	3.4-4.6	4.7-7.2	7.3-8.6	>8.6
		W/kg	<0.9	0.9-1.2	1.3-2.1	2.2-2.6	>2.6
67-68	86	ml/kg/min	<11	11-15	16-24	25-29	>29
		MET	<3.2	3.2-4.4	4.5-7.0	7.1-8.4	>8.4
		W/kg	<0.8	0.8-1.1	1.2-2.0	2.1-2.6	>2.6
69-70	74	ml/kg/min	<11	11-14	15-23	24-29	>29
		MET	<3.1	3.1-4.2	4.3-6.8	6.9-8.2	>8.2
		W/kg	<0.7	0.7-1.0	1.1-1.9	2.0-2.5	>2.5
71-72	53	ml/kg/min	<10	10-14	15-23	24-28	>28
		MET	<2.9	2.9-4.1	4.2-6.7	6.8-8.0	>8.0
		W/kg	<0.6	0.6-1.0	1.1-1.9	2.0-2.4	>2.4
73-74	47	ml/kg/min	<10	10-13	14-22	23-28	>28
		MET	<2.8	2.8-3.9	4.0-6.5	6.6-7.9	>7.9
		W/kg	<0.6	0.6-0.9	1.0-1.8	1.9-2.3	>2.3
75-76	39	ml/kg/min	<10	10-13	14-22	23-28	>28
		MET	<2.7	2.7-3.9	4.0-6.5	6.6-7.8	>7.8
		W/kg	<0.5	0.5-0.8	0.9-1.7	1.8-2.3	>2.3
77-78	12	ml/kg/min	<9	9-13	14-22	23-27	>27
		MET	<2.6	2.6-3.8	3.9-6.4	6.5-7.8	>7.8
		W/kg	<0.4	0.4-0.7	0.8-1.6	1.7-2.2	>2.2

To enable an easier comparison to other studies, Table 12 shows the equations for VO_{2max} decline with age, derived from linear regression models, and the percentual reduction by year of age in all men and women and in non-diseased men and women.

Table 12. Linear equations and calculated percentual age-related decrement in maximal oxygen consumption in all men and women and in non-diseased men and women

	l/min	**%/year**	**ml/kg/min**	**%/year**
All men (n=672)	5.29-0.047*age	2.3	53.1-0.40*age	1.6
All women (n=677)	3.26-0.027*age	1.9	42.8-0.33*age	1.6
Non-diseased men (n=117)	4.85-0.039*age	1.8	56.7-0.42*age	1.5
Non-diseased women (n=112)	3.48-0.031*age	2.3	52.5-0.45*age	2.1

Non-diseased: Individuals without cardiovascular disease, pulmonary disease, joint disease, diabetes, impaired glucose regulation, metabolic syndrome or cancer.

5.2.2 Other correlates of cardiorespiratory fitness

In men, daily smoking (10.4% lower than nonsmoking, p=0.001), use of β-blockers (16% lower than no use, $p<0.001$) and waist circumference (standardized regression coefficient β=-0.525, $p<0.001$) were inversely associated and moderate-to-vigorous PA (β=0.330, $p<0.001$) was positively associated with VO_{2max} (ml/kg/min). In women, use of β-blockers (15% lower than no use, $p<0.001$) and waist circumference (β=-0.506, $p<0.001$) were inversely associated and moderate-to-vigorous PA (β=0.290, $p<0.001$) was positively associated with VO_{2max}.

In men, those who had two diseases had a 14% lower VO_{2max} ($p<0.001$) and those with three or more diseases had a 24% lower VO_{2max} ($p<0.001$) than those who had no diseases. In women, the respective numbers were 15% ($p<0.001$) and 23% ($p<0.001$). Disease combinations that were associated with the lowest VO_{2max} were metabolic syndrome and joint disease, metabolic syndrome and diabetes or impaired glucose regulation, and joint disease and cardiovascular disease with a 20%, 19% and 15% decrement in VO_{2max} (ml/kg/min), respectively. The most common combinations of two diseases were joint disease and cardiovascular disease (n=70), respiratory and joint disease (n=60), and joint disease and diabetes or impaired glucose regulation (n=56). Individuals with one disease did not have statistically significantly lower VO_{2max} than those with no disease, except women with metabolic syndrome, who had 17% lower (p=0.008) VO_{2max} (ml/kg/min) than women with no disease.

The association between the number of diseases and VO_{2max} was weaker in men and women when VO_{2max} was expressed in l/min or when the data were adjusted for waist circumference. Adjustment for moderate-to-vigorous PA slightly weakened the association in men and women, whereas daily smoking or use of b-blockers had no effect on the association in either men or women.

5.3 CORRELATES OF LOW PHYSICAL ACTIVITY AT BASELINE (STUDY II)

Altogether, 245 (39%) men and 318 (48%) women reported no moderate or vigorous PA assessed with DR'S EXTRA PA interview, and were defined as having low PA in Study II. Women had a 1.5 (95% CI 1.2-1.8; p=0.001) times odds of low PA compared with men without adjustment for confounding factors. The association remained similar after adjustment for all 10 independent correlates of low PA shown in Table 13 (OR 1.4 [95% CI 1.1-1.8]), p=0.006). One standard deviation increase in age (5.3 years) was associated with 20% higher odds for low PA in women without adjustment, but the association was not independent of other correlates of low PA (Table 13). In men, age was not associated with low PA without adjustment. However, in the adjusted model one standard deviation increase in age (5.4

years) was associated with 27% higher odds of low PA. Divorced or separated men had 2.6 times the odds of low PA than married men without adjustment, and the association remained similar after adjustment for other correlates of low PA (Table 13). However, marital status was not associated with the odds of low PA in women without adjustment or after adjustment for other correlates of low PA. Gender modified the association between marital status and the odds of low PA without adjustment (p=0.02 for interaction) and after adjustment for other correlates of low PA (p=0.02 for interaction). Retired men had 30% lower odds of low PA than working men, and the relationship even strengthened after adjustment for other correlates of low PA (Table 13). However, labor market position was not related to the risk of low PA in women.

Poor or satisfactory perceived health and symptoms of depression (depression score ≥16) were associated with increased odds of low PA in both genders without adjustment (Table 13). A high body mass index and the suggestion of a physician or nurse to increase PA in men, and a high body mass index, cardiovascular, pulmonary, or joint disease, and having at least one chronic disease in women were associated with higher odds of low PA without adjustment (Table 13). After adjustment for all correlates of low PA, satisfactory or poor perceived health and a high body mass index were related to higher odds of low PA in both genders. In women, cardiovascular disease and symptoms of depression were also associated with higher odds of low PA after adjustment (Table 13). Gender did not modify the associations between health-related correlates of low PA and the odds of low PA, except that the suggestion of a physician or nurse to increase PA was associated with low PA in men but not in women (p=0.04 for interaction).

In men, having a weak (0 to 12) or medium (13 to 14) social network score, being a current smoker, and having medium (1 to 2) or low (0) diet score were associated with higher odds of low PA, and consuming 1 to 4 portions of alcohol per week was related to a lower odds of low PA (Table 13). Having a weak or medium social network score and having a low diet score in men were associated with a higher risk of low PA after adjustment for other correlates of low PA in the stepwise model (Table 13). In women, a weak social network score was associated with higher odds of low PA without adjustment, but not after adjustment for other correlates. Gender modified the association between diet score and the odds of low PA without adjustment (p=0.006 for interaction) and after adjustment for other correlates of low PA (p=0.05 for interaction).

Table 13. Odds ratios for low physical activity in 1303 men and women

	Men (n=636)				Women (n=667)			
	Unadjusted	**p-value**	**Adjusted[a]**	**p-value**	**Unadjusted**	**p-value**	**Adjusted[b]**	**p-value**
Demographic factors								
Age, years[c]	1.02 (0.87-1.20)	0.80	1.27 (1.02-1.56)	0.03	1.24 (1.07-1.45)	0.006		
Marital status								
Married	1		1		1			
Divorced	2.62(1.45-4.74)	0.001	2.55 (1.33-4.87)	0.005	1.10 (0.70-1.72)	0.68		
Unmarried or widow	1.26 (0.61-2.63)	0.53	1.13 (0.52-2.49)	0.75	1.04 (0.73-1.48)	0.84		
Household income, €/year								
>60000	1				1			
20001-60000	1.17 (0.88-1.80)	0.57			0.91 (0.49-1.67)	0.75		
<20000	1.51 (0.81-2.81)	0.20			1.05 (0.55-1.99)	0.89		
Education[d]								
University	1				1			
Vocational	1.08 (0.67-1.73)	0.75			0.68 (0.42-1.10)	0.22		
Basic	1.05 (0.66-1.78)	0.86			0.74 (0.44-1.21)	0.23		
Labor market position								
Working	1		1		1			
Retired	0.66 (0.43-0.99)	0.05	0.41 (0.24-0.71)	0.001	1.05 (0.68-1.63)	0.81		
Other[e]	1.07 (0.45-2.54)	0.89	1.07 (0.41-2.79)	0.89	1.25 (0.54-2.66)	0.62		
Health-related factors								
Perceived health								
Excellent, pretty good	1		1		1		1	
Good	1.65 (1.03-2.66)	0.04	1.62 (0.97-2.70)	0.07	1.26 (0.82-1.93)	0.29	1.11 (0.72-1.72)	0.64
Satisfactory, poor	3.45 (2.19-5.46)	<0.001	2.76 (1.64-4.64)	<0.001	2.81 (1.88-4.22)	<0.001	2.10 (1.38-3.23)	0.001
Body mass index, kg/m^2 [f]	1.59 (1.34-1.89)	<0.001	1.38 (1.14-1.67)	0.001	1.44 (1.22-1.69)	<0.001	1.34 (1.13-1.58)	0.001
Type 2 diabetes	1.26 (0.76-2.09)	0.37			1.74 (0.89-3.39)	0.11		
Cardiovascular disease	1.32 (0.96-1.83)	0.09			1.66 (1.20-2.31)	0.002	1.43 (1.02-2.02)	0.04
Pulmonary disease	1.41 (0.99-2.04)	0.06			1.50 (1.01-2.20)	0.04		
Joint disease	1.19 (0.87-1.64)	0.28			1.57 (1.15-2.15)	0.005		
Cancer	0.85 (0.48-1.50)	0.58			1.34 (0.82-2.21)	0.24		
Number of diseases								
0	1				1			
1	1.09 (0.70-1.69)	0.70			1.54 (1.02-2.32)	0.04		
≥2	1.47 (0.97-2.22)	0.07			2.38 (1.57-3.62)	<0.001		
Depression Score, points								
<16	1				1		1	
≥16	1.75 (1.06-2.89)	0.03			2.13 (1.37-3.29)	0.001	1.61 (1.01-2.54)	0.04
Physician or nurse suggested increasing PA	2.05 (1.48-2.84)	<0.001	1.47 (1.02-2.12)	0.04	1.27 (0.93-1.74)	0.13		

Table 13 continues

Table 13 continues

	Men				Women			
	Unadjusted	**p-value**	**Adjusted[a]**	**p-value**	**Unadjusted**	**p-value**	**Adjusted[b]**	**p-value**
Lifestyle-related factors								
Social network, points								
15-17	1		1		1			
13-14	1.60 (1.06-2.42)	0.03	1.54 (0.99-2.42)	0.06	1.28 (0.87-1.88)	0.21		
2-12	1.94 (1.33-2.82)	0.001	1.70 (1.13-2.56)	0.01	1.82 (1.26-2.63)	0.001		
Social support, points								
8	1				1			
7	0.88 (0.55-1.40)	0.58			0.98 (0.64-1.49)	0.92		
0-6	1.24 (0.87-1.77)	0.23			1.24 (0.86-1.79)	0.86		
Smoking								
Never	1				1			
Past smoker	1.34 (0.94-1.92)	0.11			0.97 (0.66-1.43)	0.89		
Current smoker	2.29 (1.39-3.78)	0.001			1.40 (0.76-2.58)	0.29		
Alcohol, portions/week								
0	1				1			
1-4	0.63 (0.40-0.99)	0.04			0.75 (0.53-1.06)	0.10		
≥5	1.02 (0.71-1.49)	0.90			0.69 (0.45-1.05)	0.09		
Diet Score, goals								
3-4	1		1		1			
1-2	1.71 (1.13-2.58)	0.01	1.27 (0.81-1.99)	0.30	1.10 (0.73-1.47)	0.83		
0	2.99 (1.78-5.00)	<0.001	1.99 (1.14-3.46)	0.02	1.14 (0.70-1.86)	0.59		

Numbers are odds ratios (95% confidence intervals) from binary logistic regression analyses.
[a]Odds ratios (95% confidence intervals) are shown only for variables selected after forward stepwise logistic regression in men including all variables in Table 13.
[b]Odds ratios (95% confidence intervals) are shown only for variables selected after forward stepwise logistic regression in women including all variables in Table 13.
[c]Odds ratios for one standard deviation (SD) increase in age: 1 SD = 5.4 years for men, 5.3 years for women.
[d]Education: basic =middle, elementary or comprehensive school, vocational = vocational school, high school, upper secondary school or higher vocational diploma, university = university graduate
[e]Unemployed, job-alternation leave.
[f]Odds ratios for one SD increase in body mass index: 1 SD = 3.8 kg/m^2 for men, 5.0 kg/m^2 for women.

5.4 INCREASE AND MAINTAINED INCREASE IN AEROBIC EXERCISE (STUDY III)

Altogether, 111 (60%) of the participants in the aerobic exercise group had increased moderate-to-heavy aerobic exercise by at least 60 minutes per week assessed at two years and 102 (55%) assessed at four years (Figure 7). The corresponding numbers of participants (proportions) in the control group were 64 (38%) and 68 (40%). Altogether, 74 (40%) participants in the aerobic exercise group and 36 (21%) participants in the control group had maintained increased aerobic exercise assessed at two and four years. Thus, 5.3 (95% CI 3.6-10.9) participants had to be treated with an aerobic exercise intervention for one individual to maintain increased moderate-to-heavy aerobic exercise of at least 60 minutes per week assessed at two and four years. The corresponding NNT value for all 467 randomized participants including dropouts and those with missing data was 6.2 (95% CI 4.2-11.9).

Participants in the aerobic exercise group had increased moderate-to-heavy aerobic exercise more than those in the control group assessed at two years (111 vs. 63 minutes/week, p=0.001) and four years (110 vs. 67 minutes/week, p=0.02) (Table 14). Participants who had maintained the increased levels of aerobic exercise in either study group had increased their moderate-to-heavy aerobic exercise on average by 194 minutes/week during two years and by 211 minutes/week during four years (Table 15).

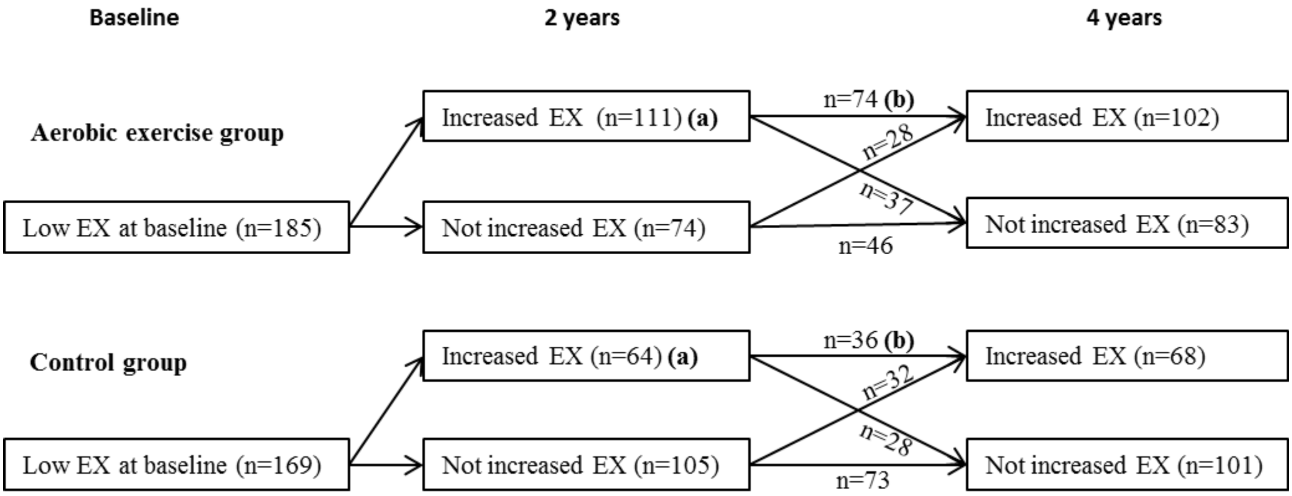

Figure 7. Increase in aerobic exercise of at least 60 minutes per week between baseline and two years (a) and maintained increase in aerobic exercise between two and four years (b) in the aerobic exercise and control groups. EX = aerobic exercise.

5.5 CHANGES IN AEROBIC EXERCISE IN RELATION TO CHANGES IN CARDIORESPIRATORY FITNESS

VO_{2max} decreased less among participants in the aerobic exercise group than among those in the control group assessed at four years (-0.15 vs -0.21 liters/minute, p=0.01) (Table 14). Participants who had maintained the increased level of aerobic exercise did not differ in VO_{2max} change from those who had not increased or maintained the increased level at two years (p=0.10) or four years (p=0.13) (Table 15).

Table 14. Change in aerobic exercise and maximal oxygen consumption in the aerobic exercise and control groups

	Aerobic exercise group	Control group	p-value
Moderate-to-heavy aerobic exercise, minutes/week			
Change (2-year follow-up – baseline)	111 (156)	63 (115)	0.001
Change (4-year follow-up – baseline)	110 (180)	67 (151)	0.02
Light aerobic exercise, minutes/week			
Change (2-year follow-up – baseline)	-30 (130)	-19 (201)	0.54
Change (4-year follow-up – baseline)	-14 (167)	-7 (224)	0.75
Maximal oxygen consumption, l/min			
Change (2-year follow-up – baseline)	-0.030 (0.21)	-0.055 (0.20)	0.26
Change (4-year follow-up – baseline)	-0.15 (0.21)	-0.21 (0.27)	0.01

Data are presented as mean (standard deviation). p-values are for differences between groups from independent samples t-test.

Table 15. Changes in aerobic exercise and maximal oxygen consumption in participants who maintained increased exercise and others

	Participants who maintained increased exercise[a] n=110	Others n=244	p-value
Moderate-to-heavy aerobic exercise, minutes/week			
Change (2-year follow-up – baseline)	194 (153)	41 (102)	<0.001
Change (4-year follow-up – baseline)	211 (194)	35 (120)	<0.001
Light aerobic exercise, minutes/week			
Change (2-year follow-up – baseline)	-40 (140)	-17 (178)	0.23
Change (4-year follow-up – baseline)	-9 (168)	-12 (208)	0.89
Maximal oxygen consumption, l/min			
Change (2-year follow-up – baseline)	-0.02 (0.21)	-0.05 (0.20)	0.10
Change (4-year follow-up – baseline)	-0.15 (0.22)	-0.19 (0.26)	0.13

Data are presented as mean (standard deviation). p-values are for differences between groups from independent samples t-test.
[a]Participants who maintained increased aerobic exercise were defined as those who had increased aerobic exercise by 60 minutes/week or more assessed at two years and had maintained the increased aerobic exercise at four years.

In men, two-year change in moderate-to-heavy aerobic exercise was not associated with two-year change in VO_{2max} expressed in l/min (linear regression coefficient β=0.02, p=0.79), but was positively associated with change in VO_{2max} expressed in ml/kg/min (β=0.16, p=0.04). In men, four-year change in moderate-to-heavy aerobic exercise was positively associated with four-year change in VO_{2max} expressed in l/min (β=0.18, p=0.02) and in ml/kg/min (β=0.20, p=0.008).

In women, two-year change in moderate-to-heavy aerobic exercise was not associated with two-year change in VO_{2max} expressed in l/min (β=0.04, p=0.61) or in ml/kg/min (β=0.06, p=0.44). In women, four-year change in moderate-to-heavy aerobic exercise was not associated with four-year change in VO_{2max} expressed in l/min (β=0.02, p=0.79) or in ml/kg/min (β=0.05, p=0.57).

5.6 MODERATORS OF THE EFFECTIVENESS OF AEROBIC EXERCISE INTERVENTION AT INCREASING AND MAINTAINING INCREASE IN AEROBIC EXERCISE (STUDY III)

Individuals in the aerobic exercise group were 2.5 (95% CI 1.6-3.8) times as likely to increase aerobic exercise by at least 60 minutes during two years as those in the control group. The aerobic exercise intervention was effective at increasing the level of aerobic exercise during two years in all subgroups of baseline characteristics, except among those who were normal weight (OR 1.5 [95% CI 0.6-3.6], p=0.42), had a pulmonary disease (1.8 [0.7-4.3], p=0.40), cancer (3.6 [0.9-14.7], p=0.08), or 2 to 5 diseases (1.8 [0.9-3.5], p=0.08), were current smokers (1.4 [0.4-4.8], p=0.86) or had high levels of light aerobic exercise at baseline (1.7 [0.9-3.0], p=0.08). Only the interaction between light aerobic exercise and study group was statistically significant (p=0.04).

Participants in the aerobic exercise group were 2.5 [95% CI 1.5-3.9] times as likely to maintain the increased moderate-to-heavy aerobic exercise from two to four years as those in the control group (Table 16). The aerobic exercise intervention was effective at maintaining increased aerobic exercise in most subgroups of the baseline characteristics (Table 16). The intervention was effective at maintaining increased aerobic exercise among individuals aged less than 68.5 years but not among older individuals (p=0.02 for interaction). Moreover, the intervention was more effective at maintaining increased aerobic exercise among individuals who were working than those who were not working (p=0.05 for interaction), among individuals with symptoms of depression than those without such symptoms (p=0.05 for interaction) and among past smokers than non-smokers or current smokers (p=0.02 for interaction). The intervention was also more effective at maintaining increased aerobic exercise among individuals with low levels of light aerobic exercise at baseline than those with high levels (p=0.02 for interaction).

5.7 ADVERSE EVENTS

Three adverse events (one angina pectoris during exercise test, one benign amnestic episode after exercise test, and one hypoglycemic attack during an interview in a participant with type 2 diabetes) were recorded during the four years of follow up among the 354 participants in Study III. No serious musculoskeletal injuries due to exercise training were recorded. The research physicians judged that it was unlikely that any of these events were caused by the interventions, and these events did not lead to the exclusion of the participants.

Table 16. Numbers of participants who maintained increased moderate-to-vigorous aerobic exercise and odds ratios of maintaining increased moderate-to-vigorous aerobic exercise according to baseline characteristics

	Numbers (%) of participants who maintained increase in aerobic exercise		**Odds ratios (95% confidence intervals) for maintained increase in aerobic exercise in aerobic exercise group compared to control group**	**p-value for association**	**p-value for interaction**
	Aerobic exercise group	**Control group**			
All	74/185 (40.0)	36/169 (21.3)	2.5 (1.5-3.9)	<0.001	
Demographic characteristics					
Gender					
Men	38/91 (41.8)	16/91 (17.6)	3.4 (1.7-6.6)	<0.001	0.20
Women	36/94 (38.3)	20/78 (25.6)	1.8 (0.9-3.5)	0.08	
Age, years					
≤62.1	27/60 (45.0)	9/58 (15.5)	4.5 (1.9-10.7)	0.001	0.02
62.2-68.4	32/64 (50.0)	13/54 (24.1)	3.2 (1.4-7.0)	0.005	
≥68.5	15/61 (24.6)	14/57 (24.6)	1.0 (0.4-2.3)	1.00	
Marital status					
Married	57/144 (39.6)	29/134 (21.6)	2.4 (1.4-4.0)	0.001	0.77
Non-married	17/41 (41.5)	7/35 (20.0)	2.8 (1.0-8.0)	0.05	
Household income, €/year					
≤40 000	54/137 (39.4)	24/112 (21.4)	2.4 (1.4-4.2)	0.003	0.83
>40 000	20/48 (41.7)	12/57 (21.1)	2.7 (1.1-6.3)	0.02	
Education, years					
≤10 years	38/95 (40.0)	20/93 (21.5)	2.4 (1.3-4.6)	0.007	0.96
>10 years	36/90 (40.0)	16/76 (21.1)	2.5 (1.2-5.0)	0.01	
Working status					
Working	21/36 (58.3)	7/38 (18.4)	6.2 (2.2-17.8)	0.001	0.05
Not working	53/149 (35.6)	29/131 (22.1)	1.9 (1.1-3.3)	0.01	
Health characteristics					
Body mass index, kg/m^2					
<25	13/38 (34.2)	10/37 (27.0)	1.4 (0.5-3.8)	0.50	0.13
25.0-29.9	33/85 (38.8)	17/81 (21.0)	2.4 (1.2-4.8)	0.01	
≥30.0	28/62 (45.2)	9/51 (17.6)	3.8 (1.6-9.2)	0.003	
Maximal oxygen consumption, (l/min)[a]					
High	38/91 (41.8)	21/88 (23.9)	2.3 (1.2-4.4)	0.01	0.71
Low	36/94 (38.3)	15/81 (18.5)	2.7 (1.4-5.5)	0.005	

Table 16 continues

Table 16 continues

	Numbers (%) of participants who maintained increase in aerobic exercise		Odds ratios (95% confidence intervals) for maintained increase in aerobic exercise in aerobic exercise group compared to control group	p-value for association	p-value for interaction
	Aerobic exercise group	**Control group**			
Perceived health					
Good-to-excellent	46/97 (47.4)	23/98 (23.5)	2.9 (1.6-5.4)	0.001	0.49
Satisfactory-to-poor	28/88 (31.8)	13/58 (18.3)	2.1 (1.0-4.4)	0.06	
Type 2 diabetes					
Yes	5/15 (33.3)	0/20 (0.0)	-		-
No	69/170 (40.6)	36/149 (24.2)	2.1 (1.3-3.5)	0.002	
Cardiovascular disease					
Yes	23/63 (36.5)	12/57 (21.1)	2.2 (1.0-4.9)	0.07	0.70
No	51/122 (41.8)	24/112 (21.4)	2.6 (1.5-4.7)	0.001	
Pulmonary disease					
Yes	9/43 (20.9)	7/40 (17.5)	1.2 (0.4-3.7)	0.69	0.17
No	65/142 (45.8)	29/129 (22.5)	2.9 (1.7-4.9)	<0.001	
Joint disease					
Yes	34/101 (30.6)	16/88 (18.2)	2.0 (1.0-3.9)	0.05	0.23
No	40/74 (54.1)	20/81 (24.7)	3.6 (1.8-7.1)	<0.001	
Cancer					
Yes	6/23 (26.1)	4/15 (26.7)	1.0 (0.2-4.2)	0.97	0.19
No	68/162 (42.0)	32/154 (20.8)	2.8 (1.7-4.5)	<0.001	
Number of chronic diseases					
0	16/32 (50.0)	12/37 (32.4)	2.1 (0.8-5.5)	0.141	0.75
1	36/76 (47.4)	12/62 (19.4)	3.8 (1.7-8.1)	0.001	
2-5	22/77 (28.6)	12/70 (17.1)	1.9 (0.9-4.3)	0.10	
Symptoms of depression					
Yes (≥16 points)	15/29 (51.7)	2/23 (8.7)	11.3 (2.2-57.0)	0.003	0.05
No (<16 points)	59/156 (37.8)	34/146 (23.3)	2.0 (1.2-3.3)	0.007	
Individuals with a disease limiting PA					
Yes	23/53 (43.4)	8/35 (22.9)	2.6 (1.0-6.7)	0.05	0.88
No	51/132 (38.6)	28/134 (20.9)	2.4 (1.4-4.1)	0.002	

Table 16 continues

Table 16 continues

	Numbers (%) of participants who maintained increased aerobic exercise		Odds ratios (95% confidence intervals) for maintained increase in aerobic exercise in aerobic exercise group compared to control group	p-value for association	p-value for interaction
	Aerobic exercise group	**Control group**			
Social and lifestyle characteristics					
Social network score, points					
Low (≤13)	39/95 (41.1)	14/85 (16.5)	3.5 (1.7-7.1)	<0.001	0.16
High (≥14)	35/90 (38.9)	22/84 (26.2)	1.8 (0.9-3.4)	0.08	
Social support score, points					
Low (0-7)	29/74 (39.2)	17/68 (25.0)	1.9 (0.9-4.0)	0.07	0.39
High (8)	45/111 (40.5)	19/101 (18.8)	2.9 (1.6-5.5)	0.001	
Alcohol consumption, portions/week					
Low (0-1)	35/94 (37.2)	19/76 (25.0)	1.8 (0.9-3.5)	0.09	0.19
High (>1)	39/91 (42.9)	17/93 (18.3)	3.4 (1.7-6.6)	<0.001	
Smoking					
Non-smoker	39/103 (37.9)	23/84 (27.4)	1.6 (0.9-3.0)	0.13	0.06[b]
Past smoker	31/63 (49.2)	10/65 (15.4)	5.3 (2.3-12.3)	<0.001	0.02[c]
Current smoker	4/19 (21.1)	3/20 (15.0)	1.5 (0.3-7.9)	0.62	0.55[d]
Diet score, goals					
Low (0-1)	31/91 (34.1)	18/90 (20.0)	2.1 (1.1-4.1)	0.04	0.50
High (2-4)	43/94 (45.7)	18/79 (22.8)	2.9 (1.5-5.6)	0.002	
Light exercise, minutes/week					
Low (<37)	42/97 (43.3)	10/74 (13.5)	4.9 (2.2-10.6)	<0.001	0.02
High (≥37)	32/88 (36.4)	26/95 (27.4)	1.5 (0.8-2.8)	0.19	
Moderate-to-heavy exercise, minutes/week					
Low (≤57.6)	37/92 (40.2)	14/87 (16.1)	3.5 (1.7-7.1)	0.001	0.17
High (>57.6)	37/93 (39.8)	22/82 (26.8)	1.8 (0.9-3.4)	0.07	
Individuals who had ever participated in competitive sports					
Yes	25/59 (42.4)	8/56 (14.3)	4.4 (1.8-11.0)	0.001	0.13
No	49/126 (38.9)	28/113 (24.8)	1.9 (1.1-3.4)	0.02	
Individuals who participated in diet intervention					
Yes	35/95 (36.8)	18/81 (22.2)	2.0 (1.0-4.0)	0.04	0.44
No	39/90 (43.3)	18/88 (20.5)	3.0 (1.5-5.8)	0.001	

Odds ratios (95% confidence intervals) from unadjusted logistic regression models. Participants who maintained increased aerobic exercise were defined as those who had increased aerobic exercise by 60 minutes/week or more assessed at two years and had maintained the increased aerobic exercise at four years.
[a]The participants were divided into two age-, tertile- and gender-specific groups of maximal oxygen consumption at median.
[b-d]Interaction analyses were performed with dummy variables: [b]non-smokers vs. past smokers and current smokers; [c]past smokers vs. non-smokers and current smokers; [d]current smokers vs. non-smokers and past smokers. PA= physical activity

6 Discussion

6.1 SUMMARY OF THE MAIN FINDINGS

The purposes of this thesis were to provide reference values for measures of cardiorespiratory fitness, to explore correlates of low PA, and to identify moderators of the effectiveness of an aerobic exercise intervention at increasing moderate-to-heavy aerobic exercise and maintaining increased exercise among older adults.

I Clinically valuable age and sex-specific reference values of cardiorespiratory fitness based on variable distribution and non-linear regression models of VO_{2max}, maximal METs and maximal work rate were presented. For easier comparison with others studies, linear models were also presented. Cross-sectional decrement of VO_{2max} was about 15% per decade and the age-related decrement was slightly steeper in men than in women. The number of chronic diseases was inversely associated with VO_{2max} in men and women.

II Men and women had partly different correlates of low PA. Satisfactory or poor perceived health and a high body mass index were independently associated with low PA in both genders. In men, advanced age, being divorced or separated, still working, having a weak social network, poor diet, and health professional's suggestion to increase PA were also associated with low PA. In women, cardiovascular disease and symptoms of depression were also associated with low PA.

III Individuals in the aerobic exercise group were 2.5 times as likely to maintain increased moderate-to-heavy aerobic exercise as those in the control group. The intervention was particularly effective at maintaining increased exercise among individuals who were less than 68.5 years of age, had not yet retired, had symptoms of depression, were past smokers or had low levels of light aerobic exercise at baseline. The change in aerobic exercise was positively associated with change in VO_{2max} in men but not in women.

6.2 METHODOLOGICAL ASPECTS

6.2.1 Study population and design

In Studies I-II the study population was formed by the baseline data of the DR's EXTRA Study. The study population was a representative sample of older men and women living in the City of Kuopio, who were randomly selected from the population register in 2002. Originally, about two thirds of the invited individuals expressed their willingness to participate in the intervention study (Figure 3). The only exclusion criteria were conditions that would have prevented safe participation in exercise training, and malignant diseases and other conditions preventing co-operation or follow-up as judged by the research physicians. The exclusion criteria resulted in a study population with varying health conditions and lifestyles. However, over the run-in period and the baseline examinations in 2005-2006, about one quarter of individuals willing to participate were lost due to reasons related to diseases, motivation or relocation. Therefore, individuals in the final study population were healthier and more motivated to participate in the lifestyle study than those who were lost during the run-in phase and before randomization. Thus, the current study sample may include a smaller proportion of individuals with low PA than the original population. This should be taken into account in the interpretation of the results. However, the study population can be considered to represent older adults in Eastern Finland. The high number of individuals studied and the wide age range of both genders provided a unique dataset to study the levels of cardiorespiratory fitness and PA separately in aging men and women, and to investigate whether gender modified the associations of targeted variables and low PA. However, it was not possible to draw conclusions about the temporal order or causality of the relationships due to the cross-sectional study design.

Study III was based on a subsample of the participants of the DR's EXTRA Study including those with insufficient aerobic exercise at baseline who were randomized into the reference group, the diet group, the aerobic exercise group or the combined aerobic exercise and diet group. The random allocation into the study group including aerobic exercise counseling or the study group not including it provided a great opportunity to study the effectiveness of the aerobic exercise intervention at increasing and maintaining increased moderate-to-vigorous aerobic exercise. The number of participants was also large enough to explore the effectiveness of the aerobic exercise intervention in subgroups of demographic, health and lifestyle variables. The long duration of the intervention and the assessment of aerobic exercise at 2-year and 4-year follow-ups provided an opportunity to study long-term changes in aerobic exercise. To the author's knowledge, this was the first long-term randomized controlled exercise intervention study in a population-based sample of older adults exploring the baseline moderators of increase in aerobic exercise and maintained increase in aerobic exercise.

Only 15 percent of individuals selected for Study III dropped out during the four years. Individuals who dropped out or had missing data had poorer health at baseline compared to those who completed the study. However, dropout rate and reasons were similar in the aerobic exercise and control groups and the final study groups were similar in their baseline characteristics (Table 9).

6.2.2 Assessment of cardiorespiratory fitness

The direct measurement of VO_{2max} during an incremental exercise stress test is the most accurate method to study maximal cardiorespiratory fitness (29). It overcomes the sources of error in non-direct and submaximal tests, e.g. individual variation in movement economy, heart rate responses and energy metabolism (25). Oxygen consumption was measured by the breath-by-breath method, which is an accurate method provided that calibration is performed carefully (29). This method can follow fast changes in oxygen consumption and is suitable for incremental tests with short stages (29).

In the present study, relatively small work rate increases per minute were used to allow a precise definition of the maximal work rate. Larger work rate increases could lead to premature test termination due to insufficient muscle power, abnormally elevated systolic blood pressure or other reasons unrelated to cardiorespiratory fitness (30,37). The recommended test duration to test VO_{2max} on a cycle ergometer in adults is between seven and 26 minutes (37). In the present study, not all individuals achieved the recommended test time and the true VO_{2max}. A plateau in oxygen consumption while the work rate is still increasing indicates that the true VO_{2max} has been reached (29). However, reaching the plateau in aging individuals is rare (29). The RER and perceived exertion were used as indicators of maximality of the exercise test. Because of the challenging definition of maximality of oxygen consumption, the expression of symptom-limited VO_{2max} is used.

An electrically braked cycle ergometer is the preferred device for exercise testing in clinical practice due to the accurate quantification of work rate, the possibility to monitor cardiac function and blood pressure simultaneously with minimal movement artifacts, and due to price and size efficiency (50). Exercise is also less weight bearing and safer on a cycle ergometer than on a treadmill (29). A limitation of cycle ergometer tests is that individuals who rarely ride a bicycle may terminate the test because of local muscle weakness before the VO_{2max} has been reached (212). This partly explains the 10-15% lower VO_{2max} on a cycle ergometer than on a treadmill observed in young-to-middle-aged adults (213-215) and healthy or diseased older adults (30,212). However, with small increases in work rate, such as in the present study, the impact of muscle weakness on the results may have been reduced (25,30,37). There is some evidence that alternative test protocols such as self-paced increments during the test and decremental or intermittent test protocols can yield higher measured values of VO_{2max} compared to conventional incremental protocols in trained and untrained subjects (216).

6.2.3 Assessment of physical activity

Two different tools to assess PA or exercise were used: DR's EXTRA PA interview assessed leisure-time PA during the previous month and DR's EXTRA PA questionnaire assessed different PAs during the past 12 months in detail. Both tools produced frequencies and mean durations of PA sessions at different intensity levels from which PA energy expenditures could be computed. DR's EXTRA PA interview was simpler to perform and analyze and was suitable for categorizing PA as was done in Study II. DR's EXTRA PA questionnaire, on the other hand, was more detailed and provided the possibility to explore certain components of PA such as aerobic exercise separately. It also provided data over a 12-month period, which was important when studying changes during a long exercise intervention.

There is no gold standard method to assess moderate-to-heavy PA; while self-reporting is prone to social desirability and recall bias, many objective measures cannot register all types of exercise like swimming and bicycling (100). In addition, using objective PA measures for a long duration is challenging for subjects and researchers (112). Self-reporting has shown moderate associations to objective measures (100,111). Increases in PA during an intervention may be larger when assessed with self-reports compared to objective measures due to social desirability, or smaller due to increased awareness and accuracy in reporting (217).

Recommendations for adults and older adults emphasize at least a moderate intensity of PA in order to enhance health (99,218). Therefore, all PA variables in the present studies were based on either reported total duration or calculated energy expenditure of at least moderate intensity PA or aerobic exercise. At least moderate intensity PA and aerobic exercise, but not light PA or aerobic exercise, correlated positively with objectively measured VO_{2max}, which supports the selection of at least moderate intensity PA and exercise as an outcome variable.

In Study II, the definition of low PA was the same as the definition of inactivity in the Physical Activity Guidelines for Americans (99). However, individuals with low PA reported a reasonable amount of light PA that exceeded the energy expenditure of daily chores but not moderate intensity level. For example, walking slowly to and from a shop was included in light PA if the continuous duration of walking exceeded 15 minutes. It is possible that for the oldest or least fit individuals who reported light intensity PA based on the pace of their PA, the relative intensity was underestimated. However, although light and non-exercise PA may also produce health benefits (2,219,220)

, individuals who have no moderate-to-vigorous PA are generally considered to be at an increased risk of developing chronic diseases (221).

In Study III, the individuals with <150 minutes of at least moderate intensity aerobic exercise and <75 minutes of heavy exercise per week were considered insufficiently active based on current recommendations and hence were selected (99,218). In addition to aerobic PA it is recommended to do strength, balance and flexibility exercises (99,218).

In study III, increase in aerobic exercise rather than the total duration of aerobic exercise or exercise adherence was explored. Previously, baseline levels of PA have been shown to be positively correlated with adherence to exercise interventions (22), which may have confounded the results concerning the predictors of adherence to exercise interventions. From a public health perspective, it is important to investigate factors that explain increased PA and maintained increase in PA, and not only adherence to an exercise intervention, in order to obtain more information about individuals who are most responsive and resistant to exercise interventions. Increase in aerobic exercise by at least 60 minutes per week has previously been defined as a meaningful increase in exercise regarding health (148), and was also used in Study III.

6.2.4 Assessment of other baseline variables

In Studies II and III a large number of correlates of low PA and moderators of the effectiveness of the aerobic exercise intervention at increasing and maintaining increased aerobic exercise were studied. Many of the assessments were detailed and validated including scores for symptoms of depression (209) and social network and support (210,211). Further, diet was assessed with a 4-day food record, which is an accurate and valid method for assessing diet (201) and has rarely been used in large population studies.

6.2.5 Statistical methods

The principal statistical methods used in the present studies were different regression models. To demonstrate the dependency of cardiorespiratory fitness on age, linear, quadratic, cubic and exponential regression models were tested in Study I, and the model with the highest adjusted R^2 was chosen for closer examination. The quadratic model had the highest R^2, and thus explained the highest proportion of variation in VO_{2max} and other measures of cardiorespiratory fitness in most subgroups of gender and health status, indicating that the association between age and cardiorespiratory fitness is not always linear.

In Study II, logistic regression analysis was used to study the odds ratios for low PA. Because many of the independent variables were intercorrelated, stepwise selection was used to find out which variables were the strongest independent correlates of low PA. There are limitations in running regression analysis using stepwise selection and in the interpretation of the results obtained (222). However, the aim of the present study was to highlight the key independent correlates of low PA and not to create a specific prediction model of low PA. The modifying effect of gender on correlates of low PA was studied by adding the interaction term into the regression models. This analysis allows the comparison of associations of low PA with its potential correlates between genders.

In Study III, NNT analysis and logistic regression analysis were used to study the effectiveness of the aerobic exercise intervention at increasing and maintaining increased aerobic exercise in the aerobic exercise group with reference to the control group. Logistic regression analyses were performed on several subgroups of baseline characteristics and interaction analyses were performed to find out which baseline characteristics modified the intervention effect. For statistical analyses, the reference and diet groups were combined into the control group and the aerobic exercise and combined aerobic exercise and diet groups were combined into the aerobic exercise group to increase statistical power. However, the number of individuals with symptoms of depression, type 2 diabetes or cancer was relatively small, which reduced statistical power in the analyses and made it more difficult to draw strong conclusions about the results.

6.3 RESULTS

6.3.1 Cardiorespiratory fitness

The decrement of VO_{2max} expressed in ml/kg/min was about 1.6% per year and 15% per decade in this population sample of men and women including healthy and diseased individuals. The rate of VO_{2max} decline with age was slightly larger in the present study than in other cross-sectional population studies of aging individuals (58,64,98) and slightly larger than in a review of adult data (55). Possible causes of the difference between VO_{2max} declines in different populations might be related to criteria for termination of the test or the prevalence of diseases. The results of a prospective population-based study suggest that VO_{2max} decline is not linear but accelerates in older age groups (16).

The decline in VO_{2max} with age is likely to be due to a decrease in maximal heart rate, stroke volume and thereby maximal cardiac output, lean body mass, and possibly a decrease in muscle oxidative capacity and decline in performance with aging (67). Some of these changes are associated with aging itself, but may also be related to prevalent and incident chronic diseases or lifestyle changes (65). In Study I, advanced age, prevalent chronic diseases, high waist circumference, low levels of moderate-to-heavy PA and use of heart rate lowering drugs were associated with decreased VO_{2max} in men and women, while daily smoking was also associated with decreased VO_{2max} in men. The age-related decline in VO_{2max} was larger when expressed in l/min than in ml/kg/min, which is due to the smaller body size of the older compared to the younger individuals. In the present study, body composition was not assessed and a possible decline in lean body mass with age could not be confirmed.

The participants of the present study with or without diseases had about 12% higher VO_{2max} than the participants of the same age and inclusion criteria in a Canadian population study (57), about 5% lower VO_{2max} than participants without known heart disease of the same age in a US population study (56), and 20% to 30% lower VO_{2max} than healthy participants of the same age in two Norwegian studies (58,59). Further, 65-year old participants in the present study had 12% lower VO_{2max} than estimated values for a 65-year old based on combined equations from several studies in healthy adults (55). The non-diseased individuals in the present study had about 20% lower VO_{2max} compared to a healthy population sample of Norwegian older adults (58), and similar VO_{2max} as the combined equations from several studies in healthy adults would predict for older adults (55). The use of a treadmill typically results in higher VO_{2max} values than the use of a cycle ergometer, which may explain the higher levels of VO_{2max} observed in three other studies (56,58,59) compared with the VO_{2max} levels in the present study. In addition to the use of a treadmill, the much higher VO_{2max} in the Norwegian HUNT 3 Fitness Study than in the present study may be partly explained by individual speed increments during the treadmill tests (58), and the use of the MetaMax II gas exchange analyzer, which has previously been shown to give 3-8% higher VO_{2max} values than a Douglas bag (223,224). In another Norwegian study, higher VO_{2max} values compared to the values in the present study could be due to the strict criteria of achieving VO_{2max}, leading to the exclusion of 16% of the tested individuals (59). On the other hand, the exclusion of patients with cardiac or cerebrovascular diseases could explain the higher VO_{2max} values in the US study compared to the VO_{2max} in the present study (56). The reason for only 5% higher VO_{2max} values in the US study could be the much smaller proportion of subjects who reached RER≥1.1 than in the present study. Although individuals with chronic diseases were included in the present study sample, 98% of the participants reached an RER of ≥1.1 and about 80% of them reported at least very heavy perceived exertion at the end of the test. The reason for the lower VO_{2max} values in the Canadian study (57) than in the present study is unknown, but the tests may not have been continued until exhaustion as often as in the present study. This assumption is based on the fact that in the Canadian study, one criterion for maximality was RER>1.0 (57), which is lower than the usual ratio in maximal aerobic effort.

In the present study, women had 20% (ml/kg/min) to 30% (l/min) lower VO_{2max} levels than men, as also reported in other studies (56-59). The decline of VO_{2max} with age slightly levelled off in older women, but accelerated in older men. In other words, the sex difference in VO_{2max} levels narrowed with increasing age. The slightly steeper decline of VO_{2max} with aging in men than in women has been reported previously (44,56), and could be partly explained by the selection of healthier older women and less healthy older men in the present study population. In two Norwegian studies, the decline rate was similar in men and women (58,59). In the present study, there was no sex difference in the rate of VO_{2max} decline in individuals without chronic diseases, unlike in some previous studies (225). The faster rate of VO_{2max} decline in men has been explained by higher initial levels of VO_{2max} and therefore greater VO_{2max} decline than in women (225). In another Norwegian study, average rate of VO_{2max} decline was similar in men and women across the age range of 20 to 85 years (59). However, the decline of VO_{2max} levels with age in individuals aged 60 to 80 years seemed to be steeper in women than in men (Table 1) (59). One reason for this finding may be that the mean age was higher in women than in men.

Levels of VO_{2max} in ml/kg/min decreased with increasing number of chronic diseases in men and women in the present study. However, the association was much weaker when VO_{2max} was expressed in l/min or the data were adjusted for waist circumference. This finding suggests that overweight and abdominal obesity partly explain the inverse association between chronic diseases and VO_{2max} in ml/kg/min. Increased fat mass often leads to increased lean body mass and blood volume and thereby to increased stroke volume (226) and skeletal muscle power during exercise, and results in increased VO_{2max} expressed in l/min. Also, PA slightly weakened the association between chronic diseases and VO_{2max} in ml/kg/min, while smoking and the use of β-blockers had little or no effect on it. However, the present data may underestimate the impact of chronic diseases on VO_{2max}, because individuals with more severe diseases were excluded or not willing to participate in the study, and because the duration and severity of diseases were not quantified in the present study.

6.3.2 Correlates of low physical activity

A high body mass index and satisfactory or poor health were independently associated with low PA in both genders. Moreover, in women, other independent correlates of low PA were health related, including symptoms of depression and cardiovascular disease. In men, other independent correlates of low PA were age, being divorced or separated, a weak social network, having a poor diet, a health professional's suggestion to increase PA, and still being at work. Women were more likely to report low levels of PA than men.

These observations add to current knowledge (106,129,130) by showing that the correlates of low PA are partly different in men and women. Interaction analyses indicate that being divorced or separated, having a poor diet, a health professional's suggestion to increase PA, and still being at work were associated with low PA in men but not in women.

According to the present results, satisfactory or poor perceived health was associated with low PA more strongly than any disease or even multiple diseases, which is in line with previous findings in older adults (106,128,227). However, self-rated health depends not only on physical and medical conditions but also on psychological and social factors (228). Thus, self-rated health may provide a better overview of general health and even readiness for lifestyle changes than prevalent diseases (229). The association of a high body mass index with low PA is also consistent with the results of previous cross-sectional studies (106,128). A high body mass index can serve as a barrier or as a motivator for PA (134). The direction of association can also be the opposite whereby an inactive lifestyle increases the risk of developing obesity and other chronic diseases (221,230).

Symptoms of depression and cardiovascular disease were independently associated with low PA in women, but in men the associations did not reach statistical significance. The gender difference in the relationship of symptoms of depression may be due to the higher prevalence of these symptoms among women than men. Another reason for these gender differences may also be other stronger correlates of low PA in men. The results of previous studies have suggested that symptoms of depression and cardiovascular disease are related to low PA in aging men and women (106,129). Prospective studies have found reciprocal associations of low PA with symptoms of depression (231) and cardiovascular disease (134). In these studies, however, there were no gender differences in the associations of PA with symptoms of depression or cardiovascular disease.

In men, being divorced or separated and having a weak social network were associated with low PA. A spouse is often the most important or only confidant for men, whereas women often have a wider network of close friends (232). Therefore, non-married men may have a higher risk of social isolation than married men or non-married women. Without the positive influence of a strong social network, people are at higher risk of unhealthy behaviors, including physical inactivity, a poor diet, heavy alcohol use, and smoking (233). Understanding of the association between marital status and low PA in aging individuals is incomplete. Previous studies in older adults have shown a slightly higher risk of low PA in non-married than married individuals (130,150,152). It is possible that in older Finnish men marriage protects against social isolation and a physically inactive lifestyle. Other explanations for the association between being divorced and low PA include changes in financial status, stress, other health behaviors, and health-related selection into and out of marriage (234).

A new finding of the present study is that a poor diet was associated with low PA in men, but not in women. Previous data on the association of diet with PA in older adults are scarce and inconclusive. Some cross-sectional studies among aging individuals have shown a modest association between low levels of PA and a lower-quality diet (235,236), but the relationship may be population-specific. For example, the association has been observed in German men and women (235) and Central European women, but not in American or Southern European men or women (236). It is also difficult to compare the results of the studies because of the different assessment methods and cut-off points for PA and diet quality.

Another new observation of the present study is that the suggestion of a physician or nurse to increase PA was associated with low PA in men but not in women. Consistent with the present findings in men, a physician's advice to increase PA was associated with the risk of not maintaining a high level of PA in a prospective study among older American men and women (237). However, it is unlikely that a discussion with a health professional about PA would truly reduce the levels of PA. A more likely explanation for the observation is that physicians and nurses typically suggest increasing PA to individuals who would benefit the most. It is also possible that individuals to whom health professionals have suggested increasing PA have had more contact with physicians and nurses because of their poor health, which itself is associated with low levels of PA.

Men who were still working were at higher risk of low PA compared to retired men, but no such association was found in women. Earlier studies have not shown such a modifying effect of gender on the association between working status and PA. The present finding in men differs from the results of previous cross-sectional studies in which no association (150) or an opposite (129) relationship has been found between working status and PA in older adults. However, the current observation in men is in line with the results of earlier longitudinal studies, which showed that retired men and women increased their leisure-time PA more than non-retired men and women (165,166). The present study did not show associations between low income or less education and low PA, unlike some previous studies among older adults (129,130). One explanation for the lack of association of education or income with PA could be that retired individuals tend to have lower income and less education but higher PA than those who are still working (135). It is also possible that socioeconomic status does not bring about accentuated differences in lifestyle among older adults in economically developed countries such as Finland.

Many of the correlates of low PA are interrelated. For example, a divorce may be associated with a weaker social network, which may be further associated with an unhealthy lifestyle such as smoking, high alcohol consumption, and a poor diet (228). Smoking and high alcohol consumption are often associated with a poor diet. This in turn tends to be associated with a high body mass index (204), which is associated with an increased risk of chronic diseases (238), poorer perceived health (227), and symptoms of depression (239). Furthermore, many of these factors have bidirectional relationships with PA. For example, a high body mass index and poor perceived health can be either a reason for or a result of low levels of PA (133,240).

6.3.3 Moderators of aerobic exercise intervention effectiveness

The present findings show that individuals who were less than 68 years of age, had not yet retired, had symptoms of depression, were past smokers or had low levels of light aerobic exercise at baseline were most likely to maintain the increased levels of aerobic exercise assessed at two and four years. Also, individuals who were overweight, without joint diseases, had a weak social network and who had participated in competitive sports during their life tended to be more likely to maintain the increased levels of aerobic exercise from two to four years. However, baseline level of light aerobic exercise was the only moderator of the effectiveness of the aerobic exercise intervention at increasing aerobic exercise during the first two years of the intervention.

Being physically active, fit, a non-smoker, and having a high self-efficacy related to PA have consistently predicted good adherence to exercise interventions among insufficiently physically active older adults (19,229). However, it is important to investigate not only predictors of adherence to exercise interventions but also factors that modify the effectiveness of exercise interventions at increasing PA assessed as actual change in PA (19). Previous levels of PA have been positively correlated with adherence to exercise interventions (22), which may have confounded the results concerning the predictors of adherence to exercise interventions. A previous randomized controlled trial investigating the modifiers of the effectiveness of an intervention at increasing PA showed that individuals in the intervention group with low levels of PA at baseline were more likely to increase PA than those with high baseline levels (24). These results support the present findings but are opposite to the observations of earlier studies exploring the predictors of adherence (229). In the same randomized controlled trial, individuals with secondary education at baseline increased PA more in the usual care group than in the intervention group (24). However, in the present study, education did not modify the intervention effectiveness.

The aerobic exercise intervention was effective at maintaining increased aerobic exercise from two to four years among individuals who were younger than 68 years of age but not among older individuals. This finding is consistent with the results of previous studies showing that older individuals were less likely to increase PA in PA interventions lasting at least 12 months (22,23). The burden of diseases may partly explain the lower likelihood of increasing aerobic exercise and maintaining increased aerobic exercise among older individuals. Older people may therefore need more individualized interventions that take prevalent diseases, disability and limited functional capacity into account to promote the long-term maintenance of increased aerobic exercise.

In the present study, an aerobic exercise intervention was more effective at maintaining increased aerobic exercise from two to four years among individuals who were working at baseline than among those who were not working. Three quarters of those who were working at baseline retired during the 4-year follow-up. This implies that the time before and soon after retirement may be a sensitive period for aerobic exercise interventions in order to facilitate the adoption of a physically more active lifestyle. In longitudinal studies, retirement has been associated with increased levels of leisure time PA (157,166,167). However, there is also some evidence that individuals with disability or adverse health behaviors may be less likely to increase PA in retirement than others (166,167). Only a few individuals in the control group who were working at baseline maintained the increased aerobic exercise from two to four years, suggesting that exercise interventions are particularly important for the long-term maintenance of increased aerobic exercise among individuals who are still working.

In the present study, about half of individuals with symptoms of depression in the intervention group were able to maintain increased aerobic exercise from two to four years, whereas only a tenth of depressive individuals in the control group were able to maintain increased aerobic exercise. These results suggest that the aerobic exercise intervention was particularly effective at achieving the long-term maintenance of increased aerobic exercise among older individuals with symptoms of depression. Individuals with symptoms of depression seem to benefit from motivational support given in exercise counseling (241).

The results of the present study suggest that past smokers benefit more from exercise counseling than non-smokers or current smokers. This finding supports the view that a beneficial change in one health behavior can facilitate the adoption of another favorable health behavior (242).

Although age, working status, symptoms of depression and smoking modified the effectiveness of the aerobic exercise intervention at maintaining increased exercise for four years, they did not modify the effectiveness of aerobic exercise at increasing exercise during the first two years of the intervention. This supports previous suggestions that determinants of the level of PA may be phase-specific, thus determinants of initiation and maintenance of PA may differ (19). Further, changes in lifestyle behavior, health, marital status, working status or other factors that may have affected responsiveness to the aerobic exercise intervention were not taken into account in the present study.

One fifth of individuals in the control group with low baseline levels of aerobic exercise had maintained increased aerobic exercise between two and four years. In the interpretation of the results, it should be noted that the maintained increase in aerobic exercise in the control group underestimates the intervention effect. The proportion of individuals in the control group who increased aerobic exercise in the current study was higher than in other intervention studies (243). This finding is surprising given the long duration of the DR's EXTRA Study. The extensive assessments of lifestyle behaviors, physical fitness and health, as well as feedback on these issues, may have increased aerobic exercise not only among individuals in the aerobic exercise group but also among those in the control group.

6.3.4 Associations between physical activity and cardiorespiratory fitness

Moderate-to-vigorous PA assessed with the DR's EXTRA PA interview and moderate-to-heavy aerobic exercise assessed with the DR's EXTRA PA questionnaire were positively associated with VO_{2max} in men and women at baseline. In addition, men and woman with low PA had lower VO_{2max} than men and women with high PA. These associations, combined with results from training studies in older adults (74), imply that regular exercise and PA contribute to the higher levels of VO_{2max}. However, the above-mentioned associations were based on cross-sectional data and it is also possible that higher cardiorespiratory fitness contributes to higher levels of PA. This has been observed in selectively bred rats: rats born as high capacity runners did much more spontaneous running that the rats with low running capacity (244). Humans with higher cardiorespiratory fitness may also be spontaneously more active than those with lower cardiorespiratory fitness (245).

Individuals in the aerobic exercise group exhibited a slightly lower decline in VO_{2max} over time than those in the control group. Among those who maintained increased exercise, the decline in VO_{2max} was also slightly less than for the other participants. Change in moderate-to-heavy aerobic exercise was positively associated with change in VO_{2max}, however this association was not seen in women. Based on previous training studies (74) and studies on the effects of ageing on VO_{2max} (16,56-59), an improvement in VO_{2max} would have been expected among those who increased and maintained aerobic exercise in the present study. Possible reasons for the lack of increase in VO_{2max} among those who maintained increased aerobic exercise include the prescription of moderate rather than vigorous intensity exercise, un-supervised exercise sessions, self-regulated intensity of aerobic exercise and self-reporting of aerobic exercise. Changes in moderate-intensity aerobic exercise may have had more pronounced effects on submaximal measures of cardiorespiratory fitness, such as ventilatory threshold, in comparison to VO_{2max}. The reason for observing an association between aerobic exercise and VO_{2max} in men but not in women may be the higher variation in change in aerobic exercise among men than women. In men, change in aerobic exercise was more strongly associated with body weight adjusted VO_{2max} (ml/kg/min) in comparison to change in absolute VO_{2max} (l/min). This may be due to exercise-induced weight loss, which can increase VO_{2max} (ml/kg/min). However, the associations between aerobic exercise and VO_{2max} were not controlled for events that happened during the intervention such as changes in health status or body weight, or other types of exercise or PA that may have affected VO_{2max}. Finally, improvements in aerobic exercise in the control group and among those who did not maintain increased aerobic exercise of at least 60 minutes per week may have attenuated the intervention effectiveness on VO_{2max}.

6.4 IMPLICATIONS FOR PROMOTION OF PHYSICAL ACTIVITY

This study showed that older age, being divorced or separated, having a weak social network or a poor diet, a health professional's suggestion to increase PA, and still being at work were associated with low PA. On the other hand, this aerobic exercise intervention was effective at increasing aerobic exercise among most older adults who had insufficient aerobic exercise at baseline, especially among those who were younger than 68.5 years, still working, had symptoms of depression or were past smokers.

These results indicate that the time near retirement may be a good time for a lifestyle intervention. Most of the individuals who were working at baseline retired during the 4-year follow-up. The time near retirement may be a sensitive period for aerobic exercise interventions in order to facilitate increases in PA. However, individuals who are close to retirement but not engaged in an exercise intervention are unlikely to increase their level of aerobic exercise, as seen in the control group.

The health care sector may provide a good setting to recruit older adults into exercise interventions (243,246). In the present study, individuals with diabetes and depressive symptoms were not likely to increase their aerobic exercise in the control group, but did so in the aerobic exercise group. Individuals with cardiovascular disease and joint disease also benefitted from the aerobic exercise intervention, increasing their aerobic exercise almost to the same extent as those without these diseases.

The oldest adults in the aerobic exercise group did not increase their aerobic exercise more than the oldest adults in the control group. Therefore, the current intervention was not effective among the oldest adults. The specific types of interventions that would be best for the oldest adults to promote long-term increases in PA are currently unknown. However, more personalized interventions including components of strength, balance and flexibility exercises, in addition to aerobic exercise, may be beneficial for older adults to improve functional capacity, muscular and cardiorespiratory fitness and health (99,103).

In the present study, aerobic intervention effectiveness was evaluated by increases in self-reported aerobic exercise. These improvements in aerobic exercise had modest associations with improvements in directly measured VO_{2max}. This study did not explore whether the intervention was effective at modulating different markers of health, morbidity or quality of life.

7 Conclusions and future perspectives

Getting older brings challenges to maintenance of previous levels of cardiorespiratory fitness and PA. However, engaging in regular PA of at least a moderate intensity can slow down the decline in cardiorespiratory fitness. There is large variation in fitness and PA levels among older adults. The present reference values of cardiorespiratory fitness for older men and women help evaluate an individual's fitness level. Multiple chronic diseases, use of β-blockers, abdominal obesity and smoking were associated with a lower level of cardiorespiratory fitness. In the future, follow-up studies on changes in cardiorespiratory fitness over the years, and on the determinants of these changes in population samples of older adults are needed.

A new observation in the present study was that the correlates of low PA are partly different in men and women. In addition to health related correlates in both genders, older age, being divorced or separated, a weak social network, having a poor diet, a health professional's suggestion to increase PA, and still being at work were associated with low PA in men. These results suggest that individuals with these features could be a reasonable target for aerobic exercise interventions.

The aerobic exercise intervention was effective at increasing aerobic exercise during two years and maintaining increased aerobic exercise from two to four years among most older adults with low baseline levels of aerobic exercise. The intervention was particularly effective at maintaining increased aerobic exercise among individuals who were younger than 68 years of age, were still working, had symptoms of depression or were past smokers. Thus, individuals near retirement or with symptoms of depression could be a reasonable target for aerobic exercise interventions. Older adults with insufficient PA who did not respond to the present intervention may need a different type of support, and could benefit from other types of interventions to increase aerobic exercise in the long term. These results are suggestive and need to be repeated in other intervention studies in different populations.

Although several studies have examined the correlates and predictors of PA (21,229), only a few intervention studies have reported the determinants of actual change in PA or exercise among older adults (22-24). The present study may be the first long-term randomized controlled trial on the moderators of effectiveness of an exercise intervention at increasing exercise in a population sample of older individuals.

More studies are needed to explore the moderators of the effectiveness of exercise interventions at increasing different types of PA, for example total daily PA, high-intensity PA or strength training. Studies on effectiveness or cost-effectiveness of increasing PA in the long term, especially in the least physically active population, are needed.

8 References

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Leena Hakola

Cardiorespiratory Fitness and Physical Activity in Older Adults

This study provided reference values of cardiorespiratory fitness in a large population sample of older adults. The study also showed that the strongest correlates of low physical activity were related to health and demographic factors in men and to health in women. This was the first long-term exercise intervention study among older adults to explore the moderators of exercise change in a randomized controlled setting. The aerobic exercise intervention was effective at increasing exercise among older adults with insufficient levels of physical activity.

UNIVERSITY OF EASTERN FINLAND

Publications of the University of Eastern Finland
Dissertations in Health Sciences

isbn 978-952-61-1730-0