Katja Borodulin

Physical Activity, Fitness, Abdominal Obesity, and Cardiovascular Risk Factors in Finnish Men and Women

The National FINRISK 2002 Study

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PHYSICAL ACTIVITY, FITNESS, ABDOMINAL OBESITY, AND CARDIOVASCULAR RISK FACTORS IN FINNISH MEN AND WOMEN

The National FINRISK 2002 Study

Academic Dissertation

To be presented with the permission of the Medical Faculty of the University of Helsinki, for public examination in Auditorium XII, University Main Building, on February 10, 2006, at 12 noon.

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To my family

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ABSTRACT

Physical inactivity, low cardiorespiratory fitness, and abdominal obesity are direct and mediating risk factors for cardiovascular disease (CVD). The results of recent studies suggest that individuals with higher levels of physical activity or cardiorespiratory fitness have lower CVD and all-cause mortality than those with lower activity or fitness levels regardless of their level of obesity. The interrelationships of physical activity, fitness, and abdominal obesity with cardiovascular risk factors have not been studied in detail.

The aim of this study was to investigate the associations of different types of leisure time physical activity and aerobic fitness with cardiovascular risk factors in a large population of Finnish adults. In addition, a novel aerobic fitness test was implemented and the distribution of aerobic fitness was explored in men and women across age groups. The interrelationships of physical activity, aerobic fitness and abdominal obesity were examined in relation to cardiovascular risk factors.

This study was part of the National FINRISK Study 2002, which monitors cardiovascular risk factors in a Finnish adult population. The sample comprised 13 437 men and women aged 25 to 74 years and was drawn from the Population Register as a stratified random sample according to 10-year age groups, gender and area. A separate physical activity study included 9179 subjects, of whom 5 980 participated (65%) in the study. At the study site, weight, height, waist and hip circumferences, and blood pressure were measured, a blood sample was drawn, and an aerobic fitness test was performed. The fitness test estimated maximal oxygen uptake (VO_{2max}) and was based on a non-exercise method by using a heart rate monitor at rest. Waist-to-hip ratio (WHR) was calculated by dividing waist circumference with hip circumference and was used as a measure of abdominal obesity. Participants filled in a questionnaire on health behavior, a history of diseases, and current health status, and a detailed 12-month leisure time physical activity recall. Based on the recall data, relative energy expenditure was calculated using metabolic equivalents, and physical activity was divided into conditioning, non-conditioning, and commuting physical activity. Participants aged 45 to 74 years were later invited to take part in a 2-hour oral glucose tolerance test with fasting insulin and glucose measurements. Based on the oral glucose tolerance test, undiagnosed impaired glucose tolerance and type 2 diabetes were defined.

The estimated aerobic fitness was lower among women and decreased with age. A higher estimated aerobic fitness and a lower WHR were independently associated with lower systolic and diastolic blood pressure, lower total cholesterol and triglyceride levels, and with higher high-density lipoprotein (HDL) cholesterol and HDL to total cholesterol ratio. The associations of the estimated aerobic fitness with diastolic blood pressure, triglycerides, and HDL to total cholesterol ratio were stronger in men with a higher WHR. High levels of conditioning and non-conditioning physical activity were associated with lower high-sensitivity C-reactive protein (CRP) levels. High levels of conditioning and overall physical activities were associated with lower insulin and glucose levels. The associations were stronger among women than men. A better self-rated physical fitness was associated with a higher estimated aerobic fitness, lower CRP levels, and lower insulin and glucose levels in men and women. In each WHR third, the risk of impaired glucose tolerance and type 2 diabetes was higher among physically inactive individuals who did not undertake at least 30 minutes of moderate-intensity physical activity on five days per week.

These cross-sectional data show that higher levels of estimated aerobic fitness and regular leisure time physical activity are associated with a favorable cardiovascular risk factor profile and that these associations are present at all levels of abdominal obesity. Most of the associations followed a dose-response manner, suggesting that already low levels of physical activity or fitness are beneficial to health and that larger improvements in risk factor levels may be gained from higher activity and fitness levels. The present findings support the recommendation to engage regularly in leisure time physical activity, to pursue a high level of aerobic fitness, and to prevent abdominal obesity.

Key words: abdominal obesity, cardiovascular diseases, epidemiologic studies, exercise, obesity, physical activity, physical fitness, risk factors, visceral adiposity

Katja Borodulin, Fyysinen aktiivisyys, kunto, keskivartalolihavuus ja sydän- ja verisuonitautien vaaratekijät suomalaisilla miehillä ja naisilla. Kansallinen FINRISKI 2002 -tutkimus.
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TIIVISTELMÄ

Vähäinen liikunta, huono aerobinen kunto ja keskivartalolihavuus ovat suoraan ja välillisesti sydän- ja verisuonitauteihin vaikuttavia vaaratekijöitä. Viimeaikaisten tutkimusten tulokset viittaavat siihen, että liikunnallisilla ja hyväkuntoisilla ihmisillä on matalampi kokonaiskuolleisuus ja kuolleisuus sydän- ja verisuonitauteihin kuin vähän liikkuvilla ja huonokuntoisilla henkilöillä riippumatta lihavuuden asteesta. Sen sijaan liikunnan, kunnon ja keskivartalolihavuuden yhdysvaikutuksista sydän- ja verisuonitautien vaaratekijöihin tiedetään vähän.

Väitöskirjatyössä tutkittiin eri vapaa-ajan liikuntamuotojen ja arvioidun aerobisen kunnon yhteyttä sydän- ja verisuonitautien vaaratekijöihin suomalaisessa aikuisväestössä. Tavoitteena oli myös tutkia uuden aerobista kuntoa mittaavan menetelmän soveltuvuutta väestötutkimukseen, aerobisen kunnon jakautumista miehillä, naisilla ja eri ikäryhmissä sekä aerobisen kunnon ja keskivartalolihavuuden yhdysvaikutuksia sydän- ja verisuonitautien vaaratekijöihin.

Väitöskirjatyö on osa kansallista FINRISKI 2002-tutkimusta, jossa seurataan sydän- ja verisuonitautien vaaratekijöiden muutoksia suomalaisessa aikuisväestössä. Yhteensä 13437 25-74-vuotiasta miestä ja naista sisältävä aineisto poimittiin väestörekisteristä ositettuna satunnaisotantana. Tutkittavat satunnaistettiin 10-vuotisikäryhmittäin, sukupuolittain ja alueittain. Erilliseen liikuntaotokseen kuului 9179 henkilöä, joista 5980 (65 %) osallistui tutkimukseen. Tutkimuspaikalla mitattiin pituus, paino, vyötärön- ja lantionympärys ja otettiin verinäyte. Lisäksi tutkittaville tehtiin lepoasennossa ilman kuormituskoetta kuntotesti, jossa mitattiin sykemittarilla epäsuorasti maksimaalista hapenottokykyä (VO_{2max}) ja jota käytettiin aerobinen kunnon mittarina. Vyötärölantiosuhde mitattiin jakamalla vyötärön ympärys lantion ympäryksellä. Vyötärölantiosuhdetta käytettiin keskivartalolihavuuden mittarina. Tutkittavat täyttivät terveyskäyttäytymistä, sairaushistoriaa ja terveydentilaa koskevan kyselylomakkeen. Liikunnan aiheuttama suhteellinen energiankulutus laskettiin yksityiskohtaisella edellistä 12 kuukautta koskevalla vapaa-ajan liikuntakyselyllä. Liikunta jaettiin kuntoliikuntaan, hyötyliikuntaan ja työmatkaliikuntaan. Kaikki 45-74-vuotiaat tutkittavat kutsuttiin myöhemmin kahden tunnin glukoosirasituskokeeseen, jossa mitattiin paasto- ja kahden tunnin glukoosi- ja insuliinipitoisuudet. Mittausten perusteella määritettiin heikentynyt glukoosinsieto ja tyypin 2 diabetes.

Arvioitu aerobinen kunto oli matalampi naisilla kuin miehillä ja laski iän noustessa. Hyvällä arvioidulla aerobisella kunnolla ja matalalla vyötärö-lantiosuhteella oli itsenäinen yhteys matalampaan systoliseen ja diastoliseen verenpaineeseen, kokonaiskolesteroliin ja triglyseriditasoihin, sekä korkeampaan HDL-kolesteroliin ja HDL-kokonaiskolesteroli-suhteeseen. Miehillä aerobisen kunnon yhteydet diastoliseen verenpaineeseen, triglyseriditasoihin ja HDL-kokonaiskolesteroli-suhteeseen olivat sitä voimakkaammat mitä suurempi oli vyötärö-lantiosuhde. Kunto- ja hyötyliikunta olivat yhteydessä matalampiin herkän C-reaktiivisen proteiinin (CRP) pitoisuuksiin ja kunto- ja kokonaisliikunta matalampiin insuliini- ja glukoositasoihin. Havaitut yhteydet olivat voimakkaampia naisilla kuin miehillä. Hyvällä itsearvioidulla kunnolla oli yhteys hyvään arvioituun aerobiseen kuntoon, matalaan CRP-pitoisuuteen ja parempiin glukoosi- ja insuliinitasoihin. Jokaisessa vyötärö-lantiosuhteen kolmanneksessa heikentyneen glukoosinsiedon ja tyypin 2 diabeteksen todennäköisyys oli suurempi ihmisillä, jotka eivät saavuttaneet 30 minuutin kuormitukseltaan kohtalaisen liikunnan vähimmäismäärää viitenä päivänä viikossa.

Tämän poikkileikkaustutkimuksen perusteella arvioidulla aerobisella kunnolla ja säännöllisellä vapaa-ajan liikunnalla on yhteys suotuisiin sydän- ja verisuonitautien vaaratekijöiden tasoihin. Kyseiset yhteydet esiintyvät kaikilla keskivartalolihavuuden tasoilla. Useimmissa yhteyksistä näkyi annos-vaste-suhde. Tämä havainto osoittaa, että jo pieni määrä liikuntaa ja kohtuullinen kunto parantavat vaaratekijöiden tasoja, mutta suuremmalla liikuntamäärällä ja paremmalla kunnolla vaikutus on vieläkin tehokkaampi. Tutkimustulokset tukevat suositusta harrastaa säännöllisesti vapaa-ajan liikuntaa, tavoitella hyvää aerobista kuntoa ja ehkäistä keskivartalolihavuutta.

Asiasanat: keskivartalolihavuus, sydän- ja verisuonitaudit, epidemiologiset tutkimukset, liikunta, lihavuus, fyysinen aktiivisuus, ruumiillinen kunto, vaaratekijät, viskeraalinen lihavuus

CONTENTS

LIST OF ORIGINAL PUBLICATIONS

I Borodulin K, Lakka TA, Laatikainen T, Laukkanen R, Kinnunen H, Jousilahti P. Associations of self-rated fitness and different types of leisure time physical activity with predicted aerobic fitness in 5979 Finnish adults. Journal of Physical Activity and Health 2004, 1, 142-153.

II Borodulin K, Laatikainen T, Lahti-Koski M, Lakka TA, Laukkanen R, Sarna S, Jousilahti P. Associations between estimated aerobic fitness and cardiovascular risk factors in adults with different levels of abdominal obesity. European Journal of Cardiovascular Prevention and Rehabilitation 2005, 12:126-131.

III Borodulin K, Laatikainen T, Salomaa V, Jousilahti P. Associations of leisure time physical activity, self-rated physical fitness, and estimated aerobic fitness with serum C-reactive protein among 3803 adults. Atherosclerosis 2005, in press.

IV Borodulin K, Tuomilehto J, Peltonen M, Lakka TA, Sundvall J, Jousilahti P. Association of leisure time physical activity, fitness, and abdominal obesity with fasting serum insulin and 2-hour post-challenge plasma glucose levels. Diabetic Medicine 2006, in press.

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ABBREVIATIONS

BMI	Body mass index
CRP	C-reactive protein
CVD	Cardiovascular disease
FINRISK	National risk factor survey in Finland
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
METh/wk	A relative energy expenditure of physical activity expressed in metabolic equivalents, MET hours per week
WHO	World Health Organization
WHR	Waist-to-hip ratio

1 INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in global terms and accounts for about 17 million deaths annually (Smith et al. 2004). In Finland, a remarkable decline in CVD mortality has occurred since the 1960's, mainly due to decreases in the prevalence of smoking and in the levels of serum total cholesterol and blood pressure and improved treatments (Vartiainen et al. 1994; Puska et al. 1998; Laatikainen et al. 2005). Despite the favorable changes in CVD risk factors, new risk factors have emerged. These include physical inactivity and obesity, both of which are considered independent and mediating factors in the development of CVD (Lakka et al. 1994; Fletcher et al. 1996; World Health Organization 2002). Physical inactivity and obesity are also associated with type 2 diabetes and metabolic syndrome, growing health hazards all over the world and major risk factors for CVD (World Health Organization 1998; World Health Organization 2000). Several scientific consensus statements have acknowledged the role of physical activity and fitness in the prevention of CVD, type 2 diabetes, and other chronic diseases and health outcomes (Bouchard et al. 1990; Bouchard et al. 1994; Kesaniemi et al. 2001).

From a public health perspective, important recommendations for health-related physical activity were first introduced by Pate et al (1995) and further emphasized in the benchmark report by the Surgeon General of the United States (U.S. Department of Health and Human Services 1996). These reports recommended at least 30 minutes of any moderate intensity physical activity, consisting of one bout or several shorter bouts, on at least five days per week. The American College of Sports Medicine (1998) recommended vigorous exercise 20-60 minutes per session three to five times per week and emphasized developing and maintaining cardiorespiratory fitness. While most previous studies have investigated the effects of more strenuous exercise aimed primarily at improving physical fitness, more research is needed to study the effect of lighter daily physical activities on various health outcomes. Furthermore, more evidence is needed to confirm the claim that 30 minutes of even low intensity physical activity would suffice to enhance health.

In Finland, physical activity behavior has changed dramatically over the past 30 years (Barengo et al. 2002; Helakorpi et al. 2004). The proportion of individuals who exercise during leisure time has increased, but physical activity at work or during commuting has decreased. Currently, about 30 percent of men and about 28 percent of women report that they do no leisure time physical activity at all. The increase in leisure time physical activity has not been sufficient to compensate for the decrease in occupational and commuting physical activity (Fogelholm et al. 1996). Moreover, international studies have reported that the availability of highly palatable energy-dense foods and drinks and increased portion sizes have increased energy intake (Prentice and Jebb 1995; Grundy 1998; Popkin and Nielsen 2003). These lifestyle changes have resulted in an overall positive energy balance. Consequently, the prevalence of overweight and obesity has increased among Finns as measured by body mass index (BMI) and waist-to-hip ratio (WHR) (Lahti-Koski et al. 2001). In The National FINRISK 2002 Study, 21% of men and 19% of women aged 25 to 74 years were classified as being obese (Laatikainen et al. 2003). In the Cardiovascular Risk in Young Finns Study, the prevalence of obesity was 14% in men and 11% in women in adults 24-39 years of age (Juonala et al. 2005). In The Health 2000 Health Examination Survey of adults over 30 years of age, 21% of men and 24% of women had their BMI higher than 30 (Aromaa and Koskinen 2002).

A major public health challenge at the moment is to tackle sedentary lifestyle, to prevent obesity and thereby to enhance health and well-being. If one wishes to devise effective health promotion measures, then it is necessary to know what types of and how much physical activity should be recommended and to recognize the population groups that are at the highest risk of obesity and CVD. Physical activity is a cost-effective way to prevent and treat cardiovascular risk factors. Certain drug therapies, although effective and ethically justified, usually improve only one or a few cardiovascular risk factors and may evoke side effects, whereas low and moderate intensity physical activity improves many risk factors with few if any side effects.

This study examines whether physical activity, fitness, and abdominal obesity are independently associated with cardiovascular risk factors and whether high physical activity or maintaining normal WHR are more effectively associated with a favorable cardiovascular risk factor profile.

2 LITERATURE REVIEW

2.1 Physical activity and fitness

2.1.1 Definitions of physical activity

Physical activity is defined as *"any bodily movement produced by skeletal muscles that results in energy expenditure"* (Caspersen et al. 1985). Energy expenditure consists of basal metabolic rate, the thermic effect of food, and physical activity (Kriska and Caspersen 1997). Physical activity behavior can also be approached from a behavioral point of view, in that individual behavior and lifestyle are governed by personal choices together with biological limitations and physical and social environment (Wankel and Sefton 1994). Physical activity is currently considered as a behavior that is a crucial part of a healthy lifestyle (Pate et al. 1995).

Different modes of physical activity refer to the context in which the activity takes place, these being typically divided into *occupational* and *leisure time physical activity* (Howley 2001). Occupational physical activity takes place at the work site and constitutes of different body movements such as sitting, standing and lifting. Leisure time physical activity refers to any activity that an individual prefers to engage in and which leads to an increased energy expenditure (Bouchard and Shephard 1994). The individual motivation to undertake physical activity may arise from various personal choices. They may involve a desire to improve health status or they may involve many other social factors (Bouchard and Shephard 1994). Leisure time physical activity can be further divided into exercise, sport, and household and other daily chores. Physical activity that is performed as a means of transportation to and from work is often referred to as commuting physical activity.

In the present study, leisure time physical activity is studied in detail by dividing it into *conditioning, non-conditioning, and commuting physical activity*, in a similar way as in the Kuopio Ischemic Heart Disease Study (Lakka and Salonen 1992a; Pereira et al. 1997). Conditioning physical activity, also called exercise, refers to activities that are performed in order to enhance fitness and health, such as walking, running, skiing, and weightlifting. Non-conditioning physical activity typically consists of activities that serve purposes other than the physical activity itself, such as household chores, gardening, fishing, snow shoveling, and wood chopping.

2.1.2 Definitions of fitness

Physical fitness can be defined in multiple ways, such as *"a set of outcomes or traits that relate to the ability to perform physical activity*" (Caspersen et al. 1985). More generally, physical fitness is approached as the capability of carrying out daily tasks with vigor and ample energy, of enjoying leisure time physical hobbies, and of meeting unforeseen emergencies. Physical fitness can be addressed from various perspectives, such as from *performance-related* and *health-related fitness* (Caspersen et al. 1985). Performance-related physical fitness refers to an optimal work or sport performance whereas health-related physical fitness refers to an ability to successfully carry out daily tasks and to maintain good health. Both health-related and performance-related fitness can be improved by regular physical activity (Haskell et al. 1985; Bouchard and Shephard 1994).

Based on the theoretical model (Figure 1) proposed by Bouchard and Shephard (1994), health-related physical fitness is divided into morphological, muscular, motor, cardiorespiratory, and metabolic fitness. Morphological fitness refers to body composition, total and abdominal fat, fat distribution, bone density, and flexibility. Muscular fitness includes power, strength, and endurance, while the motor component embraces determinants like agility, balance, coordination, and speed of movement. Cardiorespiratory fitness comprises maximal and submaximal aerobic capacity, heart and lung functions, and blood pressure. The metabolic component refers to glucose tolerance, insulin sensitivity, blood lipid metabolism, and lipid oxidation. It should be recognized, however, that these components overlap and together constitute health-related fitness and physical performance.

Cardiorespiratory fitness refers primarily to the capacity of heart and lungs to deliver oxygen to skeletal muscles, and *maximal aerobic power* is an indicator of the maximal capacity of oxygen delivery. Individuals with a high maximal aerobic power can undertake demanding physical task without suffering fatigue (Bouchard and Shephard 1994). In the present study, maximal oxygen uptake was estimated using a novel fitness test and is expressed as *estimated aerobic fitness*.

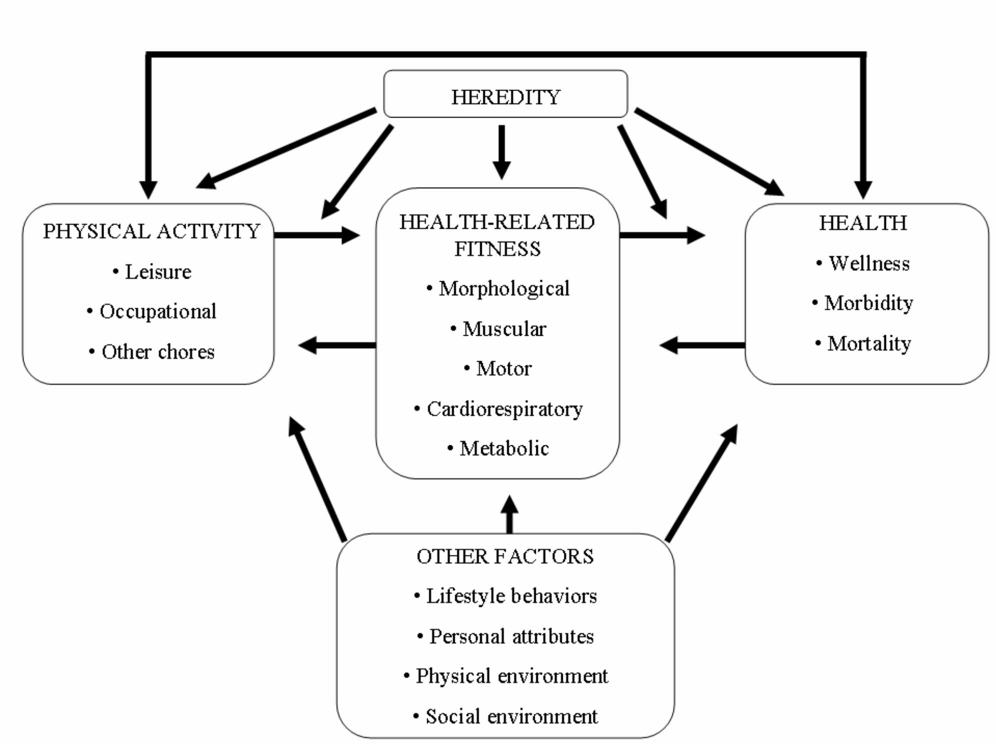


Figure 1. The theoretical model of the relationships among habitual physical activity, health-related fitness, and health status (Bouchard and Shephard 1994). Reprinted with permission from Human Kinetics.

2.1.3 Measurement of physical activity

No golden standard exists for measuring physical activity as a behavior. The level of physical activity is often expressed as the amount of energy consumed during a period of interest, such as one week. A summary of the methods used in research on physical activity is provided in Table 1. The doubly labeled water technique is the most accurate method to measure energy expenditure in field conditions. This technique assumes that the difference in elimination rates of ^2H and ^{18}O is related to CO_2 production, which is further related to energy expenditure (Schoeller and van Santen 1982). Also, direct or indirect calorimetry can be applied using heat production obtained from estimations of respired oxygen and produced carbon dioxide. These techniques are expensive and time-consuming and thus not applicable for large population studies (LaPorte et al. 1985; Lamonte and Ainsworth 2001).

Physical activity and energy expenditure can also be assessed by using heart rate monitors, accelerometers, and pedometers that are less accurate methods than the doubly labeled water technique and indirect calorimetry. Moreover, the use of heart rate monitors, accelerometers, and pedometers is challenging in large population samples, but these methods may be useful in validating questionnaire data (Montoye et al. 1996).

In large-scale population studies, data on individual behavior is self-reported (Kriska and Caspersen 1997; Lamonte and Ainsworth 2001). The most commonly used instruments are diaries, log books, recalls, and questionnaires. Diaries and log books provide detailed information on physical activity behavior and are not prone to recall bias. However, they are time-consuming and may results in high drop out rates or missing data and they may even tend to modify physical activity behavior. Recalls and questionnaires are faster and less tedious to fill in, but include less detailed information on physical activity and are affected by recall bias. Another important disadvantage of self-reported instruments is their tendency to overestimate the level of physical activity. Data can also be collected accurately via face-to-face or telephone interviews and direct observations by trained research personnel. Each measure of physical activity needs to be chosen according to the study aims, design, and sample. The important factors in selecting the measure of physical activity are often related to feasibility, age group, accuracy, cost in value and time, how activity specific the measure is, and whether it affects the physical activity behavior during the measurement period (Table 1).

The energy expenditure of physical activity can be calculated by multiplying frequency (sessions/week), the duration of the exercise bout (hours/bout), and intensity (*metabolic equivalents,* METs) and then dividing it by the period of interest (Kriska and Caspersen 1997). One MET corresponds to a resting energy expenditure of 1 kcal/h/kg. The MET values of physical activity are calculated with information on frequency (number of sessions), duration (time), intensity (degree of vigor), and type of activity (e.g. walking, gardening). Internationally accepted norms have been created for the average energy expenditures of different types and intensities of physical activities (Ainsworth et al. 1993; Ainsworth et al. 2000). An estimation of total energy expenditure, based on frequency, duration, type, and intensity, such as MET hours/week (METh/wk), thus indicates the volume of physical activity (Howley 2001). Energy expenditure in kilojoules (kilocalories) can roughly be estimated by multiplying METh/wk by body weight. Another possibility to estimate energy expenditure is to use the physical activity level (PAL) ratio, which is the ratio of daily energy expenditure to resting metabolic rate (Prentice et al. 1996).

An ideal physical activity questionnaire would provide information on energy expenditure of leisure time, occupational, and commuting physical activities (Paffenbarger et al. 1993). Two reviews have listed the range of physical activity questionnaires with information on their reliability and validity used in health-related studies (Montoye et al. 1996; Pereira et al. 1997).

Lately, there has been increasing interest in trying to define the dose-response relationship between physical activity and health (Kesaniemi et al. 2001). A good research instrument would allow the estimation of the minimum dose needed to achieve health benefits. The evaluation of dose-response relationship is also important if one wishes to create health promotion measures and recommendations of physical activity. Unfortunately, very few studies in representative population samples have use detailed questionnaires or other instruments that would allow for a detailed investigation of physical activity in terms of frequency, duration, intensity, and type. Some studies suggest that limitations in the measurement of physical activity behavior have underestimated true relationships between physical activity and various health outcomes (Blair et al. 2001; Dishman et al. 2004, p. 93).

Due to the difficulty in obtaining valid and reliable data from physical activity questionnaires, cardiorespiratory fitness can be used as a surrogate of physical activity (Blair et al. 2001). Higher levels of reported physical activity are associated with better cardiorespiratory fitness (Taylor et al. 1978; Siconolfi et al. 1985; Kohl et al. 1988) and exercise training improves cardiorespiratory fitness (Mitchell and Raven 1994).

Table 1. Assessment techniques for physical activity. Modified from LaPorte (1985) and the Report of the Surgeon General (U.S. Department of Health and Human Services 1996, p. 30)

Measurement tool	Feasible in a large scale study	Age group (child, adolescent, adult, elderly)	Accuracy	Expensive	Time-consuming	Time-consuming to subject	Activity specific	Influences behavior
Doubly labeled water	no	all	high	yes	yes	no	no	no
Direct calorimetry	no	all	high	yes	yes	yes	yes	yes
Indirect calorimetry	no	adolescent, adult, elderly	high	yes	yes	yes	yes	yes
Heart rate monitor	no	all	moderate	yes	yes	no	no	no
Accelerometer	yes	all	moderate	no	no	no	no	no
Pedometer	yes	adolescent, adult, elderly	moderate-low	no	no	no	no	no
Direct observation	no	all	high	yes	yes	no	yes	yes
Diary and log book	yes	adolescent, adult, elderly	moderate	no	yes	yes	yes	yes
Recall	yes	adolescent, adult, elderly	low	no	no	no	yes	no
Questionnaire	yes	adolescent, adult, elderly	low	no	no	no	yes	no

2.1.4 Measurement of cardiorespiratory fitness

Both physical and health-related fitness are complex attributes, and thus there is no single measurement method for these parameters. Moreover, different methods are used to measure different components of fitness, such as motor skills, muscular strength, and agility. In the present study, the main interest has been on cardiorespiratory fitness, which is one of the most important components of health-related fitness. It is worth mentioning that heritability for cardiorespiratory fitness is 40-50%, meaning that due to their genetic background many individuals have higher levels of cardiorespiratory fitness irrespective of their level of physical activity and exercise (Bouchard and Rankinen 2001).

Cardiorespiratory fitness is usually measured by indirect calorimetry in a laboratory setting as maximal aerobic power or maximal oxygen uptake ($VO2_{max}$), referring to the highest rate of oxygen uptake achieved during heavy dynamic exercise (Howley 2001). Cardiorespiratory fitness can also be estimated from peak power achieved on a cycle ergometer, total time on a standard treadmill test, or submaximal tests by estimating age-predicted value from the heart rate response.

Cardiorespiratory fitness is measured in the laboratory by using sophisticated methods and equipment, the measurement is time-consuming and expensive, but data obtained from maximal exercise stress tests are reliable and valid. Moreover, other components of health-related fitness, such as body composition, can be investigated simultaneously. Safety is an important issue when maximal exercise tests are being carried out in general populations with wide age ranges in the subjects. Maximal bicycle or treadmill exercise tests may be hazardous for older individuals and those who have CVD. Given these limitations, only a few large-scale population-based studies have measured cardiorespiratory fitness by performing exercise tests (Slattery and Jacobs 1988; Blair et al. 1989; Sandvik et al. 1993; Lakka et al. 1994; Myers et al. 2002).

Other methods than laboratory-based testing to estimate cardiorespiratory are also available. Field tests, such as the UKK 2-km walking test (Oja et al. 1991; Laukkanen et al. 1992), the

Åstrand step-test (Astrand and Ryhming 1954), and the Cooper 12-minute running test (Cooper 1968), have been found to be valid and feasible methods to assess cardiorespiratory fitness in general populations. Non-exercise methods that are carried out without performance of an actual exercise test use mathematical equations based on information on demographic variables, such as weight, height, age, sex, body composition, self-reported physical activity, and resting heart rate. Non-exercise methods have been seldom used, but have achieved a similar validity as submaximal fitness tests (Jackson et al. 1990; Williford et al. 1996).

There has been increasing interest on heart rate variability and its associations with cardiorespiratory fitness. Heart rate variability refers to the time between two consecutive heartbeats, this being regulated by the sympathetic and parasympathetic nervous systems, and varies with respiratory frequency. Ageing and heart diseases, such as an acute myocardial infarction are known to reduce heart rate variability (Bigger et al. 1992; Casolo et al. 1992; De Meersman 1993) People with good cardiorespiratory fitness have greater heart rate variability than people with poor fitness (De Meersman 1993; Rennie et al. 2003; Hautala et al. 2004).

A recently developed method, the Polar Fitness Test, uses age, sex, height, body weight, self-reported physical activity and heart rate variability of an individual to estimate maximal oxygen uptake (Väinämö et al. 1996; Väinämö et al. 1997; Väinämö et al. 1998; Kinnunen et al. 2000). The Polar Fitness Test was developed by using a matrix calculation and nonlinear equations, which have been determined by artificial neural networks. Heart rate variability is measured by using data on the variation in the intervals between consecutive R waves, called RR-intervals representing consecutive heart beats, from an electrocardiogram taken for about seven minutes. Three parameters are calculated based on filtered R-R intervals: mean R-R interval length, 99th percentile, and range between 1st and 99th percentile. Aerobic fitness is not estimated if the R-R interval data include more than 60 abnormal intervals or the abnormal intervals represent more than 25% of all intervals. A correlation between estimated aerobic fitness measured by the Polar Fitness Test and maximal oxygen consumption measured during a maximal treadmill test has varied between 0.80 and 0.95 (Kinnunen et al. 2000). This finding suggests that the Polar Fitness Test is a valid measure of aerobic fitness, but it does not prove accuracy of the method.

The public health importance of health-related fitness has lately been emphasized. While there are several performance-related fitness tests, few measures of health-related fitness are available. It is not known whether performance-related tests are a suitable and safe way to assess health-related fitness. The Consensus Statement on Physical Activity, Fitness, and Health (Bouchard et al. 1994) emphasized the need of developing and testing methods and instruments that would be suitable for assessing health-related fitness. At present, few measures of health-related fitness have been developed for studies in populations with wide age ranges.

2.2 Overweight and obesity

2.2.1 Definitions of overweight and obesity

Overweight and *obesity* are characterized as an excess amount of adipose tissue, which has resulted from a long-term positive energy balance. The Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity (1998) defined obesity as a chronic disease that is complex and multifactorial in its nature and includes an interaction of genotype with environment in its development. People have different tendencies to gain weight in different locations of the body, such as the abdomen, which is referred as *abdominal or visceral obesity*.

2.2.2 Measurement of overweight and obesity

The methods to assess body composition are numerous and also difficult to organize systematically (Wang et al. 1995). Methods that are feasible in assessing body fat mass are described here. The most accurate methods in assessing body fat mass include underwater body density measurement, body fat content estimation by dual energy X-ray absorptiometer (DEXA), magnetic resonance imaging (MRI), and computerized tomography (CT) (Heymsfield et al. 1997; Ellis 2000; Goodpaster 2002). These methods are time-consuming and require expensive equipment and thus are not feasible for large epidemiological studies.

However, bioelectrical impedance can be used in larger populations samples, because it is less time-consuming and inexpensive (Jebb and Elia 1993; Ellis 2000).

In epidemiological studies overweight, overall obesity, and abdominal obesity are typically measured by using ratios of body weight and height or body circumferences, such as BMI, waist circumference, and WHR (Garrow and Webster 1985; Revicki and Israel 1986; Despres et al. 2001; Seidell et al. 2001a; Seidell et al. 2001b). BMI is calculated as the product of weight in kilograms divided by height in squared meters (kg/m^2). BMI is highly correlated with body weight and is a surrogate measure of total body fat content but is also affected by muscle mass. WHR is a measure of abdominal fat and is calculated as the ratio of waist and hip circumferences. Waist girth is measured at the midpoint between iliac crest and lowest rib and hip girth is assessed at the widest part of pelvis.

BMI, WHR, and waist circumference are continuous variables and when used to define overweight or obesity, their cut-off points are arbitrary. The international classifications of overweight and obesity proposed by the World Health Organization (WHO, 2000, p. 8-9) and by the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults (1998) are based on an increased risk of morbidity and mortality in different populations. According to the WHO, a BMI <18.5 kg/m^2 is defined as underweight, 18.5-24.9 kg/m^2 as normal weight, 25.0-29.9 kg/m^2 as overweight, and >30.0 kg/m^2 as obesity. Obesity can be further stratified into moderate obesity (BMI 30-34.9 kg/m^2), severe obesity (35-39.9 kg/m^2), and very severe obesity (≥ 40 kg/m^2). The cut-off points of waist circumference and WHR are sex and population-specific. However, the World Health Organization has recommended the use of a cut-off point for waist circumference of 88 cm in women and 102 cm in men and for WHR of 0.85 in women and 1.0 in men to define an increased health risk (World Health Organization 2000, p. 9-11). The same cut-off points for waist circumference have been recommended by the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults (1998) and the National Cholesterol Education Program (Ford et al. 2002).

Alterative measures other than BMI may be more adequate for assessing body fat distribution. Waist girth and WHR are better measures of intra-abdominal fat and probably also of total fat than BMI when validated against computer tomography or magnetic resonance imaging (Ashwell et al. 1985; Rankinen et al. 1999; Despres et al. 2001). Also waist-to-height ratios and waist-to-thigh ratios have been used to estimate abdominal fat (Han et al. 1997b).

A simple and fairly reliable measurement of waist girth has recently been recommended to assess the amount of visceral fat (Han et al. 1995; Lemieux et al. 1996; Han et al. 1997b; Despres et al. 2001; Seidell et al. 2001b). Waist circumference appears particularly useful in the clinical setting, where both BMI and waist girth can be easily measured and followed in time (Despres et al. 2001). Waist circumference, however, is to some extent correlated with body height, and thus tall persons may falsely be categorized into the abdominally obese group (Seidell et al. 2001a). Some studies have suggested the use the ratio of waist circumference to height to overcome the potential confounding effect of height (Ashwell et al. 1996a; Ashwell et al. 1996b), but conflicting views are presented as well (Han et al. 1997a).

WHR has been criticized due to its inability to classify obesity in follow-up studies, particularly in women, if the subjects gain weight in the waist and hip areas simultaneously (Despres et al. 2001). Furthermore, it is difficult to interpret whether a large WHR is attributable to a large waist girth or to narrow hips. Previous studies suggest that both narrow waist and large hips may protect against CVD and for this reason, it is recommended that waist and hip girths should be measured in the future (Lissner et al. 2001; Seidell et al. 2001b).

The strength of WHR relates to measuring both waist and hips. Waist reflects the amount of abdominal fat and hips the overall body size (Valdez 1991; Kahn 1993; Han et al. 1997b; Seidell et al. 2001a). Although the current recommendation seems to favor the use of waist circumference in assessing abdominal obesity, WHR remains a suitable method for research purposes (Folsom et al. 2000; World Health Organization 2000, p. 10; Lakka et al. 2002).

Both BMI and WHR are confounded by sex, age, and ethnic background. Also the distribution of overweight and obesity is different across populations (World Health Organization 2000). In general, men tend to have higher amounts of visceral adipose tissue than women, particularly pre-menopausal women (Lemieux et al. 1993), older persons have larger waist circumferences than younger ones (Molarius and Seidell 1998), and morbidity risks at the same level of overweight vary across different ethnic populations (Seidell et al. 2001a). Therefore, instead of globally accepted cut-off points for obesity, there need to be age, sex, and race-specific categories for overweight and obesity (Seidell et al. 2001a).

In health-related research, BMI is more commonly used than waist circumference or WHR because of the convenience and feasibility of measuring height and weight adequately in large samples (Garrow and Webster 1985). Nevertheless, it is important to understand that BMI, waist circumference, and WHR estimate fat mass at different locations, reflect different etiological perspectives, and thus do not assess identical phenomena (Seidell et al. 2001a). Whether to choose both or only one of these methods depends on the study design and the available resources.

2.3 Health benefits of physical activity and fitness

Research on health benefits of physical activity dates back to the studies conducted in London bus drivers and fare collectors in the 1940's (Morris et al. 1953). The drivers had a lower risk of coronary heart disease than the fare collectors whose work was physically more demanding. This study was later criticized because the fare collectors may have selected a physically more demanding task. Subsequently, a large number of epidemiological studies have been carried out and international consensus statements have been created on the associations between physical activity, fitness and health (Bouchard et al. 1990; Bouchard et al. 1994; Kesaniemi et al. 2001). The latest consensus statement from a symposium held in Toronto, Canada (Kesaniemi et al. 2001), and the Report from the Surgeon General (U.S. Department of Health and Human Services 1996) emphasize that regular physical activity is one way to maintain and improve many facets of health and to reduce cardiovascular and all-cause mortality. To study the health benefits of cardiorespiratory fitness, the recommendations by the American College of Sports Medicine (1998), consisting of vigorous exercise 20-60 minutes per session three to five times weekly, may be used instead of the recommendations from the Surgeon General (U.S. Department of Health and Human Services 1996).

One commonly used theoretical model (Bouchard and Shephard 1994) on the relationships between physical activity, health-related fitness, and health emphasizes the complexity of these factors and their interrelationships. Thus, while physical activity can influence fitness, fitness can also modify the physical activity behavior. Typically, the fittest persons are physically the most active. Similarly, health has a reciprocal association with health-related fitness and physical activity: high physical activity and fitness enhance health, whereas poor health status decreases participation in physical activity and fitness. Importantly, these interrelationships are modified by individual differences, such as in genetic factors and health behaviors, as well as by physical and social environmental factors. This model also serves as the theoretical framework for this study.

Total mortality

A recent review of 44 studies, most of which are prospective cohort studies, suggested a linear reduction in all-cause mortality with increasing levels of physical activity or fitness (Lee and Skerrett 2001). Mortality was 20 to 30 percent lower at a threshold exercise energy expenditure of about 4200 kJ (1000 kcal) per week and even lower mortality at above 4200 kJ per week as compared with lower energy expenditures. At present there is insufficient evidence to quantify the dose-response relationship separately for the frequency, duration, or intensity of physical activity. The association between physical activity and all-cause mortality has been studied in Finland, and the findings are similar to the results of studies conducted in other countries (Salonen et al. 1982; Menotti et al. 2001; Hu et al. 2005b). One Finnish study found inverse associations of leisure time and occupational physical activity, but not commuting physical activity, with total mortality (Barengo et al. 2004). Another Finnish study reported decreased all-cause mortality among individuals who engaged in regular conditioning physical activity, independent of genetic and familial factors (Kujala et al. 1998). Two Finnish studies have investigated the associations of physical fitness and total mortality (Haapanen-Niemi et al. 2000; Laukkanen et al. 2001). The first study found that self-perceived physical fitness was a strong predictor of total mortality in men, but not in women (Haapanen-Niemi et al. 2000). The second study observed an inverse association of maximal oxygen uptake, as measured directly by using respiratory gas analysis, with total mortality in middle-aged men (Laukkanen et al. 2001).

Cardiovascular disease and mortality

Physical inactivity has been recognized as an independent risk factor for fatal and non-fatal CVD in men and women (Lemaitre et al. 1995; Mensink et al. 1996; Stampfer et al. 2000; Blair et al. 2001; Kohl 2001; Lee et al. 2001; Manson et al. 2002). Similar findings have also been reported in Finnish studies (Salonen et al. 1982; Lakka et al. 1994; Haapanen-Niemi et al. 2000; Barengo et al. 2004; Hu et al. 2004c). A particularly strong association has been found between physical activity and a reduced risk of coronary heart disease (Kohl 2001), while more limited evidence is available on the risk of stroke (Lee et al. 2003). The risk of CVD usually increases in a dose-dependent manner with decreasing physical activity (Blair et al. 2001; Kohl 2001). There is some evidence that weekly energy expenditure of around 4200 kJ (1000 kcal) physical activity and a minimum intensity of 4 to 6 METs are associated with lower CVD risk (Fletcher et al. 1996; Siscovick et al. 1997; Lee and Paffenbarger 2000; Lee et al. 2000).

Older studies described an association between occupational physical activity and the risk of CVD (Paffenbarger and Hale 1975; Powell et al. 1987), but newer studies have also shown associations of leisure time and commuting physical activity with CVD risk (Leon et al. 1987; Barengo et al. 2004). Generally, leisure time physical activity has been more consistently associated with CVD than occupational activity (Dishman et al. 2004, p. 88). Also, some evidence exists on the associations of different types of physical activity, such as regular walking with reduced CVD mortality (Manson et al. 2002; Tanasescu et al. 2002).

Cardiorespiratory fitness has had even stronger inverse association with CVD than physical activity, although less evidence is available and this is mainly restricted to men (Peters et al. 1983; Ekelund et al. 1988; Blair et al. 1989; Lakka et al. 1994). Two Finnish studies have measured cardiorespiratory fitness directly using respiratory gas analysis in men and have found a lower risk of coronary heart disease (Lakka et al. 1994) and stroke (Kurl et al. 2003) in highly fit as compared with unfit men.

Cardiovascular risk factors

Previous studies have shown that the CVD risk factor profile is better among individuals with higher levels of cardiorespiratory fitness or physical activity (Kokkinos et al. 1995; Fletcher et al. 1996; McMurray et al. 1998; Williams 1998; Fagard 2001; Leon and Sanchez 2001; Bassett et al. 2002; Jakes et al. 2003). However, only limited evidence is available on the detailed dose-response relationships between physical activity, fitness, and cardiovascular risk factors (Oja 2001).

Physical activity has both immediate and long-term effects on blood pressure levels (Shephard 2001; Thompson et al. 2001). Physical activity and fitness are associated with lower levels of systolic and diastolic blood pressure, and these associations seem to be somewhat weaker among women than men (Blair et al. 1984; Kelley and Tran 1995; Fagard 1999; Wilmore et al. 2001; Bassett et al. 2002; Carnethon et al. 2003; Jakes et al. 2003). Randomized controlled trials have shown that exercise training three to five times per week with 30 to 60 minutes per session at a moderate intensity level can result in a net reduction of systolic and diastolic blood pressure of 3.4 and 2.4 mmHg, respectively (Fagard 1999; Fagard 2001). There is not enough evidence to suggest that exercise at a higher intensity would lead to larger decreases in blood pressure (Fagard 2001).

Exercise training improves the serum lipid profile (Kraus et al. 2002; Kelley et al. 2004). The most consistent effect of exercise is the increase in high-density lipoprotein (HDL) cholesterol levels (Huttunen et al. 1979; Thompson et al. 2001). Exercise is also inversely associated with triglyceride and low-density lipoprotein (LDL) and total cholesterol levels (Stefanick et al. 1998; Leon and Sanchez 2001). Cross-sectional studies in male and female runners have pointed to a direct association between running kilometers and HDL cholesterol levels (Kokkinos et al. 1995; Williams 1996; Williams 1998). Studies that have addressed the dose-response relationship in general populations suggest that moderate to high intensity physical activity at 30 minutes per session three to five times per week has a favorable effect on the lipid profile, but such studies are limited in number (Lakka and Salonen 1992b; Kesaniemi et al. 2001; Leon and Sanchez 2001). There are few studies reporting the ratio of total cholesterol to HDL cholesterol in relation to physical activity or fitness and most of them have been conducted in convenience samples (Kokkinos et al. 1995; Williams 1996; Wei et al. 1997; Haddock et al. 1998; Williams 1998; Twisk et al. 2001).

In Finnish cross-sectional and prospective population-based studies, a more beneficial cardiovascular risk profile has been found among physically active individuals, but the studies are few in number and have only investigated the associations of physical activity with total cholesterol, HDL cholesterol, and systolic and diastolic blood pressure levels or the prevalence of hypertension (Tuomilehto et al. 1987; Lakka and Salonen 1992b; Hu et al. 2004a; Barengo et al. 2005).

Recently, systemic inflammation has been recognized as an independent risk factor for atherosclerosis and CVD (Jousilahti et al. 2001; Libby et al. 2002; Pearson et al. 2003). Previous studies have shown inverse associations of physical activity and fitness with levels of C-reactive protein (CRP), suggesting that physical activity has an anti-inflammatory effect (Geffken et al. 2001; Abramson and Vaccarino 2002; Church et al. 2002; Ford 2002; Lakka et al. 2005). However, there are very few studies reporting different types of physical activity in relation to CRP. A recent Finnish study reported an inverse association of overall leisure time physical activity with CRP levels in young adults (Raitakari et al. 2005). The association of physical fitness with CRP has not been studied in Finland.

Type 2 diabetes and glucose homeostasis

Epidemiological studies have shown that physical inactivity and poor cardiorespiratory fitness are associated with an increased incidence of type 2 diabetes (Manson et al. 1991; Manson et al. 1992; Lynch et al. 1996; Hu et al. 1999; Kriska et al. 2003), impaired glucose tolerance, and impaired fasting glycemia (Wei et al. 1999a; Dunstan et al. 2004). Clinical trials have pointed to a decreased risk of developing type 2 diabetes with lifestyle changes, such as regular physical activity and a healthy diet (Pan et al. 1997; Tuomilehto et al. 2001; Knowler et al. 2002). A recent Finnish prospective study showed a significantly higher risk of type 2 diabetes in men and women with lower levels of leisure time physical activity (Hu et al. 2003). The Finnish study also found an inverse association of occupational physical activity with diabetes among men and an inverse association of commuting physical activity with diabetes among women (Hu et al. 2003).

Glucose homeostasis is better among physically active individuals, and the total volume of physical activity appears to be more important than the intensity or frequency of exercise (Mayer-Davis et al. 1998; Wannamethee et al. 2000; Wareham et al. 2000; Kriska et al. 2001a; Shephard 2001; Thompson et al. 2001; Kriska et al. 2003; Lakka et al. 2003; Cox et al. 2004; Farrell et al. 2004). However, little is known about the types or dose of physical activity that most effectively improve glucose homeostasis (Kelley and Goodpaster 2001).

Obesity and weight maintenance

Obese persons are usually physically least active and conversely decreased physical activity may lead to obesity (Manson et al. 1995; Petersen et al. 2004). A large body of evidence indicates that body weight and fat mass can be reduced by increasing the short-term and long-term level of physical activity (Andersen et al. 1999; Fogelholm and Kukkonen-Harjula 2000; Ross and Janssen 2001; Donnelly et al. 2003; Jakicic et al. 2003). Weight loss due to physical activity seems to follow a dose-response manner only in short-term studies and is more effective when the exercise is combined with diet control (Ross et al. 2000; Ross and Janssen 2001; Irwin et al. 2003; Petersen et al. 2004; Slentz et al. 2004). Physical activity can reduce body mass without a loss of skeletal muscle mass (Bouchard and Shephard 1994; Klein et al. 2004, p.47). This is important because metabolically active skeletal muscle increases energy expenditure at rest and during exercise and thereby helps in the regulation of insulin release and glucose metabolism (Thompson et al. 2003).

The maintenance of healthy body weight after a substantial weight loss is a challenge. The best long-term results have been achieved by combining dietary energy restriction and regular physical activity with energy expenditure of at least 10500 kJ (2500 kcal) per week or 60-90 minutes of daily exercise (Klem et al. 1997; Jeffery et al. 2003; Saris et al. 2003; Hill and Wyatt 2005).

There is a limited amount of evidence of the associations of physical activity and cardiorespiratory fitness with a reduced abdominal obesity, independent of changes in diet (Ross et al. 2000; Ross and Janssen 2001; Donnelly et al. 2003; Irwin et al. 2003; Wong et al. 2004). One study reported that at a given BMI, men and women who had higher cardiorespiratory fitness had less abdominal and total fat than less fit men and women (Ross and Katzmarzyk 2003).

2.4 Health risks of overweight and obesity

Overweight and obesity lead to a wide variety of health problems and shorten the life span (World Health Organization 2000, p.39; Klein et al. 2004). Generally, the association of BMI with total and CVD mortality follows a U-shaped curve, while WHR and waist circumference have a direct dose-dependent relationship with mortality (Hubert et al. 1983; Folsom et al. 1993; Han et al. 1995; Manson et al. 1995; Rexrode et al. 1998; Megnien et al. 1999). Mortality from coronary heart disease has been higher already at body weights as little as 10 percent above the average (Willett et al. 1995). Morbidity and mortality are higher in individuals with obesity as compared with individuals who are merely overweight (Flegal et al. 2005; Gregg et al. 2005). Recent prospective large-scale studies have suggested that morbidity and mortality risk may be higher among underweight individuals (BMI <18.5 kg/m^2) than among normal weight persons (Flegal et al. 2005; Gregg et al. 2005). Finnish studies have shown similar associations of obesity with morbidity and mortality by using BMI, WHR, or waist circumference as measures obesity (Rissanen et al. 1990; Jousilahti et al. 1996; Haapanen-Niemi et al. 2000; Lakka et al. 2001) (Lakka et al. 2002; Hu et al. 2004c; Hu et al. 2005b).

Obesity is a major risk factor for type 2 diabetes, abnormal glucose regulation, insulin resistance, elevated blood pressure, unhealthy serum lipid profile, as well as for other chronic conditions such as gallbladder disease, sleep apnea, and breathlessness (Expert Panel on the Identification 1998; Wannamethee and Shaper 1999; World Health Organization 2000, p. 43; Despres et al. 2001). Furthermore, an excess amount of body fat is associated with high levels of CRP, proinflammatory cytokines, and hemostatic factors (Despres et al. 2001).

Visceral obesity seems to be associated even more strongly with chronic conditions than general adiposity (Folsom et al. 2000; World Health Organization 2000, p. 43-44). This is most likely due to the location of the adipose tissue adjacent to the liver, which affects glucose homeostasis and serum lipids, as well as elevating blood flow and increasing hormonal activity (World Health Organization 2000, p. 44; Dishman et al. 2004, p. 44). The adipose tissue functions as an endocrine organ, in which adipocytes secrete hormones, cytokines, and proteins essential in the regulation of cardiovascular risk factors (Mohamed-Ali et al. 1998). Individuals with abdominal obesity have an increased risk of chronic diseases independent of BMI level (Folsom et al. 1998), and the risk seems to be higher among abdominally obese individuals across each BMI category (Larsson et al. 1984; Rexrode et al. 1998; Megnien et al. 1999).

Weight loss in overweight and obese persons is associated with a reduced risk of chronic diseases, particularly type 2 diabetes and CVD (Klein et al. 2004). A reduction in body weight will improve the risk factor profile, particularly blood pressure, triglyceride, total cholesterol, LDL and HDL cholesterol levels, and glucose regulation (Thompson et al. 2003; Klein et al. 2004).

2.5 Interrelationship of physical activity, fitness, and obesity with health

Low physical activity and obesity often occur in combination, which clearly makes their independent influence on cardiovascular risk levels difficult to differentiate. In fact, there is no consensus of whether physical activity, fitness or weight reduction is more important in disease prevention (Williams 2001; Christou et al. 2005). It seems probable that both obesity and physical activity have their own independent effects on health. For example, there is one estimate in the literature that physical inactivity increases coronary mortality by 4.3% and obesity by 3.4% when all conventional risk factors are taken into account (Unal et al. 2004).

A review of 24 prospective studies indicated that health risks are attenuated by a high level of physical activity or cardiorespiratory fitness, independent of the presence of obesity (Blair and Brodney 1999). A convincing body of evidence has been published on the associations of mortality risks with physical activity or cardiorespiratory fitness across BMI categories (Lee et al. 1999; Wei et al. 1999b; Crespo et al. 2002; Farrell et al. 2002; Stevens et al. 2002). More obese individuals seemed to benefit most from their high physical activity or cardiorespiratory fitness (Blair and Brodney 1999). Similar benefits of physical activity have been reported in persons with a diagnosed chronic disease, such as type 2 diabetes (Church et al. 2004; Hu et al. 2005a), coronary artery disease, and CVD (Myers et al. 2002; Wessel et al. 2004).

To date, research on this topic has concentrated mainly on mortality as the outcome. A limited number of studies have described the interrelationships between physical activity and obesity on the risk of type 2 diabetes, impaired glucose tolerance, and impaired fasting glycemia (Helmrich et al. 1991; Burchfiel et al. 1995; Manson et al. 1995; Hu et al. 1999; Wei et al. 1999a; Carnethon et al. 2003; Kriska et al. 2003; Hu et al. 2004c). Generally, physically active or fit individuals exhibit a lower risk than inactive or unfit persons and obese persons markedly benefit from being physically active or fit.

Only a few studies have investigated the combined effect of physical activity or fitness and obesity on cardiovascular risk factor levels. One meta-analysis reported an inverse association between exercise and blood pressure in lean and obese individuals (Fagard 1999). Lower blood pressure levels have been found among physically active and fit persons who have normal weight or overweight (Paffenbarger et al. 1983; Carnethon et al. 2003; Fransson et al. 2003; Barengo et al. 2004). A healthier lipid profile has also been observed among more physically active or fitter individuals across all BMI classes (Wei et al. 1997; Carnethon et al. 2003; Fransson et al. 2003). There appear to be no published studies concerning levels of fasting insulin, glucose, or CRP in relation to physical activity or fitness and obesity.

Previous reports on the interrelationships between physical activity and obesity have utilized BMI as the measure of obesity and thus information on abdominal obesity is limited. Only two studies have reported findings on WHR or waist circumference (Lee et al. 1999; Hu et al. 2004c). The North American study (Lee et al. 1999) suggests a lower risk of all-cause and CVD mortality in fit men as compared to unfit men and the Finnish study (Hu et al. 2004c) suggests a lower risk of CVD in physically active men and women as compared to inactive persons in all abdominal obesity categories.

Studies on interrelationships of obesity and physical activity have not examined whether avoiding abdominal obesity or physical activity is more important in maintaining good health. Furthermore, more studies are needed in representative population samples with large age ranges, both sexes, and proper measurement methods of physical activity and cardiorespiratory fitness.

3 AIMS OF THE STUDY

The purpose of the present doctoral thesis was to investigate whether physical activity, estimated aerobic fitness, and abdominal obesity are independently associated with risk factors for CVD and type 2 diabetes in a large population sample of Finnish adults aged 25 to 74 years. The study also examined the interrelationships of physical inactivity and abdominal obesity with cardiovascular risk factors.

The specific objectives were:

1) to assess the distribution of estimated aerobic fitness in men and women across age groups and to study the associations of aerobic fitness with leisure time physical activity and self-rated fitness level (I).
2) to examine the association of estimated aerobic fitness with cardiovascular risk factors in men and women and to study whether the association is modified by abdominal obesity (II).
3) to study the associations of self-rated physical fitness, estimated aerobic fitness, and different types of leisure time physical activity with serum levels of high-sensitivity CRP in men and women and how abdominal obesity can modify the association of estimated aerobic fitness and CRP (III).
4) to investigate the associations of total, conditioning, non-conditioning, and commuting leisure time physical activity, self-rated physical fitness, and estimated aerobic fitness with fasting serum insulin and 2-hour plasma glucose levels (IV).
5) to study the joint association of overall leisure time physical activity and abdominal obesity with fasting serum insulin and 2-hour plasma glucose levels and with the risk of having impaired glucose tolerance or asymptomatic type 2 diabetes (IV).

4 METHODS

4.1 Study design and participants

This cross-sectional population study was part of the National FINRISK 2002 Study, which monitors cardiovascular risk factors in the Finnish adults aged 25 to 74 years. A stratified random sample was drawn from the Population Register in six geographical regions in Finland: the provinces of North Karelia, North Savo, Oulu, and Lapland, the cities of Turku and Loimaa and their 11 surrounding municipalities, and the cities of Helsinki and Vantaa. Stratification was done with region, sex, and 10-year age groups, including 250 individuals in each stratum and amounting to 13 437 subjects in total (Table 2). From this total sample, two thirds (n=9179) were randomized into the FINRISK Physical Activity Study. The participation rate was 60 percent (n=2764) for men and 70 percent (n=3216) for women. Those who did not participate in the study were more often young men from an urban environment. The Ethics Committee for the Research in Epidemiology and Public Health approved the study protocol and the participants provided their written consent. The entire study protocol, including sampling, laboratory measurements and analyses, followed closely the WHO MONICA Project protocol (World Health Organization 1988) and the recommendations of the European Health Risk Monitoring Project (Tolonen et al. 2002). The more detailed description of the number of participants and participation rates is exhibited in Figure 2.

Participants received an invitation by mail to attend a health examination at the local study site, where a trained nurse carried out measurements on weight, height, waist and hip circumferences, blood pressure, and a non-exercise fitness test. The nurse also took a fasting venous blood sample.

All men and women aged 45 to 74 years who visited the study site (n=3513) were later invited to participate in the FINRISK Blood Glucose Study, where a blood specimen for fasting plasma glucose and serum insulin was drawn and an oral glucose tolerance test was conducted**.** The limited amount of resources restricted the implementation of the oral glucose tolerance test to the total FINRISK Study population. Therefore only the participants aged 45 years and over were selected to the test.

Table 2. Sample sizes and participation rates of the National FINRISK 2002 Study and the FINRISK Physical Activity Study by 10-year age groups and sex.

Age group	**All**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**
				Men		
Original FINRISK sample (n)	6710	1480	1496	1497	1493	744
Physical Activity Study sub-sample (n)	4589	1019	1020	1020	1020	510
Participated in Physical Activity Study (n)	2764	498	581	627	709	349
Participation rate for Physical Activity Study (%)	60	49	57	61	70	68
				Women		
Original FINRISK sample (n)	6727	1490	1496	1496	1496	749
Physical Activity Study sub-sample (n)	4590	1020	1020	1020	1020	510
Participated in Physical Activity Study (n)	3216	667	721	731	754	343
Participation rate for Physical Activity Study (%)	70	65	71	72	74	67

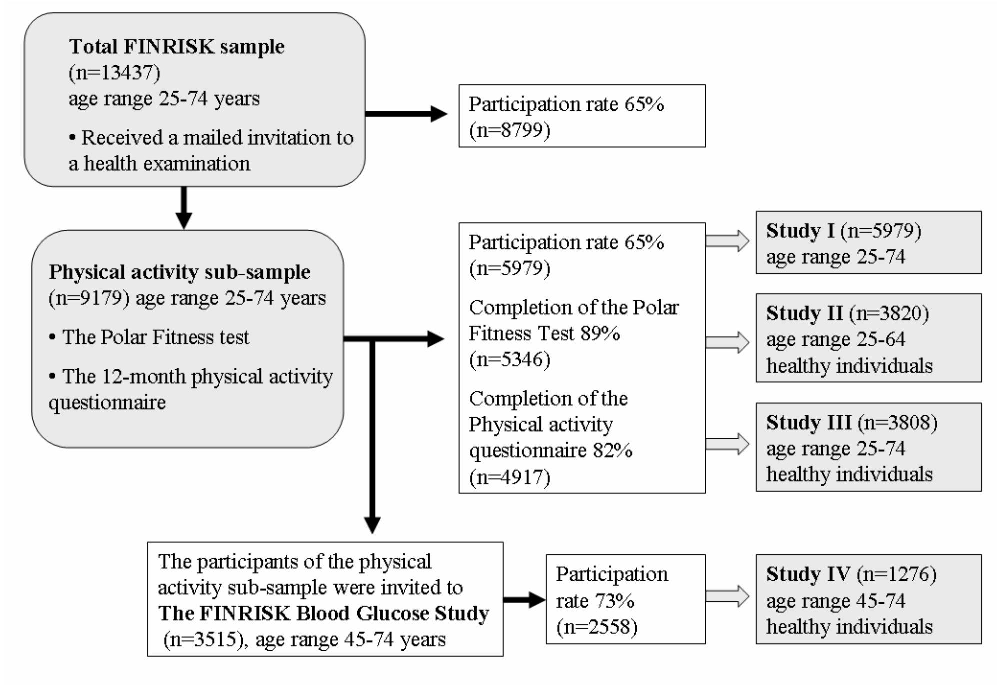


Figure 2. The participants of the National FINRISK 2002 Study, the Physical activity sub-sample, and the Blood Glucose Study.

4.2 Questionnaires

4.2.1 Leisure time physical activity

A detailed 12-month self-administered recall on leisure time physical activity (Appendix I) was adopted from the validated Kuopio Ischemic Heart Disease Risk Factor Study Questionnaire (Lakka and Salonen 1992a). A trained nurse briefly instructed the subjects in filling out the recall questionnaire. Physical activity was divided into conditioning (jogging, skiing, walking, weight training, gymnastics, swimming, etc.), non-conditioning (gardening, snow-shoveling, household chores, fishing, berry and mushroom picking, wood chopping, etc.), and commuting (walking and cycling to and from work) physical activity, and also total amount of activities was calculated. The recall allowed the estimation of frequency, duration, and intensity of each type of physical activity. The outcome measure was metabolic equivalents multiplied by hours per week (METh/wk), a relative measure of energy expenditure, where 1 MET corresponds to energy expenditure at rest. The metabolic cost of each physical activity was based on the Kuopio Ischemic Heart Disease Risk Factor Study protocol (Salonen and Lakka 1987) and other internationally accepted norms (Ainsworth et al. 1993; Ainsworth et al. 2000).

For the analyses, total, conditioning, and non-conditioning physical activities were stratified into sex-specific quarters. Commuting physical activity was divided into four categories, from no commuting activity to low, middle, and high activity. The cut-off points are reported in Studies I-IV. Overall physical activity was also dichotomized into physically active and inactive groups (Study IV) according to the current recommendations of physical activity by the Centers of Disease Control and Prevention (U.S. Department of Health and Human Services 1996). Those who were assigned to the active group undertook 30 minutes or more of moderate or higher intensity physical activity (≥3 METs) at least on five days of week.

4.2.2 Self-rated physical fitness

Self-rated physical fitness was assessed by asking “How do you consider your current physical condition?” The answer options were “very poor”, “fairly poor”, “satisfactory”, “fairly good”, and “very good”. The amount of individuals in the very poor fitness category was extremely low (n=45) and thus the categories of very poor and fairly poor were combined in the analyses.

4.2.3 Other self-reported variables

Participants received by mail a self-administered questionnaire to be filled in at home, before arriving at the study site. The questionnaire assessed medical history, smoking, and alcohol consumption in all subjects and menopausal status and the use of hormone replacement therapy in women. Medical history included questions on CVD, such as angina pectoris, myocardial infarction, coronary artery bypass surgery, coronary angioplasty, stroke, and heart failure, and other diseases, such as diabetes mellitus and acute infections. Medical history also included questions on the use of antihypertensive drug treatment and statins. Smoking behavior was assessed by the frequency of smoking, this being divided into daily smokers, ex-smokers, or non-smokers. Alcohol consumption was calculated as grams of pure alcohol per week using the recall of the preceding week. Participants were excluded from the analyses if any information on these background and confounding variables was missing.

4.3 Physical measurements

4.3.1 Anthropometric measurements

Height was measured without shoes by a measuring tape against a wall to an accuracy of 0.1 cm. Weight was determined on a balance scale in light clothing to an accuracy of 100 g. Participants had light clothing and were standing still for the measurements of waist and hip girths. Waist and hip circumferences were measured at the end of expiration. Waist circumference was measured at the midpoint between the iliac crest and the lowest rib, and hip circumference was measured at the widest part of the pelvis. Circumference was rounded up to the nearest 0.5 cm. All anthropometric measurements were carried out once. WHR was calculated as waist divided by hip, and was used in the analyses either as a continuous variable or divided into sex-specific thirds. The cut-off points are provided separately in Studies II-IV.

In the Studies II-IV, WHR was selected as the measure of abdominal obesity. All of the analyses were also run separately for waist circumference and BMI. The associations of waist circumference and BMI were statistically significant with all of the outcome variables under study. As the main aim was to examine abdominal obesity, BMI was not used as a measure of obesity in the analyses. The selection of WHR instead of waist circumference was based on the consistently stronger associations of WHR with cardiovascular risk factors and interactions between WHR and physical activity or fitness. Furthermore, the associations were more systematic in men and women with WHR as compared with waist circumference.

4.3.2 Estimated aerobic fitness

The participants underwent a non-exercise fitness test, called the Polar Fitness test (Polar Electro, Kempele, Finland) that estimates maximal oxygen uptake (VO_{2max}). The test is based on resting heart rate, heart rate variability, age, sex, height, weight, and a score of self-reported physical activity.

The nurse carried out the fitness test at the study site. The participant's information was entered into a special computer program. These data consisted of age, sex, measured height and weight, and self-reported physical activity level. Participants selected one of the four activity levels: low (no regular physical activity, occasional walking), moderate (30–90 minutes of regular recreational physical activity per week or moderate occupational physical activity), high (2–3 hours of regular heavy physical exercise per week), and very high (heavy physical exercise at least 5 times a week). Next, the participant was asked to take a comfortable seated position, with legs on the horizontal level. Following two minutes of quiet relaxation, heart rate data (R-R interval) was recorded for 5 minutes with a Polar S810 heart rate monitor (Polar Electro, Kempele, Finland). Finally, the heart rate data were entered and saved in the computer for estimations of aerobic fitness. The Polar Fitness Test was included in the Studies I-IV being referred there as either predicted aerobic fitness (I) or estimated aerobic fitness (II-IV).

The Polar Fitness Test was developed in healthy persons. CVD and drug treatment for hypertension may affect the heart rate variation, which is a crucial factor in estimating aerobic fitness by the Polar Fitness Test and thus can bias the fitness estimates. In the study population, individuals who had self-reported CVD or related condition (angina pectoris, myocardial infarction, coronary artery bypass surgery, coronary angioplasty, stroke, heart failure, or had consumed antihypertensive drug treatment during the previous seven days) were analyzed separately from healthy persons (I), were excluded (II, IV), or their diseases were adjusted in the analyses (III).

4.3.3 Blood pressure

Blood pressure was measured after five minutes' rest from the right arm in a sitting position with the mercury sphygmomanometer. The first phase of Korotkoff's sounds was recognized as systolic blood pressure and the fifth phase as diastolic blood pressure. Blood pressure was measured three times with a one-minute pause in between. The mean of the first and the second blood pressure measurements was used in the analyses. Based on the WHO MONICA protocol (World Health Organization 1988), the original FINRISK Study protocol included the measurement of blood pressure only twice. The more recent European Health Risk Monitoring Project has recommended three blood pressure measurements (Tolonen et al. 2002). Based on the decision of the research group, the mean of the first and second blood pressure measurements was used to ensure the comparability of the other FINRISK study years.

4.4 Laboratory analyses

For the venous blood specimen, participants were advised to fast for at least four hours prior to their visit at the study site. Total cholesterol, HDL cholesterol, triglycerides, and CRP levels were analyzed from serum blood samples, and later the HDL cholesterol to total cholesterol ratio was calculated. The fresh serum samples were transported to the central laboratory of the National Public Health Institute in Helsinki. Enzymatic methods were used to determine total cholesterol and HDL cholesterol levels (CHOD-PAP, Thermo Elektron Oy, Finland), and triglyceride levels (GPO-PAP, Thermo Elektron Oy). A high-sensitivity CRP concentration was determined using an immunoturbidometric method (Orion Diagnostica, Espoo, Finland) with the Optima analyser (Thermo Electron Corporation, Vantaa, Finland). The lowest detection level was at 0.2 mg/L. All values below the detection level were coded as 0.1 mg/L.

Glucose and insulin were measured according to the WHO guidelines (Alberti and Zimmet 1998). Participants were asked to fast for 12 hours prior to the test. The fasting blood sample was drawn to determine serum insulin and plasma glucose, and a 2-hour oral glucose tolerance test was performed. A blood sample was drawn 2 hours after the ingestion of the 300ml solution, containing 75g anhydrous glucose and 1.6g citric acid. Samples were first centrifuged and then frozen for transportation to the Laboratory of Analytical Biochemistry in National Public Health Institute, Helsinki. Plasma glucose was analyzed using a dehydrogenase method (ABX Diagnostics, Montpellier, France) and insulin using a microparticle enzyme immunoassay (Axsym, Abbott Diagnostics Division, Wiesbaden, Germany). Based on fasting and 2-hour plasma glucose values, impaired glucose tolerance and type 2 diabetes were defined as recommended by WHO (Alberti and Zimmet 1998). Individuals with fasting plasma glucose ≥7.0 mmol/L or 2-hour glucose ≥11.1 mmol/L were defined as having type 2 diabetes, and those with 2-hour glucose ≥7.8 and <11.1 mmol/L were defined as having impaired glucose tolerance.

4.5 Statistical methods

Some of the participants did not fill in the recall adequately to be able to quantify the relative energy expenditure. In 270 cases, the information was lacking on frequency, duration, or intensity in some physical activity items and these lacking values were replaced by the median of the same age and sex strata. In 752 cases, the information was lacking entirely and these cases were treated as missing cases. They were slightly more often men, less educated, older, and more obese as compared to those who filled in the physical activity recall.

All variables were first tested for normality. Due to their skewed distribution, physical activity in METh/wk (I), CRP (III) and insulin (IV) values were log-transformed for the analyses, but were transformed back to geometric means when presented in tables and figures. Variables on physical activity were also skewed, but they were mostly used as categorized variables or reported as medians when necessary.

One-way analysis of variance was used to study the associations between dependent and independent variables (Studies I, III and IV). Two-way analysis of covariance was applied to investigate the interactions between estimated aerobic fitness (II, III) or overall physical activity (IV) with WHR in relation to the risk factors of interest. Adjustments were made for potential confounding factors, such as age, WHR, smoking, the use of medications or hormone replacement therapy, menopausal status, a family history of diabetes, alcohol consumption, systolic blood pressure, hypercholesterolemia, and sex. Linear trends across the groups of independent variables were tested using linear regression analysis (I-IV), from where p-values for statistical interpretations were mostly adopted. In Study IV, logistic regression was carried out to assess the risk of impaired glucose tolerance and type 2 diabetes. Other statistical methods included t-test, Student-Newman-Keuls post hoc test, and Pearson partial correlation tests. All analyses were carried out using the Statistical Package for Social Sciences (SPSS, version 11.0.1, Chicago, IL, USA).

The analyses were run separately for men and women in Studies I-V, based on the assumption that cardiorespiratory fitness levels and WHR are lower in women as compared with men. The levels of most cardiovascular risk factors were lower in women than in men, which also supports analyzing the associations in men and women separately. In some parts of Study IV, men and women were combined to improve statistical power. Interaction tests were carried out for physical activity, WHR, and sex.

5 RESULTS

5.1 Estimated aerobic fitness (I)

5.1.1 Distribution of estimated aerobic fitness

The mean estimated maximal oxygen uptake was 38.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in healthy men and 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in healthy women ($p<0.001$ for sex difference, Table 3). The estimated maximal oxygen uptake declined significantly across each 10-year age group in both sexes ($p<0.001$), with a 0.12 and 0.13 $ml \cdot kg^{-1} \cdot min^{-1}$ decline per year in men and women, respectively. Persons with self-reported CVD or related condition and antihypertensive drug treatment had a lower estimated maximal oxygen uptake than healthy individuals. In these individuals, the mean estimated maximal oxygen uptake was 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and 31.9 $ml \cdot kg^{-1} \cdot min^{-1}$ in women ($p<0.001$ for difference).

Estimated maximal oxygen uptake was categorized by age and sex into seven categories of aerobic fitness from very poor to excellent according to international norms (Shvartz and Reibold 1990) (Table 4). The proportions of low, moderate, and high fitness were 33%, 25%, and 24%, respectively. Among women, the corresponding percentages were 24%, 35%, and 42%, showing that a larger proportion of women were in the high fitness group as compared with men.

Table 3. Estimated maximal oxygen uptake (VO_{2max}, ml·kg^{-1}·min^{-1}) in healthy men and women

	Years	N	Estimated VO_{2max}	95% CI	Range
Men					
	25-34	442	40.7[a]	39.9-41.4	23.6-72.4
	35-44	510	38.5[a]	37.9-39.1	24.7-66.6
	45-54	455	36.9	36.3-37.5	20.9-51.9
	55-64	400	36.7	36.1-37.2	19.1-54.1
	65-74	121	37.0	35.9-38.1	21.0-50.3
	All	1928	38.1[b]	37.8-38.5	19.1-72.4
Women					
	25-34	607	37.9[a]	37.1-38.7	16.2-69.6
	35-44	632	35.0	34.2-35.8	16.7-75.4
	45-54	558	34.8	33.9-35.6	13.2-80.6
	55-64	492	33.3	32.4-34.2	16.5-77.8
	65-74	150	32.2	30.6-33.8	17.1-74.4
	All	2439	35.1[b]	34.7-35.5	13.2-80.6

[a] Student-Newman-Keuls post-hoc test $p<0.001$ for differing from other groups

[b] T-test: $p<0.001$ between men and women

Table 4. Numbers and percentages (in parentheses) of men and women in low, middle, and high fitness categories by 10-year age groups.

	MEN			WOMEN		
Age	Low	Moderate	High	Low	Moderate	High
All	805 (33)	1017 (42)	621 (25)	696 (24)	1002 (35)	1205 (42)
25-34	277 (61)	120 (27)	54 (12)	194 (32)	307 (50)	111 (18)
35-44	228 (43)	244 (46)	59 (11)	228 (34)	292 (44)	152 (23)
45-54	197 (35)	276 (48)	97 (17)	167 (25)	165 (25)	330 (50)
55-64	94 (15)	284 (45)	247 (40)	103 (15)	171 (25)	420 (61)
65-74	9 (3)	93 (35)	164 (62)	4 (2)	67 (26)	192 (73)

The classification of fitness is based on seven original categories (Shvartz and Reibold 1990) that were divided into low (very poor, poor, fair), moderate (average, good), and high (very good, excellent) fitness categories for the present study.

5.1.2 Estimated and self-rated fitness and physical activity

A statistically significant direct association was found between conditioning leisure time physical activity and estimated aerobic fitness (age-adjusted Pearson correlation coefficient, $r=0.42$, $p<0.001$ in men, and $r=0.39$, $p<0.001$ in women). A weaker direct association was found for commuting physical activity with estimated aerobic fitness in men ($r=0.12$, $p<0.001$) and in women ($r=0.09$, $p<0.001$). The VO_{2max} was highest in those individuals who had the highest levels of conditioning and commuting physical activity. The VO_{2max} values decreased across the categories of conditioning and commuting physical activity in a dose dependent manner. Non-conditioning physical activity was not associated with estimated aerobic fitness in men or women.

Self-rated physical fitness was directly associated with estimated aerobic fitness in both sexes (ANOVA, $p<0.001$). Estimated aerobic fitness decreased across the categories of self-rated fitness (Student-Newman-Keuls post hoc test, $p<0.001$).

5.2 Estimated fitness, abdominal obesity, and cardiovascular risk factors (II)

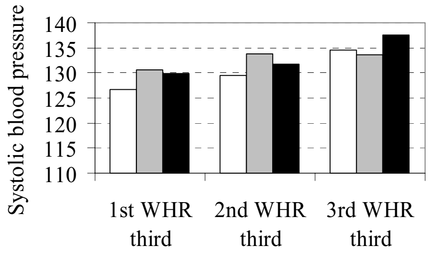
The numbers of men and women in the thirds of WHR and the categories of estimated aerobic fitness are presented in Table 5. In men (Figure 3), estimated aerobic fitness exhibited an inverse association with systolic and diastolic blood pressure and serum levels of total cholesterol and triglycerides. A direct association of aerobic fitness was found with HDL cholesterol and HDL to total cholesterol ratio. WHR exhibited a direct association with systolic and diastolic blood pressure, total cholesterol, and triglycerides, and an inverse association with HDL cholesterol and HDL to total cholesterol ratio.

To study whether the associations of estimated aerobic fitness with cardiovascular risk factors were similar in all WHR thirds, interactions were tested. Statistically significant interactions between estimated aerobic fitness and WHR were found for total cholesterol, HDL to total cholesterol ratio, triglycerides, as well as systolic and diastolic blood pressure. The association of aerobic fitness with HDL to total cholesterol ratio, triglycerides, and diastolic blood pressure tended to be stronger among men with a higher WHR than among men with lower WHR.

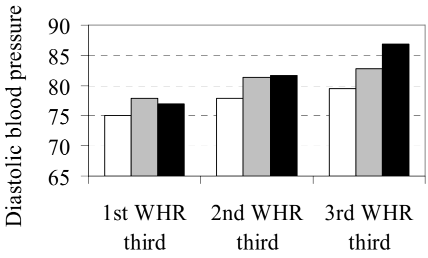
In women (Figure 4), aerobic fitness had an inverse association with diastolic blood pressure and triglycerides and a direct association with HDL cholesterol and HDL to total cholesterol ratio. WHR showed a direct association with systolic and diastolic blood pressure, total cholesterol, and triglycerides and an inverse association with HDL cholesterol and HDL to total cholesterol ratio.

Table 5. The number of men and women in WHR thirds and estimated aerobic fitness categories.

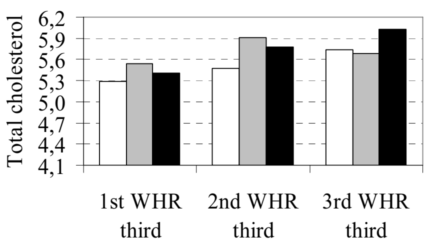
	Low fitness	**Moderate fitness**	**High fitness**	**Total**
MEN	**n**	**n**	**n**	**n**
1st WHR third	192	231	171	594
2nd WHR third	217	266	114	597
3rd WHR third	269	254	73	596
Total	678	751	358	1787
WOMEN				
1st WHR third	144	282	254	680
2nd WHR third	169	262	244	675
3rd WHR third	222	197	259	678
Total	535	741	757	2033



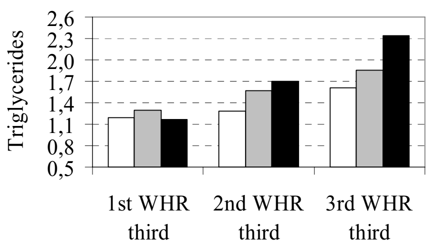
Fitness F=3.6, $p_{(trend)}$=0.027
WHR F=18.6, $p_{(trend)}$<0.001
Interaction F=3.4, p=0.009



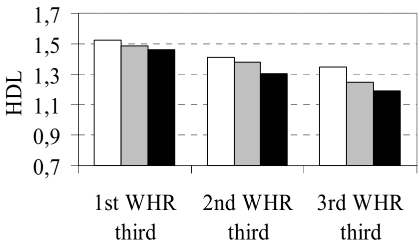
Fitness F=16.8, $p_{(trend)}$<0.001
WHR F=44.2, $p_{(trend)}$<0.001
Interaction F=5.2, p<0.001



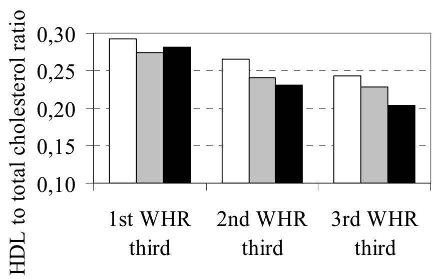
Fitness F=4.8, $p_{(trend)}$=0.009
WHR F=16.6, $p_{(trend)}$<0.001
Interaction F=4.7, p=0.001



Fitness F=7.5, $p_{(trend)}$=0.001
WHR F=33.2, $p_{(trend)}$<0.001
Interaction F=5.0, p=0.001

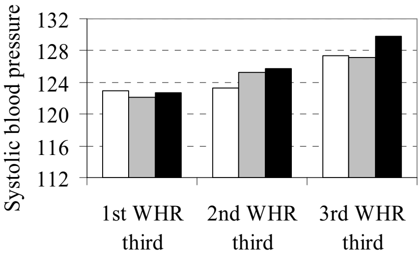


Fitness F=9.5, $p_{(trend)}$<0.001
WHR F=50.4, $p_{(trend)}$<0.001
Interaction F=1.0, p=0.39

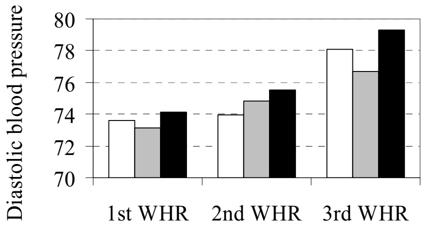


Fitness F=15.3, $p_{(trend)}$<0.001
WHR F=78.2, $p_{(trend)}$<0.001
Interaction F=3.8, p=0.005

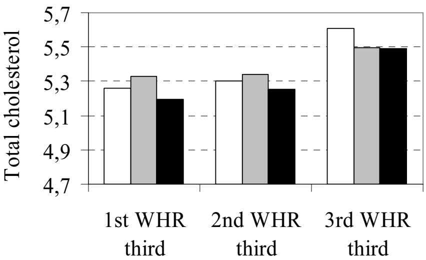
Figure 3. Systolic and diastolic blood pressure, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL), and HDL to total cholesterol ratio by estimated aerobic fitness and waist-to-hip ratio (WHR) in men. White bars represent the high fitness group, grey bars the moderate fitness group, and black bars the low fitness group, respectively. Adjusted for age, smoking, and alcohol consumption.



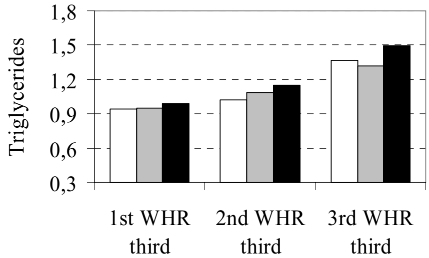
Fitness F=1.5, $p_{(trend)}$=0.23
WHR F=19.5, $p_{(trend)}$<0.001
Interaction F=0.9, p=0.45



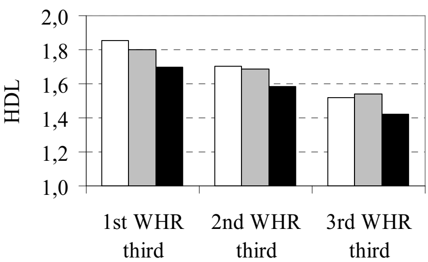
Fitness F=3.2, $p_{(trend)}$=0.027
WHR F=36.6, $p_{(trend)}$<0.001
Interaction F=1.1, p=0.35



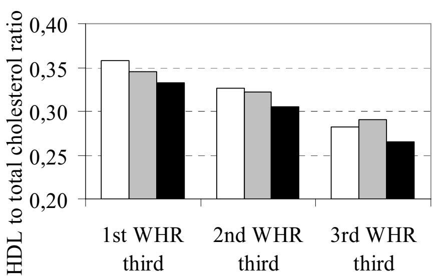
Fitness F=1.3, $p_{(trend)}$=0.26
WHR F=16.7, $p_{(trend)}$<0.001
Interaction F=0.7, p=0.58



Fitness F=5.5, $p_{(trend)}$<0.001
WHR F=94.2, $p_{(trend)}$<0.001
Interaction F=1.1, p=0.37



Fitness F=17.2, $p_{(trend)}$<0.001
WHR F=90.9, $p_{(trend)}$<0.001
Interaction F=0.7, p=0.59



Fitness F=12.6, $p_{(trend)}$<0.001
WHR F=118.5, $p_{(trend)}$<0.001
Interaction 1.2, p=0.32

Figure 4. Systolic and diastolic blood pressure, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL), and HDL to total cholesterol ratio by estimated aerobic fitness and waist-to-hip ratio (WHR) in women. White bars represent the high fitness group, grey bars the moderate fitness group, and black bars the low fitness group, respectively. Adjusted for age, smoking, alcohol consumption, hormone replacement therapy, and menopausal status.

5.3 Physical activity, self-rated and estimated fitness, and C-reactive protein (III)

Inverse age-adjusted associations of conditioning and non-conditioning physical activity with serum CRP among were found in both sexes (Table 6). After further adjustment for smoking, WHR, use of anti-hypertensive drugs and aspirin, diabetes, hypercholesterolemia, use of hormone replacement therapy, and menopausal status, the associations of conditioning and non-conditioning physical activity remained statistically significant in women ($p<0.001$ and $p=0.009$, respectively) and borderline significant in men ($p=0.076$ and $p=0.056$, respectively). Commuting physical activity had a statistically significant inverse association with CRP among women ($p=0.009$) but not among men.

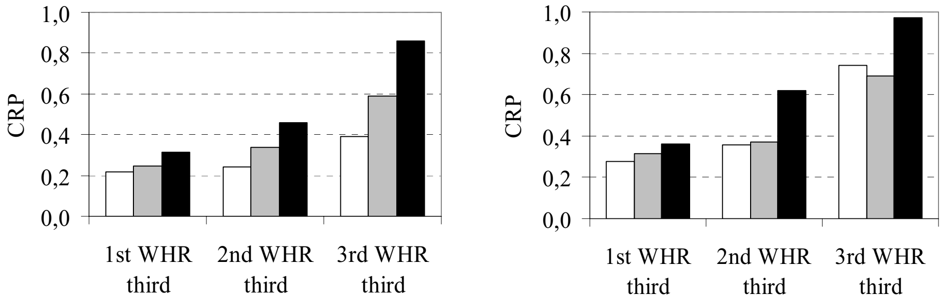
Self-rated physical fitness exhibited an inverse age-adjusted association with CRP in both sexes, and the association remained statistically significant also after further adjustment for smoking, WHR, use of anti-hypertensive drugs and aspirin, diabetes, and hypercholesterolemia in men and women and use of hormone replacement therapy and menopausal status in women ($p<0.001$ in both sexes, Table 6). Similarly, estimated aerobic fitness was inversely associated with CRP, and the association remained statistically significant after further adjustments ($p<0.001$ in both sexes, Table 6).

Estimated aerobic fitness exhibited an inverse association with CRP at all WHR levels (Figure 5), even though the relationship was somewhat inconsistent among women in the highest WHR third. The geometric mean CRP was 0.22 mg/L among men in the highest fitness category and the lowest WHR third compared to 0.87 mg/L among men in the lowest fitness category and the highest WHR third. In women, the geometric means in these corresponding groups were 0.27 mg/L and 1.02 mg/L. There were no statistically significant interactions between estimated aerobic fitness and WHR in men ($p=0.309$) or in women ($p=0.253$).

Table 6. C-reactive protein (CRP, geometric means, mg/L) by types of leisure time physical activity, self-rated physical fitness, and estimated aerobic fitness.

	Men		Women	
	N	CRP	n	CRP
Conditioning physical activity				
1st quarter	429	0.42	523	0.55
2nd quarter	427	0.40	521	0.47
3rd quarter	429	0.35	524	0.45
4th quarter	428	0.37	522	0.40
P for trend		*p=0.074*		*p<0.001*
Non-conditioning physical activity				
1st quarter	432	0.42	520	0.49
2nd quarter	424	0.39	525	0.51
3rd quarter	429	0.37	523	0.46
4th quarter	428	0.35	522	0.40
P for trend		*p=0.070*		*p=0.010*
Commuting physical activity				
No commuting activity	1190	0.39	1203	0.49
Low	173	0.35	292	0.48
Middle	169	0.38	293	0.43
High	180	0.38	302	0.39
P for trend		*p=0.936*		*p=0.012*
Self-rated physical fitness				
Poor	209	0.56	307	0.68
Satisfactory	688	0.40	852	0.48
Fairly good	686	0.35	812	0.41
Very good	130	0.29	119	0.30
P for trend		*p<0.001*		*p<0.001*
Estimated aerobic fitness				
Low	549	0.49	484	0.59
Middle	690	0.37	713	0.43
High	429	0.29	893	0.43
P for trend		*p<0.001*		*p<0.001*

Note. Adjusted for age, waist-to-hip ratio, smoking, anti-hypertensive drug use, aspirin use, diabetes and hypercholesterolemia. In women, adjusted also for hormone replacement therapy and menopausal status. Cut-off points (METh/wk): conditioning physical activity 2.4, 8.6, 20.0 in men and 3.1, 8.8, 18.0 in women, non-conditioning physical activity: 0.9, 4.0, 10.5 in men and 1.8, 4.8, 10.2 in women. Commuting physical activity: 0, 1.2, 4.5 in men and 0, 2.3, 6.9 in women.



Fitness F=18.5 , $p_{(trend)}$<0.001
WHR F= 43.0, $p_{(trend)}$<0.001
Interaction F=1.2 , p=0.31

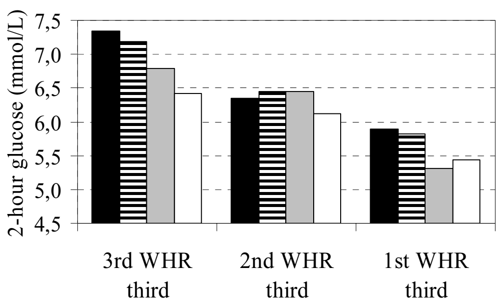
Fitness F=10,3 , $p_{(trend)}$<0.001
WHR F=64,6 , $p_{(trend)}$<0.001
Interaction F=1,2 , p=0.25

Figure 5. CRP (geometric mean, mg/L) by estimated aerobic fitness and waist-to-hip ratio (WHR) in men (left panel) and women (right panel). White bars represent the high fitness group, grey bars the moderate fitness group, and black bars the low fitness group, respectively. Adjusted for age, waist-to-hip ratio, smoking, anti-hypertensive drug use, aspirin use, diabetes and hypercholesterolemia. In women, adjusted also for use of hormone replacement therapy and menopausal status.

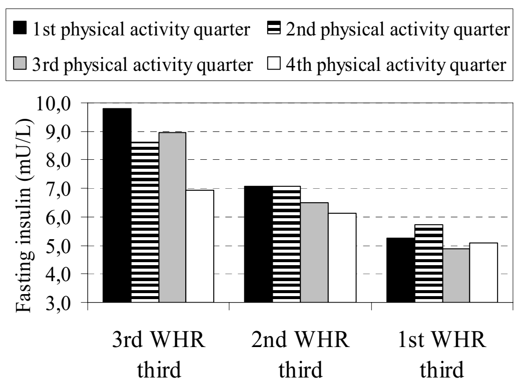
5.4 Physical activity, self-rated and estimated fitness, and glucose homeostasis (IV)

Overall and conditioning physical activity as well as self-rated and estimated fitness exhibited inverse age-adjusted associations with 2-hour glucose in men and women. All these associations remained significant after further adjustment for WHR, a family history of diabetes, systolic blood pressure, alcohol use, and smoking in women. In men, only the association of overall physical activity was significant after these adjustments. Overall and conditioning physical activity, self-rated physical fitness, and estimated aerobic fitness also showed inverse age-adjusted associations with fasting insulin in men and women. All these associations, except for that of estimated aerobic fitness in men, remained significant after further adjustments. Non-conditioning and commuting physical activity were not associated with 2-hour glucose or fasting insulin.

Two-hour glucose levels increased with increasing WHR (Figure 6). WHR did not modify the association between overall physical activity and 2-hour glucose. The highest 2-hour glucose levels were found among individuals who were abdominally most obese and physically least active. Also fasting insulin levels increased with increasing WHR (Figure 6). There was a significant interaction between WHR and overall physical activity with regard to fasting insulin levels. There were stronger associations between overall physical activity and fasting insulin as the WHR increased. The highest fasting insulin levels were observed in those individuals who were abdominally most obese and physically least active.



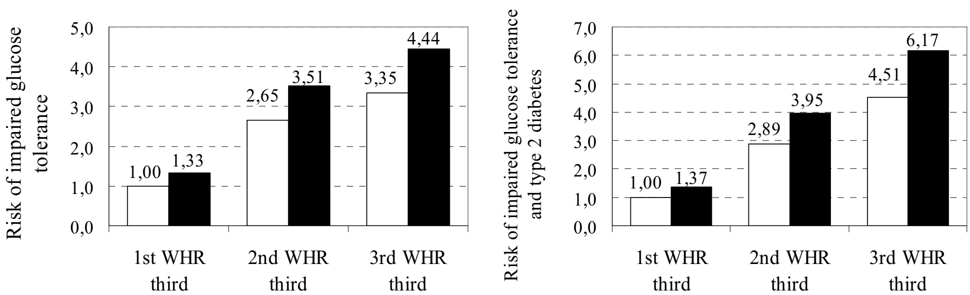
Physical activity F=4.7 , $p_{(trend)}<0.001$
WHR F=41,8 , $p_{(trend)}<0.001$
Interaction F=1,0 , p=0.426



Physical activity F=7.5 , $p_{(trend)}<0.001$
WHR F=94.1 , $p_{(trend)}<0.001$
Interaction F=2,4 , p=0.025

Figure 6. Means of 2-hour glucose and geometric means of fasting insulin in the quarters of overall physical activity by waist-to-hip ratio (WHR) in men and women combined. Adjusted for age, sex, family history of diabetes, systolic blood pressure, alcohol consumption, and smoking.

The risk of having impaired glucose tolerance and impaired glucose tolerance or type 2 diabetes was higher in physically inactive individuals who had higher WHR than in physically active persons with lower WHR after adjustment for age, sex, a family history of diabetes, systolic blood pressure, alcohol consumption, and smoking (Figure 7). The prevalence of impaired glucose tolerance and impaired glucose tolerance or type 2 diabetes was higher in the physically inactive individuals compared to their active counterparts across all WHR thirds. Physically inactive individuals who had the highest WHR had a 4.4 times higher risk of having impaired glucose tolerance and a 6.2 times higher risk of impaired glucose tolerance or type 2 diabetes than physically active persons who had the lowest WHR.



$p_{(\text{trend for physical activity})}=0.11$

$p_{(\text{trend for WHR})}<0.001$

$p_{(\text{trend for physical activity})}=0.048$

$p_{(\text{trend for WHR})}<0.001$

Figure 7. Odds ratios of impaired glucose tolerance alone and impaired glucose tolerance or type 2 diabetes combined with physical activity and waist-to-hip ratio (WHR), adjusted for age, sex, family history of diabetes, systolic blood pressure, alcohol consumption, and smoking. White bars represent physically active persons and black bars physically inactive individuals.

6 DISCUSSION

6.1 Methodological considerations

Study population and design

The present population-based study provided an excellent opportunity to investigate physical activity and aerobic fitness in relation to cardiovascular health in a large sample of Finnish men and women aged 25 to 74 years. The large sample size allowed the stratification of data by age and gender. It is important to assess whether the present findings are representative of the entire Finnish population. The participation rate was 60 percent for men and 70 percent for women, allowing us fairly well to generalize the results to the Finnish population. Most of the findings, however, deal with healthy people and some of them are restricted to particular age groups.

Sampling was implemented according to the MONICA protocol (World Health Organization 1988) from the Population Register. Therefore the stratified random sample of the general population is most likely unbiased in terms of age and gender, but should be viewed with caution in terms of geographical generalization, as the sample was drawn from six areas instead of a national random sample.

Non-participants are often different from the participants and this may result in selection bias (Campbell and Machin 1999, p. 29). Based on the available demographic data on the non-participants, those who did not attend the study were often younger men from an urban environment. Younger men are generally healthier than older men, which may have biased our results by underestimating some of the associations.

Due to the study design, only cross-sectional associations between variables of interest could be investigated. Therefore, the study does not provide evidence for causal relationships of physical activity, fitness, and obesity with cardiovascular risk factors.

Self-reported questionnaires

The different questionnaires used in this study have their inherent strengths and limitations. All of the instruments have been proven to be relatively accurate, as described in the methods section. Questionnaire data were self-reported, which may have caused recall biases. To minimize this bias, a trained nurse provided the participant with advice on filling out the questionnaires. Nevertheless, some data on leisure time physical activity from the 12-month recall were missing for 12.6% (n=752) of the subjects. The missing cases were slightly more often men, older, less educated, and more obese as compared to those who filled in the physical activity recall. If the missing cases had been included in the analyses, the statistical power would have been better and the range of the physical activity would have been larger. Thus, the associations of physical activity with the outcome variables might have been stronger if the information on all participants had been available.

Physical activity is often affected by seasonal variation. The 12-month recall overcomes the problem of seasonality, which can be considered as one of its strengths. Furthermore, the detailed quantitative assessment of 23 common types of physical activity in Finland gave us the opportunity to calculate relative energy expenditure, a method not often used in population studies.

Individuals with diseases and disease-related conditions may be physically less active and less fit than healthy persons. This could bias the results if this is not taken into account in the analyses. Some of the previous health-related studies on physical activity have been criticized for not adjusting for confounding factors, such as health behavior and medical history. One strength of the present study is that information on participants' self-reported health behavior and medical history was collected by questionnaires and included in the analyses.

Measurements at the study site

To ensure the validity and repeatability of the measurements, all nurses were specially trained to carry out the study protocol as recommended (World Health Organization 1988). During the two-week training phase, nurses practiced all the measurement methods thoroughly, including how to measure weight, height, WHR, blood pressure, perform the Polar Fitness Test, and draw the blood sample.

Regarding the accuracy of the blood sampling and their analyses, participants were advised to fast for at least four hours prior to their visit at the study site. The four-hour fasting period can be criticized for being too short for an accurate risk factor assessment from the blood samples. It should be recognized, however, that the short fasting period tends to underestimate the true associations. Blood samples were analyzed in the central laboratory of the National Public Health Institute. Analyzes were implemented systematically and reliably with recommended methods and the same personnel. The participants fasted for 12-hours prior to the 2-hour oral glucose tolerance test, this protocol being adopted from WHO (Alberti and Zimmet 1998).

Of the physical measurements, blood pressure is the most prone to measurement error. Blood pressure levels fluctuate a lot and are unstable even at individual level. To ensure a valid measurement, blood pressure was measured three times after five minutes of rest. Based on the older WHO MONICA study protocol**,** the mean of the first and second measurement was used in the analyses. The nurses who were responsible for the measurement of blood pressure were circulated in the six survey areas to avoid measurer bias.

Estimated aerobic fitness, as measured by the Polar Fitness Test, is a surrogate of cardiorespiratory fitness. Of the variables used in calculating estimated maximal oxygen uptake, the self-reported score of weekly physical activity was most prone to a recall bias, whereas other variables were measured at the study site and thus were quite accurate. Heart rate was measured accurately by using an electrocardiogram. The participants were advised to arrive to the test site in a rested and fasted state to overcome the problem of abnormal heart rate variability caused by exercise or caffeine or other stimulatory compounds.

The applicability of the Polar Fitness Test is limited to healthy individuals 25 to 64 years of age. These restrictions were taken into account by excluding persons above 65 years of age, those with self-reported CVD or a related condition, and those who were taking antihypertensive drug treatment or by adjusting for age, CVD, and medication.

WHR was selected as the measure of abdominal obesity. Waist circumference has often been suggested as the measure of abdominal obesity instead of WHR, particularly in a clinical setting (Despres et al. 2001). However, WHR remains a useful tool for defining abdominal obesity in research (Folsom et al. 2000; World Health Organization 2000, p. 10). Previous studies in Finland suggest that WHR is a better predictor for acute coronary events and accelerated progression of carotid atherosclerosis than BMI (Lakka et al. 2001; Lakka et al. 2002). In the present study, WHR, waist circumference, and BMI were significantly associated with the outcome variables. The selection of WHR instead of waist circumference as a measure of abdominal obesity was based on the stronger associations for WHR in Studies II-IV and on more systematic findings in men and women.

Statistical methods

There were 270 physical activity questionnaires in which there were missing values for the frequency, duration, or intensity of physical activity. The missing values on these components of physical activity were substituted by the median of the same age and sex strata. The substitution of missing values tends to underestimate the true associations.

The statistical methods used consist of one-way and two-way analysis of covariance and logistic regression models, which are appropriate methods in cross-sectional analyses. The normality of the dependent variables was tested in all statistical analyses. A two-way analysis of covariance was chosen to study the independent and joint associations of physical activity, aerobic fitness, and obesity with cardiovascular risk factors. The estimated means of the two-way analyses were presented in the results. The interpretation of the statistical significance of the joint associations was based on p-values of the interaction terms.

6.2 Estimated and self-rated fitness and physical activity

Estimated aerobic fitness was lower among women and decreased with age. These findings are in concordance with the results of previous studies that measured maximal aerobic power or used mathematical equations (Jackson et al. 1990; Shvartz and Reibold 1990; Fletcher et al.

1995; Jackson et al. 1995; Jackson et al. 1996). The estimated aerobic fitness of the older Finnish men and women in the present study sample was higher than values from other studies (Shvartz and Reibold 1990; Fletcher et al. 1995; Jackson et al. 1995; Rauramaa et al. 1995; Jackson et al. 1996; Paterson et al. 1999). It is possible that the participants of the present study were truly fit or else represented a selected population. Another explanation may be that the Polar Fitness Test overestimates true fitness levels. Nevertheless, this is the first study in which the Polar Fitness Test has been tested in a representative population sample. The present study indicates that the Polar Fitness Test provides similar fitness levels to international studies in the same age groups. The study also suggests that the Polar Fitness Test is a feasible, non-invasive method for measurement of aerobic fitness and that it is easy to carry out by trained nurses.

Conditioning and commuting physical activity were directly associated with estimated aerobic fitness, which is in line with the results of previous studies (Siconolfi et al. 1985; Jacobs et al. 1993; Booth et al. 1996; Wareham et al. 2002). However, non-conditioning physical activity had a weak association with aerobic fitness. The reason for the stronger associations of conditioning and commuting physical activity with aerobic fitness may be that these activities are more intensive than non-conditioning activities. The intensity of physical activity may be a more important determinant of aerobic fitness than volume.

Few studies have examined the associations of estimated and measured aerobic fitness with cardiovascular risk factors, and the methods used in these studies have varied a lot. The Polar Fitness Test uses information on regular physical activity to estimate aerobic fitness. Although the estimated aerobic fitness has a relatively high correlation with self-reported physical activity, other variables such as age and sex contributed to the estimate of aerobic fitness. For example, women and older persons had lower levels of aerobic fitness, showing that the level of physical activity did not dominate the estimates. These findings suggest that the Polar Fitness Test is a true measure of aerobic fitness and not only a measure of physical activity.

6.3 Fitness, abdominal obesity, and cardiovascular risk factors

Good estimated aerobic fitness was independently associated with a better cardiovascular risk factor profile. The estimated aerobic fitness exhibited strong associations with HDL cholesterol, HDL to total cholesterol ratio, triglycerides, and diastolic blood pressure in both sexes, and with total cholesterol and systolic blood pressure in men. These findings are similar to the results of previous studies on aerobic fitness and cardiovascular risk factors (Blair et al. 1984; Haddock et al. 1998; McMurray et al. 1998; Murphy et al. 2002; Carnethon et al. 2003). Most population studies have used self-reported physical activity instead of aerobic fitness, but their findings, nevertheless, are similar to the observations of the present study on lipid profile and blood pressure (Thune et al. 1998; Bassett et al. 2002; Fransson et al. 2003; Jakes et al. 2003; Hu et al. 2004a). The present study confirmed the previous data on the strong associations of WHR with cardiovascular risk factors (World Health Organization 2000).

The combined effect of aerobic fitness and abdominal obesity on cardiovascular risk factors has not been studied in detail before. The present study showed that unfit and abdominally obese individuals had the most unfavorable risk factor profile. The associations of the estimated aerobic fitness with diastolic blood pressure, triglycerides, and higher HDL to total cholesterol ratio were stronger as the WHR increased in men. The few previous reports on the present topic have used BMI as a measure of obesity and have only reported serum lipid profile or the prevalence of hypertension (Wei et al. 1997; Fagard 1999; Carnethon et al. 2003). In a large cross-sectional study physically active individuals with a high BMI had a better risk profile than physically inactive individuals with obesity (Fransson et al. 2003).

The associations of estimated aerobic fitness with total cholesterol and systolic blood pressure were weaker among women than among men, and this may be due to different fitness distributions in men and women or menopausal status or hormonal replacement therapy in women. However, the results remained unchanged if they were restricted to pre-menopausal women, suggesting that hormonal status is an unlikely explanation for the findings. Other studies have also suggested that the associations between physical activity or fitness with cardiovascular risk factors are weaker in women than in men (Greendale et al. 1996; Siscovick et al. 1997; Wilmore et al. 2001). Furthermore, the interactions between obesity and fitness were weaker among women. These findings suggest that fitness modifies the association between abdominal obesity and risk factors less in women than in men. Another explanation for these observations is that WHR may function differently as a measure of obesity for men and women, as has been reported previously for cardiovascular risk factors (Rankinen et al. 1999; Tanaka et al. 2002; Hu et al. 2004c; Tanaka et al. 2004).

Together with previous prospective epidemiological studies (Thune et al. 1998; Wannamethee et al. 2000; Carnethon et al. 2003) the present study provides evidence that regular physical activity and a good aerobic fitness improve the levels of traditional risk factors, such as serum lipids and lipoproteins and blood pressure, and thereby reduce the risk of CVD. The enhanced lipid profile, mostly reported as higher HDL cholesterol and lower triglyceride levels, has several possible mechanisms. These include changes in the different enzyme activities that regulate the transportation and catabolism of triglyceride and HDL cholesterol levels in blood, such as LPL and HL enzymes, lecitin:cholesterol acyltransferase, and hepatic lipase (Durstine and Thompson 2001; Dishman et al. 2004, p. 159). The blood pressure lowering effect of exercise is believed to be related to a decreased basal cardiac output and total peripheral resistance (Dishman et al. 2004, p. 141; Pescatello et al. 2004). In this perspective, the sympathetic nervous system might have an important role (Dishman et al. 2004, p. 131-144). In addition, decreased catecholamine levels, improved insulin sensitivity, and alterations in vasodilators and vasoconstrictors may all be related to the antihypertensive effects of exercise (Pescatello et al. 2004).

The amount of visceral adipose tissue can be reduced by physical activity, which is also seen as an important mechanism of how physical activity is associated with a better cardiovascular risk factor profile. The adipose tissue functions as an endocrine organ and adipocytes secrete hormones, cytokines, and proteins that may also regulate the levels of cardiovascular risk factors (Mohamed-Ali et al. 1998).

6.4 Physical activity, fitness, and C-reactive protein

Good self-rated physical fitness and estimated aerobic fitness were independently associated with decreased levels of CRP, a marker of systemic inflammation, among apparently healthy men and women. Few previous studies have reported such associations and these studies have been conducted in smaller volunteer samples or the studies have included either men or women (Church et al. 2002; LaMonte et al. 2002).

Regular conditioning and non-conditioning physical activity exhibited inverse age-adjusted associations with CRP in men and women. The associations remained statistically significant after further adjustments for variables previously associated with CRP levels in women only. Most previous studies have investigated the associations of overall leisure time physical activity or the intensity level of exercise with CRP but their findings are consistent with the present data (Geffken et al. 2001; Abramson and Vaccarino 2002; Ford 2002; King et al. 2003; Raitakari et al. 2005). Two studies pointed to a stronger association of obesity than exercise with CRP (Rawson et al. 2003; Marcell et al. 2005). There are a few intervention studies reporting that exercise training can reduce CRP levels in sedentary persons (Lakka et al. 2005), in obese women (You et al. 2004), and in persons at high risk for CVD (Smith et al. 1999).

The FINRISK Study is the first study to investigate the association between commuting physical activity with CRP. Commuting physical activity was inversely and independently associated with CRP in women, but not in men. The inconsistency among sexes could be explained by a misclassification of men into the four activity categories or by behavioral differences between men and women. A larger proportion of men (70%) than women (58%) did not engage in any commuting physical activity, and women reported higher levels of commuting physical activity than men. Also, the study was carried out in winter or early spring and possible acute anti-inflammatory effects of commuting activity, which may be more typically performed in summer, may not have been detectable.

Physical activity needs to be regular if it is to achieve health benefits. In the present study, the CRP levels were 27 percent lower among women in the highest quarter as compared with those in the lowest quarter. The highest quarter performed physical activity at least 18 METh/wk, which translates to about 3.5 hours of brisk walking per week, regularly during the 12-month study period. This amount meets the current recommendation of 30 minutes on most days of the week (U.S. Department of Health and Human Services 1996). All measured modes of physical activity were inversely associated with CRP in a dose-dependent manner.

Only one study has reported the joint relationship between aerobic fitness and obesity on CRP levels and has suggested that the inverse association between fitness and CRP levels was strongest in the most obese individuals (Aronson et al. 2004). Consistent with these findings, a steep decrease in CRP levels with increasing estimated aerobic fitness was found in individuals with the highest WHR. This finding suggests that abdominally obese individuals benefit most from good aerobic fitness. A possible explanation for this could be that CRP levels are close to normal and therefore difficult to be reduced in individuals with normal weight.

The inflammation suppressing effect of physical activity is largely unknown. Inflammation modulating cytokines, such as tumor necrosis factor-alpha and interleukin-6, are produced by adipose tissue and stimulate CRP production in the liver (Pearson et al. 2003). Indeed, physical activity may suppress inflammation by reducing the amount of adipose tissue. The present data were adjusted for obesity, suggesting that the inflammation reducing effect of regular physical activity is independent of body fat. The more direct mechanisms of how physical activity reduces CRP have been suggested as well. Previous studies suggest that exercise reduces the expression and blood levels of leukocyte adhesion molecules, inhibits interactions between monocytes and endothelial cells (Jordan et al. 1997), decreases the production of pro-inflammatory cytokines, and increases the production of anti-inflammatory cytokines by mononuclear cells (Smith et al. 1999), maintains balance between the production of pro-inflammatory and anti-inflammatory cytokines in skeletal muscles (Greiwe et al. 2001; Febbraio et al. 2003), improves antioxidative defences (Powers et al. 1999), and reduces the susceptibility of LDL to oxidation (Vasankari et al. 1998). Randomized controlled trials are needed to investigate the inflammation suppressing mechanisms in more detail.

6.5 Physical activity, fitness, and glucose homeostasis

Higher levels of overall leisure time physical activity, self-rated physical fitness, and estimated aerobic fitness were associated with improved glucose tolerance and reduced fasting serum insulin levels. These findings are in concordance with previous studies on the associations of physical activity and fitness with glucose homeostasis (Wannamethee et al. 2000; Kriska et al. 2001b; Van Dam et al. 2002; Lakka et al. 2003). In general, the associations of physical activity have been stronger with insulin than with glucose levels (Kriska et al. 2001a), but also non-significant results have been reported (Jarrett et al. 1986). Some studies have indicated that the relationship of overall physical activity with insulin or glucose is similar or stronger than that of physical fitness (Wareham et al. 2000; Kriska et al. 2001a). These results agree with the findings of the present study concerning the association of physical activity and fitness with insulin and glucose levels. There is some evidence that the improvement in insulin sensitivity in response to physical activity is related more to the duration rather than the intensity of exercise, at least in obese individuals (Houmard et al. 2004).

To support the findings of this study on conditioning physical activity, two studies have reported inverse associations of moderate to vigorous leisure time physical activity with glucose homeostasis (Mayer-Davis et al. 1998; Cox et al. 2004). Only one study has described the associations of leisure time, occupational, and commuting physical activity with the risk of type 2 diabetes (Hu et al. 2003). However, fasting insulin or 2-hour glucose levels across categories of physical activity were not reported. One study found no relationship between non-vigorous physical activities and insulin sensitivity (Mayer-Davis et al. 1998), which is in line with the data from this study on the association of non-conditioning physical activity with insulin. No previous study has reported commuting physical activity in relation to insulin or glucose. One reason for the modest associations of non-conditioning and commuting physical activity with glucose and insulin levels may be that the intensity of these physical activities does not reach the level needed to improve glucose metabolism.

In many studies, as in the present study in men, the associations of physical activity with glucose and insulin levels have disappeared after controlling for obesity (Regensteiner et al. 1991; Mayer-Davis et al. 1998). This finding suggests that obesity may be more strongly related to abnormal glucose regulation than physical activity, but may also be due to the difficulty in assessing physical activity adequately and the higher accuracy achieved for measurement of obesity (Blair et al. 2001; Seidell et al. 2001a).

Strong inverse associations of physical activity with fasting insulin and 2-hour glucose levels were found among women, whereas the associations were weaker in men. These findings disagree with some of the results of some previous studies (Jarrett et al. 1986; Regensteiner et al. 1991; Kriska et al. 2001a). The stronger relationship in women may be due to higher levels or the larger range of physical activity found in women.

The present study indicates that WHR is directly associated with 2-hour glucose and fasting insulin levels and that physical activity is inversely associated with 2-hour glucose and fasting insulin at all levels of abdominal obesity. These results suggest that it is beneficial to be physically active, even for individuals with abdominal obesity. In each WHR third, the risk of impaired glucose tolerance and type 2 diabetes was significantly higher among individuals who did not undertake 30 minutes of moderate-intensity physical activity on at least five days per week. The risks of impaired glucose tolerance and type 2 diabetes were highest among individuals who had abdominal obesity and did not reach the level of physical activity mentioned above. These findings are in line with the results of previous studies, even though they have not focused on abdominal obesity (Manson et al. 1991; Manson et al. 1992; Lynch et al. 1996; Hu et al. 1999; Kriska et al. 2003; Hu et al. 2004b). Few studies have found an association between physical activity and the risk of impaired glucose tolerance (Dunstan et al. 2004).

This is one of the first studies to report the combined effect of physical inactivity and abdominal obesity on the risk of impaired glucose tolerance and type 2 diabetes. To prevent impaired glucose tolerance and type 2 diabetes it is crucial to avoid abdominal obesity and to engage in 30 minutes of moderate-intensity physical activity on most days of the week. The favorable effect of physical activity on insulin sensitivity and glucose tolerance at the molecular level is not fully understood. Current knowledge suggests that exercise leads to an increased activity of the key enzymes and proteins involved in skeletal muscle metabolism, improves insulin sensitivity, and increases glucose uptake in the contracting skeletal muscles

(Holloszy and Hansen 1996; Albright et al. 2000; Hawley 2004). Physical activity also reduces body adiposity and thereby improves insulin sensitivity (Albright et al. 2000). Importantly, the insulin sensitivity improving effect of exercise is transitory and thus regular physical activity is required.

7 CONCLUSIONS

In the Finnish healthy population, higher levels of estimated aerobic fitness, regular leisure time physical activity, and lower levels of abdominal obesity were associated with a favorable cardiovascular risk factor profile. The risk factor levels were better among individuals with high physical activity and aerobic fitness at all levels of abdominal obesity. Avoidance of abdominal obesity may be even more important than avoidance of physical inactivity in regard to favorable cardiovascular risk factor levels.

The conclusions to the specific study questions are:

1. In healthy adults aged 25 to 74 years, the mean estimated maximal oxygen uptake was 38.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in women and decreased with increasing age. Self-rated physical fitness and conditioning and commuting physical activities showed strong direct associations with estimated aerobic fitness.

2. A good estimated aerobic fitness and a low WHR were independently associated with a better risk factor profile in healthy men and women aged 25 to 64 years. In fit men, the associations with risk factor levels were stronger than in unfit men.

3. Self-rated physical fitness and estimated aerobic fitness were associated with decreased levels of CRP among healthy adults aged 25 to 74 years. Conditioning, commuting, and non-conditioning physical activity had inverse associations with CRP in women. In men, the associations of conditioning and non-conditioning physical activity with CRP were weaker and commuting physical activity was not associated with CRP. Estimated aerobic fitness had an inverse association with CRP across the WHR thirds, showing that even obese individuals benefit from good aerobic fitness.

4. Higher levels of leisure time physical activity and estimated aerobic fitness were associated with improved glucose tolerance and reduced fasting serum insulin levels in healthy adults aged 45 to 74 years.

5. Physical activity was inversely associated with 2-hour glucose and fasting insulin at all levels of abdominal obesity. The risk of impaired glucose tolerance and type 2 diabetes was significantly higher among individuals who did not undertake 30 minutes of moderate-intensity physical activity on five days per week in comparison with physically more active persons at all levels of WHR.

8 FUTURE DIRECTIONS

Based on the findings of this study, the recommendations for future research are as follows:

1. The estimated aerobic fitness test uses a novel technique to assess maximal aerobic power without exercise stress test and is inexpensive and safe. More studies are needed to provide information on the usefulness of the test in other populations and how estimated aerobic fitness predicts morbidity and mortality.

2. Physical activity behavior and some of its associations with cardiovascular risk factors may be different among men and women. More studies are needed to understand how physical activity behavior differs between the genders and how an unfavorable cardiovascular risk factor profile could be enhanced by physical activity.

3. Higher levels of physical activity and fitness were associated with lower levels of CRP. Randomized controlled trials are needed to study the magnitude of the effect of physical activity on systemic low-grade inflammation, the dose of physical activity needed for the anti-inflammatory effect and the causal pathways underlying the effect.

4. Self-rated physical fitness has not been studied in detail and studies are needed to investigate the associations of self-rated physical fitness with morbidity and mortality.

5. More research is needed to specify the most beneficial types of physical activity and the amount and intensity of physical activity needed to prevent the development of impaired glucose tolerance and type 2 diabetes. Studies are also needed to investigate the independent and combined effects of physical inactivity and obesity on impaired glucose tolerance and type 2 diabetes.

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APPENDIX I

FINRISKI 2002

The FINRISK Physical Activity Questionnaire

Date: ____________________

1. Fitness-related physical activity

1.1 How often have you exercised, both earlier and nowadays, in your leisure time in the age groups which apply to you below. (e.g. jogging, cross-country skiing, cycling, swimming, walking, pole/Nordic walking, aerobics, ball games, ice hockey, etc.)?

	15-24	25-34	35-44	45-54	55-64	over 65
No exercise because of disability or disease						
A few times a year or less						
1-3 times a month						
Once a week						
2-3 times a week						
4-5 times a week						
More than 5 times a week						

1.2 Have you ever participated in competitive sports?

1 Never (move to question 2.1)

2 Yes

1.3 At what age did you participate in competitive sports? Between _____-_____ years

1.4 In what events did you compete? Circle the event/events in the list.

1	Running	4	Football	7	Ice hockey	10	Rowing
2	Cross-country skiing	5	Baseball	8	Orienteering	11	Wrestling
3	Gymnastics	6	Volleyball	9	Swimming	12	Track and field

13 Other, what: ____

2. Physical education

2.1 Below you will find six statements on physical education (P.E.). Recall your school years and circle the best option.

	I entirely agree	I somewhat agree	I don't know	I somewhat disagree	I entirely disagree
P.E. was interesting and pleasant.	1	2	3	4	5
I actively participated in P.E.	1	2	3	4	5
I learned useful physical activity skills in P.E. classes.	1	2	3	4	5
P.E. has motivated me to be physically active also after finishing school.	1	2	3	4	5
P.E. classes were overly oriented to competitive sports.	1	2	3	4	5
The number of P.E. classes was sufficient.	1	2	3	4	5

3. Occupational physical activity

3.1 Have you been working in the past 12 months?

1 Yes
2 No (move to question 4)

3.2 The average duration of your workday (including breaks)
______h ________min

3.3 Think about your typical workday. Estimate all the activities performed during the workday (including lunch break) and the average duration with an accuracy of 15 minutes. If you work only part of the year, the question concerns the time when at work. Commuting is not part of the workday.

Activity	Duration
Sitting	_____ h_______ min
Sitting in a car/vehicle	_____ h_______ min
Standing	_____ h_______ min
Walking on level ground	_____ h_______ min
Walking on uneven ground (forest)	_____ h_______ min
Climbing stairs, cycling or running	_____ h_______ min
Forestry, construction work or agriculture	_____ h_______ min
Loading work (or similar)	_____ h_______ min
Other, what: ____________________	_____ h_______ min

4. Leisure time physical activity in the past 12 months

Leisure time physical activity refers to commuting activity, conditioning activity, and daily chores that demand physical activity.

Filling instructions

- Fill in all activities of the past 12 months.
- Specify in each month of the past 12 months how many times (number of sessions) per month you have engaged in different types of physical activity.
- If you have not engaged in a particular event, check in the column ‘Not participating at all’.
- Into the column ’average duration’, estimate the time you normally spend in each type of activity.
- The intensity of physical activity ranges between 0-3, and the classes are defined in detail on the next page.

EXAMPLE

	Not participating at all (check in)	January	February	March	April	May	June	July	August	September	October	November	December	Average duration per session (min)	Intensity class (0-3)
Commute: walking (one way =1 session)	X														
Commute: cycling (one way =1 session)						6	4	10						10	1
Jogging, running, orienteering					2	2				4		4		45	2
Cross-country skiing		1	4											45	3
Walking, pole/Nordic walking, hiking	X														
Leisure time cycling, stationary cycling	X														
Swimming, water gymnastics	X														
Gymnastics	X														
Aerobics	X														
Floorball	X														
Golf	X														
Other ball and racket games	X														
Downhill skiing, snowboarding	X														
Skating, roller skating	X														
Rowing (distance, indoor)	X														
Dance										2	2	3	3	60	1
Weight training	X														
Bowling	X														
Hunting, berry/mushroom picking, fishing										1	1			90	0
Gardening/yard work, snow shoveling						1	3	3	5	1				20	0
Carpentry and renovation hobbies	X														
Forest work	X														
house work, cleaning		6	6	6	6	6	6	6	6	6	6	6	6	15	0
Other, what:															
Other, what:															

Which of the following activities have you performed during the last 12 months?
Estimate your most usual intensity category of each activity by choosing one of the following classes:

Class	Intensity	Breathlessness
0	Light	None
1	Moderate	Some
2	Strenuous	Out of breath
3	Very strenuous	Heavy breathing

Fill in the following table according to the example on the previous page.

	Not participat-ing at all (check in)	January	February	March	April	May	June	July	August	September	October	November	December	Average duration per session (min)	Intensity class (0-3)
Commute: walking (one way =1 session)															
Commute: cycling (one way =1 session)															
Jogging, running, orienteering															
Cross-country skiing															
Walking, pole/Nordic walking, hiking															
Leisure time cycling, stationary cycling															
Swimming, water gymnastics															
Gymnastics															
Aerobics															
Floorball															
Golf															
Other ball and racket games															
Downhill skiing, snowboarding															
Skating, roller skating															
Rowing (distance, indoor)															
Dance															
Weight training															
Bowling															
Hunting, berry/mushroom picking, fishing															
Gardening/yard work, snow shoveling															
Carpentry and renovation hobbies															
Forest work															
house work, cleaning															
Other, what:															
Other, what:															

5. Leisure time physical activity during the past 7 days

Reply by writing on the empty line or checking in the box.

When replying • **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. • **Moderate** physical activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

5.1 During the past week, on how many days did you do **<u>vigorous</u>** physical activities like heavy lifting, snow shoveling, aerobics, cross-country skiing or running. Think only of those physical activities that you did for at least 10 minutes at a time.

_________ days per week
☐ None (*Move to question 5.3*)

5.2 How much time, in total, did you usually spend on one of those days doing vigorous physical activities?

______ hours _____minutes

5.3 During the past week, on how many days did you do **<u>moderate</u>** physical activities like carrying light loads, home gymnastics or light jogging. **Do not include walking.** Think only of those physical activities that you did for at least 10 minutes at a time.

_________ days per week
☐ None (*Move to question 5.5*)

5.4 How much time, in total, did you usually spend on one of those days doing **<u>moderate physical activities?</u>**

______ hours _____minutes

5.5 During the past week, on how many days did you **<u>walk</u>** for at least 10 minutes at a time? This includes walking at work or home, walking to travel from place to place, and any other walking that you did solely for recreation and exercise.

_________ days per week
☐ None (*Move to question 5.7*)

5.6 How much time in total did you usually spend walking on one of those days?

______ hours _____minutes

5.7 How much time did you spend *<u>sitting</u>* **on a normal weekday?** This includes sitting at work and during leisure time, at home, while visiting friends, studying and traveling. This includes time spent sitting or lying down to read or to watch television.

______ hours _____minutes

5.8 Were the last 7 days **typical** (normal work/school week) or **untypical** (holiday/sick)?

☐ Typical
☐ Untypical

6. Importance of leisure time physical activity and physical activity skills

6.1 What is your opinion on your own leisure time physical activity?

1 I am physically active enough. (Move to question 6.3.)
2 I am physically active, but not enough.
3 My leisure time physical activity is completely inadequate.

6.2 What are the most important reasons for your physical inactivity? Circle those options you find most important.

1 I am lacking in time.
2 Equipment is too expensive.
3 Facilities are too far or out of reach.
4 Entrance fees are too high.
5 I am lacking the skills to do physical activities.
6 I don't have a friend or group to be physically active with.
7 I don't like to exercise.
8 I have a disease or injury that restricts my engagement in physical activity.
9 Other reason, what? ____

6.3 What is your opinion on the statements regarding physical activity and health that are listed below? Circle the option that best reflects your opinion.

	I entirely agree	I somewhat agree	I don't know	I somewhat disagree	I entirely disagree
Insufficient physical activity is hazardous to health.	1	2	3	4	5
Finns would be healthier if they were physically active more often.	1	2	3	4	5
Physicians say enough to their patients about the importance of physical activity in health promotion and disease treatment.	1	2	3	4	5
I know enough about the health benefits of physical activity.	1	2	3	4	5
Physicians should be allowed to prescribe physical activity instead of, or alongside with, prescribed medication.	1	2	3	4	5
The social security system should compensate expenses on physical activity prescribed by physicians (e.g. swimming hall and fitness club, exercise counselling, etc.) as it compensates medication or other treatment costs.	1	2	3	4	5

6.4 Has a physician or a nurse ever advised you to exercise?

1 Yes
2 No

6.5 A list of the most popular physical activities among Finns follows below. Please give an estimation of your skills in each physical activity by circling the best option.

	I cannot at all	I can, but poorly	I can pretty well	I can very well
Cross-country skiing	1	2	3	4
Running	1	2	3	4
Track and field	1	2	3	4
Swimming	1	2	3	4
Gymnastics	1	2	3	4
Dance	1	2	3	4
Orienteering	1	2	3	4
Golf	1	2	3	4
Floorball	1	2	3	4
Football	1	2	3	4
Skating	1	2	3	4
Volleyball	1	2	3	4
Baseball	1	2	3	4
Downhill skiing	1	2	3	4
Weight training	1	2	3	4
Roller skating	1	2	3	4
Bowling	1	2	3	4

Thank you for your reply!

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Physical activity study
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