TURUN YLIOPISTON JULKAISUJA
ANNALES UNIVERSITATIS TURKUENSIS

SARJA - SER. D OSA - TOM. 873

MEDICA - ODONTOLOGICA

PHYSICAL ACTIVITY IN ADOLESCENCE

- with special reference to cardiovascular health

by

Katja Pahkala

TURUN YLIOPISTO
UNIVERSITY OF TURKU
Turku 2009

From the Research Centre of Applied and Preventive Cardiovascular Medicine, the Paavo Nurmi Centre and the Department of Pediatrics, University of Turku, Finland.

Supervised by

Professor Olli J. Heinonen
Paavo Nurmi Centre
Turku, Finland

Adjunct professor Hanna Lagström
Turku Institute for Child and Youth Research
Turku, Finland

Adjunct professor Paula Hakala
Research Department of the Social Insurance Institution
Turku, Finland

Reviewed by

Professor Tuomo Rankinen
Pennington Biomedical Research Center
Baton Rouge, LA, USA

Professor Willem van Mechelen
VU University Medical Center
Amsterdam, the Netherlands

Dissertation opponent

Adjunct professor Mikael Fogelholm
Academy of Finland
Helsinki, Finland

ISBN 978-951-29-4064-6 (PRINT)
ISBN 978-951-29-4065-3 (PDF)
ISSN 0355-9483
Painosalama Oy – Turku, Finland 2009

To Petri

ABSTRACT

Katja Pahkala

PHYSICAL ACTIVITY IN ADOLESCENCE - with special reference to cardiovascular health

The Research Centre of Applied and Preventive Cardiovascular Medicine, the Paavo Nurmi Centre and the Department of Pediatrics, University of Turku, Turku, Finland.
Annales Universitatis Turkuensis. Medica – Odontologica, Turku, Finland, 2009.

The development of atherosclerotic cardiovascular disease is a long process that begins in childhood. Lack of physical activity has a detrimental effect on cardiovascular disease and its risk factors throughout life.

The aim of this study was to investigate physical activity and its association with cardiovascular health among adolescents. The subjects comprised adolescents who participated in a longitudinal atherosclerosis prevention study (STRIP) at age 13 years and provided data on their leisure-time physical activity (n=560). Data on anthropometric and laboratory measures, vascular endothelial function and diet were assessed.

A low level of leisure-time physical activity was common among girls. Low leisure-time physical activity was associated with higher screen time among boys, but not girls. Maternal, but not paternal, leisure-time physical activity and body weight were associated with the child's leisure-time physical activity. Girls with little leisure-time physical activity were already since age two years more often overweight than their physically more active peers. Clustering of cardiovascular disease risk factors was more prevalent among the adolescents with low rather than high leisure-time physical activity. Boys who do little leisure-time physical activity had impaired endothelial function compared to their physically more active peers. This is an important finding since vascular endothelial function may indicate cardiovascular health before structural changes occur.

Lack of leisure-time physical activity was common in adolescents, especially girls. A lack of leisure-time physical activity was adversely associated with cardiovascular disease risk factors and vascular endothelial function. To support cardiovascular health, active efforts are needed to promote a physically active lifestyle in adolescents.

Key words: children, physical activity, exercise, CVD, risk factor, obesity, lipids, cluster, endothelium, health promotion

TIIVISTELMÄ

Katja Pahkala

LIIKUNTA JA SYDÄN- JA VERISUONITERVEYS NUORILLA
Sydäntutkimuskeskus; Paavo Nurmi -keskus ja lastentautioppi, Turun yliopisto, Turku.
Annales Universitatis Turkuensis. Medica – Odontologica, Turku, 2009.

Aikuisiällä ilmenevien sydän- ja verisuonisairauksien kehitys alkaa lapsuudessa. Vähäinen liikunta lisää vaaraa sairastua sydän- ja verisuonisairauksiin sekä vaikuttaa haitallisesti näiden sairauksien riskitekijöihin läpi elämän.

Tämän tutkimuksen tavoitteena oli tutkia nuorten liikuntaa ja sen yhteyttä sydän- ja verisuoniterveyteen. Sydän- ja verisuoniterveyttä tutkittiin riskitekijöiden sekä valtimon laajentumiskyvyn avulla. Tutkittavat koostuivat nuorista, jotka osallistuivat pitkäaikaisen sepelvaltimotaudin ehkäisytutkimuksen (STRIP) 13-vuotistutkimuskäynnille ja jotka raportoivat vapaa-ajan liikuntatottumuksensa (n=560). Liikunnan lisäksi nuorten pituus, paino, verenpaine ja olkavaltimon laajentumiskyky mitattiin sekä analysoitiin laboratorionäytteitä (otettiin verinäyte) ja selvitettiin ruoankäyttöä.

Vähäinen vapaa-ajan liikunta oli yleistä etenkin tytöillä. Vapaa-ajallaan vähän liikkuvat pojat viettivät enemmän aikaa televisio- ja tietokoneruudun ääressä kuin vapaa-ajallaan paljon liikkuvat pojat. Äidin, toisin kuin isän, vapaa-ajan liikunta ja paino olivat yhteydessä lapsen vapaa-ajan liikuntaan. Vähän liikkuvat tytöt olivat olleet jo kahden vuoden iästä saakka useammin ylipainoisia kuin runsaammin liikkuvat ikätoverinsa. Sydän- ja verisuonisairauksien riskitekijöiden kasautuminen oli tavallisempaa vähän kuin paljon liikkuvilla nuorilla. Vähän liikkuvilla pojilla oli lisäksi huonompi olkavaltimon laajentumiskyky kuin paljon liikkuvilla pojilla. Tämä on tärkeä löydös, koska valtimon laajentumiskyky kuvannee sydän- ja verisuoniterveyttä jo ennen rakenteellisten muutosten ilmaantumista.

Useat nuoret, etenkin tytöt, liikkuivat vähän vapaa-ajallaan. Vähäisellä vapaa-ajan liikunnalla oli haitallinen yhteys sydän- ja verisuonisairauksien riskitekijöihin sekä valtimon laajentumiskykyyn. Nuorten kannustaminen liikunnalliseen elämäntapaan on erittäin tärkeää sydän- ja verisuoniterveyden edistämiseksi sekä nuoren että kansanterveyden kannalta.

Avainsanat: lapset, liikunta, sydän- ja verisuonisairaudet, riskitekijä, lihavuus, lipidit, kasautuminen, endoteeli, terveyden edistäminen

CONTENTS

ABBREVIATIONS

AN(C)OVA	analysis of (co)variance
Apo	apolipoprotein
BMI	body mass index
bpm	beats per minute
CI	95% confidence interval
CVD	cardiovascular disease
E%	percentage of total energy intake
FMD	flow-mediated dilatation
HDL-C	high-density lipoprotein cholesterol
hs-CRP	high-sensitivity C-reactive protein
IQR	inter-quartile range
kcal	kilocalorie
LDL-C	low-density lipoprotein cholesterol
MET	metabolic equivalent
PAI	leisure-time physical activity index
OR	odds ratio
RANOVA	repeated measures analysis of variance
SD	standard deviation
SE	standard error
SFA	saturated fatty acids
STRIP	Special Turku coronary Risk factor Intervention Project for children

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals:

I Pahkala K, Heinonen OJ, Lagström H, Hakala P, Sillanmäki L, Simell O. Leisure-time physical activity of 13-year-old adolescents. Scand J Med Sci Sports 2007;17:324-330.

II Pahkala K, Heinonen OJ, Lagström H, Hakala P, Sillanmäki L, Viikari JSA, Simell O. Parental and childhood overweight in sedentary and active adolescents. Scand J Med Sci Sports 2008; Nov 5 [Epub ahead of print]

III Pahkala K, Heinonen OJ, Lagström H, Hakala P, Hakanen M, Hernelahti M, Ruottinen S, Sillanmäki L, Rönnemaa T, Viikari JSA, Simell O. Clustered metabolic risk and leisure-time physical activity in adolescents. Submitted.

IV Pahkala K, Heinonen OJ, Lagström H, Hakala P, Simell O, Viikari JSA, Rönnemaa T, Hernelahti M, Sillanmäki L, Raitakari OT. Vascular endothelial function and leisure-time physical activity in adolescents. Circulation 2008;118:2353-2359.

1 INTRODUCTION

Physical activity is good for your health. This is hardly news for anyone. Indeed, already more than two millennia ago, Hippocrates (ca. 460 BC – ca. 370 BC) is cited as having stated that "Walking is man's best medicine". Since the times of Hippocrates, what folk medicine took for granted regarding the health benefits of physical activity has been scientifically proven. The first modern studies on the relationship between physical activity and health emerged in the 1950's. In these reports, occupation was used as an indicator of physical activity. The classic study by Morris and co-workers (1953) compared the drivers and conductors of the London's double-decker busses. The incidence of coronary heart disease was higher among drivers, who were not physically active during work, than among conductors, who were active by walking up and down the bus stairs. Gradually as jobs began to be physically less demanding, physical activity during leisure-time took the focus of interest. As for occupational physical activity, leisure-time physical activity was shown to provide protection against coronary heart disease (Paffenbarger et al. 1978, Morris et al. 1980). The health benefits of physical activity were corroborated in studies assessing cardiorespiratory fitness. Consistently, the incidence of cardiovascular disease (CVD) and all-cause mortality was highest in the least fit (Taylor et al. 1970, Blair et al. 1996, Kujala et al. 1998). Today, physical activity is known to have a favorable effect on a wide range of diseases also other than CVD, e.g., type 2 diabetes, certain types of cancer, osteoporosis and mental health.

Along with growing evidence of the importance of physical activity on health, several recommendations for physical activity have been released. Currently, the consensus is that adults should accumulate 30 minutes of moderate intensity aerobic activity, e.g., brisk walking, on at least five days of the week and do muscle-strengthening activities at least twice a week (U.S. Department of Health and Human Services 2008). Additional health benefits are gained with more physical activity. Despite all the knowledge and efforts to increase physical activity, many people fail to reach the recommendation (Troiano et al. 2008). Interestingly, turning it around – is limiting the daily sitting, lying and other sedentary behaviors to only 23.5 hours really an unattainable target?

In terms of physical activity, our way of life has indeed changed considerably. A few decades ago, physical activity was an essential part of daily life for nearly everyone. Today, the jobs of the modern society require hardly any physical effort. We live surrounded by gadgets designed to make our lives easier but which at the same time save any energy that might be expended at daily chores. Furthermore, instead of walking or cycling, we often rely on a car or a bus to take us even short distances. Physical activity is currently more or less something we need deliberately to set out to do. This change in our exposure to physical activity is problematic, since everybody is obviously not interested in deliberately engaging in physical activity. Also given the possibility to avoid incidental physical activity associated with, e.g., transport, we may truly live a life of minimal physical activity today.

Despite many advances in our knowledge of medicine and nutrition, CVD is still a major cause of death in the world (Yach et al. 2004). The development of CVD begins in childhood, but it takes decades before overt disease emerges. Because of the increasingly sedentary lifestyle also among children, we are now in a new, worrisome situation, where CVD may again turn up at an earlier age. This study was conducted to investigate physical activity and its relation with cardiovascular health among adolescents in the modern society, which favors a sedentary lifestyle.

2 REVIEW OF THE LITERATURE

Health benefits of physical activity are many – indeed, physical activity should be regarded as a “polypill” able to prevent and treat a wide range of diseases. This thesis focuses on the physical activity of adolescents (Figure 1). Special emphasis is put on the effects of physical activity on cardiovascular health, indicated by CVD risk factors and vascular endothelial function. In this thesis, an adolescent is considered to be a person aged 13 to 17 years.

2.1 Physical activity in adolescence

2.1.1 Physical activity and sedentary behaviors

Physical activity is defined as any bodily movement produced by skeletal muscles that results in increased energy expenditure (Caspersen et al. 1985). Physical activity is characterized by its intensity, frequency and duration, and it can been seen as a continuum from physical inactivity to extreme activity. Thus, when physical activity increases, inactivity decreases, and *vice versa*. People can be placed along the continuum according to their physical activity, and regarded as, e.g., physically inactive, moderately active or active. There is no consensus on the definition of a physically inactive person. Inactivity can be defined as not meeting the recommendation for physical activity or by an artificial cut-off point that relates to the distribution of physical activity in the given study group.

In adolescence, the opportunities for physical activity consist mainly of active commuting to school, physical education, physical activity during lesson breaks and during leisure-time, participation in sports and of unorganized physical activity. There are two consistent findings on physical activity in children and adolescents: boys are physically more active than girls (Tammelin et al. 2007, Horst et al. 2007, Currie et al. 2008, Nader et al. 2008) and physical activity declines through childhood to adolescence (Kimm et al. 2002, Trost et al. 2002, Riddoch et al. 2004, Currie et al. 2008). The current recommendation for physical activity states that school-aged youth should engage in moderate to vigorous physical activity at least one hour daily to promote health (Strong et al. 2005, U.S. Department of Health and Human Services 2008). This is in line with the recent Finnish guidelines (Tammelin & Karvinen 2008). However, the number of adolescents who do not meet the recommendation is alarmingly high. In the U.S., 69% of 15-year-old adolescents do not meet the recommendation during weekdays, and the corresponding proportion is even higher, 83%, during weekends (Nader et al. 2008). Similarly, in the Health Behaviour in School-aged Children study covering 41 countries, the proportion of adolescents who reported not meeting the recommendation for physical activity varied from 65% to 95% in 13-year-old girls and from 49% to 86% in boys of similar age (Currie et al. 2008). Furthermore, 90% of Finnish girls and 77% of Finnish boys reported failing to meet the recommendation of one hour of moderate to vigorous activity daily (Tammelin et al. 2007). Of note is, however, that the mean time of moderate to

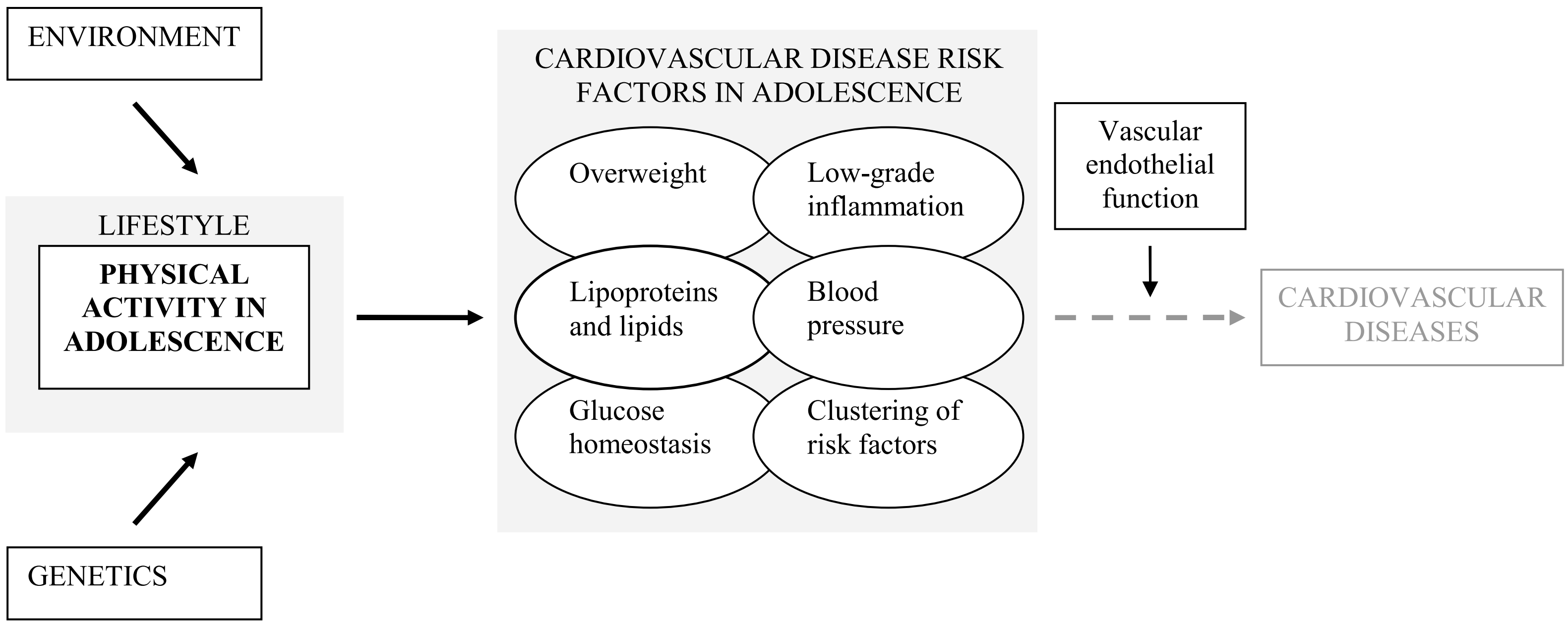

Figure 1. Physical activity, selected cardiovascular disease risk factors and vascular endothelial function in adolescence.

vigorous physical activity assessed objectively in adolescents varies greatly from 16 to 99 minutes per day (Riddoch et al. 2004, Ness et al. 2007, Nader et al. 2008). This is partly a result from the different definitions of moderate to vigorous activity and makes it difficult to compare pertinent reports on this subject. Nevertheless, all in all a great number of adolescents are currently not sufficiently active with regard to maintenance of good health.

Studies not only try to capture the physically active time of adolescents, but assess also the time spent sedentary. TV viewing, or in broader terms, screen time, is often used as a marker of sedentarism. The displacement theory suggests that physical activity and sedentary behaviors replace each other. For instance, if an adolescent watches a lot of TV, he does not have time to be physically active. The findings of an association between physical activity and sedentary behavior in adolescents are, however, contradictory (Feldman et al. 2003, Ekelund et al. 2006, Vandewater et al. 2006, Tammelin et al. 2007, Horst et al. 2007). The lack of association between physical activity and sedentary behaviors is not all that surprising, because sedentary behavior is not the opposite of physical activity (Katzmarzyk et al. 2007, Horst et al. 2007), and the sedentary behaviors assessed generally cover only a limited proportion of the total sedentary time, e.g., only TV viewing. Furthermore, a person may fulfill the recommendation for physical activity and thus be regarded as physically active and, at the same time, spend the rest of the day sedentary. Sedentary behaviors (Strong et al. 2005) and, more precisely, entertainment media time (American Academy of Pediatrics 2001), should be limited to two hours per day for children and adolescents according to current recommendations. Approximately half of all adolescents exceed this recommendation in terms of TV viewing alone (Tammelin et al. 2007, Currie et al. 2008).

2.1.2 Effect of genetics

Physical activity has a genetic component that was first shown in family and twin studies (Kaprio et al. 1981, Perusse et al. 1989). Twin studies differ from family studies in that monozygotic twins allow the discrimination of genetic influences from environmental influences, which is not possible in family studies. The magnitude of the genetic effect is investigated in twins by comparing the concordance of physical activity between monozygotic and dizygotic twin pairs. The literature on this topic reports the genetic contribution to physical activity most inconsistently: the genetic contribution ranges from low to relatively high heritability (Simonen et al. 2002, Stubbe et al. 2006, Teran-Garcia 2008). This variation is, in part, explained by differences in the assessment of physical activity (Stubbe et al. 2005). Also on a general level, twin studies provide greater heritability estimates than family studies (Simonen et al. 2002). In the largest twin study conducted, the median heritability of exercise participation was 62% with a range of 27% to 71% (Stubbe et al. 2006). Of note, heritability plays a role in both ends of the physical activity continuum (Simonen et al. 2002, Carlsson et al. 2006); a low activity level as well as a high activity level have genetic components.

Sex-specific data on the heritability of physical activity among adults are scarce and inconsistent (Maia et al. 2002, Stubbe et al. 2006). In adolescents, the genetic contribution to physical activity may be stronger in males than in females (Beunen & Thomis 1999, Maia et al. 2002). It is unclear whether the genetic effect differs across age groups (Kaprio et al. 1981, Stubbe et al. 2005, Carlsson et al. 2006). The genetic contribution may be stronger to vigorous than to total physical activity (Kujala et al. 2002), and to inactivity than to moderate or vigorous physical activity or to total physical activity (Simonen et al. 2002). The genetic contribution may also vary between different types of physical activity, e.g., sports/exercise participation and habitual or leisure-time physical activity (Perusse et al. 1989, Maia et al. 2002).

There is not much data on specific genes contributing to physical activity. The candidate genes include the dopamine D_2 receptor, angiotensin converting enzyme, leptin receptor, melanocortin 4 receptor, calcium-sensing receptor and aromatase (CYP19A1) (Teran-Garcia et al. 2008).

Taken together, genetics partly determine the level of a person's physical activity. Detailed data on the genetic component of physical activity is, however, still limited.

2.1.3 Effect of environment

The environment has many features which contribute to physical activity in adolescence. The key features potentially associated with adolescent physical activity are here classified into the following levels: home, school, neighborhood and city/municipality and region/country (Ferreira et al. 2006).

At the *home level*, the availability of exercise equipment, family structure, modeling of physical activity from parents, siblings or friends, support from parents, friends or more broadly, from significant others and parental socio-economic status have been studied as factors possibly associated with adolescent physical activity (Ferreira et al. 2006). The impact of these determinants are generally inconsistent and there is usually no association with adolescent physical activity (Ferreira et al. 2006). For instance, half of the studies assessing the effect of support from parents on adolescent physical activity found a direct association while the other half found no association. Regarding general support from significant others, mother's education level and family income, most studies support a direct association with adolescent physical activity (Ferreira et al. 2006). The finding that physical activity of the adolescent increases with increasing parental education level is also supported by a more recent review (Horst et al. 2007). However, there was no association between adolescent physical activity and parental physical activity or socio-economic status (Horst et al. 2007). Parental concerns about traffic safety are strongly related to active commuting to school: children and adolescents are more likely to actively commute to school if their parents have few compared to many traffic safety concerns (Kerr et al. 2006). In longitudinal studies, maternal physical activity during pregnancy and parental physical activity when the child was 21 months old are directly associated with physical activity at age 11-12 years (Mattocks et al. 2008) whereas a low birth order is related to an increased risk of a sedentary lifestyle in similarly aged children (Hallal et al. 2006b).

At the *school level*, role modeling or support from teachers and instruction on health benefits of physical activity are generally not related to physical activity in adolescence (Ferreira et al. 2006), while physical education seems to increase adolescent physical activity (Horst et al. 2007). After-school programs aiming to increase physical activity may also positively associate with adolescent physical activity (Beets et al. 2009). The association between adolescent physical activity and problems with classmates (teasing) is not clear (Ferreira et al. 2006). The type of school is associated with adolescent physical activity in that students attending non-vocational schools are more active than vocational school students (Ferreira et al. 2006). The adolescents' engagement in physical activity during school recess periods is positively influenced by improvements in the activity areas and adult supervision of the activities (Sallis et al. 2001).

At the *neighborhood level*, the availability of physical activity equipment or facilities is unrelated to adolescent physical activity in most studies reviewed by Ferreira and co-workers (2006) and Horst and co-workers (2007). The effect of the distance to physical activity facilities is not clear (Ferreira et al. 2006). However, the vicinity and the number of commercial physical activity facilities are positively associated with physical activity level and intensity among adolescent girls (Dowda et al. 2007, Pate et al. 2008). The walkability in the neighborhood, the number of stores within a 20 minute walk, walking and biking facilities (e.g., sidewalks) and the esthetics of the neighborhood are for one positively related to active commuting to school (Kerr et al. 2006). Higher perceived traffic safety supports active transport to recreation sites for physical activity (Grow et al. 2009). Crime incidence and crime threat are inversely associated with adolescent physical activity (Ferreira et al. 2006, Grow et al. 2009).

Only a few studies have investigated the effect of the environment on adolescent physical activity at the *city/municipality* and *region/country level* determined by the location of residence (Ferreira et al. 2006). Residence in an urban versus rural environment is not associated with physical activity, and the effect of season or weather is not clear (Ferreira et al. 2006). Recently, ambient temperature was positively associated with physical activity of children while rainfall was associated with a reduction in activity (Duncan et al. 2008).

Both genetic and environmental factors affect physical activity in adolescence. It is not known whether heritability or environment is more important. Familial resemblance in physical activity reflects both shared genetic and environmental factors. In all, it is important to understand that due to genetic predisposition, the ease or difficulty of engaging in physical activity varies between individuals. Likewise, the environment may encourage or discourage physical activity of an adolescent.

2.1.4 Assessment of physical activity

Physical activity is assessed with several methods. Objective methods include the doubly labeled water technique, indirect calorimetry, direct observation, heart rate monitoring, accelerometry and pedometry. Recently, devices which combine heart rate monitoring and accelerometry have emerged (Corder et al. 2008). Although objective measurement of physical activity would be the ideal choice, practical and financial reasons often limit their use. Thus, subjective methods, i.e., questionnaires, proxy-reports and diaries are used to assess physical activity. In all, the assessment physical activity is challenging.

Objective methods

While no golden standard for the measurement of physical activity as a behavior exists, the *doubly labeled water technique* is considered as the reference method for the assessment of energy expenditure (Armstrong & Welsman 2006). The technique presumes that the difference in the elimination rates of hydrogen and oxygen isotopes (^{2}H, ^{18}O) is related to carbon dioxide production, which in turn is related to energy expenditure. The strength of the method is that it gives accurate data on total energy expenditure. However, the energy expenditure caused specifically by physical activity cannot be directly obtained. The method is also very expensive.

Similarly to the doubly labeled water technique, *indirect calorimetry* is used to measure energy expenditure. Due to its inconvenience in everyday life, it has mainly been used to validate heart rate monitors, accelerometers and pedometers (Armstrong & Welsman 2006).

Contrary to the methods measuring energy expenditure, physical activity patterns, even those lasting for a short time, can be captured with *direct observation*. The method is, however, labor-intensive, time consuming and thus costly. A further limitation of the direct observation method is that the observer might influence the subject's behavior.

Heart rate monitoring was the first widely used objective measure of physical activity in children and adolescents (Rowlands & Eston 2007). Heart rate is, however, not a direct measure of physical activity. Rather, it gives an indication of the stress placed upon the cardiorespiratory system by physical activity (Armstrong 1998). Heart rate monitoring results can be used in different ways, the most popular being prediction of energy expenditure and reporting the time spent above fixed heart rate thresholds (Armstrong & Welsman 2006). Among children and adolescents, a heart rate ≥140 bpm is generally used as the threshold for moderate intensity activity, e.g., brisk walking, whereas a heart rate ≥160 bpm indicates vigorous activity, e.g., jogging (Armstrong & Welsman 2006). An important limitation of the method is that physical activity is not the only factor that affects heart rate. For instance, emotional stress, anxiety, level of fitness, active muscle group, hydration, humidity and the ambient temperature may affect heart rate, especially when the intensity of physical activity is low. Heart rate monitoring should thus primarily be used to assess the time spent during moderate to vigorous activity, while heart rates <120 bpm may not be considered as valid estimates of physical activity (Riddoch & Boreham 1995).

A *pedometer* is a simple mechanical motion sensor which records the acceleration and deceleration of movement in one direction (Rowlands & Eston 2007). It is commonly used to estimate the distance walked or the number of steps taken. The method – which was, incidentally, introduced by Leonardo da Vinci – is objective, cheap and unobtrusive, and thus ideal for large population surveys or studies where only a measure of total activity is required. The major disadvantages of the pedometer include its inability to measure the intensity of physical activity, e.g., walking versus running, or to record counts during cycling or swimming. As the heart rate monitor, pedometer use may change physical activity behavior, and thereby give unreal results on the subject's habitual physical activity. The method is also not fully comparable among different pedometer brands: different brands give different outputs, especially at low walking speeds (Corder et al. 2008). Pedometer data should be expressed as steps per day rather than distance or energy expenditure because of the uncertainty of predicting these measures (Corder et al. 2008).

Since 2001, when *accelerometry* was introduced, the method is now one of the most commonly used objective methods to assess physical activity among adolescents (Corder et al. 2008). Similar to pedometers, accelerometers measure movement directly, but they also assess the temporal pattern and intensity of the physical activity (Rowlands & Eston 2007). Accelerometers measure acceleration in one to three orthogonal planes. Their output is a dimensionless unit commonly referred to as the accelerometer "count". The counts are arbitrary and depend on the specifications of the given device, and thus cannot be compared between different accelerometers (Rowlands & Eston 2007). Typically, the counts are integrated over a time interval from one second to several minutes, and called an epoch. There is still a lack of standardization regarding how accelerometers should be used and how the output should be interpreted. For instance, there are several accelometer count thresholds to assess the time spent in different physical activity intensities (Rowlands & Eston 2007). This discrepancy makes it difficult to compare studies on, e.g., achieving the physical activity recommendation. Further challenges are related to accelerometers' insensitivity to cycling, locomotion on a gradient or other activities with limited torso movement (Armstrong & Welsman 2006).

Subjective methods

Self-reported physical activity is the most widely used method to assess physical activity in epidemiological studies (Armstrong & Welsman 2006). Self-report methods comprise various *questionnaires* and activity *diaries*. The benefits of questionnaires include their relative ease to the researcher and subject and low cost. They may, however, be confounded by recall bias, especially by children. The spasmodic nature of children' physical activity makes accurate assessment of physical activity still more difficult. Recently, the use of self-reports to estimate absolute energy expenditure or moderate to vigorous activity at an individual level in youth has been criticized (Corder et al. 2009). Physical activity diaries might provide more accurate data than questionnaires, but they are substantially more laborious and may affect physical activity habits (Armstrong & Welsman 2006). It is commonly suggested that people overestimate their self-reported physical activity, but interestingly children may also underestimate especially moderate intensity activity compared to objective measurement (Epstein et al. 2001, Armstrong & Welsman 2006). In young children, *proxy reports* by parents and/or teachers have been used to assess physical activity (Corder et al. 2008), but this method is limited by the ability of the adults to recall the child's physical activity.

All of these methods to assess physical activity can be used in adolescents. When choosing the appropriate physical activity assessment method, several aspects should be considered. Most importantly, one has to know what kind of activity data is needed and which is the most feasible method for the subject and for the researcher. Cost-effectiveness must also be considered. If the cost of an appropriate method is too high, a compromise should be carefully considered. Ultimately, the choice of the method is often a trade-off between feasibility and validity. The use of objective methods is becoming more common although they too still have limitations.

2.1.5 Physical activity and fitness

While physical activity is a behavior, physical fitness is an adaptive state which relates to the ability to perform physical activity (Caspersen et al. 1985). Physical fitness is divided into several subcategories, e.g., musculoskeletal, motor and cardiorespiratory fitness (Bouchard & Shephard 1994). In this thesis, fitness refers to cardiorespiratory fitness.

Physical activity and fitness are closely interrelated – physical activity influences fitness and *vice versa* (Bouchard & Shephard 1994). In general, physically active people tend to be more fit than those whose activity level is low, and for most individuals, increases in physical activity produce also increases in fitness. Although fitness is used as a surrogate of physical activity, they do not overlap completely. Physical activity for instance needs to be of sufficient intensity to improve fitness. Furthermore, since fitness is also influenced by genetics (Bouchard et al. 1998, Bray et al. 2009), similar physical activity levels yield different fitness levels in different individuals. The fact that fitness improves with variable increments at similar exercise training shows also that genetics play a role in the association between physical activity and fitness (Bouchard & Rankinen 2001).

An interesting question is whether physical activity or fitness is more important for health (Figure 2). From the physical activity's point of view, the complex interrelationship between physical activity and fitness makes it difficult to distinguish whether the effect on a health outcome is due to physical activity *per se*, or is physical activity merely a marker of fitness. In general, the relationship between physical activity and health outcomes is weaker than that of fitness (Blair et al. 2001, Hurtig-Wennlöf et al. 2007). This may, however, be due to methodological problems in assessing physical activity compared to the more precise measurement of fitness (Blair et al. 2001, Ekelund 2008). The development and wider use of objective methods to assess physical activity will probably give more insight into the association. Recently both objectively measured physical activity and fitness were found to be independently associated with metabolic health in children and adolescents (Ekelund et al. 2007). A thorough review concerning adults concluded that it is impossible to say which is more important for health – physical activity or fitness (Blair et al. 2001). Furthermore, while genetic factors affect physical activity and fitness, they also influence susceptibility to diseases, and the genetics of these characteristics may be partly shared. One such selective mechanism may be the inherited difference in the proportion of slow versus fast twitch skeletal muscle fibers (Kujala et al. 2000). A high proportion of slow twitch muscle fibers is associated with increased physical activity, fitness as well as a favorable lipid and lipoprotein profile (Tikkanen et al. 1998), lower blood pressure (Hernelahti et al. 2005) and lower BMI (Tanner et al. 2002). Genetic variability may thus make it easier for some people to be physically active, fit, and also favor them with reduced occurrence of diseases (Kujala et al. 2000). Altogether, physical activity is the only behavioral, and thus the only modifiable determinant of fitness, making it the relevant target for health improvement.

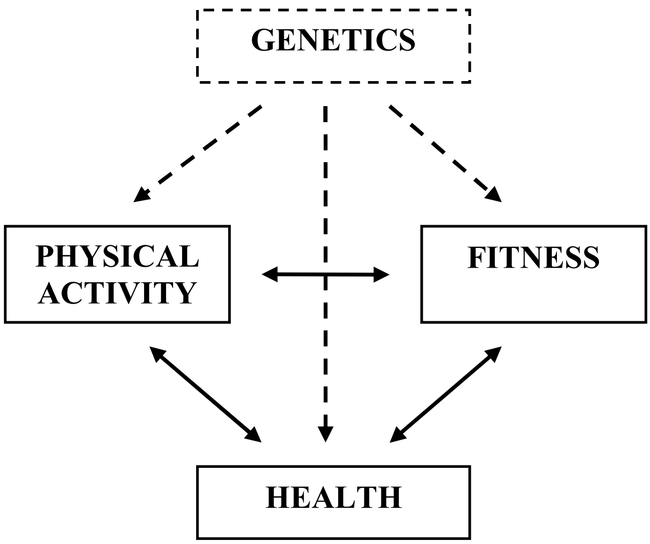

Figure 2. Model of association between genetics, physical activity, fitness and health. Genetics is depicted with dotted lines indicating its role as an underlying factor for the other characteristics.

2.2 Physical activity and cardiovascular disease risk factors

Atherosclerotic CVD begins in childhood and there is typically a long preclinical phase before overt disease. CVDs have numerous risk factors; already 30 years ago, 246 risk factors for coronary heart disease only were described (Hopkins & Williams 1981). There is consensus that lack of physical activity and low fitness raise the risk for CVD. Indeed, the relative risk of CVD mortality associated with low fitness is at least as great as that of several traditional risk factors (Blair et al. 1996). Furthermore, the benefits of physical activity/fitness go beyond body weight, race/ethnicity, health status and CVD risk factor profile (Wei et al. 1999, Myers et al. 2002, Kokkinos et al. 2008). Recently, low fitness has emerged as an important feature of the metabolic syndrome (Hassinen et al. 2008). The importance of fitness on health is highlighted in Figure 3. Other key risk factors for atherosclerotic CVD than physical activity/fitness and association of the risk factors with physical activity are described in the following chapters.

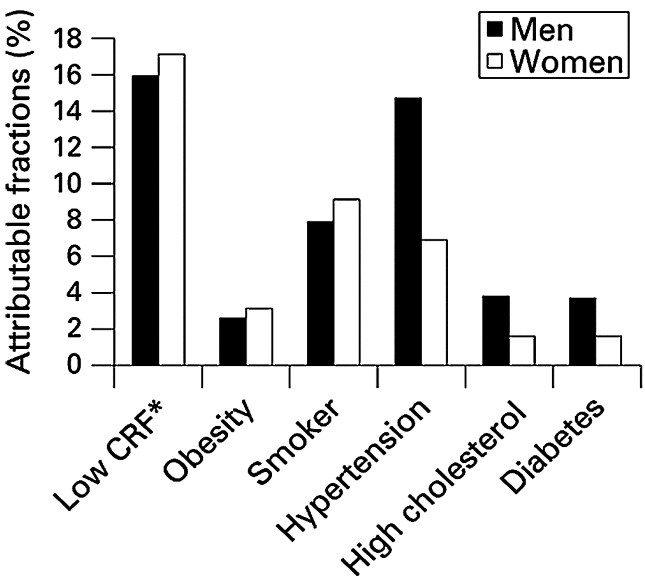

Figure 3. Attributable fractions (%) for all-cause deaths among 40 842 (3333 deaths) men and 12 943 (491 deaths) women in the Aerobics Center Longitudinal Study. The attributable fractions are adjusted for age and each other items in the figure.
*Cardiorespiratory fitness determined by performance at maximal treadmill exercise test.
The attributable fraction is an estimate of the number of deaths in a population that would have been avoided if a specific risk factor had been absent (Blair 2009).
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2.2.1 Overweight

Obesity is fundamentally the result of a long-term positive energy balance. It is a strong risk factor for CVDs (Jousilahti et al. 1996b, Rexrode et al. 1998) and linked to other CVD risk factors, e.g., low HDL-C, high triglyceride, high hs-CRP and high insulin concentrations, hypertension and has adverse effects on vascular structure and function (Yudkin et al. 1999, Després et al. 2001, Lakka et al. 2001, Brook 2006). These unfavorable effects on cardiovascular health emerge already in childhood and adolescence (Freedman et al. 1999, Tounian et al. 2001, Moran et al. 2005). Obesity in adolescence is associated with an increased risk for CVD (Baker et al. 2007) even without obesity in adulthood (Must et al. 1992, Freedman et al. 2008). Overall, obesity is very persistent through adolescence and obese adolescents are likely to become obese adults (Whitaker et al. 1997, Wardle et al. 2006). Several methods and criteria are used to define overweight and obesity in adolescents. Here, overweight refers to both overweight and obesity.

Since physical activity is the main modifiable determinant of energy expenditure, one would assume that lack of physical activity contributes to overweight. The association between physical activity and overweight is, however, not straightforward in adolescents (Janssen et al. 2005, Thompson et al. 2005, Ness et al. 2007, Horst et al. 2007, Fogelholm et al. 2008). One reason for this is that many different methods and criteria are used to assess physical activity and overweight. The results are further complicated by, e.g., gender differences (Ekelund et al. 2005, Klein-Platat et al. 2005) and the effect of activity intensity as vigorous activity, in contrast to moderate intensity or total activity, is associated with lower body fatness (Gutin et al. 2005, Ruiz et al. 2006). Prospective studies show that physical activity protects against overweight in adolescence (Kimm et al. 2005, Must & Tybor 2005, Stevens et al. 2007), although the amount of physical activity needed to prevent overweight is unknown. Taken together, lack of physical activity in part contributes to adolescent overweight.

2.2.2 Lipoproteins and lipids

High serum concentrations of total cholesterol and low-density lipoprotein cholesterol (LDL-C) are major risk factors for CVDs (Thomas et al. 1966). Especially the predominance of small, dense low-density lipoprotein particles is detrimental for cardiovascular health (Austin et al. 1988). High concentrations of triglycerides and lipoprotein (a) and a low concentration of high-density lipoprotein cholesterol (HDL-C) also raise the CVD risk (Gordon et al. 1977, Hulley et al. 1980, Dahlén 1994). Lipoprotein and lipid levels track from childhood to adulthood (Webber et al. 1991, Porkka 1994) and they are affected by pubertal maturation (Niinikoski et al. 2007).

Physical activity relates favorably to lipoproteins and lipids in children, adolescents and adults (Boreham et al. 1997, Raitakari et al. 1997, Leon & Sanchez 2001, Kraus et al. 2002, Andersen et al. 2006). In general, the effect is, however, modest in youth (Strong et al. 2005). Overall, the effect of physical activity varies between individuals, as similar exercise training in different individuals results in a decrease, no change or an increase of a given lipoprotein concentration (Bouchard & Rankinen 2001). The favorable association between physical activity and lipoproteins and lipids is strongest for HDL-C and triglycerides and weaker for total cholesterol and LDL-C (Leon & Sanchez 2001, Strong et al. 2005). The effect on the HDL-C/total cholesterol and the HDL-C/LDL-C ratio is, however, beneficial.

2.2.3 Impaired glucose homeostasis

Impaired glucose homeostasis is predominantly characterized by an elevated blood glucose concentration. Resistance to the action of insulin, the key stimulator of glucose uptake by cells, is one of the principal underlying factors (Goldstein 2002, Stumvoll et al. 2005). Combined with pancreatic β-cell dysfunction, insulin resistance can lead to impaired glucose tolerance, hyperglycemia and eventually type 2 diabetes (Goldstein 2002). All these conditions are linked to an increased CVD risk (Rader 2007). Also type 1 diabetes is associated with an increased risk for CVD (Stamler et al. 1993).

Physical activity increases glucose uptake also independently of insulin (Shepherd & Kahn 1999), and may improve insulin sensitivity by increasing the oxidative capacity of skeletal muscle (Gill & Malkova 2006). The beneficial effects of physical activity on glucose homeostasis occur in children, adolescents and adults (Houmard et al. 2004, LaMonte et al. 2005, Imperatore et al. 2006, Krekoukia et al. 2007, Rizzo et al. 2008). Lifestyle modifications, including regular physical activity, may prevent or delay the development of type 2 diabetes in subjects with impaired glucose homeostasis (Tuomilehto et al. 2001, Knowler et al. 2002, Orozco et al. 2008). Physical activity also ameliorates the excess CVD mortality risk of insulin resistant individuals (Gill & Malkova 2006).

2.2.4 Low-grade inflammation

Inflammation contributes to the initiation and progression of atherosclerotic CVD (Ross 1999). Inflammatory markers considered as predictors of CVD risk include, e.g., adhesion molecules, cytokines and acute-phase reactants such as fibrinogen, serum amyloid A and C-reactive protein (Pearson et al. 2003). Currently, high-sensitivity C-reactive protein (hs-CRP) is one of the most studied inflammatory markers as a predictor of atherosclerotic CVD (Pearson et al. 2003, Ridker et al. 2008). A hs-CRP concentration <1 mg/l relates to low cardiovascular risk while 1-3 mg/l indicates moderate and >3 mg/l high risk (Pearson et al. 2003).

In general, regular exercisers have a lower hs-CRP concentration than their physically less active counterparts (Petersen & Pedersen 2005, Borodulin et al. 2006, Plaisance & Grandjean 2006, Fischer et al. 2007). This finding is further supported by exercise training studies showing that hs-CRP can be reduced in response to training especially among those with high hs-CRP levels (Obisesan et al. 2004, Lakka et al. 2005). Indeed, physical activity lowers hs-CRP as much as or even more than statins (Plaisance & Grandjean 2006). In children and adolescents, studies on the association between physical activity and hs-CRP are limited and no obvious association has been reported (Moran et al. 2005, Ruiz et al. 2007, Thomas et al. 2008, Kelishadi et al. 2009).

2.2.5 Blood pressure

Until as late as in the 1930's, hypertension was not perceived as detrimental for cardiovascular health. Rather, hypertension was seen as the body's adaptation to sclerotic blood vessel disease and thus its treatment was undesirable (Mancia 2007). Today, in contrast, hypertension is regarded as one of the strongest risk factors for CVD. The CVD risk increases incrementally with blood pressure indicating that there is no threshold (Kannel & Wolf 2008). With increasing age, the adverse cardiovascular consequences of hypertension shift in importance from diastolic to systolic hypertension and finally to pulse pressure hypertension (Kannel & Wolf 2008).

A physically active lifestyle is associated with a lower blood pressure level and a decreased risk for the development of hypertension compared to a sedentary way of living (Carnethon et al. 2003, Barengo et al. 2005). Furthermore, a reduction in blood pressure has been found in response to exercise training (Cornelissen & Fagard 2005a, Cornelissen & Fagard 2005b). Especially hypertensive individuals benefit from exercise (Fagard 2001, Cornelissen & Fagard 2005a). As for lipoproteins, the blood pressure response to exercise training varies between individuals (Bouchard & Rankinen 2001). In previous studies involving children and adolescents, there was no clear association between physical activity and blood pressure (Kelley et al. 2003, Strong et al. 2005), but more recently a modest favorable association between physical activity and blood pressure in youth has been reported (Leary et al. 2008, Mark & Janssen 2008).

2.2.6 Clustering of risk factors

The risk factors for CVD are interrelated and thus a person is likely to express a combination of several risk factors. The risk for CVD increases as the number of risk factors increases (Berenson et al. 1998, McGill et al. 2008). Risk scores which integrate the risk factors have been developed, e.g., the Framingham risk score which provides a quantative prediction of the future disease risk (Wilson et al. 1998). Since introduced more than 20 years ago (Reaven 1988), the metabolic syndrome has been a widely studied cluster of CVD risk factors. Overweight is suggested to be one of the key underlying factors for the clustered risk. There is, however, a high prevalence of clustering of cardiometabolic abnormalities also in individuals with normal body weight (Wildman et al. 2008). Although children and adolescents are not considered to be at risk for clinical CVDs, the development of a clustered risk at an early age is certainly an undesirable condition which tracks into adulthood (Bao et al. 1994).

As is the case for individual CVD risk factors, physical activity is associated with a reduced clustered risk for CVD in adults (Lakka et al. 2003, Wildman et al. 2008). In general, also physically active children and adolescents have fewer risk factors than their physically less active peers (Andersen et al. 2006, Steele et al. 2008).

2.2.7 Other risk factors

Smoking and an unhealthy diet carry an established risk for CVD (Ambrose & Barua 2004, Gidding et al. 2009). Together with lack of physical activity they are the central lifestyle risk factors and root causes of CVD (Mozaffarian et al. 2008). One of the key dietary aims to prevent CVD is to limit the intake of saturated fat. Generally, the risk of CVDs increases with age and is more prevalent in males (Jousilahti et al. 1999, McGill et al. 2008). For genetic reasons, some individuals are more prone to CVD than others (Jousilahti et al. 1996a). Furthermore, for instance fibrinogen, homocysteine, infectious agents and psychosocial factors are associated with CVD risk (Rozanski et al. 1999, Hackam & Anand 2003).

2.3 Physical activity and vascular endothelial function

The development and progression of atherosclerosis is associated with adverse functional and structural changes of the arteries (Ross 1993). Ultrasonography allows noninvasive assessment of these changes, mainly impairment of the arterial vasodilatory function, decreased arterial elasticity and thickening of the arterial wall.

The endothelium is the innermost luminal cell layer lining the blood vessels. This thin layer of cells plays a key role for several vascular functions. Impairment of the endothelial vasodilatory function is an important early step in the atherosclerotic process, which apparently precedes structural changes, e.g., thickening of the arterial wall (Ross 1986). Impairment of the endothelial function is associated with the extent and severity of coronary atherosclerosis (Neunteufl et al. 1997), and is a predictor of cardiovascular events (Yeboah et al. 2007). Endothelial function is also inversely associated with carotid artery intima-media thickness, a subclinical marker of atherosclerosis (Juonala et al. 2004). Moreover, those with impaired endothelial function have a more rapid progression of carotid intima-media thickness, independent of traditional CVD risk factors (Halcox et al. 2009).

Physical activity enhances endothelial function in adults (Clarkson et al. 1999, Hambrecht et al. 2000, Gokce et al. 2002, Vona et al. 2009) and counteracts the loss of endothelium-dependent vasodilatation associated with aging (Seals et al. 2008). The beneficial effect of physical activity is suggested to be mediated by exercise-induced enhancement of blood flow leading to augmented shear stress, which further stimulates nitric oxide production and bioavailability, followed by arterial structural adaptations that increase the diameter of the vessel lumen (Green et al. 2004). Among overweight and obese children and adolescents, prone to impaired endothelial function (Fernhall & Agiovlasitis 2008), exercise training improves endothelial function independently of changes in body weight or BMI (Kelly et al. 2004, Watts et al. 2004, Woo et al. 2004). The effect of exercise training is substantially attenuated when training ceases, regardless of age (Watts et al. 2004, Woo et al. 2004, Vona et al. 2009). Thus, physical activity should be maintained if the benefits of exercise on endothelial function are to be sustained. Overall, there are very few population-based studies on the relation between habitual physical activity and endothelial function in children and adolescents.

In fact, only one such study has been conducted in children (Abbott et al. 2002) but none in adolescents.

2.4 Physical activity in adolescence and cardiovascular health later in life

Physical activity during adolescence may influence the risk factors for CVD in adulthood through three pathways (Twisk et al. 2002a) (Figure 4). First, there may be a direct relationship between adolescent physical activity and adult cardiovascular health (1). Second, the effect of physical activity during adolescence on adult cardiovascular health may be mediated through tracking of physical activity from adolescence to adulthood (2) or, third, through the effect of adolescent physical activity on adolescent cardiovascular health (3), which in turn predicts adult cardiovascular health. The direct effect of physical activity during adolescence on adult CVD risk factors is not supported since high physical activity in adolescence does not predict a better adult CVD risk factor profile (Twisk et al. 2002b, Hallal et al. 2006a, Kvaavik et al. 2009). High adolescent fitness, however, is generally associated with better CVD risk factor levels later in life (Twisk et al. 2002b, Kvaavik et al. 2009, Ruiz et al. 2009). The reported lack of an association between physical activity in adolescence and adult CVD risk factors may be related to difficulties in quantifying physical activity. There is a lack of data on the association between physical activity during adolescence and adult CVD morbidity and mortality.

The indirect pathway from physical activity during adolescence to adult cardiovascular health through adult physical activity seems plausible, partly at least because physical activity during adulthood is positively associated with cardiovascular health. However, tracking of physical activity from adolescence to adulthood is only weak to moderate (Hallal et al. 2006a, Parsons et al. 2006, Herman et al. 2008). This indicates that many people change their physical activity habits with advancing age, and that a physically active lifestyle during adolescence is not necessarily sustained over the years. In fact, a sedentary lifestyle may track even more strongly than an active lifestyle (Raitakari et al. 1994, Malina 1996). The other indirect pathway mediated through adolescent cardiovascular health is supported by data on good tracking of CVD risk factors from childhood to adulthood (Porkka et al. 1994, Whitaker et al. 1997). The modest association between physical activity and CVD risk factors in adolescence attenuates, however, this pathway (Twisk et al. 2002b).

Taken together, there is probably no direct relationship between adolescent physical activity and adult cardiovascular health. The indirect pathways are also challenged by the rather weak tracking of physical activity and the weak associations between physical activity and CVD risk factors in adolescence. The key for adult cardiovascular health seems thus to be to maintain a physically active lifestyle during adulthood. Preferably, the active lifestyle should begin in childhood.

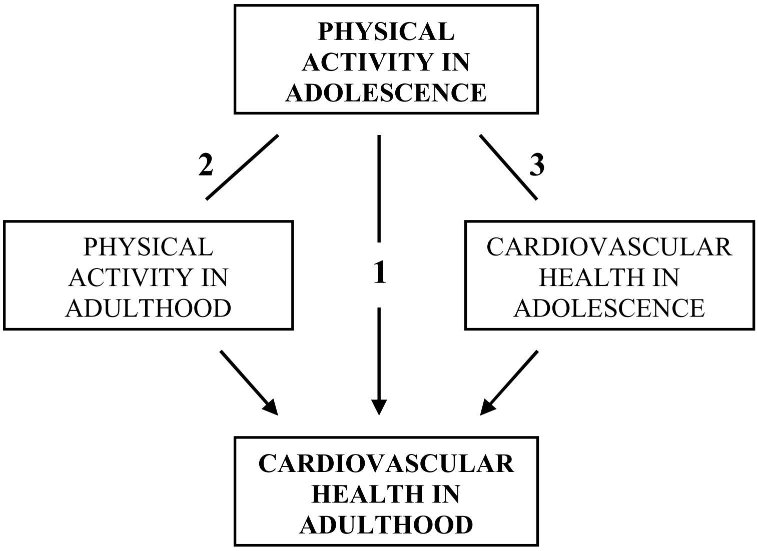

Figure 4. Pathways through which physical activity in adolescence may influence cardiovascular health in adulthood. Modified from Twisk and co-workers (2002a).
1 = direct association, 2 = indirect association mediated by tracking of physical activity, 3 = indirect association mediated by tracking of cardiovascular health.

2.5 Summary of the literature review

- Today, a great number of adolescents are physically insufficiently active for health.

- Physical activity in adolescence is affected both by genetic and by environmental factors.

- Physical activity can be assessed with several methods, all of which have their distinctive strengths and weaknesses.

- Physical activity is associated with fitness but these terms are not synonyms. Whether physical activity or fitness is more important for health is not known. Physical activity is at any rate the only means to improve fitness.

- CVDs have numerous risk factors which are closely interrelated. In general, physical activity is beneficially associated with the key metabolic risk factors for CVD. In adolescents, some of the associations are weak or absent.

- Arterial changes associated with the development and progression of atherosclerotic CVD can be assessed noninvasively with ultrasonography. Physical activity improves vascular endothelial function in adults, but it is not known if this occurs also in healthy adolescents.

- There does not seem to exist a direct pathway from adolescent physical activity to adult cardiovascular health. Maintaining a physically active lifestyle from adolescence through adulthood most likely provides cardiovascular health benefits at adult age.

3 AIMS OF THE STUDY

Adolescents in the modern society are subject to a sedentary lifestyle, which may adversely affect cardiovascular health. The main aim of this study was to investigate physical activity and cardiovascular health among 13-year-old adolescents (Figure 5).

The specific aims were:

1. to assess leisure-time physical activity and the intensity of physical activity of the adolescents, and to study whether leisure-time physical activity is associated with screen time (Study I)

2. to investigate if the parents' leisure-time physical activity and body weight is linked to the leisure-time physical activity of their child (Studies I and II)

3. to study whether leisure-time physical activity is associated with CVD risk factors and the clustering of risk factors in adolescents (Studies II and III)

4. to examine if leisure-time physical activity is related to vascular endothelial function in adolescents (Study IV)

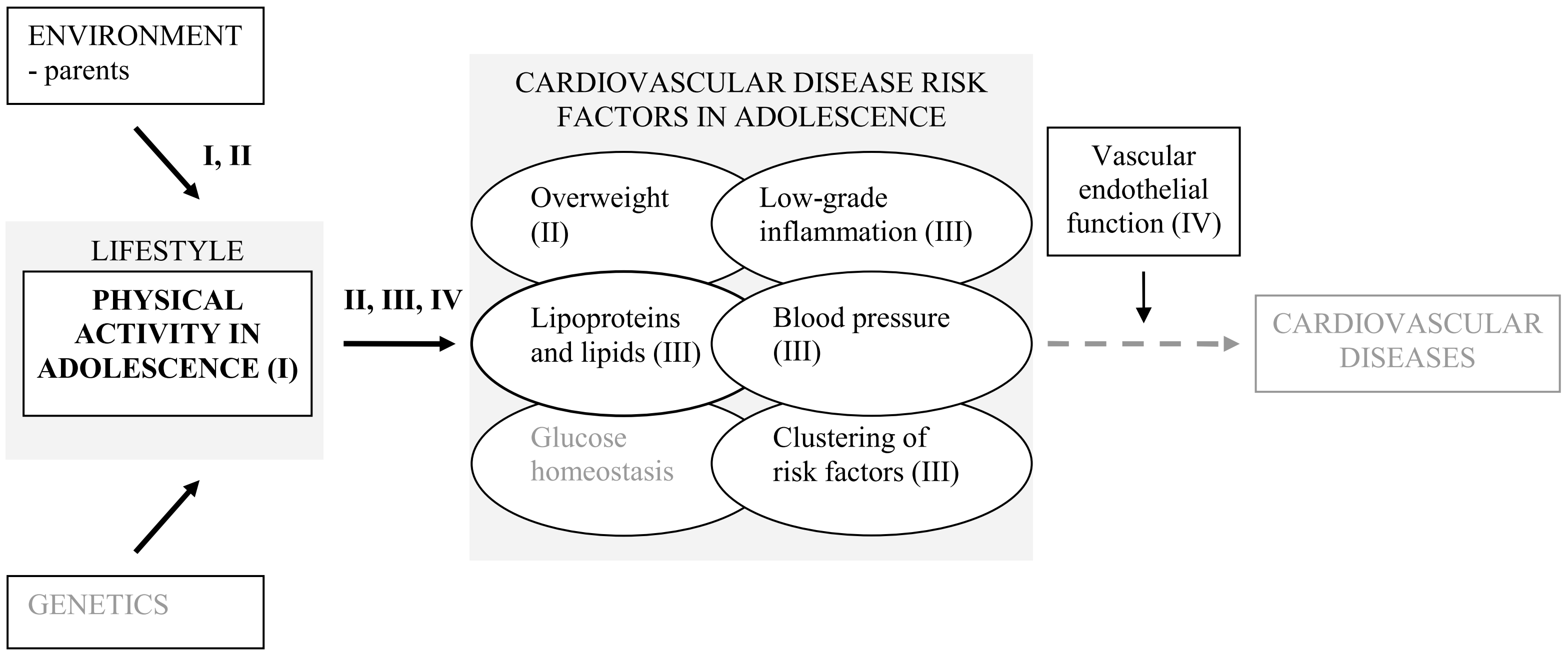

Figure 5. Physical activity, selected CVD risk factors and vascular endothelial function in adolescence. The Roman numerals refer to the studies of the original publications. The effect of the parents on the physical activity of their adolescent child is incorporated under the heading "environment", since the effects of environment and hereditary factors cannot be separated in this study.

4 SUBJECTS AND METHODS

The subjects consisted of adolescents who participated in the longitudinal Special Turku coronary Risk factor Intervention Project for children (STRIP) at age 13 years and provided data on their physical activity. Also the parents of the adolescents were included in studies I and II.

4.1 Special Turku coronary Risk factor Intervention Project for children

The aim of the prospective, randomized STRIP study is to reduce exposure of the intervention children to the established CVD risk factors (Niinikoski et al. 2007). The recruitment of families to the STRIP study was done by well-baby clinic nurses in Turku, Finland. During the regular visits, the parents of 5-month-old children (n=1880) were informed about the STRIP study and invited to participate. Of the families, 1105 were interested and finally 1054 families with 1062 children (56.5% of the eligible age-cohort) volunteered. At age seven months, the children were randomly allocated into a dietary intervention group (n=540) or into a control group (n=522). The first recruited family paid their study visit in February 1990 and the last in June 1992. The study is still ongoing.

Before the child was two years old the families in the intervention group had visited the research center at 1- to 3-month intervals and the families in the control group at 4- to 6-month intervals. Thereafter, study visits in both groups took place biannually until the child was seven years old, after which the control families continued to visit the research center annually. At each visit, the family met a nutritionist, a physician and/or a nurse. During the study visits, anthropometric and laboratory data were collected together with data on food consumption by the children and parents. Vascular ultrasonography studies of the children were introduced when the children were 11 years old.

The intervention group has received individualized dietary counseling at least biannually since the beginning of the study (Talvia et al. 2004). The main aim of the counseling has been on the quality of dietary fat. Suggestions to make dietary changes have been made individually based on the food records. Counseling on primary prevention of smoking has been initiated when the children were nine years old. The hobbies of the child have been discussed during the visits, but although a physically active lifestyle has been encouraged, physical activity *per se* has not been a formal, continuous component of the intervention.

4.2 Study design and subjects

Of the 565 adolescents aged 13 years examined between June 2002 and November 2004, 560 (99%) provided data on their physical activity (Figure 6). Two adolescents were excluded from the study due to congenital physical impairment. The study group thus comprised 558 adolescents (264 girls, 294 boys). In studies II-IV, additionally 11

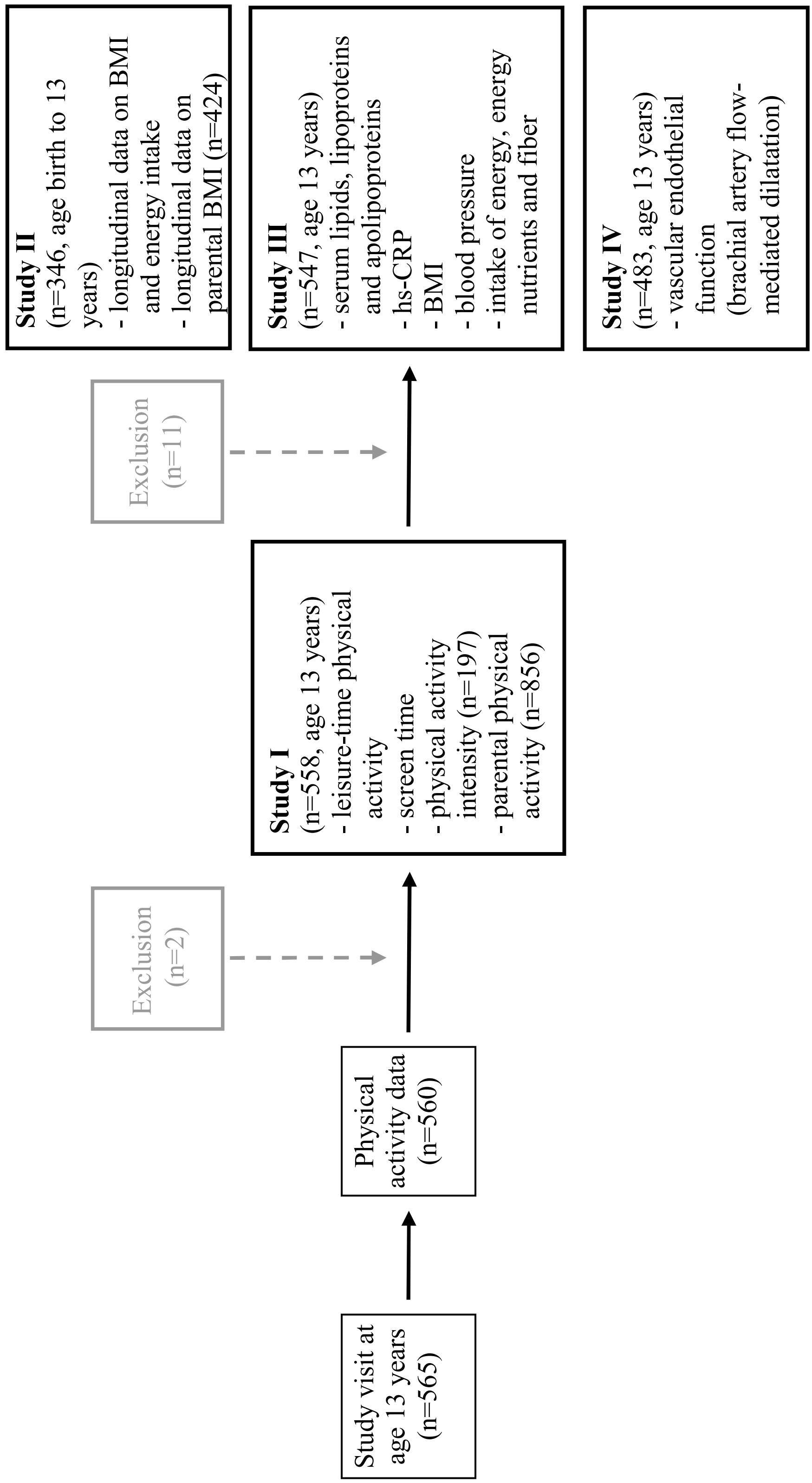

Figure 6. Participants and data assessed in studies I-IV.

adolescents were excluded (type 1 diabetes, familial hypercholesterolemia). Data on only the physically least and most active adolescents were used in study II. Girls and boys were examined separately in all studies. The STRIP intervention was not associated with the physical activity of the adolescent (I, IV), hence the intervention and control boys were studied as one group, as were the intervention and control girls.

In study I, leisure-time physical activity of the adolescents and the association of leisure-time physical activity with screen time, i.e., the sedentary time of day spent watching TV or videos and playing computer games, were studied at age 13 years. In addition, the association between leisure-time physical activity of the adolescents and their parents was studied. In a subgroup of the 13-year-old adolescents, the intensity of the physical activity was assessed using heart rate monitoring and the association with leisure-time physical activity was studied.

The association between leisure-time physical activity of the adolescents at age 13 years and overweight since age two years was studied longitudinally in study II. Also, the association between the 13-year-old adolescents' leisure-time physical activity and energy intake since age 13 months, waist circumference since age 7 years, and parental overweight since their child was seven months old, were investigated.

In study III, the association between leisure-time physical activity of the adolescents and clustering of cardiometabolic risk factors (HDL-C, triglycerides, blood pressure and BMI) was studied at age 13 years. In addition, association of leisure-time physical activity with individual risk factors and the intake of energy, energy nutrients and fiber were investigated.

The association between leisure-time physical activity of the adolescents and brachial artery endothelial function was studied at age 13 years in study IV.

4.3 Leisure-time physical activity and screen time (I)

Leisure-time physical activity was assessed with a self-administered questionnaire. The questionnaire has been widely used in studies involving children, adolescents and adults (Raitakari et al. 1996, Leino et al. 1999, Lehtonen-Veromaa et al. 2000). The questionnaire included three multiple choice questions on the frequency, duration and intensity of habitual leisure-time physical activity. For the frequency of the leisure-time physical activity, the choices were: a) less than once a month, b) once a month, c) two to three times a month, d) once a week, e) two to six times a week, and f) once a day. For the average duration of the leisure-time physical activity, four choices were given: a) less than 20 minutes, b) 20-40 minutes, c) 40-60 minutes, and d) more than 60 minutes. For habitual leisure-time physical activity intensity, the choices were: a) never sweating and becoming breathless, b) some sweating and becoming breathless, c) heavy sweating and becoming breathless. Based on the questions, a Leisure-time Physical Activity Index (PAI) was calculated as MET h/wk (range 0 - 93.35) by multiplying the frequency, mean duration in minutes and mean intensity of weekly leisure-time physical activity as described (Raitakari et al. 1996). A MET is a multiple of the resting metabolic rate. One MET is equivalent to the resting metabolic rate, e.g., quiet sitting, while for instance six METs are equivalent to an energy expenditure six times higher than the resting metabolic rate, e.g., riding a bicycle with light effort (Ainsworth et al. 2000). From the PAI data, tertile cut-off points were calculated and the girls and boys were divided into Sedentary, Moderately Active and Active groups, respectively. The PAI values tended to cluster, and consequently the group sizes were not identical (girls: Sedentary n=89, Moderately Active n=121, Active n=54; boys: Sedentary n=114, Moderately Active n=89, Active n=91).

In the questionnaire, screen time on a weekday and on a weekend day was also reported. Screen time is the sum of time spent by the subject watching TV, videos or playing computer games. According to the screen time, two groups were formed: 1) ≤2 h/day and 2) >2 h/day. The leisure-time physical activity of the parents was also estimated with the self-administered questionnaire. As for the adolescents, PAI (MET h/wk) was calculated for the parents and the mothers and fathers were divided into Sedentary, Moderately Active or Active groups, respectively, by PAI tertile cut-off points.

4.4 Heart rate monitoring (I)

The heart rate of the adolescents was monitored to collect data on physical activity intensity. The subjects wore the monitor (Polar Vantage NV, Polar Electro Oy, Kempele, Finland) for three days from waking up until bed time. The monitoring was successful if each day contained at least eight hours of recording. From the heart rate monitoring data, time spent at a heart rate of 120-139 beats per minute (bpm), 140-159 bpm and ≥160 bpm were calculated. These heart rate thresholds represent light, moderate and vigorous exercise, respectively.

4.5 Anthropometric measures and pubertal status (II-IV)

Recumbent length was measured until age 21 months and thereafter, standing height with a Harpenden stadiometer. Until age 15 months, weight was measured using an infant scale and thereafter, with an electronic scale. The height of the parents was also measured with the stadiometer, and weight with the electronic scale. Since the age of seven years, waist circumference of the children, midway between the iliac crest and lowest rib at the midaxillary line, was measured with a flexible measuring tape.

BMI was calculated as weight (kg)/height^2 (m^2). The children were classified as being overweight if their BMI exceeded the international age- and sex-specific criteria (Cole et al. 2000). A distinction between overweight and obese adolescents was not made due to the small proportion of obese adolescents (Table 2). Thus, the group of adolescents with overweight included also those who were obese. The parents were considered overweight if their BMI was ≥25 kg/m^2. As for the adolescents, a distinction between overweight and obese parents was not made.

The pubertal status was recorded as of age nine years according to Tanner staging (Niinikoski et al. 2007).

4.6 Laboratory measures and blood pressure (III, IV)

A fasting venous blood sample was drawn for the determination of serum lipid, lipoprotein and apolipoprotein concentrations. The serum cholesterol concentration was determined using an enzymatic method (CHOD-PAP, Merck, Darmstadt, Germany) with an AU 400 automatic analyzer (Olympus, Hamburg, Germany). The serum HDL-C concentration was analyzed after precipitation of LDL-C and very-low density lipoprotein cholesterol with dextran sulphate. The interassay (intra-assay) coefficients of variation of the total cholesterol and HDL-C were 2.0% (1.5%), and 1.9% (1.2%), respectively. The serum triglyceride concentration was analyzed using a colorimetric method (GPO-PAP, Merck) with an Olympus AU 400 analyzer. Apolipoproteins A-I (ApoA-I) and B (ApoB) were determined using ApoA-I and ApoB kits (Orion Diagnostica, Helsinki, Finland). The interassay (intra-assay) coefficients of variation of the ApoA-I and ApoB determinations were 3.0% (1.8%) and 4.5% (3.3%), respectively. The Friedewald formula was used to calculate the LDL-C concentration (Friedewald et al. 1972). The formula could be used throughout all studies because all triglyceride values were <4 mmol/l. The hs-CRP concentration was assayed by a turbidimetric immunoassay (Wako Chemicals GmbH, Neuss, Germany). Values >10 mg/l were excluded (n=4). All analyses were done at the National Public Health Institute in Turku, Finland.

The seated blood pressure of the adolescents was measured twice with an oscillometric device. The mean of the measurements was used.

4.7 Cluster of risk factors (III)

The adolescent was defined as having a high risk factor level if the triglyceride concentration, the BMI, the systolic or the diastolic blood pressure was in the highest, and in the case of HDL-C in the lowest, quintile of the sex-specific distribution of the risk factor (Table 1). To form the cluster of risk factors, only one blood pressure variable, systolic or diastolic blood pressure, was used. The children were divided into two groups according to the number of risk factors: 1) 0-1 risk factors and 2) 2-4 risk factors.

Table 1. Cut-off points for risk factors.

	Girls	**Boys**
BMI, kg/m^2	21.95	21.23
HDL-C, mmol/l	1.04	1.00
Triglycerides, mmol/l	1.20	1.10
Systolic blood pressure, mm Hg	118	119
Diastolic blood pressure, mm Hg	66	66

4.8 Food consumption (II, III)

Dietary intake of energy, energy nutrients and fiber was estimated annually using a 4-day food record. Household measures or a scale were used to estimate the food amounts. Type and brand of foods, and preparation method of dishes were also recorded. During each study visit, a nutritionist reviewed the food records and if needed, schools, restaurants and manufacturers were contacted to obtain detailed information. Dietary intakes were calculated using a Micro Nutrica® program based on the Food and Nutrient Database of the Social Insurance Institution of Finland. While the program originally calculated 66 nutrients in 1208 foods and 890 dishes, it has continuously been updated with new foods and recipes.

4.9 Vascular endothelial function (IV)

Endothelial function of the left brachial artery was studied with ultrasonography (Acuson Sequoia 512 mainframe) as described (Raitakari et al. 2005). The method is based on the measurement of the brachial artery diameter at baseline and after increased blood flow (Figure 7). The flow-mediated dilatation (FMD) of the brachial artery is a marker of systemic arterial endothelial function (Celermajer et al. 1992).

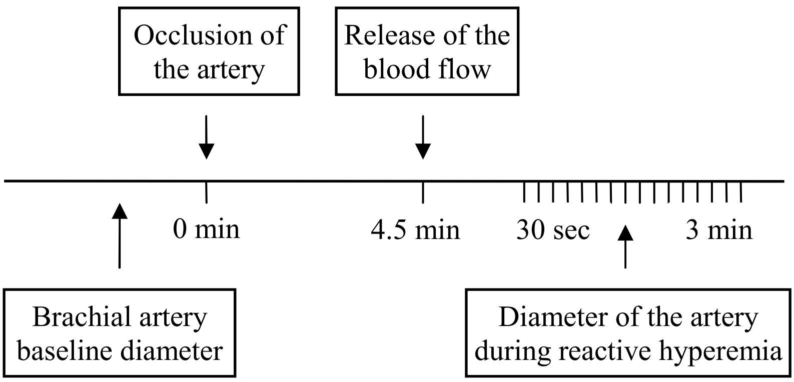

Figure 7. Study protocol for the assessment of brachial artery endothelial function.

At first, the luminal diameter of the brachial artery was measured at rest at a fixed position at end diastole, incident with the R-wave on electrocardiography (Figure 8, left). The artery was then occluded by inflating a blood pressure cuff placed around the forearm to a pressure of 250 mm Hg. After 4.5 minutes, the cuff was deflated; this caused increased blood flow, reactive hyperemia, in the artery. A continuous scan was then recorded for 30-180 seconds after deflation of the cuff. During this time, the dilatation of the artery from baseline was measured offline at end diastole, incident with the R-wave on electrocardiography, at 10-second intervals (Figure 8, right). From these data, the maximum FMD (FMDmax, %), the absolute FMD (ΔFMD, mm) and the FMD after 60 seconds of cuff release (FMD 60 sec, %) were measured. The total dilatation response, defined as the area under the dilatation response versus time curve between 40-180 seconds after hyperemia (FMDauc, %×s), was also assessed. The interobserver variation (coefficient of variation) of FMD measurements was 8.6%, and the between-study coefficient of variation was 9.3% in our laboratory.

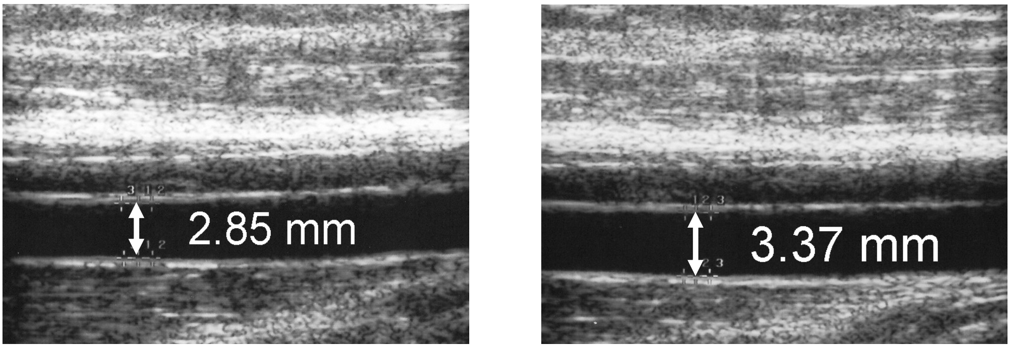

Figure 8. Diameter of brachial artery at baseline (left) and during reactive hyperemia (right).

4.10 Statistical analyses (I-IV)

All statistical analyses were done with the statistical software package SAS release 9.1 (SAS Institute Inc., Cary, NC, USA). P-values <0.05 were considered significant. The adolescents were analyzed gender wise since the girls had lower activity levels than the boys (I, IV). PAI was used as a categorical variable in all studies, i.e., the Sedentary, Moderately Active and Active groups were compared. In study IV, PAI was in addition used as a continuous variable.

In study I, the Kruskall-Wallis test was used to study gender difference of PAI among all adolescents and in the activity groups, and to study the association between the activity groups and screen time. Differences in physical activity intensity in the activity groups were analyzed with analysis of variance (ANOVA). The association between leisure-time physical activity of the adolescents and their parents was studied with Spearman's rank-order correlation.

In study II, repeated measures ANOVA (RANOVA) with covariates (pubertal status and STRIP study group) was used to study the longitudinal differences in height, weight, BMI, waist circumference and energy intake between the Sedentary and Active adolescents. RANOVA was also used to study longitudinal differences in BMI of the mothers and fathers of the Sedentary and Active adolescents. Multivariate logistic regression analysis with pubertal status and STRIP study group as covariates was used to study longitudinal differences in the proportion of overweight children in the Sedentary and Active groups. Logistic regression analysis was also used to study the association between leisure-time physical activity of the adolescent and weight status of the mother and father.

Univariate and multivariate logistic regression analysis was used to study the association between leisure-time physical activity and clustered metabolic risk in study III. The STRIP study group and pubertal status were used as covariates. Univariate and multivariate logistic regression analysis was also used to study the association between screen time and clustered metabolic risk. The multivariate analyses were adjusted for leisure-time physical activity, and additionally for STRIP study group and pubertal status. The association between leisure-time physical activity and BMI, serum lipid, lipoprotein, apolipoprotein and hs-CRP concentrations, blood pressure as well as the intake of energy, energy nutrients and fiber were studied with univariate and multivariate linear regression analyses. Triglycerides and hs-CRP were logarithmically transformed since these variables were non-normally distributed. In the multivariate linear regression analyses, BMI and the STRIP study group were used as covariates with the exception of the association between leisure-time physical activity and BMI, where adjustment was made only for the STRIP study group. Further adjustment was made for pubertal status. The association between leisure-time physical activity and pubertal status was studied with the Cochran-Mantel-Haenszel statistics for general association.

The association between PAI and vascular ultrasonography measurements (excluding hyperemia) were studied with multivariate linear regression analyses adjusted for the brachial artery baseline diameter in study IV. The association between PAI and FMDmax and FMDauc was also studied with multivariate linear regression analyses, where BMI, HDL-C, LDL-C, triglycerides, hs-CRP, blood pressure and brachial artery baseline diameter were included in the model. RANOVA with covariates was used to study whether the magnitude of the FMD responses differed between the Sedentary and Active adolescents. In these analyses, time, interaction between activity group and time, and brachial artery baseline diameter were used as covariates. The difference of the FMDmax between girls exercising 10-20 MET h/wk versus 40-60 MET h/wk and boys with the same activity criteria was studied with ANOVA (gender × physical activity interaction).

The association between body weight (normal weight versus overweight) and leisure-time physical activity at age 13 years was studied with logistic regression analysis. The *t*-test was used to study the difference in hs-CRP between normal weight and overweight Sedentary, Moderately Active and Active adolescents, respectively. The hs-CRP values were logarithmically transformed.

4.11 Ethics

The STRIP study (registered clinical trial; NCT00223600) was approved by the Ethics Committee of the Intermunicipal Hospital District of Southwest Finland (formerly the Joint Commission on Ethics of the Turku University and the Turku University Central Hospital). Written informed consent was obtained from the parents.

5 RESULTS

5.1 Characteristics of participants

This study examined the physical activity, CVD risk factors and vascular endothelial function of more than 500 adolescents aged 13 years. Approximately 15% of the them were overweight and a clustering of risk factors was found in 23% (Table 2).

Table 2. Characteristics of 13-year-old adolescents.

	Girls (n=260)	**Boys** (n=287)
Birth weight, g	3491 (468)	3667 (521)
Height, cm	160.5 (6.6)	159.8 (8.3)
Weight, kg	50.4 (10.1)	49.2 (10.1)
BMI, kg/m^2	19.5 (3.2)	19.2 (3.1)
Overweight[a], %	14.8	16.0
Obese[b], %	3.5	2.9
Waist circumference, cm	69.8 (8.7)	70.6 (8.7)
Waist/height	0.43 (0.05)	0.44 (0.05)
Energy, kcal/day	1752 (417)	2010 (442)
Fat, E%	31.0 (5.3)	31.9 (4.9)
SFA, E%	12.3 (3.0)	12.5 (2.7)
Carbohydrate, E%	52.4 (5.8)	51.3 (5.3)
Protein, E%	16.6 (2.9)	16.8 (2.8)
Fiber, g/1000 kcal	8.2 (2.1)	7.7 (1.9)
Total cholesterol, mmol/l	4.29 (0.74)	4.14 (0.71)
HDL-C, mmol/l	1.21 (0.22)	1.19 (0.24)
HDL-C/total cholesterol	0.29 (0.06)	0.29 (0.06)
LDL-C, mmol/l	2.69 (0.66)	2.58 (0.60)
Triglycerides, mmol/l	0.80 (0.40)	0.70 (0.50)
ApoA-I, g/l	1.35 (0.18)	1.33 (0.21)
ApoB, g/l	0.79 (0.18)	0.76 (0.18)
ApoA-I/ApoB	1.81 (0.50)	1.85 (0.54)
hs-CRP, mg/l	0.17 (0.29)	0.21 (0.38)
Systolic blood pressure, mm Hg	110 (10)	110 (10)
Diastolic blood pressure, mm Hg	60 (7)	60 (7)
Clustered metabolic risk[c], %	23.9	22.6
FMDmax, %	9.8 (4.4)	9.5 (4.3)
FMDauc, %×s	706 (498)	730 (506)

Data are mean (SD), except for triglycerides and hs-CRP, where median (IQR) are given.
[a]BMI >22.58 kg/m^2 girls, >21.91 kg/m^2 boys at age 13 years (Cole et al. 2000)
[b]BMI >27.76 kg/m^2 girls, >26.84 kg/m^2 boys at age 13 years (Cole et al. 2000)
[c]≥2/5 risk factors (see Chapter 4.7)

Of the parents, 52% were overweight (Table 3). 2.8% of the girls and 0.8% of the boys were prepubertal (Tanner stage M1/G1), while 4.4% of the girls and 0.8% of the boys had passed puberty (Tanner stage M5/G5). Hence, in nearly all adolescents puberty was ongoing. One of the adolescents reported regular smoking.

Table 3. Characteristics of parents at child's age 13 years (I).

	Mothers (n=451)	**Fathers** (n=405)
Age, years	43.5 (4.9)	45.5 (5.7)
Height, cm	166.3 (5.4)	180.3 (5.9)
Weight, kg	68.9 (12.0)	85.3 (12.2)
BMI, kg/m^2	24.9 (4.3)	26.2 (3.3)
Overweight[a], %	39.6	64.2

Data are mean (SD).
[a]BMI ≥25 kg/m^2

Physical activity and pubertal status (III)
Leisure-time physical activity was not associated with pubertal status either among the girls (P=0.53) or among the boys (P=0.19).

Physical activity and diet (II, III)
The mean daily intake of energy increased with increasing leisure-time physical activity in boys, but not in girls at age 13 years (Table 4). Similarly, when the mean daily energy intake of the 13-year-old physically least and most active boys was compared since early childhood, the Active boys had a higher energy intake than the Sedentary boys between 13 months and 13 years of age (Figure 9). Among the girls, the mean daily energy intake was similar for the 13-year-old Sedentary and Active girls throughout the study (Figure 10). Leisure-time physical activity was not associated with the intake of energy nutrients or fiber in boys or girls at age 13 years (Table 4). Thus, the analyses of the association of physical activity with CVD risk factors (III) and endothelial function (IV) were not adjusted for these dietary factors.

Table 4. Mean (SD) dietary intake of energy, energy nutrients and fiber by physical activity group and association with physical activity at age 13 years (III).

	Sedentary	Moderately Active	Active	Univariate model β^a (SE)	Multivariate model[b] β^a (SE)
GIRLS (n=236)					
Energy, kcal/day	1711 (415)	1759 (413)	1830 (433)	57.75 (37.17)	54.48 (37.11)
Fat, E%	31.0 (5.4)	31.0 (5.7)	30.8 (4.7)	-0.054 (0.48)	0.0097 (0.48)
SFA, E%	12.2 (2.9)	12.5 (3.2)	12.1 (2.9)	0.023 (0.27)	0.10 (0.26)
Protein, E%	16.7 (3.2)	16.5 (2.8)	16.8 (2.9)	0.048 (0.26)	0.056 (0.26)
Carbohydrate, E%	52.4 (5.5)	52.5 (6.3)	52.4 (5.4)	0.0010 (0.52)	-0.063 (0.52)
Sucrose, E%	9.0 (2.8)	9.6 (4.1)	9.0 (3.2)	0.084 (0.31)	0.086 (0.31)
Fiber, g/1000 kcal	8.3 (2.3)	8.1 (1.8)	8.3 (2.1)	-0.000018 (0.00018)	-0.000029 (0.00018)
BOYS (n=264)					
Energy, kcal/day	1922 (409)	1998 (386)	2139 (507)	107.64 (32.26)*	112.56 (31.87)#
Fat, E%	32.1 (5.3)	31.3 (4.3)	32.2 (4.8)	0.047 (0.36)	0.080 (0.36)
SFA, E%	12.8 (2.9)	12.3 (2.5)	12.3 (2.7)	-0.23 (0.20)	-0.18 (0.19)
Protein, E%	16.6 (2.9)	17.0 (2.6)	16.9 (3.0)	0.14 (0.21)	0.11 (0.21)
Carbohydrate, E%	51.3 (5.6)	51.7 (5.0)	50.9 (5.1)	-0.18 (0.39)	-0.19 (0.39)
Sucrose, E%	9.2 (3.9)	9.4 (3.3)	9.3 (3.4)	0.055 (0.26)	0.083 (0.26)
Fiber, g/1000 kcal	7.7 (2.0)	7.7 (1.8)	7.6 (2.0)	-0.000073 (0.00014)	-0.00011 (0.00014)

[a]Regression coefficient for change in the variable when leisure-time physical activity increases by 1 activity group
[b]Adjusted for STRIP study group
*P=0.001; #P=0.0005

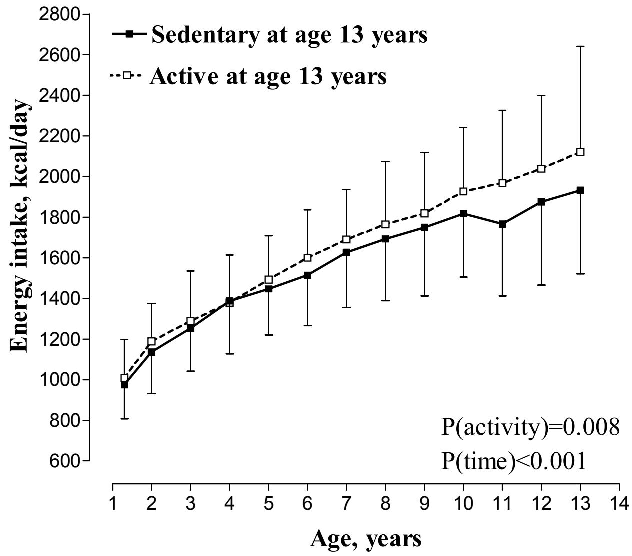

Figure 9. Mean (SD) energy intake among 13-year-old Sedentary and Active boys since age 13 months (II).

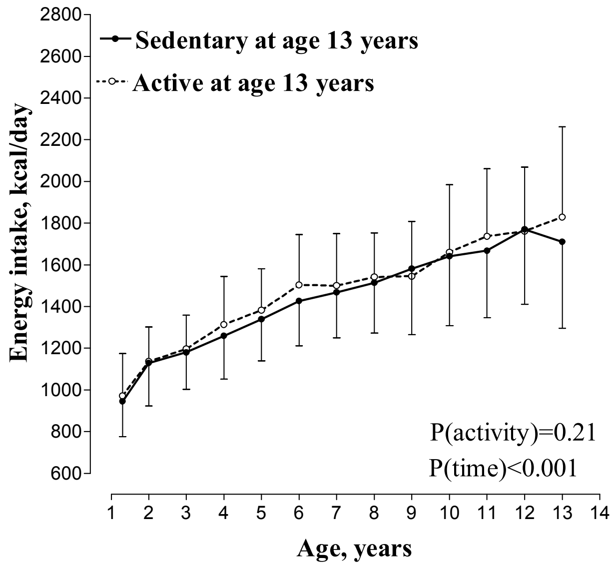

Figure 10. Mean (SD) energy intake among 13-year-old Sedentary and Active girls since age 13 months (II).

5.2 Physical activity in adolescence

5.2.1 Leisure-time physical activity and screen time (I)

The boys were physically more active than the girls during their leisure-time [median (IQR) PAI: 31.3 (44.2) MET h/wk versus 19.5 (26.3) MET h/wk, P=0.0002], (Figure 11). The PAI tertile cut-off points were similar for the Active girls (31.3 MET h/wk) and the Active boys (32.6 MET h/wk). Among the Sedentary girls, however, the cut-off point was only 5.0 MET h/wk compared to 19.5 MET h/wk among the Sedentary boys. Thus, one third of the girls exercised only ≤5 MET h/wk in leisure-time.

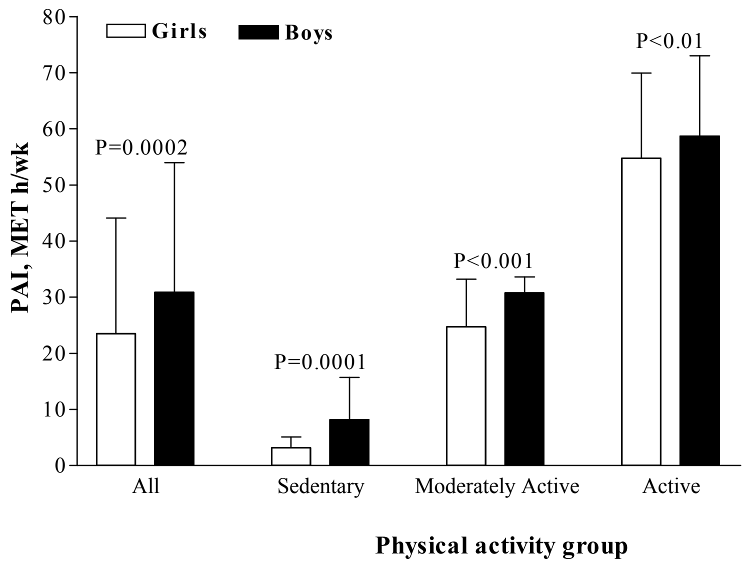

Figure 11. Mean (SD) leisure-time physical activity index in all adolescents and by physical activity group (I).

The Sedentary boys spent more time watching TV, videos or playing computer games than their physically more active peers (Figure 12). In girls, leisure-time physical activity was not associated with screen time. The mean (SD) screen time in the girls was 2.0 (1.1) h/weekday and 2.8 (1.4) h/weekend day, while the boys spent 2.4 (1.2) h/weekday and 3.2 (1.6) h/weekend day by the screen.

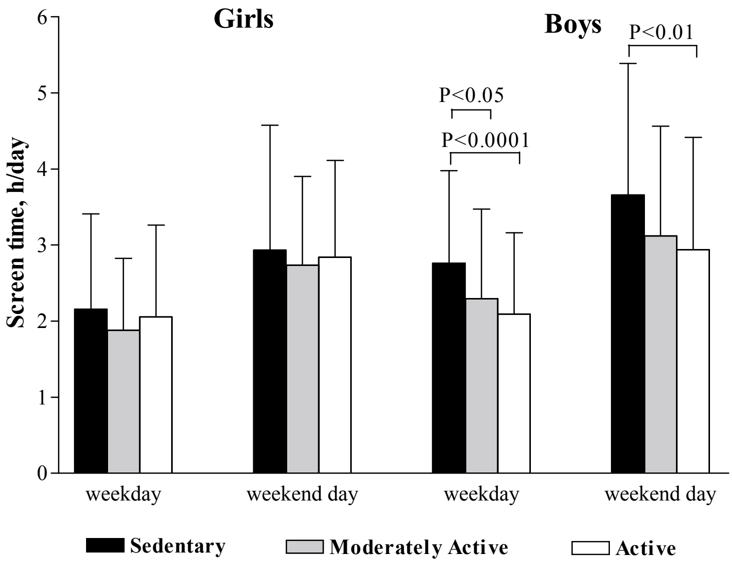

Figure 12. Mean (SD) screen time by physical activity group (I).

5.2.2 Intensity of physical activity (I)

The mean times spent at physical activity intensities of 120-139 bpm, 140-159 bpm and ≥160 bpm were similar in the Sedentary, Moderately Active and Active girls (Table 5). The times spent at the activity intensities by the boys were also similar by activity groups, with the exception of the Moderately Active boys, who spent more time than the Sedentary boys at physical activity intensity of ≥160 bpm. The results were similar when those with longer monitoring time (>10 h/day or >12 h/day) were studied. PAI was similar in those who participated in the heart rate monitoring study to those who refused, and in those who completed of the monitoring to those who did not provide adequate data.

Table 5. Mean (SD) time (min/day) spent at different physical activity intensities in the activity groups (I).

	GIRLS, min/day (n=90)			**BOYS**, min/day (n=107)		
	Sedentary	Moderately Active	Active	Sedentary	Moderately Active	Active
Physical activity intensity						
120-139 bpm	64 (28)	57 (27)	47 (17)	67 (28)	57 (25)	54 (29)
140-159 bpm	20 (15)	21 (15)	20 (11)	22 (13)	27 (15)	22 (12)
≥160 bpm	8 (11)	10 (9)	13 (12)	11 (11)	20 (18)*	16 (12)

*P<0.05 for Moderately Active versus Sedentary boys.

5.2.3 Effect of parental leisure-time physical activity and body weight (I, II)

Leisure-time physical activity of the mother was associated with the leisure-time physical activity of the child (r=0.12, P=0.010), i.e., the Active mothers tended to have Active children and the Sedentary mothers Sedentary children. In fact, the children of the Active mothers were three times more often Active than the children of the Sedentary mothers. Gender wise analysis revealed that the leisure-time physical activity of the mother was associated especially with the leisure-time physical activity of the daughter (r=0.15, P=0.023) but not with the son (r=0.10, P=0.14). Leisure-time physical activity of the father was not associated with the child's leisure-time physical activity (r=0.08, P=0.096).

Among the girls, leisure-time physical activity at age 13 years was associated with the mother's body weight; the Sedentary girls had more often an overweight mother than the Active girls already since age seven months (Figure 13). The mean BMI of the mothers of the Sedentary girls was ~1.2 kg/m^2 (~5%) higher during the study than the mean BMI of the mothers of the Active girls (P=0.035). Among the boys, the body weight of the mother was not associated with leisure-time physical activity of the son. The body weight of the father was not associated with the leisure-time physical activity of the daughter or son. During the 13 years of follow-up, the proportion of overweight mothers increased from 25% to 39%, and the proportion of overweight fathers from 44% to 61%.

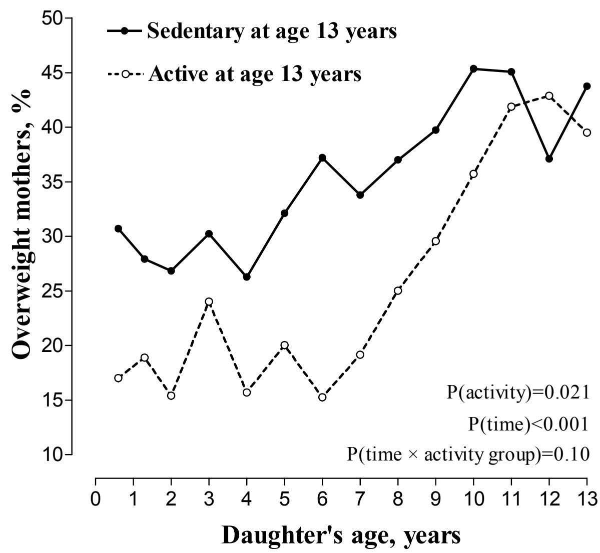

Figure 13. Proportion of overweight mothers by daughter's leisure-time physical activity at age 13 years (II). P(time × activity group): interaction indicating difference in proportion of overweight mothers in the activity groups between time points.

5.3 Physical activity and cardiovascular disease risk factors

5.3.1 Overweight (II, III)

The 13-year-old Sedentary girls were over twice more often overweight than their physically more active peers [OR(Sedentary versus Active)=3.2, CI=1.1-9.0, P=0.0032; OR(Moderately Active versus Active)=1.1, CI=0.4-3.2, P=0.22] (Figure 14). Among the boys, the prevalence of overweight was similar throughout all activity groups [OR(Sedentary versus Active)=1.0, CI=0.5-2.2, P=0.64; OR(Moderately Active versus Active)=0.8, CI=0.4-1.8, P=0.50]. The association between leisure-time physical activity and overweight remained similar when girls and boys with more extreme activity levels (<5 MET h/wk versus >50 MET h/wk) were compared (girls: OR=3.53, CI=1.13-11.00, P=0.030; boys: OR=1.49, CI=0.66-3.36, P=0.34).

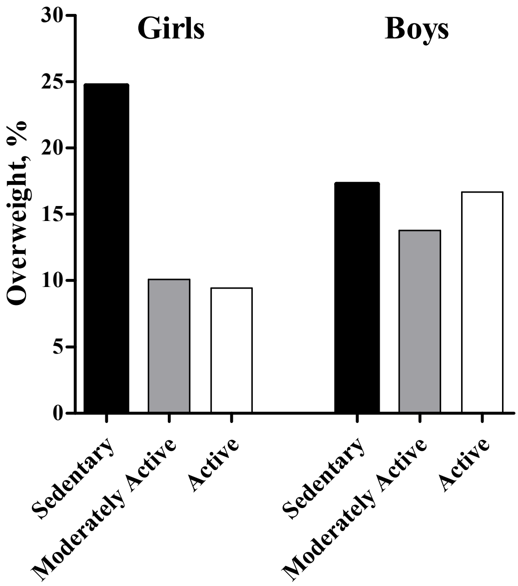

Figure 14. Proportion of overweight adolescents by physical activity group.

Moreover, the girls who were Sedentary as adolescents were more likely to be overweight than the Active girls already since the age of two years (Figure 15). In contrast, the proportion of overweight boys was similar between the ages of two and 13 years regardless of whether they were Sedentary or Active at age 13 years (Figure 16).

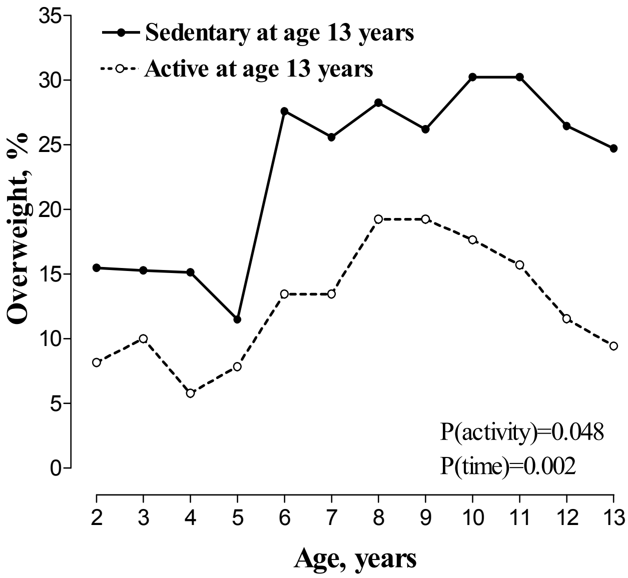

Figure 15. Proportion of overweight children among 13-year-old Sedentary and Active girls since age two years (II).

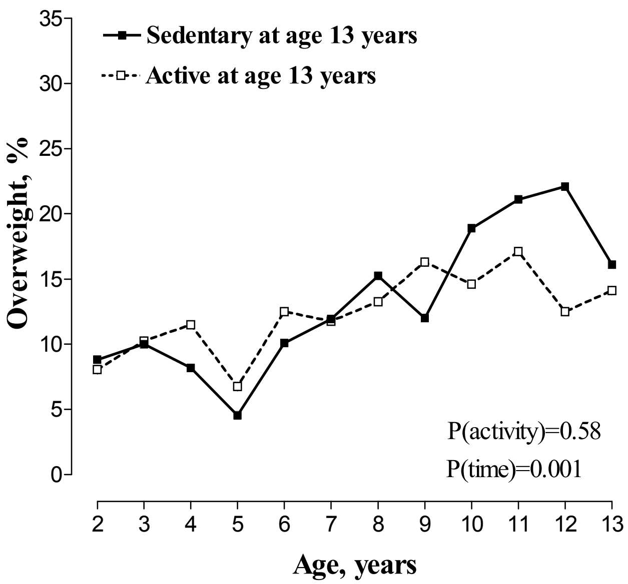

Figure 16. Proportion of overweight children among 13-year-old Sedentary and Active boys since age two years (II).

As was the case for the prevalence of overweight, the mean BMI of the Sedentary girls at age 13 years (20.1 kg/m^2) was higher than the mean BMI of the physically more active peers (Moderately Active: 19.2 kg/m^2, Active: 19.1 kg/m^2) (β=-0.57, P=0.039). However, the mean BMI of the Sedentary and Active girls was similar when analyzed since birth (II). Among the boys, the mean BMI was similar in the activity groups at age 13 years (Sedentary: 19.3 kg/m^2, Moderately Active: 18.8 kg/m^2, Active: 19.3 kg/m^2) as well as between birth and age 13 years (II).

The mean waist circumference was similar in the Sedentary and Active girls, and in the Sedentary and Active boys, respectively, at age 13 years (II) as well as between age seven and 13 years (Figures 17 and 18).

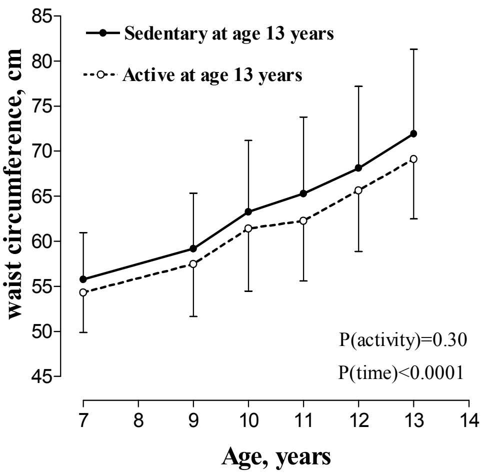

Figure 17. Mean (SD) waist circumference among 13-year-old Sedentary and Active girls since age seven years.

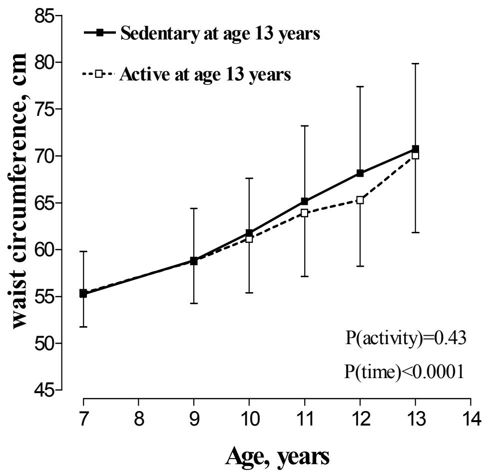

Figure 18. Mean (SD) waist circumference among 13-year-old Sedentary and Active boys since age seven years.

5.3.2 Lipoproteins and lipids (III)

HDL-C among the girls (Table 6) and the boys (Table 7) increased with increasing leisure-time physical activity. Among the girls, leisure-time physical activity was, however, no longer associated with HDL-C after adjustment for BMI and STRIP study group. An increase in leisure-time physical activity was associated also with a higher HDL-C/total cholesterol ratio in girls. Other lipoproteins, lipids or apolipoproteins were not associated with leisure-time physical activity in either gender. Additional adjustment for pubertal status did not affect the results.

Table 6. Lipoproteins, lipids, apolipoproteins, hs-CRP and blood pressure by physical activity group and their association with leisure-time physical activity in girls (III).

	Sedentary	**Moderately Active**	**Active**	**Univariate model** β^a (SE)	**Multivariate model**[b] β^a (SE)
Total cholesterol, mmol/l	4.27 (0.63)	4.33 (0.81)	4.20 (0.73)	-0.027 (0.064)	-0.033 (0.064)
HDL-C, mmol/l	1.16 (0.20)	1.22 (0.24)	1.25 (0.22)	0.045 (0.019)*	0.033 (0.19)
HDL-C/total cholesterol	0.28 (0.06)	0.29 (0.06)	0.30 (0.05)	0.012 (0.0049)[#]	0.010 (0.0049)[‡]
LDL-C, mmol/l	2.68 (0.59)	2.74 (0.72)	2.55 (0.59)	-0.054 (0.057)	-0.055 (0.57)
Triglycerides, mmol/l	0.80 (0.40)	0.70 (0.40)	0.80 (0.40)	-0.030 (0.034)	-0.018 (0.034)
ApoA-I, g/l	1.32 (0.16)	1.36 (0.19)	1.37 (0.18)	0.024 (0.015)	0.015 (0.015)
ApoB, g/l	0.79 (0.18)	0.79 (0.19)	0.76 (0.16)	-0.014 (0.015)	-0.0090 (0.016)
ApoA-I/ApoB	1.76 (0.49)	1.82 (0.53)	1.87 (0.44)	0.056 (0.043)	0.043 (0.043)
hs-CRP, mg/l	0.19 (0.31)	0.16 (0.19)	0.20 (0.50)	0.035 (0.092)	0.12 (0.083)
Systolic blood pressure, mm Hg	111 (10)	110 (11)	107 (8)	-1.78 (0.88)[‖]	-1.07 (0.83)
Diastolic blood pressure, mm Hg	61 (7)	60 (7)	59 (6)	-1.00 (0.58)	-0.93 (0.58)

Data are mean (SD) except for triglycerides and hs-CRP where median (IQR) are given.
[a]Regression coefficient for change in the variable when leisure-time physical activity increases by 1 activity group
[b]Adjusted for BMI and STRIP study group
*P=0.019; [#]P=0.011; [‡]P=0.040; [‖]P=0.042

Table 7. Lipoproteins, lipids, apolipoproteins, hs-CRP and blood pressure by physical activity group and their association with leisure-time physical activity in boys (III).

	Sedentary	Moderately Active	Active	Univariate model β[a] (SE)	Multivariate model[b] β[a] (SE)
Total cholesterol, mmol/l	4.10 (0.77)	4.16 (0.71)	4.18 (0.64)	0.038 (0.050)	0.053 (0.050)
HDL-C, mmol/l	1.16 (0.24)	1.18 (0.25)	1.24 (0.24)	0.043 (0.017)*	0.043 (0.017)[#]
HDL-C/total cholesterol	0.29 (0.05)	0.29 (0.06)	0.30 (0.05)	0.0064 (0.0040)	0.0057 (0.0039)
LDL-C, mmol/l	2.57 (0.61)	2.59 (0.63)	2.60 (0.56)	0.017 (0.043)	0.027 (0.043)
Triglycerides, mmol/l	0.75 (0.40)	0.80 (0.40)	0.60 (0.40)	-0.054 (0.030)	-0.047 (0.028)
ApoA-I, g/l	1.31 (0.20)	1.32 (0.20)	1.36 (0.21)	0.024 (0.015)	0.026 (0.015)
ApoB, g/l	0.76 (0.19)	0.77 (0.18)	0.74 (0.16)	-0.0082 (0.013)	-0.0037 (0.012)
ApoA-I/ApoB	1.82 (0.47)	1.84 (0.67)	1.91 (0.48)	0.045 (0.038)	0.039 (0.038)
hs-CRP, mg/l	0.23 (0.40)	0.21 (0.34)	0.19 (0.27)	-0.066 (0.081)	-0.074 (0.074)
Systolic blood pressure, mm Hg	111 (10)	110 (11)	111 (10)	-0.23 (0.72)	-0.29 (0.66)
Diastolic blood pressure, mm Hg	61 (6)	60 (7)	60 (6)	-0.46 (0.47)	-0.37 (0.47)

Data are mean (SD) except for triglycerides and hs-CRP where median (IQR) are given.
[a]Regression coefficient for change in the variable when leisure-time physical activity increases by 1 activity group
[b]Adjusted for BMI and STRIP study group
*P=0.013; [#]P=0.010

5.3.3 Low-grade inflammation (III)

Sedentary girls (Table 6) and boys (Table 7) had a similar hs-CRP concentration as their physically more active peers. Adolescents with overweight had a higher hs-CRP than adolescents with normal body weight, regardless of leisure-time physical activity (Figure 19). Only 10.4% had hs-CRP ≥1 mg/l; clearly, the CRP concentrations were overall very low.

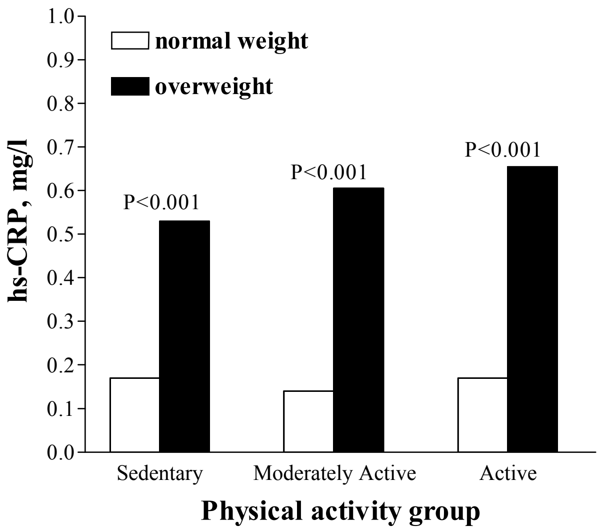

Figure 19. Median hs-CRP by physical activity group and body weight.

5.3.4 Blood pressure (III)

Among the girls, the systolic blood pressure decreased with increasing leisure-time physical activity (Table 6). The association was not significant after adjustment for BMI and STRIP study group. Among the boys, there was no association between leisure-time physical activity and blood pressure (Table 7).

5.3.5 Clustering of risk factors (III)

A decrease in leisure-time physical activity was associated with an increased risk for clustered metabolic risk among the girls (OR=1.55, CI=1.03-2.34, P=0.038), but not among the boys (OR=1.17, CI=0.84-1.64, P=0.35) (Figure 20). The results were similar after adjustment for STRIP study group and pubertal status (girls: OR=1.59, CI=1.04-2.42, P=0.031; boys: OR=1.14, CI=0.79-1.66, P=0.48). Of the girls, 15.3% had 2 risk factors, while 6.7% had 3 and 2.0% had 4 risk factors. Among boys, 14.6% had 2 risk factors, 5.2% 3 risk factors, and 3.1% all 4 risk factors. Of note, 39.3% of the girls and 33.9% of the boys who had clustered metabolic risk (≥2 risk factors) had the cluster without having a high BMI level (BMI in the uppermost quintile), indicating that a cluster of risk factors was not solely determined by BMI.

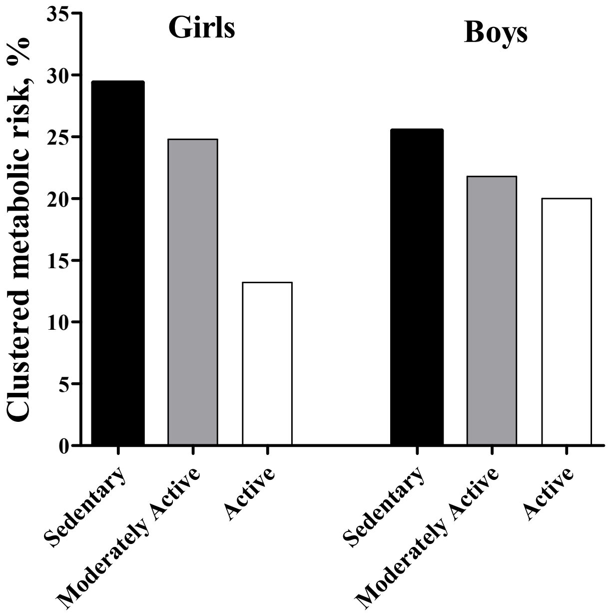

Figure 20. Proportion of adolescents with clustered metabolic risk by physical activity group (III).

To further explore the association between leisure-time physical activity and clustered metabolic risk, the extreme physical activity groups (<5 MET h/wk versus >50 MET h/wk) were compared. When more strict criteria for activity groups were used, low leisure-time physical activity was associated with an increased risk for clustered metabolic risk also in the group of boys (girls: OR=2.85, CI=1.07-7.55, P=0.036); boys: OR=2.10, CI=1.00-4.40, P=0.049).

A screen time >2 h compared with ≤2 h on a weekday was associated with an increased risk for clustered metabolic risk among the girls (OR=2.32, CI=1.28-4.20, P=0.005), but not among the boys (OR=1.01, CI=0.58-1.77, P=0.97). The association was similar regardless of leisure-time physical activity (girls: OR=2.43, CI=1.33-4.45, P=0.0041; boys: OR=0.95, CI=0.53-1.69, P=0.86). Of the Active girls who watched TV, videos or played computer games ≤2 h/weekday, 11.1% (n=36) had a clustered metabolic risk, while the corresponding prevalence of clustered risk was 41.7% (n=24) among those Sedentary girls whose screen time exceeded 2 h/weekday. Screen time on a weekend day was not associated with clustered metabolic risk among the girls or the boys.

5.4 Physical activity and vascular endothelial function (IV)

Endothelial function expressed as brachial artery flow-mediated dilatation improved in boys, but not in girls, with increasing leisure-time physical activity (Table 8).

Table 8. Mean (SD) brachial artery flow-mediated dilatation by physical activity group and the association between leisure-time physical activity and endothelial function (IV).

	Sedentary	Moderately Active	Active	Multivariate model[a] β[c] (SE)	Multivariate model[b] β[c] (SE)
GIRLS					
FMDmax, %	10.0 (4.2)	9.3 (4.2)	10.6 (4.8)	0.0069 (0.014)	0.0071 (0.014)
FMDauc, %×s	729 (503)	667 (494)	759 (504)	0.24 (1.57)	0.54 (1.62)
FMD 60 sec, %	7.9 (4.4)	7.2 (4.6)	8.4 (5.0)	0.0074 (0.014)	0.0063 (0.015)
ΔFMD, mm	0.28 (0.12)	0.26 (0.11)	0.29 (0.13)	0.00020 (0.00038)	0.00019 (0.00039)
BOYS					
FMDmax, %	9.1 (4.3)	9.4 (4.1)	10.1 (4.5)	0.026 (0.011)*	0.028 (0.012)*2
FMDauc, %×s	671 (482)	721 (480)	811 (555)	3.67 (1.31)#	4.033 (1.36)#2
FMD 60 sec, %	7.2 (4.4)	7.7 (4.4)	8.4 (4.8)	0.032 (0.012)‡	0.036 (0.012)‡2
ΔFMD, mm	0.27 (0.12)	0.28 (0.12)	0.30 (0.13)	0.00083 (0.00034)‖	0.00088 (0.00035)‖2

[a]Adjusted for brachial artery baseline diameter
[b]Further adjusted for BMI, HDL-C, LDL-C, triglycerides, hs-CRP and systolic blood pressure.
[c]Regression coefficient for a 1-unit change in PAI
*P=0.020; *2P=0.016; #P=0.0055; #2P=0.0032; ‡P=0.0080; ‡2P=0.0041; ‖P=0.014; ‖2P=0.012

When the Sedentary and Active boys were compared, the FMD had an identical pattern over time, but the magnitude of the response was smaller among the Sedentary than the Active boys (Figure 21). Among the Sedentary and Active girls, the temporal development of FMD and the magnitude of the response over time were similar (Figure 22).

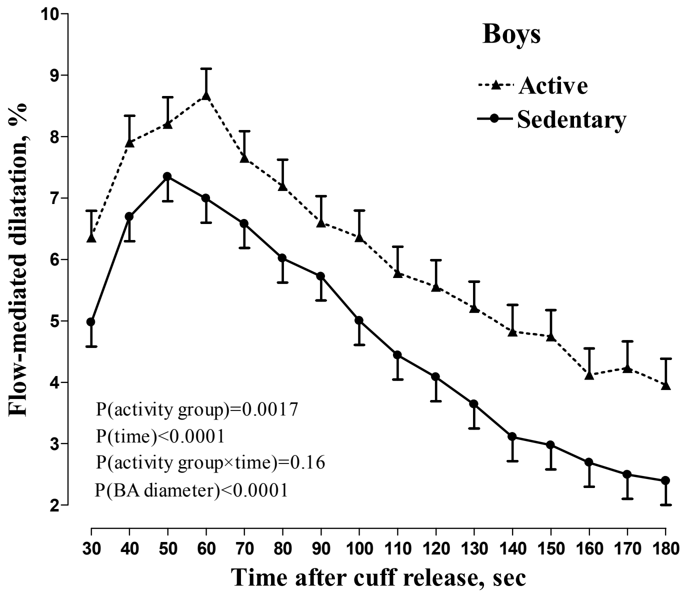

Figure 21. Mean (SE) flow-mediated dilatation in the Active and Sedentary boys (IV). P(activity group×time)=significance for interaction indicating difference in FMD in the activity groups between time points. BA indicates brachial artery.

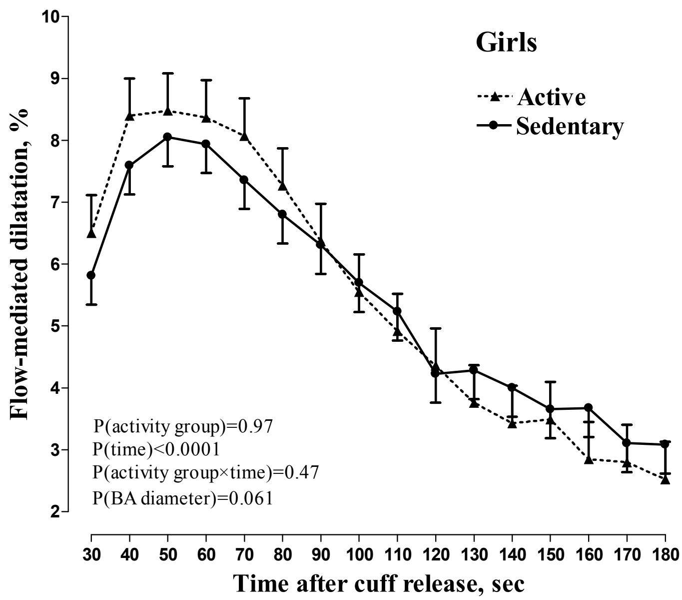

Figure 22. Mean (SE) flow-mediated dilatation in the Active and Sedentary girls (IV). P(activity group×time)=significance for interaction indicating difference in FMD in the activity groups between time points. BA indicates brachial artery.

The gender difference was further studied by comparing the change in FMDmax between girls exercising 10-20 MET h/wk (n=33) and 40-60 MET h/wk (n=36) versus boys with similar activity. The mean (SD) FMDmax was 8.9 (4.9)% for the girls exercising 10-20 MET h/wk and 10.1 (4.7)% for the girls exercising 40-60 MET h/wk during leisure-time. The corresponding FMDmax measures were 9.3 (4.7)% for the boys exercising 10-20 MET h/wk (n=37) and 10.1 (4.8)% for the boys exercising 40-60 MET h/wk (n=67). Thus, with a similar increase in physical activity, FMDmax of the girls increases in a similar manner as of the boys (P=0.78).

5.5 Summary of the results

A lack of leisure-time physical activity was common especially among the girls and it was adversely associated with CVD risk factors and vascular endothelial function (Figure 23).

The main findings were:

- Low leisure-time physical activity was common among girls; in about one-third of the girls the amount of leisure-time exercise corresponded to less than 10 minutes of brisk walking daily (<5 MET h/wk). The Sedentary boys spent more time watching TV, videos or playing computer games than their physically more active peers.

- The leisure-time physical activity of the mothers and their daughters was linked; the Sedentary girls had more often a Sedentary mother than the Active girls. The mothers of the Sedentary girls had also more often been overweight than the mothers of the Active girls during the past 13 years.

- The girls who were Sedentary at age 13 years were more often overweight already since age two years than their physically more active peers, while no association was found among the boys. Clustering of metabolic risk factors was more common in the Sedentary than Active adolescents and in the group of girls spending screen time >2 h/day.

- The endothelial function of the Sedentary boys was decreased compared to the Active peers.

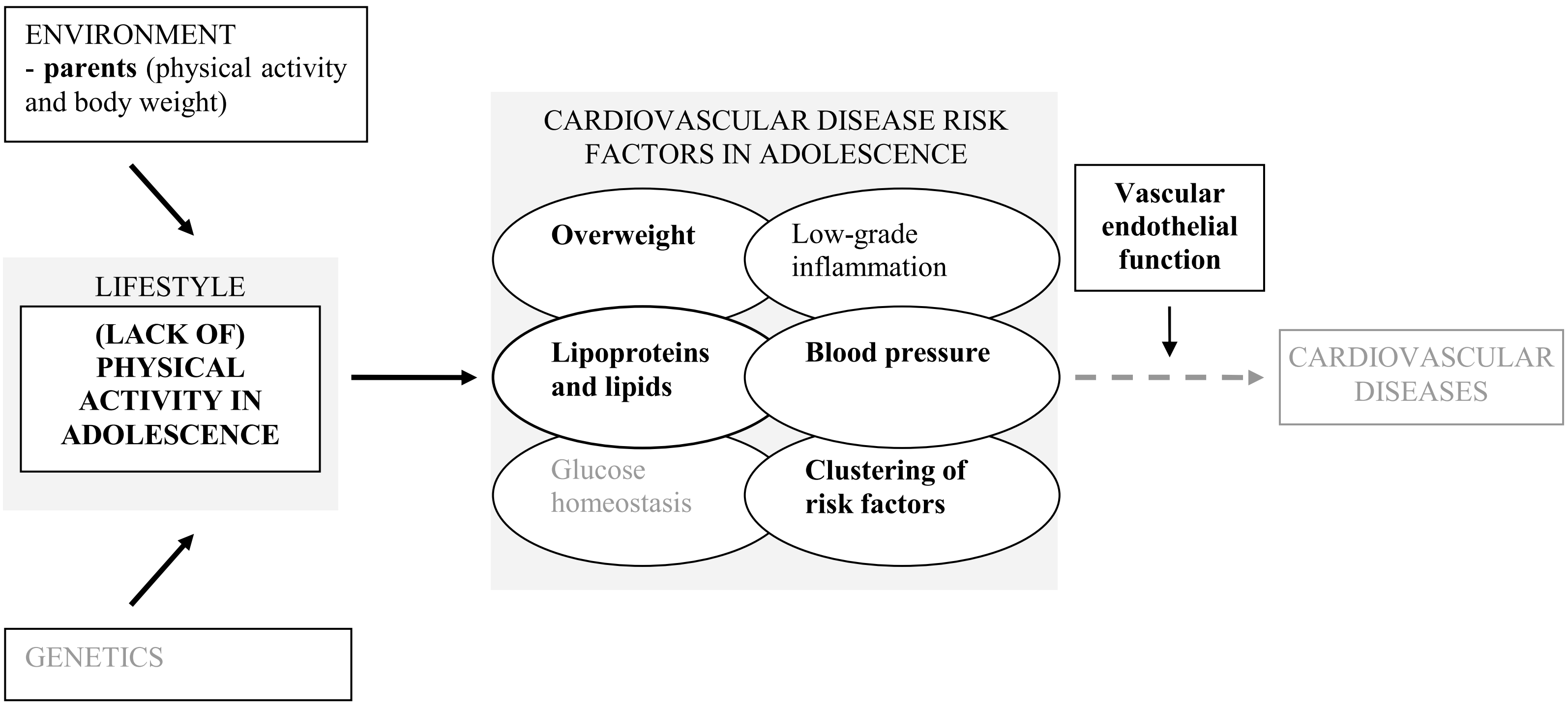

Figure 23. Summary of the results. Risk factors affected by (lack of) physical activity are bolded.

6 DISCUSSION

In the modern society our daily physical activity is reduced by increasing mechanization at work and home, easy transportation and attractive alternatives to spend leisure-time sedentary (Blair & Morris 2009). There is ample evidence that the modern lifestyle constitutes a major threat to the health of individuals and also to public health. The present study confirms previous reports showing that many adolescents spend their leisure-time in a rather sedentary way. Being sedentary causes unfavorable effects on CVD risk factors. While it takes decades before these risk factors may cause disease, the noninvasive ultrasonography provides new insights into the very first signs of atherosclerosis *in vivo*. In this study, assessment of the vascular endothelial function by ultrasonography demonstrated indisputably the detrimental effect of being sedentary on cardiovascular health in adolescence.

6.1 Subjects and methods

6.1.1 Subjects

The study comprised 13-year-old adolescents who were participants of a longitudinal atherosclerosis prevention study. In a longitudinal study, it is inevitable that some subjects are lost to follow-up. In the STRIP study, less than half of the initially recruited families discontinued their participation during the first 13 years of the study. The most common reasons for withdrawing were changed family situation or domicile. The characteristics of those still participating in the STRIP study and those lost to follow-up have been compared repeatedly and no major differences have been found regarding body weight, BMI, total cholesterol or SFA intake (Rask-Nissilä et al. 2000, Raitakari et al. 2005, Hakanen et al. 2006). Furthermore, the mean BMI of the adolescents who remained in the study at age 13 years was similar to the mean BMI of those who had discontinued participation at the beginning of the study as well as at age 13 months, two years, five years and ten years.

Practically all adolescents participating in the 13-year-visit provided data on their leisure-time physical activity which eliminated selection bias. Importantly, the fact that the adolescents have been participants of the STRIP study since the age of seven months also eliminates the possibility of enrollment to the study due to interest in physical activity.

6.1.2 Leisure-time physical activity – questionnaire

Data on leisure-time physical activity was obtained using a self-reported questionnaire. Reported habitual leisure-time physical activity intensity, duration and frequency were combined to provide a single leisure-time physical activity variable (PAI) expressed as a comparable unit (MET h/wk). The PAI was originally introduced in the Young Finns Study (Raitakari et al. 1996) and has subsequently also been used in the STRIP study.

The use of a subjective method to assess physical activity is a limitation of this study. Although widely used, the questionnaire has not been thoroughly validated against an objective physical activity assessment method, e.g., accelerometry or calorimetry, as these studies would be, if not impossible, at least very difficult to conduct. In this study, leisure-time rather than total daily physical activity data was used. In the questionnaire, data on physical education and active commuting to school and hobbies were also reported, but these data were limited with regard to activity intensity and/or duration. Thus, they could not be calculated as MET h/wk and combined with PAI. In all, the PAI estimates leisure-time physical activity and it may sometimes describe preferentially participation in organized physical activity while unorganized, recreational activity may go underreported. Arbitrary PAI cut-off points (tertiles) were used to divide the adolescents into activity groups in face of the lack of established criteria for a sedentary or an active adolescent based on leisure-time physical activity.

The time span used to define leisure-time physical activity was not determined strictly as, e.g., over the past month. Rather, the amount of "habitual" physical activity related to the current leisure-time physical activity was assessed. The benefit of using the definition "habitual" is that it is not subject to recent or short-lasting changes in physical activity. Seasonality may also affect physical activity. In this study, seasonality was hardly a confounding factor, since the study covered two and half years.

Although a questionnaire in itself is a relatively easy way to assess physical activity, designing one is difficult. Questions that require precise definitions are, for instance: What are the characteristics, e.g., age, of the study objects? What aspects of physical activity are assessed? How are the questions to be formulated to be clear and unambiguous? In a longitudinal study from childhood to adolescence, the challenge is also how to get comparable physical activity data throughout these years while taking into account the changing physical activity habits of the growing child. Every effort should also be put into stringent data collection, as missing data may bias the results. In this study, the high response rate was in part obtained through sending the questionnaire in advance, by making systematic enquiries of the questionnaire at the study visits and by revision of the questionnaire to avoid missing data. Those who failed to return the questionnaire at the study visit were repeatedly contacted to provide the information.

All physical activity assessment methods have pros and cons. These may be best overcome by the use of both objective and subjective methods. In epidemiological studies, my best choice within the current physical activity assessment tools would be an accelerometer or a pedometer used together with a questionnaire. There hardly is a simple answer to what is the best question or questionnaire to assess physical activity – except that "it depends".

6.1.3 Physical activity intensity – heart rate monitoring

Heart rate monitoring was used to assess time spent by the adolescents in physical activity at an intensity of ≥120 bpm. This heart rate cut-off point was chosen because lower heart rates are more likely to be confounded by other factors than physical activity (Riddoch & Boreham 1995). Eight hours of monitoring per day was the minimum time for successful data assessment (Epstein et al. 2001). The heart rates were recorded for three days, including one weekend day. The number of monitoring days has varied from one to seven in previous studies (Epstein et al. 2001). The monitoring days were not necessarily consecutive allowing the participant to choose the day to wear the device. This may have influenced the results, since physically more active days may have been selected. Furthermore, simply wearing the heart rate monitor may have inspired the adolescents to be physically more active than usually. Exclusion of the first monitoring day could have limited this effect (Corder et al. 2008), but it was not done in this study because not more than three days were monitored.

Because of the limited number of devices, 27% of the eligible adolescents could not be invited to wear the heart rate monitor. Refusal of the heart rate monitoring was not common (9%) and was not associated with PAI, which implies that participation was not affected by leisure-time physical activity. The main reason for refusal was a perceived inconvenience of the monitoring. Over half (53%) of the adolescents provided heart rate monitoring data which met the study criteria. Completion of the monitoring was not associated with PAI.

In practice, the adolescents were invited to the heart rate monitoring study at the 13-year-visit. The use of the monitor and the study protocol were introduced to the adolescent and his parent/older sibling and written instructions were given. Although the heart rate monitor was readily accepted by most, there were challenges in the adherence to the study protocol. Especially, the monitor had been removed during exercise training. For instance, those engaged in soccer, ice-hockey, floor ball and gymnastics reported that wearing a heart rate monitor which could harm oneself or others was not allowed during training. In water sports, again, social pressure was a reason for not wearing the monitor. Thus, lack of wearing the monitor during exercise has probably reduced the time spent at heart rates ≥120 bpm assessed in this study.

Ideally, the heart rate data is received immediately after each monitoring day and analyzed. If the study criteria are not met, extra monitoring time is required. This study protocol would obviously be inconvenient for the subject and laborious for the researcher. In this study, the heart rate monitor was mailed back after completing the monitoring days. If the data assessment was unsuccessful, the monitoring was occasionally repeated. A greater effort to recollect the monitoring data would have provided a more complete study sample. Altogether, given the effort needed to obtain representative heart rate data, the use of heart rate monitoring to assess physical activity in adolescents should be carefully considered within large studies.

6.1.4 Vascular endothelial function – ultrasonography

The possibilities provided by ultrasonography to study the development and progression of atherosclerotic CVD *in vivo*, even before structural alterations occur, are fascinating. Instead of measuring the factors that might contribute to the disease development, ultrasonography allows the direct visualization of the function and structure of the vascular system. For instance, high LDL-C may in part predispose to the formation of an atherosclerotic plaque, but with ultrasonography it is possible study whether there are changes in the arterial wall or not. Impairment of the vascular endothelial function is suggested to occur before the structural changes (Ross 1986) and is, of course, of major interest.

The noninvasive assessment of endothelial function by ultrasonography used in this study was first introduced in 1992 (Celermajer et al. 1992). It is based on the measurement of the brachial artery luminal diameter at baseline and after an increase in blood flow. In the endothelial function test, FMD of the artery describes the proportional change in the diameter of the artery. Traditionally, the FMD has been measured during a rather strict time interval, 40-60 seconds, after the release of blood flow (Celermajer et al. 1992). However, there is considerable variation in the time needed to achieve maximum FMD (Järvisalo et al. 2002). Therefore, to assess the true maximum FMD, dilatation of the artery was measured 30-180 seconds after blood flow release in this study. In addition, arterial dilatation during the entire measurement time (FMDauc) was used to describe endothelial function.

Brachial artery FMD is associated with coronary endothelial function and it is used as a marker of systemic arterial endothelial function (Celermajer et al. 1992, Anderson et al. 1995). There is day to day variation in FMD, but the long-term within subject variation during weeks and months is small (Sørensen et al. 1995). Thus, the measurement of FMD is reproducible (Sørensen et al. 1995). The future will show if assessment of endothelial function along with risk factors for CVD will be useful in clinical practice.

6.2 Results

6.2.1 Physical activity in adolescence

A considerable number of the adolescents, especially girls, reported low leisure-time physical activity. In line with other recent studies (Kimm et al. 2002, Tammelin et al. 2007, Currie et al. 2008) this is a cause for great concern. In one-third of the girls, the reported leisure-time physical activity was at most five MET hours/week. This amount of physical activity corresponds to only ten minutes of brisk walking daily. It should be kept in mind, however, that the PAI gives an estimate of the leisure-time physical activity and unorganized activity may be underreported. Thus, it is possible that the Sedentary girls are physically somewhat more active than indicated by the PAI. Nevertheless, such a low PAI value as only five MET h/wk likely indicates low leisure-time physical activity level. Self-report methods to assess physical activity tend, on the other hand, to overestimate physical activity. If this is the case here, the finding that many adolescents report an extremely low leisure-time physical activity is even more worrisome.

The PAI cut-off point for the group of Sedentary boys was 19.5 MET h/wk. This amount of leisure-time physical activity corresponds to, e.g., four to five hours of brisk walking weekly. It can thus be speculated whether the boys defined as Sedentary in this study were truly sedentary. However, the mean PAI among the Sedentary boys was 8.2 MET h/wk, showing that the majority of the Sedentary boys were considerably less active than indicated by the cut-off point.

The results concerning physical activity assessed by a heart rate monitor gave a somewhat different picture of the adolescents' physical activity than the reported leisure-time activity. Although all day was not covered, the Sedentary girls spent on average 28 minutes and the Sedentary boys 33 minutes in moderate to vigorous physical activity (≥140 bpm). In addition, they exercised approximately an hour at the intensity of 120-139 bpm. This indicates a fairly good amount of daily physical activity. Overall, there was nearly no association between reported leisure-time physical activity and the times spent doing these activities. Only the Moderately Active boys spent, on average, more time in vigorous physical activity than the Sedentary boys. Enthusiasm to test the heart rate monitor and, on the other hand, its removal during exercise training has probably influenced the results and has leveled off any possible differences between the activity groups. Moreover, physical activity assessed by these two different methods do not give directly comparable results because they assess different aspects of physical activity.

It cannot be concluded how many of the adolescents in this study reached the current recommendation for physical activity (U.S. Department of Health and Human Services 2008, Tammelin & Karvinen 2008). The entire day was not captured by the heart rate monitoring and those who reported low physical activity during leisure-time may, in theory, have been physically active enough in other times of the day. Among adolescents, other opportunities for physical activity besides leisure-time activities are active commuting to and from school and physical education lessons during school. Although lesson breaks also offer an opportunity to be physically active, adolescents seldom use it. The number of weekly physical education lessons is unfortunately small, typically only two (1.5 hours), for adolescents in Finland. Furthermore, part of this time is allocated to changing clothes, listening to instructions and waiting for own turn. Hence, with minimal leisure-time physical activity, two weekly physical education lessons are clearly not enough to meet the recommendation for physical activity. Furthermore, commuting in urban areas is often done by bus or car, limiting its role in terms to provide physical activity. Hence, I claim that many of the adolescents who reported low leisure-time physical activity were not able to compensate for it during other times of the day and that their physical activity level was indeed low.

Screen time

Screen time is a common indicator for sedentary time. Indeed, much of the daily time today, both at work and leisure, is spent in front of a TV and computer screens. TV and computers are a part of daily life already from early childhood on. Even small children have access to these devices and they know how to use them. A computer connected to the Internet is nearly a necessity in today's home. Watching TV and leisure use of a computer are sometimes criticized for wasting time from more useful activities. I suspect, however, that not many people would like to go back to the time before them. The challenge is to avoid spending too much time by the TV and computer screens. It is worrisome that there are children and adolescents who do spend practically their whole leisure-time watching TV, playing video or computer games, or browsing and chatting through the Internet.

In practice, it is probable that if much time is spent being sedentary, less time is left for physical activity. In this study, the Sedentary boys reported spending more time by the screen than their physically more active peers, but no association was found in girls. This is in line with previous studies showing that physically active adolescents spend less time by a TV and/or computer screen than those who are less active or that there is no association (Ekelund et al. 2006, Tammelin et al. 2007). Furthermore, a reduction in TV viewing and computer use was not associated with increased physical activity in children (Epstein et al. 2008). This indicates that the sedentary behaviors are not necessarily replaced by physical activity. Lack of an association between physical activity and screen time may be caused by the fact that TV and computer screen time does not constitute the whole time spent sedentary, or that adolescents simply have time for both. Interestingly, new video/computer games designed to physically activate the player (exergames) may in part change screen time from being an indicator of sedentary time. Indeed, all time spent in front of a screen is not necessarily sedentary today.

6.2.2 Physical activity and cardiovascular disease risk factors

A lack of physical activity has a detrimental effect on several CVD risk factors. The Sedentary adolescents of this study were more often overweight and had a higher prevalence of clustered metabolic risk than their physically more active peers.

Obesity is a major health problem worldwide today. In the U.S., approximately two-thirds of all adults are overweight or obese (Kumanyika et al. 2008). The proportion of overweight children and adolescents has increased steadily during the last decades, and heavy children and adolescents are getting heavier. An indicator of this is the emergence of type 2 diabetes also as a pediatric disease. However, some leveling off of the prevalence of youth overweight has taken place in the recent years (Ogden et al. 2008).

A sedentary lifestyle may contribute to overweight regardless of age. In this study, being Sedentary was clearly associated with a higher prevalence of overweight in girls. Interestingly, this was evident already since the age of two years. The girls who were

Sedentary at age 13 years were twice as often overweight as their Active peers already eleven years ago. Although it is not possible to state which comes first, overweight or lack of physical activity, this finding implies that children with overweight may be more prone to a sedentary lifestyle in adolescence. Rather than the cause, the lack of physical activity may be the consequence of overweight (Petersen et al. 2004, Mortensen et al. 2006). For instance, overweight children may find physical activity involving, e.g., running, strenuous and they may feel that they are not as good as their leaner peers, and thus withdraw from it. Of note, if being overweight already at the age of two years increases the likelihood of being sedentary in adolescence, the prevention of overweight to support a healthy, physically active lifestyle later in life needs to be started at a very early age.

The marked increase in the proportion of overweight children at age six years, especially among the girls who were Sedentary at age 13 years, further emphasizes early prevention of overweight. This age is characterized by adiposity rebound, which refers to an increase in BMI after reaching its lowest level, and which is a period of increased risk for the development of obesity (Steinbeck 2001). One explanation for the increase in the proportion of overweight children among the Sedentary girls at age six years, is that the energy intake of the Sedentary girls who had a normal body weight both at age 5 and 6 years was lower at age 6 years than the energy intake of the Sedentary girls who had a normal body weight at age 5 years but who were overweight at age 6 years (II).

Not only a sedentary lifestyle but also the abundance of foods that contain much energy relative to the food amount indeed challenges the maintenance of a normal body weight today. These energy-dense foods make it especially easy to consume more energy than what the body needs. The same amount of energy is also far more easily eaten than expended in physical activity. For instance, a typical hamburger meal contains approximately 4.2 megajoules (~1 000 kcals) of energy. It would take for an adolescent weighing 50 kg about three hours of jogging (7 METs) to expend it. Thus, in order to prevent overweight, both avoidance of a sedentary lifestyle and moderation of energy intake are needed.

The potential benefits of physical activity on CVD risk factors are not restricted to body weight. For instance, lipoproteins and lipids, blood pressure and glucose homeostasis are also favorably affected by physical activity. Importantly, the effects of physical activity on cardiovascular health are not only a result of reduced body weight *per se* but are evident irrespective of whether one is of normal weight, overweight or obese (Church et al. 2005). Furthermore, those who are regarded as fat but fit in terms of cardiorespiratory fitness, have a lower risk of CVD mortality than those who have a normal body weight but are unfit (Church et al. 2005). The important message to those who have overweight is that physical activity is good for health even if there is no reduction in body weight. On the other hand, although the beneficial association between physical activity and, e.g., blood pressure would be partly caused by lower body weight in those who are active, it does not diminish the importance of physical activity as the underlying factor. Overall, the risk factors for CVD tend to cluster and the disease risk increases as the number of risk factors increases (McGill et al. 2008). The present study shows that those adolescents who are Sedentary have a higher prevalence of clustered risk than those who are physically more active, which confirms earlier reports (Lakka et al. 2003, Andersen et al. 2006). Given the wide benefits of physical activity on CVD risk factors, physical activity seems to be the ideal prevention and treatment of clustered CVD risk.

6.2.3 Physical activity and vascular endothelial function

This study showed for the first time in healthy adolescents that being Sedentary in leisure-time was associated with impaired endothelial function compared with physically more active peers. Previous studies have reported the beneficial effect of physical activity on endothelial function of healthy adults (Clarkson et al. 1999) and of those with coronary artery disease or type 2 diabetes (Hambrecht et al. 2000, Maiorana et al. 2001, Vona et al. 2009). Exercise training has also improved endothelial function of children and adolescents with overweight (Watts et al. 2004, Woo et al. 2004). Of note, those boys who were Sedentary had a smaller flow-mediated dilatation of the artery than those who were Active – independent of several other CVD risk factors, i.e., the cholesterol and triglyceride concentration, BMI, hs-CRP or blood pressure. The lack of association in girls may be due to lower physical activity level rather than gender, since when the maximum FMD was studied in girls and boys with the same activity level, girls experience a similar increase in maximum FMD than boys. In all, the detrimental effect of the lack of physical activity on cardiovascular health as assessed *in vivo* emphasizes the importance of avoiding a sedentary lifestyle since childhood.

6.3 Promotion of a physically active lifestyle

It is evident that many people in the Western societies are sedentary and the sedentary way of life is associated with adverse health effects. Despite all the knowledge on the benefits of a physically active lifestyle, we are generally reluctant to take the “exercise medicine”. As a consequence, the burden may be high for the individual and for society. The physical activity promotion message has traditionally focused on the importance of engaging in physical activity. The recommendation for physical activity guides us to collect a certain amount of at least moderately intense aerobic activity and to do strength training. The message could, however, also be turned around. Instead of emphasizing the need to increase physical activity, we could be guided to avoid a sedentary lifestyle. Naturally, this includes the message that physical activity is good for the health and that it is important to engage in it, but at the same time, it takes into account the whole spectrum of activities. The idea is that reduction of the time spent sedentary would simultaneously lead to an increase in physical activity. TV viewing might not be replaced with jogging, but even a slight increase in activity is for the better. Moreover, this message may be more readily taken up by those who are not so keen on physical activity *per se*. In addition to promoting avoidance of a sedentary lifestyle, the primary target should be those currently sedentary since they are the ones to benefit the most.

The sedentary way of life may begin in early childhood. Thus, this is a good time to start preventive actions. Among young children, promotion of physical activity could be done by implementing physical activity as an essential part of the functions in cay-care centers as well as supported in the well-baby clinics. In the clinics, parents could be asked about the physical activity habits of the family, and the parents could be given information about the benefits of physical activity and guided how to increase physical activity in practice. From the view point of activity-friendly environment, families should, e.g., have an easy access to safe play grounds. Although a physically active lifestyle in children and adolescents needs to be supported through many ways, parents have, in my opinion, a key role – lifestyle habits and attitudes may be passed from parents to children. Ideally, parents themselves should be physically active and show a good example for their children. This is especially important regarding everyday physical activity associated with, e.g., commuting and other daily chores. Indeed, although structured exercise hobbies are to be encouraged they should not be a necessity for a child or an adolescent to be physically active. Given the parents' possibility to influence the physical activity of their children, guidance to avoid a sedentary lifestyle should be family-oriented and also include promotion of the parents' physical activity.

In a broader perspective, promotion of a physically active lifestyle could in part be done through activity-friendly environments. Neighborhoods built to support physical activity for instance can contribute to increased physical activity in children, adolescents and adults (Gordon-Larsen et al. 2006, Sallis et al. 2009, Tester et al. 2009). This approach is especially important in that it can involve also those who are not interested in physical activity as such. Changing the environment again requires making also changes through politics and legislation. Particularly among the youth, branding of physical activity as something fun and "cool" could also be used as a tool to promote physical activity (Asbury et al. 2008).

Altogether, physical activity is one of many lifestyle factors associated with cardiovascular health. Thus, in addition to promoting physical activity, an overall healthy lifestyle including, e.g., non-smoking and a healthy diet should be emphasized, as they together best support health. A healthy lifestyle choice should also be an easy, attractive choice.

6.4 Perspectives

Lack of physical activity in adolescents is of great concern. There is abundant, scientifically valid evidence that physical activity has wide-ranging beneficial health effects at all ages. Accordingly, recommendations for physical activity are available. It is important that we understand the mechanisms how physical activity affects health. However, the momentous great challenge of today is to get sedentary people to be physically more active.

7 CONCLUSIONS

Among healthy 13-year-old adolescents, lack of leisure-time physical activity was common. Parental leisure-time physical activity and body weight were associated with leisure-time physical activity of the child. Being Sedentary was adversely associated with CVD risk factors and vascular endothelial function. In specific:

- a great number of the adolescents, especially girls, reported an alarmingly low leisure-time physical activity. Sedentary adolescents should thus be put into focus for active efforts to support a physically active lifestyle.
- the Sedentary girls' mothers were more often Sedentary or overweight than the mothers of the physically more active girls. A healthy lifestyle should be encouraged for parents for personal health benefits and as a good role model for their children.
- the girls who were Sedentary at age 13 years were more often overweight already since early childhood than the Active girls. The Sedentary adolescents had a higher prevalence of clustering of metabolic risk factors for CVD than their physically more active peers.
- endothelial function, an *in vivo* indicator of cardiovascular health, was impaired in the Sedentary adolescents compared to those who were physically more active.

Avoidance of a sedentary lifestyle should be emphasized to support cardiovascular health in adolescents.

8 ACKNOWLEDGEMENTS

This study was carried out at the Research Centre of Applied and Preventive Cardiovascular Medicine (CAPC) and the Paavo Nurmi Centre, University of Turku in collaboration with the Departments of Pediatrics and Medicine, University of Turku, and the National Public Health Institute, Turku, Finland, during the years 2002-2009.

The study was financially supported by the Finnish Ministry of Education, the Finnish Cultural Foundation, the Juho Vainio Foundation, the Finnish Cardiac Research Foundation, the Academy of Finland, the Sigrid Juselius Foundation, the Special Governmental Grants for Health Sciences Research/Turku University Hospital, the Yrjö Jahnsson Foundation, the C.G. Sundell Foundation, the Foundation for Pediatric Research and the Turku University Foundation. Polar Electro Oy is acknowledged for technical assistance.

I owe my deepest gratitude to my principal supervisor, Professor Olli J. Heinonen. It is difficult to find the words to describe my appreciation for the time, patience and commitment you have devoted to my thesis, and above all, for educating me to be a scientist. Countless times you have challenged me to think instead of giving a quick answer and taught me to be critical. During these years you have encouraged and guided me, and shared the ups and downs of scientific work. I could not think of a more dedicated teacher – I have truly been privileged to have you as my supervisor.

I warmly thank my supervisor Adjunct professor Hanna Lagström for your valuable experience in the STRIP study, the numerous conversations and for always being available to answer my questions and listen to my ideas. Thank you also for accompanying me on my first congress trip and emphasizing the importance of life outside work.

I am grateful for my supervisor Adjunct professor Paula Hakala for your friendly support and patient guidance during these years. I highly appreciate our profound discussions especially at the beginning of my thesis project.

I am indept to Professor Olli Simell, the principal investigator of the STRIP study, for providing me the opportunity to work in the STRIP study. I am proud to be a part of this study. I highly admire your effort in establishing the STRIP and keeping it going through the past 20 years. I am also thankful that you were open-minded to propose physical activity as the topic of my thesis and had faith in me during the years.

I have been very fortunate to co-work with Professor Jorma Viikari, Professor Tapani Rönnemaa and Professor Olli Raitakari, the director of CAPC. Despite your busy schedules, you have always had time to share your vast knowledge and experience to improve my work. I truly admire your expertise, enthusiasm and dedication to science.

I am deeply thankful for the reviewers of this thesis, Professor Tuomo Rankinen and Professor Willem van Mechelen, for your time and valuable comments to improve the thesis. I was honoured that you accepted to review my thesis. I sincerely thank also Adjunct professor Robert Paul for the skillful language revision of this thesis.

My heartfelt thanks to my friends and co-writers Maarit Hakanen, Tuuli Kaitosaari and Soile Ruottinen, for sharing the joys and challenges of preparing a thesis and the cheerful moments not related to research work. Maarit, special thanks for the many stimulating conversations and your invaluable support during this year when we completed our theses. I am very happy that I could share this demanding, yet very rewarding time with you.

I am very grateful to my co-writers Lauri Sillanmäki, Adjunct professor Minna Aromaa and Miika Hernelahti for your contribution. Thank you Lauri for the statistical analyses and showing so much patience in answering my endless questions about the methodology and teaching me how to do statistical analyses myself. Minna and Miika, your valuable comments and constructive critisism have greatly improved the articles.

I warmly thank the investigators of the STRIP study, Katariina Kallio, Sanna Talvia, Marika Viitala, Maarit Laurinen, Johanna Lehtomäki, Marika Havola, Susanna Anglé, and Iina Volanen for the countless vivid discussions and fun moments throughout the years. Thank you Sanna for introducing me the possibility to become a researcher in the STRIP. I also thank Päivi Raittinen and Arja Sääkslahti for collaboration in studies on physical activity.

My co-workers and friends, Asta Myyrinmaa and Soile Kotilainen – the "grand ladies" of the STRIP study – and Minna Hyppönen, Tiina Peromaa, Nina Aalto, Nina Ruotsalainen, Maiju Saarinen, Pekka Heino, Anni Pakarinen and Mia Laakkonen, I warmly thank you for your expertise, help, as well as for your company and unforgettable time during the years. If laughing really makes you live longer, I have gained many extra years because of you.

All the people at the CAPC and the Paavo Nurmi Centre are warmly acknowledged for making it pleasant to come to work and for the nice time together. I am grateful to Professor Pekka Kääpä, the former director of CAPC, for providing the facilities and creating a good atmosphere to work in. Jaakko Kytölä and Jarmo Jalonen, thank you for always being willing to give your help in various technical and statistical problems. Thank you also Hanna Soukka for encouragement and optimism. Marja Piippo and Marketta Kiviniitty are sincerely acknowledged for helping me in many practical matters. Thank you Irina Lisinen for your professional help and company at and outside work. I am also thankful to Costan Magnussen for the discussions on physical activity and improving the language of the thesis.

I have been fortunate to meet many charming and inspiring people from the field of science during these years. I wish to warmly acknowledge you all. Special thanks to

Tuija Tammelin, Katja Mjøsund, and Adjunct professor Raija Laukkanen for your enjoyable company during scientific meetings.

I especially acknowledge all the children of the STRIP study and their families. Your contribution and admirable dedication have made the study possible. I also owe my deep gratitude to those people who in addition to Professor Simell contributed to the establishment of the STRIP.

Special warm thanks to all of my family and friends for bringing joy to my life and being there for me. I especially owe my love and gratitude to my parents Marjatta and Arvi for your unreserved love and support. My dear friend Salla, my heartfelt thanks to you for sharing the ups and downs of life with me for more than 20 years.

Above all, I thank from all my heart my husband Petri for the love and life together. Your incredible support and interest in my work have made the preparation of this thesis considerably easier. You are the most precious to me.

Turku, October 2009

Katja Pahkala

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