UNIVERSITY OF SOUTHAMPTON

Faculty of Medicine, DOHAD, Institute Of Human Nutrition

Doctor of Philosophy

Comparison of different methods of categorization for physical activity on Coronary Heart Disease Risk Factors

by

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ABSTRACT

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Objective: There is a general agreement that physical activity (PA) has a beneficial effect on health and those who are more active have a reduced risk of developing many chronic diseases, such as coronary heart disease (CHD). However, the amount, type and intensity of PA deemed to be sufficient to achieve good health remains unclear. Different methods have been used to categorise activity behaviour, but the level of agreement, consistency and coherence between methods and how this might influence their relationship with CHD risk factors and estimated CHD (eCHD) risk are poorly understood. This uncertainty is reflected in many different messages communicated to the public as to how active they should be to prevent chronic diseases. The primary objective of this thesis was to determine whether the methods used to categorise PA (as either inactive/active or level of PA) influence the extent to which PA is associated with CHD risk factors and eCHD risk.

Methods: This thesis was divided into two parts. The first part was to conduct a secondary analysis of data on activity and CHD risk factors (blood pressure and lipid profile) obtained from the 2004 UK National Diet and Nutrition Survey (NDNS) in 1658 adults aged 19-64 years. Using the information obtained from the NDNS 7-day diary, it was possible to extend the original observations and to re-categorise individuals according to measures of PA in terms of number of days and minutes of at least moderate PA, total activity expressed as metabolic-equivalents (METs) and self-perception of PA. Each of these methods was then used to examine the proportion of the variance in CHD risk factors and the eCHD risk attributable to differences in PA using General Linear Modelling with adjustment for BMI, age and smoking. Partial eta squared a "proportion of variance due to physical activity plus error that is attributed to physical activity alone" was used. In the second part, the concurrent validity of measures of PA derived from the NDNS 7-day diary, using different systems for coding and classifying of different physical activities, was compared against those measures of PA obtained from the International Physical Activity Questionnaire (IPAQ) in a group of medical students (n = 26).

Results: Taken together, this thesis revealed: 1) poor agreement across different methods of categorisation of PA level, 2) no support to justify a curvilinear dose-response relationship between PA level and CHD risk factors and eCHD risk and that a linear model was sufficient, 3) the differences in CHD risk factors or eCHD risk that could be directly attributable to differences in PA in men was modest (generally < 5%) although no associations evident in the women, 4) effect was most obviously demonstrable as improvements in lipid profile, no demonstrable effect on blood pressure, 5) a potential problem might arise when using one system and applying its results to different guidelines established by different systems.

Conclusion: These findings support the view that being physically active is associated with markers of better health and lower CHD risk; a small but consistent effect that was the same irrespective of which method of categorizing PA was used and even after adjustment for differences in age, BMI and smoking. The effects were most evident in men and largely attributable to improvements in lipid metabolism.

Dedication

My parents

My wife and children

Nawaf Al-Haifi and Dr John Jackson

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Bibliography

1. Abstract accepted by the 16th European Congress on Obesity (ECO 2008) in Geneva, Switzerland.

The relative importance of BMI and physical activity on cardiovascular disease risk factors

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Introduction: There is no clear consensus whether body mass index (BMI) or physical activity (PA) is more important in cardiovascular disease (CVD) prevention. Only a limited number of studies have compared the relative effects of BMI and PA on the risk factors for CVD. Therefore, the aim of this study was to compare the relative importance of BMI and PA on the levels of systolic blood pressure (SBP), total cholesterol (TC) and high-density lipoprotein (HDL).

Methods: This was a secondary data-set analysis of 1658 adults (aged 19-64 years) obtained from the 2004 UK National Diet and Nutrition Survey (NDNS). PA was a categorized metabolic-equivalent (MET) value extracted from the NDNS self-reported seven-day diary. A General Linear Model was used to calculate the partial-eta-squared percent (proportion of variability) with adjustment for age and smoking, and individuals taking medications were excluded.

Results: In women, the partial-eta-squared percent of BMI vs PA for SBP, TC and HDL were 11.4% (P<0.001) vs 1.4% (P=0.195), 6.6% (P<0.001) vs 0.5% (P=0.759), and 8.2% (P<0.001) vs 0.5% (P=0.719), respectively. In men, the partial-eta-squared percent explained by BMI vs PA for SBP, TC and HDL were 6.4% (P<0.001) vs 1.0% (P=0.289), 1.0% (P=0.511) vs 4.0% (P=0.009), and 7.1% (P<0.001) vs 6.3% (P<0.001), respectively.

Conclusion: The evidence from this data set suggests that BMI explains a greater proportion of the variation in the CHD risk factors than does PA, particularly in women.

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List of abbreviations

AAS:	Active Australia Survey
ACSM:	American College of Sports Medicine
AEE:	activity energy expenditure
AHA:	American Heart Association
BRFSS:	Behavioural Risk Factor Surveillance System surveys
BF:	Body Fat
BMI:	body mass index (Weight kg/ Height metre2)
BHS:	British Hypertension Society
CAD:	coronary artery disease
CDC:	Center for Disease Control
CAD:	coronary artery disease
CHD:	coronary heart disease
CRP:	C-reactive protein
CVD:	cardiovascular disease
DH:	Department of Health
DHHS:	Department of Home and Health Services
DIY:	Do It Yourself
eCHD risk:	estimated of coronary heart disease risk
EE:	energy expenditure
FRS:	Framingham Risk Score
GP:	General Practicener
HDL-C:	high-density lipoprotein-cholesterol
IPAQ:	International Physical Activity Questionnaire
Kcal:	kilo calories
Kg:	kilo gram
KJ:	kilo joule
Km:	kilo meter
LDL-C:	low density lipoprotein-cholesterol
LTPA:	leisure-time physical activity
MET:	metabolic equivalent (k-cal/kg/hour)
MRFIT:	Multiple Risk Factor Intervention Trial
NDNS:	National Diet and Nutrition Survey.
NHS:	National Health Service
NIDDM:	non-insulin dependent diabetes mellitus
OR:	odds ratio
PAEE:	physical activity energy expenditure
PAL:	physical activity level
REE:	resting energy expenditure
PKC:	protein kinase C
RMR:	resting metabolic rate
RR:	relative risk
SD:	standard deviation
SHBG:	sex hormone-binding globulin
SI:	special intervention
TC:	total cholesterol
TEE:	total energy expenditure
TG:	triglycerides
UK:	United Kingdom

US:	United States
VLDL:	very low density lipoprotein
VO_2max:	maximal oxygen uptake
WC:	waist circumference
WHO:	World Health Organization
WHR:	waist hip circumference

Physical activity terminology

Aerobic exercise: exercise in which energy needed is provided by using oxygen inspired to combust metabolites.

Anaerobic exercise: exercise in which energy needed exceeds oxidative processes (metabolism in the absence of oxygen).

Cardiorespiratory fitness: refers to the ability of the circulatory and respiratory systems to supply oxygen to skeletal muscles during sustained physical activity. Regular exercise makes these systems more efficient by enlarging the heart muscle, enabling more blood to be pumped with each stroke, and increasing the number of small arteries in trained skeletal muscles, which supply more blood to working muscles.

Detraining: means when subjects did not train. It leads to reductions in maximal and submaximal exercise capacity, causes muscle weakness because of reduced motor neuron activity and muscle wasting, and causes a decline in the activity of enzymes involved in oxidative energy conversion.

Dose: refers to the total amount of energy expended in physical activity.

Exercise capacity: reflects the maximum ability to undertake physical work.

Intensity: reflects the rate of energy expenditure during such activity. It can be defined in absolute or relative terms. Relative intensity refers to the percent of aerobic power utilized during exercise and is expressed as percent of maximal heart rate or percent of Vo_2max.

Isotonic exercise: is defined as a muscular contraction resulting in movement, primarily provides a volume load to the left ventricle, and the response is proportional to the size of the working muscle mass and the intensity of exercise.

Isometric exercise: is defined as a muscular contraction without movement (eg, handgrip) and imposes greater pressure than volume load on the left ventricle in relation to the body's ability to supply oxygen.

Leisure-time physical activity (LTPA): is the daily physical activity accumulated during free time, such as sport or exercise activities. Leisure-time physical activity can be calculated based on the number of months spent completing the specific activity per year, average number of times for the specific activity each month, total time per each specific activity session, and an activity-specific intensity code.

Low-intensity activities: are those performed at a relative intensity of less than 40% of Vo_2max (or absolute intensity of <4 METs).

Maximum Oxygen Uptake or maximal oxygen consumption ($VO_{2\ max}$): is the greatest amount of oxygen a person can take in from inspired air while performing dynamic exercise involving a large part of total muscle mass. It is considered the best measure of cardiovascular fitness and exercise capacity. $VO_{2\ max}$ represents the amount of oxygen transported and used in cellular metabolism. It is convenient to express oxygen uptake in multiples of sitting/resting requirements. $VO_{2\ max}$ is influenced by age, sex, exercise habits, heredity, and cardiovascular clinical status.

Metabolic equivalent (MET)*:* is considered as a shorthand method for estimating the amount EE during physical activity. Each activity can be assigned a MET value which represents the ratio of the EE of the activity to the resting metabolic rate (RMR), where 1 MET being equivalent to 60 kcal/hr for an adult with a body weight of 60 kg. Therefore, MET value can be taken as numerically equivalent to EE using the following equation: MET*hr x (weight in kilograms/60 kilograms).

Moderate-intensity activities: are those performed at a relative intensity of 40% to 60% of Vo_2max (or absolute intensity of 4 to 6 METs).

Occupational activity: on-the-job activity, such as a job requiring lifting of loads ≥ 20 pounds at least hourly throughout the day or constantly moving any size load from place to place without mechanized aid.

Physical activity level (PAL): is defined as the ratio of TEE to REE.

Physical activity: any bodily movement produced by skeletal muscles that results in energy expenditure.

Physical inactivity: is the activity equivalent of < 30 minutes of brisk walking/day.

Physical fitness: is a set of outcomes or traits that relate to the ability to perform physical activity.

Resistance exercise: combines both isometric and isotonic exercise (such as free weight lifting).

Training: refers to physical activity and conditioning leading to fitness.

Vigorous-intensity activities: are those performed at a relative intensity of >60% of Vo_2max (or absolute intensity of > 6 METs). For example, brisk walking at 4.8 km $\cdot$ h^{-1} (3 miles $\cdot$ h^{-1}) has an absolute intensity of ≈ 4 METs. In relative terms, this intensity is considered light for a 20-year-old healthy person but represents a vigorous intensity for an 80-year-old person.

Chapter 1: General introduction

Chapter 1 General introduction

There is a general agreement that physical activity has a beneficial effect on health and those who are more active have a reduced risk of developing many chronic diseases, especially coronary heart disease (CHD). Whilst the general association is well accepted, the amount, type and intensity of physical activity deemed to be sufficient to achieve good health remains unclear. This uncertainty is reflected in many different messages communicated to the public as to how active they should be to protect against ill-health and prevent disease. For example, people can be described as being active if they achieve 30 minutes or more of at least moderate physical activity on at least 5 days of the week (Department of Health, 1996), if they achieve 30 minutes or more of at least moderate physical activity on at least 3 days of the week (Gwinup, 1975; Pollock et al., 1975) or if they accumulate more than 40 MET*h/d (Blair et al., 1984 and 1985). Here, two different methods are used to communicate the recommended level of activity. The first describes the recommendation in terms of three components – accumulated time (30 minutes), intensity (at least moderate) and frequency (number of days that this level of activity is achieved) over the week. In this example, achieving this amount of activity on three occasions each week would reflect a lower target than achieving this amount of activity on five days each week. Any activity of a lesser intensity, or where moderate or higher intensity activity is performed for less than 30 minutes, or where the recommended activity is performed on less days than the recommendation would not be seen as contributing to or being sufficient to promote good health. The other method describes the recommended level of activity in terms of an activity score which requires knowledge of the amount, duration and type of activity performed each day, together with information on the energy cost of each activity. This method embraces any type, duration and intensity of physical activity into consideration and represents a sum or aggregate statement of total activity.

Examination of the previous literature revealed that little is known of the level of agreement, consistency and coherence between these different methods of categorising activity. It is self-evident that categorisation according to whether an individual does or does not achieve 30 minutes of activity on 3 or 5 days each week would be likely to result in differences in the distribution between levels of activity because individuals who achieve 30 minutes of activity on 4 days of the week would be categorised as 'inactive' by one method and 'active' by the other. Thus, the possibility of incorrectly categorizing an individual is likely to be high as different methods are used such that the same individual could be categorised as sufficiently active by one method and not another, and vice versa.

Measurement of physical activity in terms of intensity, type, measure, duration and total physical activity is a challenging task. The relative contribution of each of these components can vary considerably both within and among individuals and populations. In addition, the way in which each is adequately captured using different instruments or expressed in a single statement of activity will markedly differ. Not surprisingly, given the potential lack of consistency and coherence between different methods to categorising activity, there is also inconsistency in the evidence relating activity to measures of ill-health or health risk factors of ill-health. For example, even when the same outcome variable (i.e. total cholesterol) is used, some studies report associations with activity whilst others do not. There are fundamental differences in the pattern of occupational and leisure time activity and the tasks of daily living among the different study populations. These differences, taken together with the pronounced changes in the way we live our lives over the recent years, would also make it difficult to identify one single method of categorising activity levels that adequately embraces all individuals or can be used with equal applicability in all settings or populations.

As part of an effort to improve public health in the United Kingdom (UK), the Department of Health recommended that adults should participate in at least 30 minutes of physical activity, of at least moderate intensity similar to brisk walking, on five or more days of the week (Department of Health 1996). This guideline is similar to the guideline published by the Center for Disease Control/American College of Sports Medicine (CDC/ACSM, 1995). More recent research has challenged this guideline and emphasised the importance of the consideration of other levels of physical activity. This is reflected in the latest Center for Disease Control/American College of Sports Medicine guidelines (CDC/ACSM 2007) that have outlined physical activity recommendations for healthy adults and older adults and are an update from the 1995 CDC/ACSM guideline. To acknowledge the preferences of some adults for vigorous-intensity physical activity, the US updated guidelines have been clarified to encourage participation in either moderate- and/or vigorous-intensity physical activity. In addition, the CDC/ACSM updated guidelines have acknowledged the importance of muscle contractions, muscular strength and endurance in relation to cardiovascular health. Moreover, to meet the current CDC/ACSM updated guidelines, the ACSM and the American Heart Association recommend a minimum goal that should be in the range of 450 to 750 MET*min/week of at least moderate activity.

These concepts of vigorous-intensity, muscle strength and MET score are not specifically addressed within the 1996 Department of Health guideline.

Therefore, there is a need to determine how much physical activity is needed for adults to improve or maintain good cardiovascular health and to be able to identify those who are inactive and most likely to benefit from increasing activity in an easier way. There is a need to examine the interrelationship between intensity, type, measure, and duration in capturing level of habitual physical activity. Without a more careful and complete description of activity and how this is related to chronic disease, it is difficult to adequately advise the public health authorities on the optimal level of physical activity which can bring improvements in cardiovascular health.

The purpose of the work described herein was to explore the inter-relationship between different methods of categorizing physical activity (using methods which underlie current activity recommendations) and the extent to which differences in activity level could account for differences in metabolic behaviour and CHD risk after adjustment of other known factors that would contribute to ill-health. The analysis sought to determine whether the methods used to categorise physical activity (as either inactive/active or level of physical activity) influence the extent to which physical activity is associated with CHD risk factorsand estimated CHD risk.

The findings of this thesis will provide the literature and the public health authorities with data regarding the assessment of physical activity levels that may be influenced by using different methods or systems for physical activity within the same population. Addressing this issue, will have important implications in policy determination, interpretation and implementation, whereby different guidelines of physical activity are used to predict the CHD risk in both research and clinical settings. This, in turn, will have substantial benefits for public health policies as well as improve the overall quality of life in the society.

This thesis is arranged into Chapters, of which this Introduction to the overall field of research is the first (*Chapter* 1). *Chapter* 2 starts by providing a conceptual framework to characterise physical activity, and the different methods that can be used to characterise and measure physical activity before critically reviewing what is known about current levels of physical activity in the UK. The *Chapter* will also address the nature of possible dose-response relationships between physical activity and health and reviewing the current recommendations and guidelines for physical activity. In addition, the evidence from observational and interventional studies of the relationship between physical activity and cardiovascular disease (CVD) risk and CVD risk factors will also be explored. Attention is directed towards providing the reader with a framework through which these issues can be explored whilst highlighting the limits of current knowledge and understanding before presenting the hypothesis and aims of the research in *Chapter* 3.

The thesis is then divided into two parts. The purpose of the first part was to conduct a secondary analysis of an extensive published data-set that included measures of diet, activity and health. The National Diet and Nutrition Survey (NDNS) of adults aged 19-64 years published in 2004 includes four measures of physical activity – a 7 day activity diary and self-perceived activity level – together with measures of lipid metabolism and blood pressure. Although a cursory initial examination of the activity data have been reported (NDNS, 2004), the data-set offer a unique opportunity to more systematically examine different methods of categorising activity behaviour and their relationship with CHD risk factors[systolic blood pressure (SBP) and diastolic blood pressure (DBP), total cholesterol (TC) and high-density lipoprotein-cholesterol (HDL-C)] and then use the CHD risk factorswith a risk engine to estimate CHD risk (eCHD). The hypothesis examined was that subjects who are categorised as physically inactive (or with lower levels of activity) would exhibit a phenotype with greater risk of CHD, than those who are categorised as active (or with higher levels of physical activity), an effect that persists after adjustment for differences in age, BMI and smoking. The magnitude of this effect is influenced by the method used to categorise physical activity. The general Methods underlying this secondary analysis are given in *Chapter* 4.

The results of the secondary analysis are given in *Chapters* 5 through 11. The aims of these Chapters were:

- to investigate the hypothesis that individuals deemed inactive/less active by one method of categorization would not necessarily be deemed inactive/less active by another method (*Chapter* 5);
- to compare the values of the CHD risk factors(SBP and DBP, TC and HDL-C) and eCHD risk in inactive versus active within each categorization method for physical activity (used in guidelines) before and after adjustments for age, BMI and smoking (*Chapter* 6);
- to repeat the analysis of *Chapter* 6 excluding those subjects who were taking medications (*Chapter* 7);

- to create a new categorization method that combines the physical activity expressed in number of days of at least 30 minutes of moderate physical activity with the total physical activity expressed in MET*hr/day (*Chapter* 8);
- to explore the nature of the dose-response relationship of expressing physical activity, using different measures, in terms of a) increasing the number of categories within each guideline approach, and b) expressing the absolute values as a continuous variable on the CHD risk factorsand eCHD risk (*Chapter* 9);
- to explore how subjects would describe their own activity behaviour in terms of overall and job activities and to examine the effect of these activities with the CHD risk factorsand eCHD risk, and to compare these outcomes with those measures of activity behaviour derived from the activity diary (e.g. number of days/week and minutes/day of at least moderate activity or total MET*h/day) (*Chapter* 10);
- to examine whether those deemed inactive by which ever method of categorization for physical activity (used in guidelines) would have higher eCHD risk than those deemed active and that the magnitude of the difference between inactive and active groups varies depending on the method of categorization used (*Chapter* 11).

In the second part (*Chapter* 12), the aim was to examine the concurrent validity of the NDNS 7-day diary against the International Physical Activity Questionnaire (IPAQ) by exploring the agreement in MET scores assessed in a group of volunteers (first-year medical students) using three different systems for physical activity coding and classifications. In addition, this part aimed to determine the extent to which different physical activity guidelines are met using different calculation systems in the same volunteers.

The principal findings and their interpretation are presented together with a discussion of the strengths and weaknesses of the work (*Chapter* 13) and the conclusions drawn are given in *Chapter* 14. The implications of these findings for Public Health are then presented together with recommendations for future work (*Chapter* 15).

Finally, the appendices contain additional information on the Dimensions, instruments and measures of physical activity (Appendix 1), details of the respondents and non-respondents rate of the NDNS (Appendix 2), description of the protocols used in the NDNS (Appendix 3), the data record sheets for the NDNS activity diary and the IPAQ (Appendix 4), a copy of the letter from the School of Medicine Ethics Committee (Appendix 5) and a copy of the Participation Information Sheet (Appendix 6) for Part 2 of the work and finally, an example of the approach used to calculate total physical activity scores (Appendix 7).

Chapter 2: Literature review

Chapter 2 Literature review

2.1. Electronic literature search:

While the Medline, as an electronic database of published studies in the biomedical field, it focuses on the English language. Published papers on the associations of physical activity/fitness with the CHD/CVD and risk factors for CHD/CVD have been commonly included as key-words. The current search of Medline spanned the period all through to November 2008. Over this period, while a large number of the reviewed articles have shown a relationship between physical activity/fitness and CHD/CVD, searching the Medline for each key-word was used in combination as follows:

- physical activity/fitness and CHD/CVD (575 articles),
- physical activity/fitness and metabolic syndrome (243 articles)
- physical activity/fitness and blood lipids (303 articles)
- physical activity/fitness and systolic and diastolic blood pressures (624 articles)
- physical activity/fitness and diabetes (7815 articles), and
- physical activity/fitness and BMI or waist circumference (4578 articles)

The present review is limited to the 117 articles. This is mainly because these articles were the only ones that have addressed physical activity and fatness with CHD/CVD risk factors in details. Additionally, governmental and non-governmental agencies' reports (e.g. Department of Health, Centre for Disease Control, World Health Organization) were sought. Furthermore, 51 articles have been identified to address other risk factors (e.g. endothelial function) that are related to CHD/CVD.

2.2. Dimensions and instruments of Physical Activity:

Attempts to characterise differences in physical activity behaviour are confounded or complicated by the imprecise use of terminology. To avoid confusion in this review, the terms 'dimension', 'measure' and 'instrument' are defined in the following way. The term dimension is used to refer to the different aspects of physical activity such as self-reported activity, body movement, total energy expenditure, and fitness. The term instrument refers to the device or tool that is used to characterise each specific dimension of physical activity. The term measure refers to the objective information, data or values generated by the instrument.

Physical activity has been classified into four dimensions: a) subjective physical activity,

b) objective physical activity, c) energy expenditure, and d) physical fitness. Examples of the different dimensions, instruments and measures obtained in their use to describe different dimensions are given in *Appendix* 1. Whilst each dimension in itself is an important component of physical activity, none of these dimensions is sufficient to adequately describe all aspects of physical activity. Therefore, differences in these dimensions of physical activity may have implications for the prevention of CHD or metabolic syndrome, and may limit the ability to detect associations between physical activity and health risk factors. On the other hand, there are various instruments currently available to measure physical activity which may vary greatly in their applications in epidemiologic research, intervention studies, clinical practice, and personal assessment. Each of these instruments has different strengths and weaknesses based upon the population being studied and the research objectives.

2.2.1. Dimension of subjective physical activity:

Subjective physical activity behaviour can be measured by questionnaires, direct observations, diaries, and records. A physical activity questionnaire is typically chosen for population studies as it possesses the characteristics of non-reactiveness (does not alter behaviour of subjects), practicality (reasonable study cost and participant convenience), applicability (can be designed to suit particular population), and reliable (but not accurately enough) (Kriska and Bennett, 1992). The disadvantage is that vigorous and moderate-intensity activities or sports are easily recalled, while light-intensity activities, such as general household activities are less likely to be accurately recalled. In addition, physical activity recalled from a previous week or month may not accurately represent an individual's true year round activity pattern (Schutz et al., 2001). Moreover, direct observations and physical activity diaries and records yield information about specific activity patterns. Although these instruments are not practical for use in large population studies, they are useful with small samples (Fletcher et al., 2001).

2.2.2. Dimension of objective physical activity:

Objective physical activity behaviour can be measured by portable pedometers and accelerometers. These instruments can measure physical activity behaviour of individuals in free-living situations. Pedometers are simple mechanical movement counters which have been designed to count steps and thus provide a potentially useful measure of distance walked or run during leisure and work. However, the high variability among pedometers and the lack of stable calibration mechanism make them unsuitable for estimating physical activity. They also tend to underestimate distances walked at slower speeds and overestimate distances during fast walking or running (Montoye and Taylor, 1984; Livingstone, 1997).

Accelerometers measure body movements to detect differences in speed, steps, position, motion, and gait which can estimate the relative intensities as well as the duration of various physical activities. The energy cost of activities can be obtained from accelerometers data to estimate total energy expenditure (TEE) of individuals from standard regression equations (against indirect calorimetry) based on the subject's characteristics of age, height, weight, and sex (Bouten et al., 1994; Freedson et al., 1998). Other advantages of accelerometers devices include their small size (permitting subjects to wear the monitors without interfering with normal movement) and their ability to record data continuously for periods of days, weeks, and even months (Westerterp, 1999). In addition, accelerometers can accurately measure differences in the levels of physical activity. A well-recognised limitation of accelerometers is their inability to detect the additional energy cost of upper body movement (unless sensors are placed on the upper limbs), load carriage (static work), or moving on soft or graded terrain (Bouten et al., 1994; Hendelman et al., 2000). Basically, accelerometers data demonstrates a better relationship with walking compared to other common household activities, such as house cleaning and yard work, or recreational activities, such as playing golf.

2.2.3. Dimension of energy expenditure (EE):

Heart rate monitors have been used frequently in recent years to measure EE. Recordings of heart rate can be used to estimate the person's oxygen consumption and, in turn, EE in free-living conditions. Heart rate and oxygen uptake have been shown to be moderately correlated during field and laboratory activities (Strath et al., 2000). These monitors are quite practical as they are available of low-cost, portable. In addition, they are capable of measuring and storing minute-by-minute data over several hours and averaged data over days or weeks, and permits preselection of a threshold heart rate above the sedentary level. The use of these monitors in assessing physical activity is largely limited by the lack of established relationships between heart rate and energy expenditure for a wide range of activities encountered in daily living. In addition, this method of assessment is not a good predictor of EE at low levels of physical activity (Livingstone, 1997).

Assessment of physical activity based on indirect calorimetry can provide accurate measurements of average daily EE at rest under controlled laboratory conditions, by which oxygen consumption and carbon dioxide production can be determined in a sample of air by using gas analysers (Westerterp et al., 1988). In well-ventilated surroundings the oxygen and carbon dioxide content of inspired (atmospheric) air can be assumed to be 20.9 % and 0.03 %, respectively (Westerterp et al., 1988). Although the indirect calorimetry is used for short-term measurements of EE at rest, it is not practical for most epidemiological studies or free-living individuals. This is mainly because it has a relatively high cost, not ideal for use during heavy exercise, and unable to determine the type, intensity, frequency, and/ or duration of any single bout of activity (Westerterp et al., 1988; McNeill, 2000).

Doubly-Labelled Water (a particular type of metabolic rate test) is another test which can be used to calculate EE by giving free-living subjects an oral dose of specified amounts of water labelled with the stable isotopes deuterium (^{2}H) and oxygen-18 (^{18}O) based to their body weight (Westerterp et al., 1988). The rate of loss of these isotopes from the body can be calculated by measuring the change in isotopic enrichment in the body pool over a period of time. This can be measured using urine (most usual in humans), saliva or blood plasma. The difference between the rate of loss of ^{18}O and ^{2}H reflects the rate of CO_2 production, which in turn can be used to estimate EE. This technique has the advantages of obtaining data with little effort by the subjects and has been shown to be more accurate when compared with indirect calorimetry. However, the use of this test is limited by it is quite costly and does not provide us with any information regarding the type, intensity, frequency, and/or duration of any single bout of activity (Westerterp et al., 1988; McNeill, 2000).

2.2.4. Dimension of physical fitness:

Physical fitness can be determined by the maximal oxygen uptake (VO_2max) exercise test of work performance on cycle ergometer or treadmill. The cycle ergometer is usually less expensive, fairly small in size, and is less noisy than a treadmill. Upper body motion is usually reduced, making it easier to obtain blood pressure measurements. However, discomfort and fatigue of the quadriceps muscles is a major limitation to the use of cycle ergometer testing. Therefore, leg fatigue in an inexperienced subject may cause them to stop before reaching a true O_2 max. It has been observed that O_2 max is 10 % to 15 % lower in cycle versus treadmill testing in those not accustomed to cycling (Wilmore, 1989).

Fitness level measured by treadmill can determine the strength of a large muscle work. However, it may be influenced by the capacity of subjects to withstand submaximal effort. This is mainly due to limitations in their physical condition, and the fact that they get halted by impending circulatory failure. In addition, several different treadmill protocols are currently in use and are defined according to treadmill speed, grade, stage, and duration which may result in different O_2 max (Wilmore, 1989).

Physical fitness can also be measured by handgrip dynamometers which determine the sustained maximal voluntary isometric grip force (Strath et al., 2000). Measures based on grip strength which provides useful information about different types of muscle function and is specific to the muscle group. However, the testing of one muscle group does not provide accurate information about the strength of other muscle groups (Strath et al., 2000). Thus, to be effective, strength testing must involve at least several major muscle groups, including the upper body, trunk, and lower body.

2.3. What is known about the current physical activity in the UK?

In the UK, despite the benefits of physical activity, James (1995) has observed an average of 800 kcal/d decline in EE from since the World War II until 1995. This suggested a decline in activity levels equivalent to walking about 16 km less per day (at an energy cost of around 50 kcal/km for a 70 kg man) (Ainsworth et al., 2000). In addition, the National Travel Survey (Department for Transport, 2001) has reported that both walking and cycling on the public highway declined dramatically between 1975 and 1998. The total miles traveled per year on foot and by bicycle reduced by 27 % and 25 %, respectively.

2.3.1. Health Survey for England 1998:

The Health Survey for England represents a series of annual surveys commissioned by the Department of Health, which is part of the National Health Survey (NHS). The objective of the survey is to monitor trends in the nation's health of people living in private residential accommodations in England. The survey plays a key role in monitoring the effectiveness of the government's policies and the extent to which its targets are achieved in order to help plan NHS services to meet the health needs of the population. In 1998 the major focus of the survey was on CVD. Topics included: experience of CVD symptoms, physical activity, eating habits, drinking, smoking and general health. The sample (approximately 13,700 addresses) has been selected based on the Postcode Address File. There were two parts to the survey, an interviewer-administered interview (Stage 1), followed by a nurse visit to carry out measurements and take a blood sample (Stage 2). All people in this study aged 16 and over and up to children aged 2-15 at an address were eligible to be interviewed.

The target was set of reducing the death rate from CHD and stroke amongst people aged less than 75 years by at least two fifths (based on 1996 data) by the year 2010. For the purpose of this survey, informants were classified as having a CVD condition if they reported having had any of the following conditions diagnosed by a doctor: angina, heart attack, stroke, heart murmur, abnormal heart rhythm, 'other heart trouble', diabetes and high blood pressure. This survey also reviewed the current prevalence among adults of a number of risk factors for CVD, such as alcohol consumption, cigarette smoking, eating habits, body mass, blood pressure and blood analytes.

Physical inactivity is one of the major risk factors for CHD which has been targeted by government health strategies since the early 1990s (The Health of the Nation, 1992; Shaper AG and Wanamathee G, 1991). Four main types of activity were asked about in the 1998 survey; occupational activity (activity at work), activity at home (housework, gardening, DIY), walks of 15 minutes or more, and sports and exercise activities. For each activity type, informants were asked on how many days in the last four weeks they had participated in the activity for at least 15 minutes time. They were then asked how long they had usually spent participating in the activity. The activities have been classified into four intensity levels, based on an estimate of the energy cost of the activities. The intensity levels are:

1. Vigorous: activities with an energy cost of at least 7.5 kcal/min
2. Moderate: activities with an energy cost of at least 5 kcal/min but less than 7.5 kcal/min
3. Light: activities with an energy cost of at least 2 kcal/min but less than 5 kcal/min
4. Inactive: activities with an energy cost of less than 2 kcal/min

Then, the activity levels of the individuals were grouped into three classifications:

1. **Group 1 - low activity**: up to three occasions of moderate or vigorous activity of at least 30 minutes' duration in the last four weeks (less than once a week)
2. **Group 2 - medium activity**: four to 19 occasions of moderate or vigorous activity of at least 30 minutes' duration in the last four weeks (at least once, less than five days a week)

3. **Group 3 - high activity**: fulfils the current physical activity recommendations; 20 or more occasions of moderate or vigorous activity of at least 30 minutes' duration in the last four weeks (at least five days a week)

This survey has reported that while there were 27.9 % and 27.8 % men and women, respectively, diagnosed as having a CVD condition, the CVD prevalence increased with age in both sexes. Men had a higher prevalence of CVD conditions than women. The prevalence of the most severe category of CVD conditions (i.e. heart attack or stroke) was twice as high in men as in women.

This survey also showed that men were far more likely to be classified in Group 3 (37 %) (fulfils the current activity guideline) compared to women (25 %). Among men, the proportion in Group 3 fell steadily with age from 58 % (age of 16-24) to 7 % (age of 75 and over). Among women, the proportion in Group 3 was fairly at the level of 32 % for 16-54 yr age group, before falling with age to about 4 % among those aged 75 and over.

Men were more likely than women to have participated in all activity types except heavy housework. The activity type most commonly reported by men was sports and exercise: 42 % of men had participated in some sports and exercise (of at least 15 minutes' duration) in the past four weeks. Participation by women in sports was lower at 36 %. The most common activity type for women was heavy housework; 58% of women had participated in this, compared to 38 % of men. Similar proportions of men (44 %) and women (41 %) reported that when at work they were mainly walking about. Furthermore, 22 % of men were classified as at least moderately active at work (on the basis of their occupation and their own rating of their physical activity at work), compared to 12 % of women. Nearly half of men (49 %) considered that their work involved lifting and/or carrying heavy loads compared to 41 % of women. Men were far more likely than women to say their work involved climbing (30 % compared with 8 %).

Combining all activity types, 80 % of men and 76 % of women reported at least one occasion of physical activity (of at least 15 minutes' duration) in the last four weeks. This proportion tended to fall with age, particularly after the age 35. Overall, 38 % of men and 25 % of women took part in physical activities for 7 hours or more per week, that is, at least one hour a day on average. Nearly a third of men (32 %) and 22 % of women had participated in activity at a vigorous level.

2.3.2. National Diet and Nutrition Survey (NDNS) 2004:

The NDNS 2004 was commissioned and funded by the Departments of Health and the Food Standards Agency (in England, Wales and Scotland). It was carried out between July 2000 and June 2001 by the Social Survey Division of the Office for National Statistics in collaboration with the Medical Research Council Human Nutrition Research, Cambridge. Its aim is to provide a comprehensive cross-sectional picture of the dietary habits and the nutritional status of the population of Great Britain. In addition, the survey includes information on physical activity levels. The survey gives valuable information on adults aged 19 to 64 years and provides a sound basis for future food policy as it affects this group, and for the development of nutrition education programmes.

The main purpose in collecting physical activity information in this survey was to investigate of the relationships between physical activity levels and total dietary intakes (percentage food energy from total fat, protein, total carbohydrate and non-milk extrinsic sugars and percentage total energy from alcohol), body size (BMI and waist to hip ratio), and blood pressure. *Chapter* 4 (Methodology) illustrates in more details the dietary habits, nutritional status and physical activity.

Overall, 36 % of men and 26 % of women fulfilled the current UK guidelines (spent 30 minutes or more per day in activities of at least moderate intensity on five or more days). In fact, 17 % of men and 16 % of women did not record spending any time in activities of at least moderate intensity during the seven-day recording period. This survey showed that 39 % of men and 28 % of women recorded spending some time in activities of vigorous/very vigorous intensity over the seven-day recording period. Generally, the proportion of men and women who recorded spending time in activities of vigorous/very vigorous intensity significantly decreased with age ($P < 0.05$).

For all sex/age groups, the mean time spent in activities of at least moderate intensity was considerably higher than the median value. This indicates that there were a small number of respondents within each sex/age group who recorded spending relatively long periods of time in activities of at least moderate intensity. It is likely that the longer periods of time spent in activities of at least moderate intensity at the upper end of the distribution are due to the fact that respondents working in occupations were categorized as moderate or hard/very hard work.

On average, men spent 2.2 hours per day and women 1.2 hour per day in activities of at least moderate intensity (medians 0.6 hours and 0.5 hours) ($P < 0.01$). Within each age group, men spent significantly more time than women in activities of at least moderate intensity. Generally, for men, the mean hours spent in activities of at least moderate intensity decreased with age. Overall, younger men were more active than older men. Compared to older men (50-64 year), the younger men spent significantly more time in activities of at least moderate intensity (19 to 24 year: $P < 0.05$; 25 to 34 year: $P < 0.01$). There were no significant age differences among women. Men spent significantly more time in activities of vigorous/very vigorous intensity than women ($P < 0.01$). Closer examination of time spent in different types of activity demonstrated that the data were not normally distributed, with the result that the mean values tended to be higher than the median values for all groups.

This survey provided some superficial analysis (conducted by the Food Standards Agency) regarding the correlation coefficients for the relationships between the time (hours) spent in activities of at least moderate intensity and dietary intake, as measured by average daily total energy intake, body size and blood pressure. Based on the data from this survey, there was low correlation (*r* ranged 0.0 to 0.19) between the time spent in activities of at least moderate intensity and the measures of average intake of energy and macronutrients, in both men and women. Despite the low correlation, in men, there was significant correlation between the time spent in activities of at least moderate intensity and average daily total energy intake, total fat, and protein, other macronutrients were not significant. In women, only the percentage of total energy from alcohol was significantly correlated with time spent in at least moderate intensity.

In addition, there was no significant correlation between the time spent in activities of at least moderate intensity and the measures of BMI and waist to hip ratio, in both men and women. According to the blood pressures (SBP and DBP), there is significant association between the time spent in activities of at least moderate intensity and SBP (in women only) and DBP (in men and women). It should be noted that wherever correlations are statistically significant the relationship between the two variables may not necessarily be causal; other factors (e.g. the respondent's smoking and BMI which were not adjusted) may have affected the size of the correlation. The correlation between the time spent in activities of at least moderate intensity and blood analytes (e.g. TC and HDL-C) was not considered by the NDNS 2004.

2.3.3. Health Survey for England 1998 versus NDNS 2004:

Questions on CVD in the Health Survey for England 1998 were very similar to those asked in the NDNS 2004, including health risk factors, body size, cigarette smoking, alcohol consumption, general health. Notably, the 1998 survey provided information regarding the prevalence of CVD, whereas the NDNS did not.

In general, for men and women, there were no significant differences between these surveys regarding physical activity levels. Nevertheless, the proportion of men age groups of 35-44 and 55-64 years in the NDNS meeting the current UK guideline was significantly lower ($P < 0.05$) (32 % and 21 %, respectively) than that of the 1998 survey (43 % and 32 %, respectively). However, there were several important differences between the Health Survey for England 1998 and the NDNS 2004 in terms of the methods used for the data collecting. In particular, it should be noted that while the NDNS used a 7-day diary, the Health Survey used a 4-week recall questionnaire. In this regard, only activities lasting less than 10 minutes were excluded in the NDSN, whereas those lasting less than 15 minutes were excluded in the Health Survey. Furthermore, in the Health Survey the youngest age (16 years) was three years lower than that used in the NDNS (19 years).

2.4. Physical Activity and health outcomes:

In the UK, CVD, including CHD, has remained the most common cause of death over the last 90 years among both males and females (National Statistics, 2004). Cross-sectional and prospective studies (Lakka et al., 2002; Wilson et al., 2005; Ford and Li, 2006) have generally indicated that individuals with adverse phenotypic traits (including blood glucose impairment, insulin resistance, excess abdominal/body fat, dyslipidemia, and elevated blood pressure) are at risk of developing CVD. Efforts to control the epidemic of phenotypes (or health risk factors) related to CVD have largely focused on lifestyle interventions including physical activity. Many epidemiological studies have shown that low level of physical activity is a strong and independent risk factor for both CVD and all-cause mortality including hypertension, high TC, and low HDL-C (Peltonen et al., 1981; Seals et al., 1984; Haffner et al., 1992; Torjesen et al., 1997; Eriksson et al., 1997; Kujala et al., 1998; Dunn et al., 1999; He and Whelton, 1999; Johansson and Sundquist, 1999; Andersen et al., 2000; Lehmann et al., 2001; Crespo et al., 2002; Ricardo et al., 2002; Franks et al., 2004). For example, sedentary lifestyle is responsible for approximately 30 % of deaths which are mainly due to CHD (Powell and Blair, 1994).

From a public health perspective (Lee and Skerrett, 2001b), helping people to change from an inactive level to the next levels of activity will produce the greatest reduction in risk. This concept is illustrated below in *Figure* 2.1. Although this *Figure* is documented in the Department of Health's report (2004) for physical activity, it is unclear whether the level of physical activity or fitness is more related to the level of risk of disease or not. Essentially, the Department of Health guideline advises people to stay active in order to reduce the risk of CHD. However, the Department of Health's document recommends 5 days per week of moderate activity but does not clearly indicate whether there would be no benefit unless this target is fully achieved or if this recommendation relates to a maximum effect. The document illustration in *Figure* 2.1 appears to show a dramatic reduction in the risk is obtained from low level of activity, but no further reduction seems to be attained with a higher level and there is no time scale is displayed. In addition, the curvilinear dose-response curve of the *Figure* generally related only to CHD and type 2-diabetes, rather than other health risk factors. It should be noted that the health outcomes can be judged using different parameters such as incidence of CHD or mortality, predicting active disease (e.g. CHD) using estimation programmes, or CHD risk factors(e.g. TC).

Applying different categories for physical activity measures (number of days/week, minutes/day and MET*hr/day), would be expected to show one or more of the five possible "dose-response" relationships between physical activity and health risk outcomes and CHD risk. The five potential models for the physical activity and health risk outcomes relationships are depicted in *Figure* 2.2. Curve D illustrates a relationship where risk decrease linearly as a function of increasing physical activity level (i.e. the greater the dose, the greater the response). Curve A represents curvilinear relationships, where a dramatic reduction in the risk is obtained from low level of activity, but no further reduction would be obtained with a higher level. On the other hand, curve E represents another curvilinear relationship where a reduction in risk is obtained only with high levels of physical activity. Curve B indicates a U-shape relationship where the risk drops significantly as the subject turns from inactive to slightly- moderately active but starts to increase with more vigorous physical activity. Curve C demonstrates that the risk is constant and not affected by the level of physical activity.

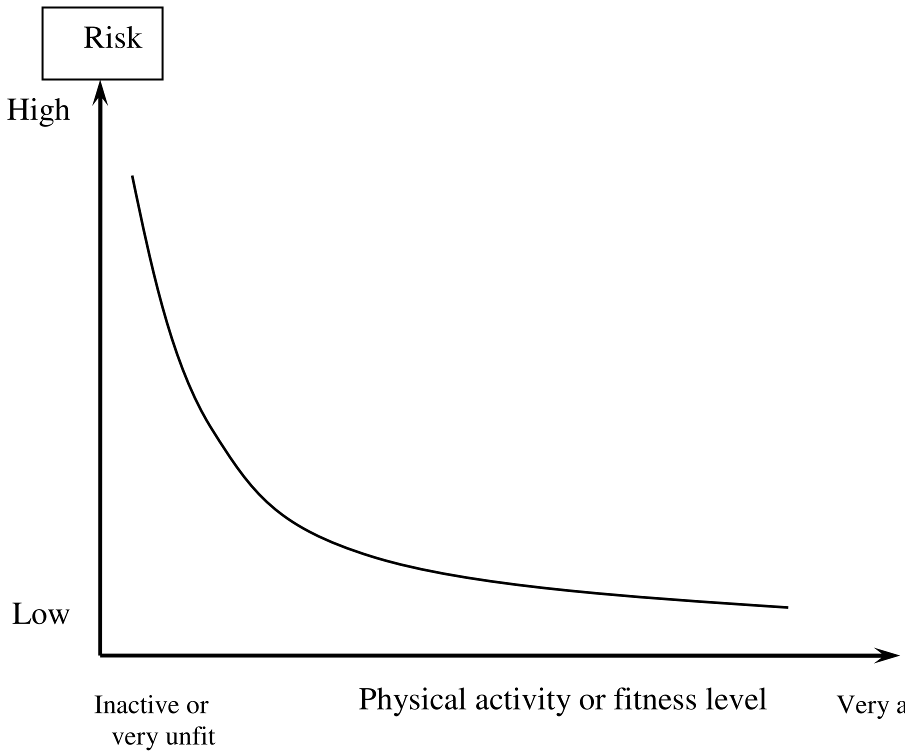


Figure 2.1: The dose-response relationship between physical activity level and risk of disease.

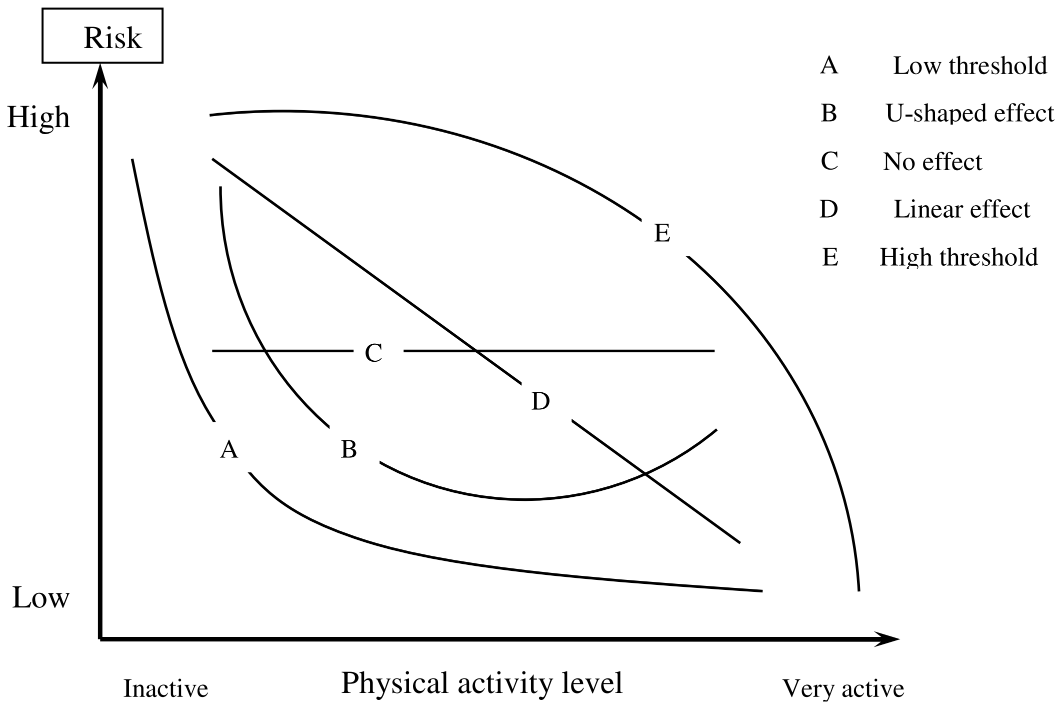


Figure 2.2: Five possible dose-response relationships between physical activity level on the one hand and CHD risk factors and CHD risk on the other. Curve A (fast effect) indicates that the greatest reduction in risk originates from increases in the lower levels of activity.

2.5. Physical Activity, CVD/mortality, and health risk factors:

2.5.1. CVD and mortality:

Observational studies:

Observational-based prospective studies have relied largely on questionnaire or self-report methods to assess physical activity levels. These methods are susceptible to measurement bias which may affect its relationship with CVD risk factors (Sallis and Saelens, 2000). In addition, recent advances in motion sensing techniques such as heart rate monitors, accelerometers and pedometers can be used to measure daily living activities in large populations, however, they have also been noted to be susceptible to measurement bias (Mahar and Ainsworth, 2000; Raven, 2000). Many investigators have found an inverse association between physical activity and CVD risk (Folsom et al., 1990; Bijnen et al., 1998; Hu et al., 2000; Lee et al., 2003). Other studies have shown a U-shaped association where there is either no association between physical activity and CVD incidence or mortality (Nakayama et al., 1997; Lee and Paffenbarger, 1998; Lee et al, 1999). A review by Lee and Skerrett (2001b) has concluded that there is insufficient evidence to indicate that vigorous physical activity (exemplified by jogging) conferred an additional benefit beyond that of moderate-intensity physical activity (equivalent to a brisk walk) on mortality. However, this review failed to reveal data on the duration and frequency of physical activity as might be related to all-cause mortality rates.

The Multiple Risk Factor Intervention Trial (MRFIT) is a randomized, multicenter, primary prevention trial conducted at 22 US clinical centres from 1973 to 1982 to test the hypothesis that reductions in cigarette smoking, high blood pressure and elevated serum cholesterol reduce the risk of dying from CHD in 12,866 men aged 35 to 57 years at high risk for CHD (Kjelsberg et al., 1997). Volunteers were randomly assigned to either special intervention (SI) or usual care groups. The SI group received dietary instructions for reducing blood cholesterol, smoking cessation programme, and drug therapy to lower blood pressure. No exercise programme was provided or encouraged for the SI group.

At the initial 7-year follow-up, Leon et al., (1987) has shown that in MRFIT men who reported a moderate amount of leisure-time physical activity (LTPA) (47 minutes/day), there were 63 % fatal CHD events, 67 % fatal CVD events, and 71% total deaths in men with lower levels of LTPA (29 minutes/day) ($P < 0.01$). Mortality rates with high LTPA were similar to those in moderate LTPA. However, combined fatal and nonfatal major CHD events were 20 % lower in high compared to low LTPA ($P < 0.05$). The level of

LTPA was determined by the Minnesota LTPA questionnaire with subjects classified into tertiles (low, moderate, and high).

In 1991 and 1997, Leon et al., also studied the effect of habitual LTPA on the total and cause-specific mortality rates in 12,138 men who participated in the MRFIT over a 10 and 16-year follow up. The least active men (low LTPA) had excess mortality rates of 22-29 % and 22-27 % for CVD and CHD, respectively, compared to more active men in the moderate LTPA, whereas the high LTPA groups was not associated with further attenuation of mortality rates. No further decrement in mortality rates was noted in those in the higher LTPA. These associations remained significant ($P < 0.05$) after proportional hazards adjustments for additional possible confounding variables. These data suggested that a relatively small amount (10 to 36 min/d) of daily moderate intensity LTPA can significantly reduce premature mortality, particularly from CHD, in middle-aged and older men at high risk for CHD.

Manson and colleagues (1999) on the other hand have found that about 30 % of the cases of CHD and stroke are prevented by 2.5 hours of brisk walking each week, compared to those who performed less than this amount of physical activity ($P < 0.001$) in 72,488 female nurses (40 to 65 years old) after controlling the age, body mass index (BMI), history of hypertension, and other covariates. They have also indicated that regular vigorous exercise [> or = 6 metabolic equivalent, expressed as MET)] is associated with similar risk reductions (30 to 40 %). MET value is considered as a shorthand method for estimating the amount EE during physical activity. Each activity can be assigned a MET value which represents the ratio of the EE of the activity to the resting metabolic rate (RMR) (Blair et al., 1985; Ainsworth et al., 2000), where 1 MET being equivalent to 60 kcal/hr for an adult with a body weight of 60 kg (Blair et al., 1985; *Fletcher et al., 2001*). Therefore, MET value can be taken as numerically equivalent to EE using the following equation: MET*hr x (weight in kilograms/60 kilograms).

In addition, Manson and co-workers (2002) have found the increase in the total physical activity score (measured in MET score) is significantly and inversely associated with CVD ($P <0.001$) in 73,743 postmenopausal women (50 to 79 years of age). Walking and vigorous exercise were associated with similar risk reductions, and the results did not vary substantially after controlling the ethnic group, age, and BMI.

Tanasescu et al., (2002) has assessed the amount, type, and intensity of physical activity in relation to risk of CHD in a cohort of 44,452 US adult men. They have found that total physical activity, running, walking, weight training, and rowing are inversely associated with risk of CHD. Men who ran for an hour or more/ week (42 %; relative risk (RR) = 0.58), trained with weights lifting for 30 minutes or more/ week (23 %; RR = 0.77), rowing for 1 hour or more/ week or brisk walking for half-hour or more /day (18 %; RR = 0.82) had significant reduction in CHD risk ($P < 0.03$ for trend) compared to those who did not have any training at all. The RRs corresponding to moderate (4-6 METs) and vigorous (6-12 METs) activity intensities were 0.94 and 0.83, respectively, compared to low activity intensity (< 4 METs) ($P = 0.02$ for trend). They have concluded that the total physical activity, running, weight training, and walking are associated with reduced CHD risk, and the average exercise intensity is associated with reduced risk independent of the number of MET spent in physical activity.

In contrast, a follow-up cohort study of 7.4 years by Siscovick et al., (1988) has found no association between regular vigorous activity, the incidence of CHD death and nonfatal myocardial infarction among 1,533 hypercholesterolemic men aged 35-59 years. The men were free of clinical heart disease at entry, and the adjustment by the age, LDL-C, smoking, family history of CHD, and occupation had no effect on this finding. This observation suggests that reported regular physical activity may not be related to the risk of CHD among asymptomatic, hypercholesterolemic, middle-aged men. However, they determined the level of each participant's self-perception habitual physical activity by the response to only two questions asked to select a target heart rate for the baseline graded exercise tolerance test. The first question was, "Do you regularly engage in strenuous exercise or hard physical labor?" Participants who answered no to the first question were classified as inactive. If the answer was yes, the participants were then asked, "Do you labor or exercise strenuously at least three times a week?"

Sesso et al., (2000) has examined the association of the quantity and intensity of physical activity with CHD risk in 12 516 middle-aged and older men (mean age 57.7 years) from 1977 through 1993. Physical activity was assessed at baseline in kilojoules per week (4.2 kJ = 1 kcal) based on the number of blocks walked, flights climbed, and the participation in sports or recreational activities. Compared to men expending < 2100 kJ/wk in physical activity, men expending 2100 to 4199, 4200 to 8399, 8400 to 12 599, and ≥ 12 600 kJ/wk had multivariate RR of 0.90, 0.81, 0.80, and 0.81, respectively (P for trend = 0.003). When the independent effects of specific physical activity components were considered, only total sports or recreational activities (P for trend = 0.042) and vigorous activities (P for trend = 0.02) were inversely associated with the risk of CHD. Therefore, it was concluded that moderate and light activities, which may be less precisely measured, have non-significant inverse associations with CHD risk. However, both total physical activity and vigorous activities showed the strongest reductions in CHD risk.

In addition, the optimal intensity of LTPA to decrease the risk of all causes, CVD and CHD mortality have been examined by Yu et al., (2003) in a prospective study (average 11 year follow up) of 1975 British men aged 49–64 years with a free medical history and clinical evidence of CHD at baseline examination. A record of leisure activity questionnaire during the preceding 12 months derived from the Minnesota LTPA was used in the study. When different intensities of activity were considered, light and moderate intensity LTPA had inconsistent and non-significant relations with all cause, CVD, or CHD mortality whether adjusted only for age or for other cardiovascular risk factors. However, a significant dose–response relation was found for vigorous intensity LTPA for all cause, CVD, and CHD mortality as they were fully adjusted for other risk factors. These data suggest that only leisure exercise classified as heavy or vigorous was independently associated with reduced risk of premature death from CVD.

On the other hand, Lee et al., (2003) has reviewed the overall associations between physical activity or cardiorespiratory fitness and stroke incidence or mortality in a meta-analysis of 18 cohort and 5 case-control studies. The ethic groups, age, sexes, and outcome measured were separately analyzed. For cohort studies, highly active or fit individuals had a 25 % lower risk of stroke incidence or mortality (RR = 0.75) compared to low-active individuals. For case-control studies, also highly active or fit individuals had a 64 % lower risk of stroke incidence (RR = 0.36) than their low-active counterparts. When they combined both the cohort and case-control studies, highly active or fit individuals had a 27 % lower risk of stroke incidence or mortality (RR = 0.73) than did low-active individuals. In addition, they found similar results in moderately active individuals as compared to inactive persons (RR = 0.83 for cohort, RR = 0.52 for case-control, and RR = 0.80 for combined both studies).

Blair et al., (1989) has evaluated the relationship between changes in physical fitness levels and risk of mortality in 10,224 men and 3120 women for about 8 years follow-up. Physical fitness was measured by a maximal treadmill exercise test. Mortality rate declined across the physical fitness quintiles from 64.0 per 10,000 persons in the least-fit men compared to 18.6 per 10,000 person/years in the most-fit men. Corresponding values for the least-fit women were 39.5 per 10,000 person/years to 8.5 per 10,000 person/years in the most-fit. These trends remained statistically significant after correction for age, smoking habit, cholesterol level, systolic blood pressure, fasting blood glucose level, parental history of CHD, and the follow-up interval. Also, in 1995, Blair et al., has conducted a prospective study to evaluate the relationship between changes in physical fitness and risk of mortality in a group of a 9777 men for an average follow-up period of 5.1 years. Physical fitness was measured by a maximal treadmill exercise test. After controlling the age, health status, and other risk factors of premature mortality, men who improved from unfit to fit had a reduction in mortality risk of 44 % compared to men who remained unfit. In addition, the researcher observed that for each minute increase in maximal treadmill time, there was a corresponding 7.9 % ($P < 0.001$) decrease in risk of mortality.

Moreover, another large cohort sample of 5721 asymptomatic women (52 ± 11 years old), Gulati et al., (2003) has hypothesised that reduced exercise capacity is associated with an increased risk of death. The participants underwent an exercise capacity measured in MET by treadmill until fatigue. Framingham Risk Score (FRS)-adjusted hazards ratios of death associated with MET levels of <5, 5 to 8, and >8 were 3.0, 1.9, and 1.0 respectively. In this study, it has been revealed that the FRS -adjusted mortality risk decreased by 17 % for every 1-MET increase. The FRS is a recommended model used to predict the risk of cardiac disease and has been described previously by Wilson et al., (1998).

It has been identified that low level of cardiorespiratory fitness is a strong independent factor for CVD mortality in cross-sectional studies (Cooper et al., 1976). In addition, cardiorespiratory fitness has also been found to be a more important independent predictor of CHD risk factors than physical activity as measured by accelerometer over one week in 222 healthy adult men and women (Suzuki et al., 1998). In this regard, Myers et al., (2002) has prospectively examined the effect of exercise on mortality rate in more than 6000 symptomatic men for a follow up mean of 6.2 years. Surprisingly, it has been indicated that fitness level was more predictor in death rate than the age and for each 1 MET increase in exercise capacity, there was a 12 % reduction in all-cause mortality rate.

In addition, in a prospective observational study (Wei et al., 1999), the influence of low cardiorespiratory fitness (measured by a treadmill) on CVD and all-cause mortality has been evaluated in 25,714 normal-weight, overweight, and obese adult men (mean age was 43.8 years) who received a medical examination. The RR for all-cause mortality was 3.1 both in obese men with either low fitness or diabetes mellitus. However, it has been found that the RRs slightly higher in obese men who either smoked or had high cholesterol levels. In addition, obese men with low fitness had attributable risk of 39 % for CVD mortality and 44 % for all-cause mortality after adjustment for other mortality predictors (age, BMI, type 2 diabetes mellitus, high serum cholesterol level, hypertension, current cigarette smoking). These findings have also indicated that the low cardiorespiratory fitness was equally significant compared to other CVD risk factors, such as high serum cholesterol level, hypertension, current cigarette smoking.

In addition, the relation of fitness to mortality adjusted for BMI and within levels of BMI has been quantified in a cohort 2,196 men with diabetes (average age 49.3 years) who underwent a maximal treadmill exercise test (Church et al., 2004). It has been shown that the risk of mortality was 4.5, 2.8, and 1.6 for the first, second, and third fitness quartiles, respectively, with the fourth quartile (highest fitness level) as the referent (P for trend <0.0001). However, there was no significant trend of change when the fitness-mortality relation was examined within levels of body composition. Therefore, it has been suggested that the inverse gradient between fitness and mortality was independent of BMI. In contrast, Rosengren and Wilhelmsen, (1997) have found that there was a significant 40–50 % reduction in mortality risk associated with physical activity within BMI categories in middle-aged Swedish men.

In a prospective 16 years follow-up study, the independent associations and the possible interaction of BMI, LTPA and perceived physical fitness and functional capability with the risk of mortality have been investigated in men (n= 1,090) and women (n= 1,122) 35-63 years old (Haapanen-Niemi et al., 2000). After adjustment for age, marital and employment status, perceived health status, smoking and alcohol consumption, it has been shown that compared with the most active subjects, men and women with no weekly vigorous activity had relative risks of 1.61 and 4.68, respectively for CVD mortality. When compared with men who perceived their fitness as better than their age-mates, men with least fit had a relative risk of 3.29 for all-cause mortality and 4.37 for CVD mortality. Another prospective follow-up study of 22 528 men and 24 684 women aged 25-64 years by Hu et al., (2005) has indicated that physical activity had a strong independent effect on mortality from BMI. However, Tanaka et al., (1998) has found that higher total and abdominal body fatness is associated with a less favourable metabolic CHD risk profile, and high levels of habitual aerobic exercise did not appear to negate the deleterious effects of adiposity on the coronary risk profile in 38 healthy middle-aged and older women. In addition, physical activity was not found to be associated with a reduced in risk of all-cause mortality obese subjects (BMI = 27 kg m-2) 15–96 year old American males (n 698) and women (n 763) in a 29- year prospective follow-up (Dorn et al., 1999).

Interventional studies:

There are few interventional studies examining the relative impact of physical activity or fitness on CVD and mortality, especially in healthy people. In 1982, Carson P et al has randomly divided 303 men who reported acute myocardial infarction (heart attack) in the last 6 weeks into exercise and control groups. The exercise group participated in the hospital gymnasium twice weekly for a three-month period. Although there was no significant difference between the groups, the exercise group had lower incidence of death (8 %) compared to 14 % of the control group during the period of the study. Another randomized study conducted by Belardinelli et al., (1999) who has tested whether long-term moderate exercise training improves functional capacity and quality of life in patients with chronic heart failure in 99 patients with stable chronic heart failure (average age was 59 years). Fifty participants underwent exercise training at 60 % VO_2 max; initially 3 times a week for 8 weeks, and then twice a week for 1 year and 49 subjects were control group. Without any adjustments undertaken, researchers have indicated that exercise training was significantly associated with lower mortality (P = 0.01) and hospital readmission for heart failure (P = 0.02).

In contrast, the effect of regular exercise (composed mainly of gymnastics and walking without any special equipment) over 5 years on mortality have been evaluated in 245 elderly men and women (76.5 years) by Oida et al., (2003). Of these individuals, 155 (56 males and 99 females) were voluntarily participated in the exercise group, and the remaining 90 individuals (29 males and 61 females) were considered as a control group. Age, presence or absence of cardiovascular or musculo-skeletal disorders and functional fitness level were adjusted. Among men, the RR of death in the intervention and control groups were similar (RR = 1.0). However, among women the RR of death in the intervention group was 0.16 compared to 1.0 in the control groups. It has been suggested that the improved mortality and state of independence in the female of the intervention group occurred resulted from the increase in physical exercise levels in daily life. This means other confounding factors between the intervention and the control groups should be controlled.

While the importance of physical fitness for greater longevity and reduced risks of CVD and all-cause mortality is well-established in the literature, the precise association between subjective physical activity (questionnaire), CVD and mortality remains obscure. It should be noted that the recommendation for physical activity by the Department of Health was based on a measure of physical activity rather than physical fitness.

2.5.2. Metabolic syndrome:

The term 'metabolic syndrome' has evolved to embrace a constellation of adverse phenotypic traits which when taken together are associated with an increased risk of cardio-metabolic disease and all cause mortality (Lakka et al., 2002; Eckel et al., 2005; Unwin, 2003). This is a poorly defined pathophysiological syndrome that has many different meanings and definitions that has resulted in some controversy over the criteria used to define the syndrome and whether it has any specific value in clinical practice beyond current established markers of risk associated with CVD and type 2 diabetes (Ford, 2005a; Guize L et al., 2008).

Currently, there are several definitions and criteria for diagnosing the metabolic syndrome such as WHO (WHO, 1999), Third National Cholesterol Education Program Adult Treatment Panel III (NCEP III) (NCEP III, 2001; Grundy et al., 2005), International Diabetes Federation (IDF) (IDF, 2005), American Association of Clinical Endocrinologists (AACE) (Einhorn et al., 2003), and European Group for the Study of Insulin Resistance (EGSIR) (EGSIR, 1999). These are concordant on the essential components such as glucose intolerance, obesity, hypertension, and dyslipidemia. The cut-points for each component and the approaches used in combining components also differ. Table 2.1 (next page) shows different criteria proposed for clinical diagnosis of metabolic syndrome.

The NCEP III 2001 and 2005 criteria are those most frequently reported and require at least three from the following five components: Waist circumference (WC), blood pressure, TG, HDL-C and fasting plasma glucose. The cut-off points for several of these are less stringent than usually required to identify a categorical risk factor. It is important to note that it is possible for the same term to be applied to very different phenotypes depending on which three components are present (i.e. with or without obesity, with or without insulin resistance).

The WHO criteria viewed insulin resistance as a required component for diagnosis and included BMI in place of WC, and microalbuminuria is listed as one criterion. The WHO criteria require presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, and two components that relate to CVD such as BMI, blood pressure, TG, HDL-C and urinary albumin.

The EGSIR criteria requires insulin resistance defined as the top 25 % of the fasting insulin values among non-diabetic individuals plus two or more CVD risk factors such as

WC, blood pressure, TG and fasting plasma glucose. The AACE criteria appear to be a mixture of those of NCEP III and WHO metabolic syndrome. However, no defined number of risk factors is specified; diagnosis is left to clinical judgment. More recently, the IDF attempted to rationalise many of these differing approaches within a single unified definition. For a person to be defined as having the IDF metabolic syndrome, they must have central obesity (WC ≥ 94 cm for men and ≥ 80 cm for women, with ethnicity specific values for other groups) plus two other factors such as blood pressure, TG, HDL-C and fasting plasma glucose.

Table 2.1: Different criteria proposed for clinical diagnosis of metabolic syndrome.

Metabolic syndrome defined by	**Clinical measure**
World Health Organization criteria (1999)	Requires presence of diabetes mellitus, IGT, IFG or insulin resistance, AND two of the following: • blood pressure: ≥ 140/90 mmHg • TG ≥ 1.7 mmol/L and HDL-C ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female) • waist/hip ratio > 0.90 (male); > 0.85 (female), and/or BMI > 30 kg/m^2 • urinary albumin excretion ratio ≥ 20 mg/min or albumin: creatinine ratio ≥ 30 mg/g
The European Group for the Study of Insulin Resistance criteria (1999)	Requires insulin resistance defined as the top 25% of the fasting insulin values among non-diabetic individuals AND two or more of the following: • WC ≥ 94 cm (male), ≥ 80 cm (female) • TG ≥ 2.0 mmol/L and/or HDL-C < 1.0 mmol/L • blood pressure ≥ 140/90 mmHg • fasting plasma glucose ≥ 6.1 mmol/L
The US National Cholesterol Education Program Adult Treatment Panel III criteria (2001)	Requires at least three of the following: • WC ≥ 102 cm (male), ≥ 88 cm (female) • TG ≥ 1.7 mmol/L (150 mg/dl) • HDL-C < 40 mg/dL (male), < 50 mg/dL (female) • blood pressure ≥ 130/85 mmHg • fasting plasma glucose ≥ 6.1 mmol/L
American Association of Clinical Endocrinologists criteria (2003)	Requires IGT or IFG plus any of the following based on clinical judgment: • BMI ≥ 25 kg/m^2 • TG ≥ 150 mg/dL and HDL-C <40 mg/dL (male) or < 50 mg/dL (female) • blood pressure ≥ 130/85 mmHg • Other features of insulin resistance
International Diabetes Federation criteria (2005)	Requires increased WC (WC ≥ 94 cm for men and ≥ 80 cm for women) plus any 2 of the following: • TG ≥ 150 mg/dL • HDL-C < 40 mg/dL (male) or <50 mg/dL (female) • blood pressure ≥ 130/85 mmHg • glucose ≥ 100 mg/dL

BMI, body mass index; HDL-C, high density lipoprotein-cholesterol; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; TG, triglycerides; and WC, waist circumference.

Each of these definitions agree that the core criteria of metabolic syndrome includes blood glucose impairment (hyperglycemia and/or insulin resistance), excess abdominal/body fat (increased waist and/or obesity), dyslipidemia (low HDL-C and/or high TG), and elevated blood pressure. However, criteria and cut-off values differ between these definitions, implying that different definitions may identify different individuals with differing phenotypes, but increased risk. For example, recently, Kelliny et al., (2008) found that the agreement between three definitions for metabolic syndrome (WHO, NCEP III and IDF) was limited in 1255 subjects aged 25-64 years in a country of the African region. They found a fairly similar prevalence of metabolic syndrome according to different definitions except the different between these definitions actually identified different subjects as having metabolic syndrome. Therefore, recommendations of one definition over another may lead to different values of metabolic syndrome.

Observational studies:

Cross-sectional and prospective studies have generally found that high levels of physical activity and fitness are inversely related to the prevalence of this syndrome, regardless of the definition used (Laaksonen et al., 2002; Ford and Li, 2006; Churilla and Zoeller, 2008). For instance, Laaksonen et al., (2002) has studied the associations of Leisure Time Physcial Activity and cardiorespiratory fitness with development of the metabolic syndrome (using the WHO 1999 and NCEP 2001 definitions) in a population-based cohort of 612 middle-aged men who when they entered the study di not have the metabolic syndrome. LTPA was classified was follow: low-intensity (< 4.5 METs), moderate-high-intensity (4.5-7.5 METs), and vigorous intensity (≥ 7.5 METs). A graded maximal exercise test was performed on cycle ergometer in order to assessed fitness level. At the 4-year follow-up, men engaging in > 3 hours/week of moderate or vigorous LTPA were half as likely as sedentary men to have the metabolic syndrome after adjustment for major confounders (age, BMI, smoking, alcohol, and socioeconomic status) or potentially mediating factors (insulin, glucose, lipids, and blood pressure). Vigorous LTPA had an even stronger inverse association. Fit men were 75 % less likely than unfit men to develop the metabolic syndrome, even after adjustment for major confounders. However, the adjustment for possible mediating factors attenuated the association fitness and metabolic syndrome. Associations of LTPA and fitness with development of the metabolic syndrome, as defined by the NCEP, were qualitatively similar.

Therefore, it has been suggested that poor fitness could be considered a feature of metabolic syndrome (Lakka et al., 2003; Hassinen et al., 2008). For example, Hassinen et al., (2008) has explored the associations of fitness with metabolic syndrome (as defined by the NCEP 2005) in a population sample of 1347 men and women aged 57–79 years at baseline of the Dose-Responses to Exercise Training Study (which is an ongoing 4-year randomized controlled trial) on the health effects of regular physical exercise and diet. Fitness level was assessed by respiratory gas analysis during a maximal bicycle exercise test. They found that men and women who were in the lowest sex-specific third of fitness level had a 10 times higher risk of metabolic syndrome than those who were in the highest third, after multivariable adjustments. Recently, Park et al., (2008) has determined associations between habitual physical activity (using pedometers/accelerometers) and metabolic syndrome (defined by the NCEP 2001 criteria) in elderly persons 65–84 years old. They showed that the risk of metabolic syndrome was 4.3 and 3.3 times greater in the least active quartiles of participants (taking < 4700 steps/day and spending < 9 minutes/day at > 3 METs, respectively) relative to the most active quartiles (taking > 8500 steps/day and spending > 24 minutes/day at >3 METs, respectively).

Sedentary behaviour is also known to predict progression toward CVD and metabolic syndrome in adults (Ford et al., 2005b; Ford and Li, 2006; Laaksonen et al., 2002). For instance, Ford et al., (2005) has examined the associations among physical activity, sedentary behaviour, and metabolic syndrome (defined by the NCEP 2001 criteria) in a total of 1626 men and women ≥ 20 years old from National Health and Nutrition Examination Survey. They found that the OR of the participants who did not engage in any moderate or vigorous physical activity during leisure time had higher metabolic syndrome (OR = 1.46) compared to those who reportedly engaged in ≥ 150 minutes/week of such activity after adjustment for age, sex, race or ethnicity, educational status, smoking status, and alcohol use.

A cross-sectional study by Farrell et al., (2004) has studied the prevalence of the metabolic syndrome (defined by the NCEP 2001 criteria) in 7104 women who underwent a maximal treadmill exercise test (VO_2max) after adjustment for the age and smoking. Women were divided into cardiorespiratory fitness quintiles categories. In this study, it has been demonstrated that there is a lower prevalence of the metabolic syndrome at progressively higher maximal MET levels (P for trend = 0.001). The HDL-C, TG, SBP and DBP, and WC were significantly lower among women with high level of fitness (P for trend = 0.001) than women with low fitness level.

However, the associations of physical activity and fitness with the metabolic syndrome have varied. For example, a study by Franks et al., (2004) has examined the associations of physical activity and fitness with the metabolic syndrome (defined by the WHO 1999 criteria) in a total of 874 healthy Caucasians (mean age for men and women was 54 and 53 years respectively). Participants wore heart rate monitors continuously during the waking hours over 4 days to measure physical activity energy expenditure (PAEE), and the VO_2max was measured by measuring the oxygen uptake during an exercise stress test on a cycle ergometer. It has been revealed that the VO_2max was inversely related to the metabolic syndrome score after adjusting for age, gender, and PAEE ($P = 0.03$). After bivariate error correction, the association between fitness and metabolic syndrome dropped to a level of borderline significance ($P = 0.06$). However, the association between PAEE and the metabolic syndrome score was more than three times stronger than the associations for VO_2max. PAEE was significant in models adjusted for age, gender, and VO_2max ($P < 0.0001$) and even after adjustment for age, gender, VO_2max, and bivariate measurement error ($P = 0.0042$). Therefore, it has been suggested that the association between VO_2max and metabolic syndrome was substantially weaker than the association between PAEE and metabolic syndrome.

In addition, a cohort study of 605 healthy middle-aged adults (249 were men) over 5 years by Ekelund et al., (2005) has indicated that the PAEE (measured by heart rate monitor) was a more predictable factor ($P = 0.046$) on metabolic syndrome (defined by the WHO 1999 criteria) than aerobic fitness (VO_2max measured by cycle ergometer at different workloads), after adjusting for gender, baseline age, smoking, socioeconomic status, and follow-up time. They underscored the importance of physical activity for metabolic disease prevention even when an improvement in aerobic fitness is absent.

In contrast, Brage et al., (2004) has indicated that physical fitness has more influence in CVD risk factors than physical activity. In their study, they examined the relationship between the metabolic syndrome (defined by the WHO 1999 criteria), objective habitual physical activity (assessed by accelerometer) and fitness (determined by a maximum cycle-ergometer test until exhaustion) in a younger population of a total of 589 Danish children (310 girls, 279 boys; mean age 9.6 years). After adjusting for all confounding factors (gender, ages, BMI, ethnicity, socioeconomic status, parental smoking), they have observed that habitual physical activity was inversely associated with insulin ($P = 0.018$) and borderline significantly associated with TG ($P = 0.052$). However, they have shown that there was no evidence of associations with glucose, HDL-C, SBP and DBP, or skinfold thickness. Interestingly, physical fitness has been found to be inversely associated with insulin, TG, SBP, and skinfold thickness ($P \leq 0.033$), and positively associated with HDL-C ($P = 0.002$), but not with glucose or DBP, following adjustment for all confounding factors.

In addition, Irwin et al., (2002) has determined the association of moderate-intensity physical activity, vigorous-intensity, and maximal treadmill duration with the metabolic syndrome (defined by the NCEP 2001 criteria) among African-Americans (n = 49), Native-Americans (n = 46), and white (n = 51) women (ages, 40 to 83 years). Moderate physical activity and vigorous physical activity were determined based on detailed physical activity records during two consecutive 4 day periods. Maximal treadmill duration (VO_2max) was determined from a graded exercise test. Age, ethnicity, study site, menopausal status, and use of hormone-replacement therapy were controlled. They have found that the adjusted OR for the metabolic syndrome was 0.18 for women in the highest category of moderate physical activity compared to women in the lowest category ($P < 0.01$). Similar associations have been observed for the metabolic syndrome with vigorous physical activity ($P < 0.01$ for trend) and the maximal treadmill duration ($P < 0.01$ for trend).

In this regard, a cross-sectional study by Rennie et al., (2003) has examined the relationships between moderate (≥ 3 – < 5 METs) and vigorous (≥ 5 METs) physical activity and the metabolic syndrome (defined by the NCEP 2001 criteria) in the Whitehall II study of 10,308 (3,414 women) civil servants (age 45-68 years). In this study, while the self-reported LTPA was categorised into moderate and vigorous activity intensities, cardiovascular fitness was assessed as resting heart rate (HR) by an electrocardiogram. They hence found that in the top categories of moderate activity, low BMI and TG levels and higher HDL-C levels were observed in men only (all $P < 0.05$), and lower waist hip circumference (WHR) in both genders ($P < 0.01$). In contrast, no associations were observed with 2-hour glucose or SBP. In the top categories of vigorous activity, while BMI was lower in both genders ($P < 0.01$), lower TG, SBP, 2-hour glucose level, and WHR and higher HDL-C were found only in men (all $P < 0.01$). Also, the ORs for having the metabolic syndrome in the top categories of vigorous and moderate activity were 0.52 and 0.78, respectively. These results persisted after the adjustment for the age, gender, smoking, alcohol intake, and socioeconomic status. However, when the BMI and resting HR were considered, both of the above associations were substantially attenuated. This suggests that both body fatness and fitness are mediators of the benefits of both activity intensities in this middle-aged population.

Interventional studies:

Interventional studies are limited but suggest that regular exercise reduces the incidence of metabolic syndrome. Katzmarzyk et al., (2003a) has reported that the effects of a 20-week supervised aerobic training program on prevalence of the metabolic syndrome (defined by the NCEP 2001 criteria) in 621 men and women who were enrolled in the HERITAGE Study. After the exercise intervention, 30.5 % of the participants with the metabolic syndrome at baseline were no longer classified as having the metabolic syndrome. In addition, Tjonna et al., (2008) has compared moderate and high exercise intensity with regard to variables associated with cardiovascular function and prognosis in 32 patients (average aged 52 years) with the metabolic syndrome defined by WHO 1999 criteria. The patients were randomized to equal volumes of either moderate continuous moderate exercise (70 % of highest measured heart rate) or aerobic interval training (90 %), or to a control group. Both exercise groups performed endurance training as walking/running "uphill" on a treadmill 3 times a week for 16 weeks. They demonstrated that high-intensity exercise training is superior to moderate-intensity training in reversing risk factors of the metabolic syndrome. In general, the amount and intensity of physical activity required to prevent or reverse metabolic syndrome has yet to be determined.

2.5.3. Blood lipids:

Observational studies:

Lakka and Salonen, (1992) have found that total physical activity measured by a self-reported questionnaire (classified according to EE into eight groups) is associated inversely with TG ($P < 0.001$) and positively associated with HDL-C ($P < 0.001$) in 2,492 Finnish men aged 42-60 years after controlling the age. Moreover, in another study, Dey et al., (2002) has evaluated the effects of total physical activity (expressed as energy expended in joules/kg of body weight) on selected CHD risk factors of older former athletes (162 people aged 46.5 years) and to compare these selected risk factors with age-matched older non-athletes. After controlling the age, BMI and body fat %, it has been shown that active older athletes had significantly lower mean values in TC, LDL-C, TG, ratio of TC/HDL-C, weight, BMI, and body fat % than in sedentary older athletes and sedentary older non-athletes. In addition, a cross-sectional study of 141 Flemish males aged 40 old, Delvaux et al., (2000) has found that when WC is considered, there were significant differences in the levels of TG, TC/HDL-C ratio, and the body fat % (all $P < 0.001$) among the fitness groups (measured on a bicycle until exhaustion).

However, Bijnen et al., (1996) has investigated of the association of three different categories for total physical activity (minutes/week for each activity) assessed by self-administered questionnaire with cardiovascular risk factors. Activities were grouped by level of intensity using the intensity codes and categories proposed by Caspersen et al. (1991): light (e.g., tending animals), moderate (e.g., walking, low-speed bicycling, fishing), and heavy (e.g., brisk walking, bicycling at normal or high speed, gardening, farming, dancing). They have indicated that total physical activity was not associated with TC and LDL-C in 1,402 men (aged 69-90 years) after controlling the age, cohort, smoking, BMI, and alcohol intake. Also, blood pressure and BMI were reported to be not significant. However, the total physical activity was only positively associated with HDL-C ($P < 0.01$).

In addition, Danielson et al., (1993) has found no significant differences in TC, HDL-C, LDL-C, or TG across tertile of total physical activity in 634 elderly postmenopausal women (mean age 70.7 years) after adjusting for the age, BMI, education, and oral estrogen use. The total physical activity measured in kilocalories/week was assessed by the Paffenbarger Questionnaire, a composite index of sports/recreation, stair climbing, and walking. Young et al., (1993) has found in a cohort sample of 807 men and women (18 and 74 year), that improvements in total physical activity (expressed in MET scores) were significantly associated with an increase in the HDL-C in men and women ($P = 0.005$ and $P = 0.028$ respectively), but not TC in both genders. Also, they reported that BMI was significantly decreased in men only ($P = 0.001$).

<u>Interventional studies:</u>

A review study by Durstine et al., (2001) has indicated that moderate training programme of 24 to 32 km (15 to 20 miles) per week of brisk walking or jogging that elicit 1200 to 2200 kcal/week is associated with 2 to 3 mg/dl increases in HDL-C and TG reductions of 8 to 20 mg/dl. A previous study by Peltonen, (1981) has also observed that serum HDL-C increased by about 7 % ($P < 0.01$), HDL/TC ratio by 11 % ($P < 0.001$), and decreased in LDL-C ($P < 0.05$) in 27 middle-aged men after participation in a moderate training program of 15-week compared to non-training control subjects. Also, Ballantyne., (1982) has found that after an incremental moderate exercise program on treadmill, the TG and LDL-C levels decreased significantly ($P < 0.001$ and 0.05, respectively) and HDL-C levels significantly increased ($P < 0.001$) in the trained men (n= 19) compared to a control group (n= 23) for 6 months.

In a small randomised controlled trial, Sugiura et al., (2002) has evaluated the effects of a

24-month period of moderate exercise (90-minute physical education class once a week measured by a pedometer for 24 months) on serum lipids in 27 menopausal women (aged 40-60 years). Mean of daily steps was found to be significantly higher in the exercise group (n = 14) from about 6,800 to over 8,500 steps (P < 0.01) than the control group (n = 13). They have also observed significant reductions in TC levels (P < 0.05) and TC/HDL-C ratios (P < 0.05), and an increase in HDL-C levels (P < 0.05) among the exercise group, but not in the control group.

On the other hand, it has been reported that a weekly running 24-48 km of vigorous exercise programme on treadmill at 75 % VO_2max to reach 800 kcal/session, significantly increased the level of HDL-C (P < 0.05) in 12 trained premenopausal women aged 22 years old (Gordon et al., 1998). In addition, Zmuda et al., (1998) has evaluated the level of lipids after a weekly 4 supervised vigorous exercise sessions (elicit 60–80 % of the subjects' VO_2max) in 17 men aged 26–49 years with low and normal HDL-C. Diets habits, changes in lipids, lipase activities, and fat tolerance were controlled. It has been found that while the levels of HDL-C were significantly increased (P = 0.001) and the TG levels decreased by 12 % with exercise training in the normal HDL-C group (P<0.05), but not in low HDL-C group. LDL-C was nearly significantly lower (P = 0.07) in the normal HDL-C group. No significant difference was found in TC, weight, and BMI.

In contrast, without any adjustment undertaken, it has been indicated that after one year of moderate exercise programme on treadmill, the changes in levels of fitness and/or regular exercise did not substantially influence HDL-C, TC, and TG levels in either trained or control group of 223 post-coronary men, aged 30 to 64 (LaRosa et al., 1982). Another study by Hinkleman and Nieman, (1993) has evaluated the effect of 45 minute of brisk walking at 62 % VO_2max 5 times/week for 15 weeks on lipid profiles. They have indicated that HDL-C was only significantly increased (P = 0.035) in overweight exercised women (n = 18) compared to a non-exercise women (n = 18). However, the pattern of changes in serum TG, TC, and LDL-C was not significant. In addition, they have reported that the total body weight was significantly reduced in the exercise group (P = 0.002), but the percentage of body fat was not significantly different between the groups.

In addition, after adjusted smoking habits, Raz et al., (1988a) has indicated that a vigorous program of sub-maximal aerobic exercise (a 45-minute work phase at 70% to 85% of maximal capacity determined by self-measured heart pulse rate) 3 days/week for 9 weeks has no significant difference in TC, HDL-C, LDL-C between the exercise (n = 28) and control (n = 27) groups of healthy men with low HDL-C who were sedentary and non-obese (24 to 26 year old). The level of TG was only significantly lower by 19 mg/dl in the exercise group compared to the control group ($P < 0.05$). In addition, they reported that body weight and skinfold thickness of both groups remained essentially unchanged after 9 weeks. Moreover, Hicks et al., (1987) has recruited 12 men (19-41 years) to run an equivalent distance on a treadmill on two separate occasions: performed at a speed that elicited 60 % of VO_2max, and then performed at a speed that elicited 90 % of VO_2max. Without any adjustment considered, they found significant increases in HDL-C ($P < 0.01$) with exercise at both intensities, but greater increases with the higher intensity exercise. However, TG did not differ between conditions.

Ready et al., (1995) has also examined the effect of a moderate exercise (walked an average of 54 minutes/d, 5 days/w, at an intensity of 54 % of maximum heart rate, for 6 months) on TC, TG, HDL-C, LDL-C, body composition and cardiovascular fitness (VO_2 max) in 25 subjects (15 walkers, 10 controls) mildly hyperlipidemic postmenopausal women. After adjusting for diet, smoking and hormone replacement therapy, significant reductions have been found in TC, TG, TC/HDL-C ratio, BMI and fat mass in the walkers compared to controls ($P < 0.05$). However, it has been suggested that these changes are related more to the loss in body fat rather than to increased activity level.

2.5.4. Blood pressure:

<u>Observational studies:</u>

It has been found that individuals who performed moderate-to-vigorous LTPA has a 25 % lower hypertension prevalence in 16,246 adults compared to those performed no LTPA (Bassett et al., 2002). The activity levels of LTPA were classified as none, 0.1-4.9 bouts/week at any intensity, and ≥ 5 bouts/week of moderate-to-vigorous activity. This finding was obtained after controlling the gender, age, income, smoking, BMI, salt intake, rural/urban dwelling, and alcohol intake. In addition, they have observed that black people had an OR for hypertension of 1.77 compared to non-Hispanic whites. This may suggest that ethnicity has an effect on the relationship between physical activity and hypertension.

After adjustment for several possible confounders, Mensink et al., (1999) has found that women (aged 50-69) with modest levels of moderate-to-vigorous LTPA (≥ 5 kcal/kg/h conducted ≥ 5 times a week) have significantly lower SBP (-1.8 %) and resting heart rate (-3.1 %) values than sedentary women. In addition, this study has revealed that, among women, light activities (3-4.5 kcal/kg/h) were significantly associated with favourable lower DBP (-1.4 %) and resting heart rate (-2.3 %). They have also reported that BMI decreased 2.9 % and 2.2 % in women and men, respectively. They concluded that even less physical activity than currently recommended, is likely to improve the cardiovascular risk profile for sedentary elderly. Likewise, Cavelaar et al., (2002) has shown that increasing the physical activity level (measured by accelerometer) from a very low level (e.g. watching television) to a moderate level (e.g. shopping) caused an average reduction of 11.6 mmHg and 7.0 mmHg in SBP and DBP respectively in 27 subjects. However, the response to moderate physical activity had a small effect on the SBP levels in overweight subjects.

In contrast, a cross-sectional study by Chan et al., (2003) has addressed the associations between walking (measured by pedometer-determined steps/day) and blood pressure in adult women (n = 153) and men (n = 21). The mean number of steps/day for women and men were 7230 and 8265, respectively. In this study, it has been found that pedometer was inversely associated with DBP (P = 0.04) in all participants, and SBP was nearly significant (P = 0.06). Also, they have also reported that pedometer-determined steps/day were inversely associated with BMI (r = -0.40, P < 0.0001) in all participants and WC in females only (r = -0.43, P < 0.0001). In addition, despite the daily number of steps was positively associated with self-reported occupational activity (P = 0.0002), self-reported occupational activity was not associated with blood pressure both in men as well as in women.

<u>Interventional studies:</u>

The hypothesis that walking activity would lower blood pressure in 24 postmenopausal women with high blood pressure has been tested by Moreau et al., (2001). Fifteen women were assigned into the exercise group walked 3 km/day above their daily lifestyle walking, whereas 9 women in the control group did not change their activity. Walking activity was self-measured with a pedometer in both groups. It has been found that the resting SBP dropped in the exercise group after 12 week by 6 mm Hg (P < 0.005) and further decreased by 5 mm Hg at the end of 24 week (P < 0.005) with no significant change in DBP. The controlled group experienced no change in blood pressure at 12 or 24 weeks.

In addition, Murphy et al., (2006) has examined the effects of 45 minutes self-paced walking programme at 62 % of maximum heart rate, 2 days/week for 8 weeks on SBP, body composition, and lipids in previously 37 sedentary 24 women (average aged 41.5 years). The participants were randomly assigned to either walking group or no training group (control group). The mean steps for the walking and control groups were 9303 and 5803, respectively. Compared to the control group, the walking group showed a significant reduction in SBP ($P < 0.05$). Moreover, it has been shown that body fat level significantly decreased in the walking group compared to the control group ($P < 0.05$). However there were no significant changes in lipid profiles. These findings suggest that walking twice per week for 45 minutes at approximately 62 % of maximum heart rate reduces SBP and prevents an increase in body fat in previously sedentary adults. This walking prescription, however, failed to induce significant improvements in other markers of CVD risk following eight weeks of training.

In contrast, a 6-month randomized controlled trial by Stewart et al., (2005) has evaluated the combined aerobic and resistance training (until fatigue) in 51 participants (aged 55-75 years), and 53 controls. They have found that the aerobic and resistance training significantly lowered DBP ($P=0.02$) among exercisers, but not SBP in both groups. Also they have reported that the exercisers significantly improved their aerobic fitness and body composition (increased lean mass, and reduced general and abdominal obesity). They indicated that body composition (e.g BMI, WC) improvements explained 8 % of the systolic blood pressure reduction ($P = 0.006$) and 17 % of the DBP reduction ($P<0.001$). These findings suggested that body composition improvements were associated with blood pressure reductions and may be a pathway by which exercise training improves cardiovascular health in older men and women.

It has been suggested that moderate aerobic exercise alone should not be considered a replacement for pharmacologic therapy in 99 non-obese men and women with mild hypertension (Blumenthal et al., 1991). After 4 months of moderate exercise training, it has been revealed that aerobic exercise group did not exhibit greater reductions in blood pressure than subjects in the control group. Cox et al., (2006) has evaluated 6 months of supervised moderate swimming or walking on blood pressure in previously sedentary, normotensive, older women aged 50-70 years ($n = 116$). The participants were randomly assigned to a supervised 6-month swimming or walking programme. The exercise programme was comprised 3 sessions/week with a warm-up, cool down, and 30-minutes of moderate intensity walking or swimming. After adjustment for initial blood pressure, age, hypertension treatment status and change in weight, swimming increased supine and standing SBP relative to walking by 4.4 mmHg ($P = 0.008$) and 6.0 mmHg ($P = 0.001$), respectively. This finding may have important implications for exercise prescription on blood pressure in previously sedentary older subjects.

2.5.5. Diabetes:

Observational studies:

Insulin resistance is the key factor linked to the clustering of several CVD risk factors, including abdominal obesity, hyperglycaemia, dyslipidaemia and elevated blood pressure (Eckel et al., 2005; Chew et al., 2006). One of the mechanisms of physical activity improves the risk factors for CVD is through insulin resistance (Goodyear and Kahn, 1998). Briefly, it has been demonstrated that an increase in level of physical training may improve insulin sensitivity by increasing skeletal muscle oxidative capacity and glucose uptake in skeletal muscle (Oshida et al., 1989, Tonino, 1989, Young, 1989, Dunstan et al., 1998, Maiorana et al., 2002, Zierath, 2002; Bruce et al., 2003; Wojtaszewski et al., 2003; Christ-Roberts and Mandarino, 2004; Holloszy, 2005). This effect of lowering TG, decreasing body fat, and increasing HDL-C is observed among both diabetic and non-diabetic subjects (Mayer-Davis et al., 1998; Gordon et al., 1994).

In a cross-sectional study by Waden et al., (2005), the association between LTPA and glycemic control, insulin dose, and estimated glucose disposal rate has been addressed in 1,030 patients with NIDDM participating in the Finnish Diabetic Nephropathy Study. LTPA was assessed by a validated 12-month questionnaire and expressed in MET scores. Patients were grouped as sedentary (LTPA < 10 MET*hr/week, n = 247), moderately active (LTPA 10-40 MET*hr/week, n = 568), and active (LTPA > 40 MET*hr/week, n = 215). After adjustment for age and BMI, it has been found that in both sexes, sedentary patients had lower estimated glucose disposal rate than active patients ($P < 0.01$). Low levels of LTPA were associated with poor glycemic control in type 1 diabetic women whereas increased LTPA levels were associated with increased insulin sensitivity. Finally, they also reported that men seemed to use less insulin when physically active.

In a random sample of younger population of 1137 girls and boys (aged 9 and 15 years), Wennlof et al., (2005) have been indicated that the total physical activity measured by accelerometer was negatively related to insulin ($P = 0.002$). Also they reported that TG was significantly decreased ($P = 0.039$), but TC and HDL-C were not significant. When the analysis was separated by the age and gender, the association of total physical activity with insulin persisted only in the 15-year-old girls ($P=0.014$) and boys ($P=0.038$).

Interventional studies:

Evidence from large intervention studies in the US (The Diabetes Prevention Program), Finland (The Finnish Diabetes Prevention Program) and China (The China Da Qing

Diabetes Prevention Study) have shown that sustainable lifestyle interventions in people at high risk of developing type 2 diabetes, lead to significant reductions in the incidence of diabetes.

The Diabetes Prevention Program (DPP) (2002), a federally funded study conducted from 1996 to 2001, was a major multicenter clinical research study in the United States aimed at discovering whether modest weight loss through dietary changes and increased physical activity or treatment with the oral diabetes drug could prevent or delay the onset of type 2 diabetes in study participants. The DPP participants (n = 3234) ranged from age 25 to 85, with an average age of 51 years. Upon entering the study, all the participants had impaired glucose tolerance as measured by an oral glucose tolerance test, and all were overweight, with an average BMI of 34. The study participants were randomly divided into three different treatment groups: 1) intensive lifestyle modification (aimed of reducing body weight by 7 % through healthy diet and moderate physical activity of 30 minutes a day 5 days a week), 2) standard care plus the drug metformin (850 mg twice a day), and 3) standard care plus placebo (a pill that has no effect). The DPP found that participants who lost a modest amount of weight (5 to 7 %) through dietary changes and increased physical had 58 % lower chances of developing diabetes compared with placebo group. Participants randomly assigned to treatment with metformin had a 31 % lower incidence of type 2 diabetes. In addition, about 5 % of the lifestyle intervention group and 7.8 % of the metformin group developed diabetes each year during the study period, compared with 11 % of those in the placebo group. These effects were similar in men and women, and in all racial and ethnic groups.

The risk reduction with lifestyle intervention found in the DPP study was the same as that found in a similar study conducted in Finland (Tuomilehto et al., 2001), and was higher than the study in China (Pan et al., 1997). In the Finnish Diabetes Prevention Program study (Tuomilehto et al., 2001), about 522 middle-aged, overweight subjects with impaired glucose tolerance (172 men and 350 women; mean age = 55 years; mean BMI = 31) were randomly assigned to either the intervention group or the control group. Each subject in the intervention group received individualized counselling aimed at reducing weight (≥ 5 % of body weight), total intake of fat, and intake of saturated fat and increasing intake of dietary fibre and physical activity (moderate exercise for at least 30 minutes per day). The mean duration of follow-up was 3.2 years. The cumulative incidence of diabetes after four years was 11 % in the intervention group and 23 % in the control group. During the trial, the risk of diabetes was 58 % lower in the intervention group than in the control group (P < 0.001) in the intervention group. They indicated that the reduction in the incidence of diabetes was directly associated with changes in the lifestyles of both women and men at high risk for the disease.

In 1986, 577 adults with impaired glucose tolerance (using WHO criteria) from 33 clinics in the city of Da Qing, China, were recruited to join the China Da Qing Diabetes Prevention Study and randomly assigned to either a control group or to one of three active treatment groups: diet only, exercise only, or diet plus exercise (Pan et al., 1997). The intervention took place over 6 years. After adjustment for differences in baseline BMI and fasting glucose, participants who were randomly assigned the diet, exercise, and diet-plus-exercise interventions had 31 % (P = 0.03), 46 % (P < 0.001), and 42 % (P = 0.005) lower in risk of developing diabetes, respectively, compared with control participants. These same subjects were revisited 20 years later and those in the combined lifestyle intervention groups had a 43 % lower incidence of diabetes, after adjustment for age, that those in the control group (Li G et al 2008). The average annual incidence of diabetes was 7 % for intervention participants versus 11 % in control participants, with 20-year cumulative incidence of 80 % in the intervention groups and 93 % in the control group.

The results from other smaller studies also provide evidence that changes in physical activity levels are effective in preventing diabetes, however the magnitude of the benefit in these studies was varies. For instance, a clinical trial of 18 overweight, inactive women (mean age 53 years), Swartz et al., (2003) has evaluated the effectiveness of walking programmes accumulating 10,000 steps/day for 8-week (measured by pedometer) on glucose tolerance, without any changes in diet. It has been found that the beneficial changes in 2-hour glucose levels (P < 0.001) in those participants who had increased their accumulated steps/day by 85 % to 9213 steps/d. Also, they reported, SBP (P < 0.001), and DBP (P = 0.002) significantly decreased, however, no changes in BMI, body fat %, and WC were found after 8-week walking programme.

In this respect, the effect of a 20-week endurance training programme has been determined by Boule et al., (2005) in healthy, previously sedentary participants (316 women and 280 men: 173 blacks and 423 whites) on measures derived from an intravenous glucose tolerance test (GTT). Participants were asked to exercise on cycle ergometers 3 days per week for 60 sessions. The exercise intensity was progressively increased from 55 % VO2max for 30 minutes/session to 75 % VO2max for 50 minutes/session. Analysing the results, it has been shown that the mean insulin sensitivity increased by 10 % (P < 0.001) following the intervention with higher improvements in men than in women ($P = 0.02$). There were also significant mean increases in the glucose disappearance index (3 %, $P = 0.02$), glucose effectiveness (11 %, $P < 0.001$). In contrast, the glucose area below fasting levels during the GTT dropped by 7 % ($P = 0.02$).

The hypothesis that residual effects of the last bouts of exercise play an important role in the insulin concentration has been examined by Heath et al., (1983). Eight well-trained subjects stopped training for 10 days. It has been indicated that there were no significant changes in VO2max, estimated percent body fat, or body weight. The maximum rise in plasma insulin concentration in response to a 100-g oral glucose load was 100 % higher after 10 days without exercise than when the subjects were exercising regularly. Despite the increased insulin levels, blood glucose concentrations were higher after 10 days without exercise. One bout of exercise after 11 days returned the insulin and glucose responses to an oral 100-g glucose load almost to the initial "trained" value. In addition, a study by Arciero et al., (1998) has evaluated two identical tests of different days on glucose tolerance in 8 athletes (21 years old). The first test was participation in normal endurance training bout by cycle ergometer to exhaustion, and the other test was after 7-10 days of inactivity. Without any adjustment undertaken, they found that the fasting plasma glucose concentrations increased significantly ($P < 0.05$), and glucose tolerance was significantly reduced after 7-10 days of inactivity compared to the training test.

In contrast to the above studies, some authors have revealed different results about the relationship between exercise training with insulin and glucose (Lampman et al., 1987, Raz et al., 1988b, Kang et al., 1996, Ligtenberg et al., 1997, Pratley et al., 2000, Fenicchia, 2004; Baynard et al., 2005). For example, a randomized prospective study have been performed by Ligtenberg et al., (1997) on 51 subjects with type 2 diabetes to investigate the role of physical activity programme (consisted of 3 sessions/week, aiming at 60-80 % of the VO2max for 12 week supervised period followed by a 14 week non-supervised one) in the treatment of type 2 diabetes. It has been concluded that blood glucose control and insulin sensitivity did not change during the study, while the levels of TG and TC significantly decreased ($P < 0.01$ and $P < 0.05$, respectively), after 12 weeks of training programme consisted of 3 sessions/week, aiming at 60-80 % of the VO2max.

In another study, Pratley et al., (2000) has also examined the effects of aerobic exercise training on glucose-stimulated insulin responses in 17 middle-aged and older men. Subjects walked, jogged, or cycled at 50 to 60 % heart rate three times per week for 30 to 45 minutes and progressed over 6 to 9 months until subjects were training at 80 to 85 % of heart rate for 45 to 60 minutes 3 to 4 times per week. Fasting glucose and insulin levels, and glucose responses during the oral glucose tolerance tests did not change. However, the insulin responses during the oral glucose tolerance tests decreased significantly to 16 % (P = 0.027) after training. Multiple regression analyses showed that changes in waist circumference (r = 0.68, P < .0001) and percent body fat (r = 0.08, P = .049) were independent predictors of the reductions in the late phase insulin responses with exercise training. It has been concluded that the decrease in glucose-stimulated insulin secretion with aerobic exercise training in middle-aged and older men appears to be mediated, at least in part, by reductions in the amount of abdominal fat.

In addition, it has been indicated that 3 days/week of acute bout of resistance exercise for 6 weeks is sufficient to improve whole body integrated glucose concentration in type 2 diabetes women (n 7) for at least 24 hours post-exercise as compared to age-matched controls with normal glucose tolerance (n = 8) (Fenicchia, 2004). However, the insulin concentrations were not affected by exercise. Moreover, Baynard et al., (2005) has found that exercise (one 30-minute or three 10-minute bouts of exercise) or no exercise did not alter the insulin response to the oral glucose tolerance tests in women (average age 53 years) either with type 2 diabetes (n = 9) or the control group (n = 6). Despite a higher glucose response to the glucose load, an acute exercise bout (single or multiple bouts) did not appear to alter glucose control the following day for either group.

2.5.6. Body composition:

Observational studies:

Several investigators have suggested that the favourable effects of exercise or physical activity on CVD risk factors may be mediated through differences in body composition (BMI, WC, body fat %, or total visceral body fatness) (Després et al., 1991; Katzel et al., 1995; Hunter, 1997). Although the widely held notion that maintaining or reducing body weight or body fat is facilitated by an increase in physical activity, the relation between physical activity and body composition is inconsistent (Rising et al., 1994; Westerterp and Goran, 1997), and little is known about what intensity of exercise might be optimal to reduce the risk of obesity.

In an epidemiologic study of adult individuals, it has been found that those who engaged in greater amounts of free-living vigorous physical activities (expressed as kcal/kg of body weight/hr of activity) had lower general and central adiposity than those not performing these activities, even after control for total PAEE (Tremblay et al., 1990). Schoeller et al., (1997) conducted a prospective study to test whether physical activity measured soon after weight loss predicted weight maintenance and to determine how much physical activity was required to optimize maintenance. Thirty-two women (mean age 38 years and mean BMI 24) were recruited through local advertising within 3 months of reaching their target for weight loss (23 ± 9 kg). Total EE (TEE) was measured by the doubly labeled water method, and resting metabolic rate (RMR) was measured by respiratory gas exchange. While women in the physically active group [physical activity level (PAL) (ratio of TEE to RMR) = 1.89] gained 2.5 kg during the 12 months after reaching their target for weight loss, moderately active women (TEE/RMR = 1.64) gained 9.9 kg, and sedentary women (TEE/RMR = 1.44) gained 7.0 kg ($P < 0.01$). Retrospective analyses of weight regain as a function of EE in physical activity have indicated a threshold for weight maintenance of 11 kcal/kg body weigh/day. This corresponds to an average of 80 minutes/day of moderate activity or 35 minutes/day of vigorous activity added to a sedentary lifestyle.

Paul et al., (2004) has evaluated the relation between PAEE and the percentage of body fat (BF) in a sample of 91 healthy persons (women aged 48 years, n = 47; and men aged 47 years, n = 44). Resting energy expenditure (REE) was measured by indirect calorimetry for 40 minutes whereas the TEE was obtained by using the doubly labelled water method. Physical activity level (PAL) was calculated as the ratio of TEE to REE. In this regard, while it has been reported that the relation of TEE to the % BF was only significant in women ($P < 0.001$), the relation of PAEE and PAL to the % BF was significant in men ($P < 0.03$) but not in women. In addition, Jia et al., (2005) has indicated that the REE measured by indirect calorimetry was closely related with the area of abdominal visceral fat in 109 Chinese adults men (n= 52) and women (n = 57). They have also found that the RMR was significantly lower in overweight/obesity subjects than in normal-weighted subjects, and significantly lower in subjects with abdominal obesity than in subjects with non-abdominal obesity.

In contrast, it has been indicated that the RMR of obese subjects did not increase with increasing BMI tertiles in 87 obese non-diabetic outpatients mean age 45 years (de Luis et al., 2005). In agreement, another study conducted by Lahti-Koski et al., (2002) has found that subjects who are moderately or highly active at leisure time were less likely to be obese than subjects with a low level of activity. These associations, however, disappeared after controlling for all the other lifestyle variables such as dietary habits. In addition, although the higher steps (measured by pedometer) was inversely associated with BMI ($P < 0.001$) and WC ($P < 0.001$), self-reported occupational activity had no relationship to any of these health indicators in 182 sedentary working subjects (Chan et al., 2003).

Interventional studies:

Slentz et al., (2004) has determined the effects of different amounts and intensities of exercise training in 120 sedentary, overweight men and women (aged 40-65 years) with mild to moderate dyslipidemia who were recruited from in North Carolina (USA). The intervention exercise programme lasted for 8-month with 3 groups: (1) high amount/vigorous intensity (calorically equivalent to approximately 20 miles [32.0 km] of jogging per week at 65-80 % peak oxygen consumption); (2) low amount/vigorous intensity (equivalent to approximately 12 miles [19.2 km] of jogging per week at 65-80 %), and (3) low amount/moderate intensity (equivalent to approximately 12 miles [19.2 km] of walking per week at 40-55 %). Subjects were counselled not to change their diet and were encouraged to maintain body weight. In this study, it has been shown that the high-amount/vigorous-intensity group lost significantly ($P < 0.05$) more body mass and fat mass than the low-amount/moderate-intensity group, the low-amount/vigorous-intensity group, and the controls. Compared to control group, all exercise groups significantly had a decrease in abdominal, minimal waist, and hip circumference measurements. Therefore, it has been concluded that a higher amount of activity in the absence of changes in dietary intake is necessary for weight maintenance and that the positive caloric balance observed in the overweight controls is small and can be reversed by a modest amount of exercise. This may suggest this amount of exercise can be accomplished by walking 30 min/day.

Consistently, Bryner et al., (1997) has tested the effect of exercise intensity without dietary manipulation on body composition and/or weight loss in 15 normal weight young women aged 18 to 34 years. Subjects were randomly assigned to 1) low heart rate intensity exercise group (LI, N = 7) which exercised 40 to 45 minutes approximately four times weekly at a mean heart rate of 132 beats/minute; and 2) high heart rate intensity group (HI, N = 8) which exercised 40 to 45 minutes approximately four times weekly at a mean HR of 163 beats/minute. All subjects were given a maximal exercise test prior to and during weeks 8, 12 and 16. The first 4 weeks served as a control period, followed by approximately 11 weeks of exercise. Analysing the results has shown that there was a significantly decreased in the fat percentage in HI ($P < 0.05$), but not in LI. This may imply that the high heart rate intensity exercise training without dietary manipulation results in a decrease in body fat, but not weight change. This may be due to in an increase in lean body mass. In addition, an intervention study of adults suggested that high-intensity physical training led to greater reductions in fatness than did moderate-intensity physical training (Tremblay et al., 1994).

In contrast, it has been indicated that moderate aerobic exercise training (five 45-min at 78.5 % of VO2max) during a 12-week period has no marked effects on body composition in 91 dieting obese women (Utter et al., 1998). In this regard, Tully et al., (2005) has assigned one group (intervention group n= 11) in a randomised controlled trial into a walk briskly programme for 30 minutes, 5 days/ week in one session or in shorter bouts of no less than 10 minutes for 12 weeks, and the other group was control (n = 10) subjects (aged 50-65 years). They found no significant changes in anthropometric measurements, as with blood lipid profiles. However, they have observed significant decreases in both SBP and DBP ($P = 0.02$ and $P < 0.001$ respectively) and a reduction in the stroke risk ($P < 0.001$) in the walking group compared to the control group.

Moreover, Borg et al., (2002) has investigated whether walking or resistance training improves weight maintenance (WM) after weight loss in 90 healthy, obese men aged 35-50 year-old (mean BMI 32.9 and waist 112.5 cm). The subjects were randomized into three groups (control, walking, resistance training) for 6 months' WM programme and 23 months' unsupervised follow-up. Exercise diaries and dietary records were used to assess energy balance (expressed as kilojoules/week). It was found that the exercise training did not improve on short or long-term WM compared to the control group. However, resistance training attenuated the regain of body fat mass during WM (P = 0.0l), but not during the follow-up. In the combined groups, the estimated TEE of reported physical activity was associated with less weight regain during WM. This may indicate that exercise training of moderate intensity does not seem to improve long-term weight maintenance.

Similarly, in a juvenile intervention study, skinfold fat has been shown to decline in the low and high-intensity physical training groups (Savage et al., 1986). Gutin et al., (2002) has also found there is no evidence that the moderate and high-intensity physical training differ in their effects on body composition obese adolescents (n = 80) aged 13-16 years. Physical training was offered 5 days/week, and the target EE for all subjects in physical training groups was 250 kcal/session. However, it has been suggested that for enhancement of cardiovascular fitness it is reasonable to advise obese youths to exercise as vigorously as they can sustain.

Accumulating evidence from cross-sectional and intervention studies have thus far indicated that it is not clear what level of physical activity is beneficial in reducing the risks of the cluster of metabolic syndrome and, more precisely, whether both moderate and vigorous activity are beneficial or not. More specifically, the dose-response relationship (i.e., intensity, frequency, duration, type) between physical activity and health, particularly with regard to the different health outcomes remains uncharacterised. For example, if a particular index (e.g. TC) is the main outcome, both observational and intervention studies have shown discrepant results. This reviewed literature suggests that the effect of physical activity on CVD risk factors may be mediated, in part, through differences in the measures and levels of physical activity utilized, age, subjects with different health status and body composition, and other health risk factors.

2.6. Physical activity and other health risk factors:

2.6.1. Risk factors exist in the pathway:

Physical activity may reduce the risk of CVD through other risk factors that may exist in the causal pathway. Even after controlling for the traditional risk factors for CVD (such as blood pressure, TC, HDL, insulin resistance and body fatness) physical activity/fitness has still been shown to be an independent risk factor for CVD (DHHS-US, 1996). This may indicate that physical activity influences CVD risk through other non-classical mechanisms. Potential mechanisms by which physical activity and fitness may influence CVD risk are described briefly below.

Inflammatory markers:

There is increasing evidence that systemic inflammatory markers such as higher levels of C-reactive protein (CRP), serum amyloid A, fibrinogen, interleukine-6 and white blood cell count are predictors of CVD independently from other cardiovascular risk factors (Ross, 1999; Danesh et al., 2000; Rifai and Ridker, 2002). It has also been found that there is an inverse relationship between the inflammatory markers and other risk factors of CHD, such as age, gender, smoking habits, obesity, diabetes mellitus, LDL and HDL, high TG levels, insulin resistance and physical activity (Geffken et al., 2001; Wannamethee et al., 2002; Reuben et al., 2003; Heilbronn and Clifton, 2002; Yudkin et al., 1999; Festa et al., 2000).

For clinical purposes, the strongest predictor and most useful inflammatory bio-marker appears to be CRP (Pearson and Mensah, 2003; Yeh and Willerson, 2003; Delanghe et al., 2002), which has been found to correlate with insulin resistance (Chambers et al., 1999; Frohlich et al., 2000; Cook et al., 2000; Danesh et al., 2000). The reduction of cardiovascular risk by exercise has been linked to lower CRP levels (Heilbronn and Clifton, 2002; Lagrand et al., 1999; Tchernof et al., 2002). In a review by Plaisance and

Grandjean, (2006) it has been showed that reductions in CRP concentrations by higher levels of physical activity and cardiorespiratory fitness range from 16% to 41%, an effect that may be independent of baseline levels of CRP, body composition and/or weight loss. In addition, lower aerobic capacity levels are associated with higher circulating CRP levels in middle-aged and older adult women and men independent of the higher BMI and the larger waist circumferences (LaMonte et al., 2002; Church et al., 2002). This stimulated the idea that it might be possible to reduce cardiovascular risk and the progression of atherosclerosis by reducing circulating levels of inflammatory markers. This may supports the idea that the inflammatory markers might be related to the mechanisms linking physical activity to the levels of the SBP, DBP, TC and HDL-C.

Protein kinase C (PKC):

PKC constitutes a family of important regulators of metabolism, differentiation, and cell growth that are classified into subfamilies based on amino acid similarity and mode of activation (Farese, 2001) which is involved in many cellular responses (Dempsey et al., 2000). It has been indicated that PKC has a role in insulin resistance (Cortright et al., 2000; Itani et al., 2002; Beeson et al., 2003) and exercise-mediated glucose transport (Chen et al., 2002; Beeson et al., 2003). A single bout of exercise has been found to induce changes in gene transcription and protein synthesis, constituting a possible mechanism for the chronic adaptations to regular physical exercise (Booth and Thomason, 1991). Therefore, the effect of exercise on PKC may provide evidence in mediating the increase in insulin sensitivity on glucose transport in skeletal muscle (Thong et al., 2003). This may combat several diseases including cardiac and type 2 diabetes (Dzimiri et al., 2004).

Endothelial function:

Endothelium function plays an important role in the local regulation of vascular tone and the maintenance of cardiovascular homeostasis (Rubanyi, 1993; Glasser et al., 1996), mainly through production of the relaxing factor nitric oxide, which acts by protecting the vessel wall from the development of atherosclerosis and thrombosis (Luscher and Vanhoutte, 1990). Endothelium dysfunction characterized by reduced nitric oxide availability induced by oxidative stress, causing the most of the cardiovascular risk factors including dyslipidemia, insulin resistance, and essential hypertension (Celermajer et al., 1992; Goodfellow et al., 1996; Ghiadoni et al., 2001). This dysfunction is related to increased oxygen free radicals production (Taddei et al., 2001; Eskurza et al., 2004) and a gradual loss of antioxidant capacity (Rinder et al., 2000), leading together to impaired nitric oxide availability (Taddei et al., 2001).

Available evidence supports the beneficial effect of physical activity such as maximal exercise testing (70-75 % of maximal heart rate) performed on a treadmill or 30 minutes of brisk walking 5 to 7 times/week on endothelium function (Rinder et al., 2000) and nitric oxide availability (Higashi et al., 1999; DeSouza et al., 2000; Taddei et al., 2000; Franzoni et al., 2005). Therefore, given the clinical importance of endothelial function to cardiovascular health, physical activity represents an important therapeutic strategy on endothelial function which may improve health risk factors.

<u>Haemostatic function:</u>

The protective effect of physical activity may result in part from its favourable influence on haemostatic function (e.g. fibrinogen, coagulation and platelet count). It has been found in a 20 year follow-up of men in the British Regional Heart Study (Wannamethee et al., 2002), habitual LTPA showed significant and inverse dose-response relationships with fibrinogen, plasma and blood viscosity, platelet count, and coagulation, even after adjustment for potential confounders. Randomized intervention studies have also consistently found that regular moderate-intensity exercise produces significant improvements in fibrinolytic capacity in formerly sedentary individuals (Lee and Lip, 2003; Smith et al., 2003). In addition, regular physical exercise has been shown to improve the balance between two systems that play a crucial role in thrombogenic processes, such as coagulation and fibrinolysis, in relation to the heart and blood vessels (van den Burg et al., 2000, Smith, 2003). Therefore, a disturbance in this function is an important risk factor for CVD (Barold et al., 1985, Ciampricotti et al., 1990).

2.6.2. Other confounding factors:

There is conflicting evidence about the importance of metabolic syndrome itself as a predictor of CVD risk compared to the characteristics of the people (such as birth weight, family history, genetic) (Malik et al., 2004; Stern et al., 2004; Sundstrom et al., 2006). For example, it has been suggested that the Framingham risk assessment tool seems to be a better predictor of short-term (10-year) in the risk of CVD than metabolic syndrome (Stern et al., 2004). This is not surprising, as it includes potent cardiovascular risk factors that are not included in the metabolic syndrome definition, such as age and smoking. Therefore, many studies have indicated that other confounding factors such as birth weight, family history, genetic, hormonal function and skeletal muscle properties may affect the relationship between physical activity and risk factors for CVD. This section highlights the important associations between characteristics of the people and CVD that are not routinely measured in clinical practice. It should be noted that the age, BMI and smoking are adjusted in this thesis and, therefore, their effects on the CVD are not discussed in this section.

Fetal growth/ birth weight**:**

Data from a large number of epidemiological studies in a wide range of populations has suggested that fetal growth measured by birth weight link with many chronic diseases. These studies have indicated that low-birth weight, shortness or thinness at birth increases the risk of insulin resistance, hypertension and CVD later in adult life (Barker, 2004; Law et al., 1993, Hales et al., 1991, Hales and Barker, 2001; Phipps et al., 1993, Prokopec and Bellesle, 1993, Simmons, 2005; Weihang et al., N 1994). When these important cardiovascular risk factors are present in childhood, they may persist into adulthood, suggesting origins in early life.

In addition, it has been suggested that fetal growth programmes lean mass and physical activity/fitness level later in adult life. Recent studies have shown that birth weight is positively correlated with adult muscle mass (Kensara et al., 2005; Kensara et al., 2006; Phillips, 1995, Gale et al., 2001, Kahn et al., 2000), muscle metabolism (Phillips, 1994), and muscle strength (Aihie Sayer, 1998). Therefore, adult muscle mass and strength might be modifiable by environmental influences acting at critical periods during early life development. Although the evidence that there is a link between fetal growth and chronic diseases later in life is strong, there are still limited studies that have investigated the impact of early life development on physical activity levels and its effects on health risk factors.

Family history:

It is suggested that the magnitude of the relationship between physical activity and CVD may be modified by a family history. It has previously been reported that cardiovascular risk factors such as hypertension, hyperlipemia, serum lipoprotein levels, BMI, waist-to-hip ratio, and fibrinogen are associated with a positive family history (Harrap, 1994; Humphries et al., 1995; Margaglione et al., 2000; Pankow et al., 1997). In addition, it has been reported that family history was found to be an independent factor from other factors (e.g. gender, smoking) in determining CVD risk factor in a number of different studies (Boer et al., 1999; Li et al., 2000; Liao et al., 1997; Myers et al., 1990; Nora et al., 1980; Pohjola-Sintonen et al., 1998; Roncaglioni et al., 1992). For example, a positive family history is generally associated with about a 1.5 to twofold increase in the risk of CHD among first-degree relatives (Friedlander, 1998). Thus, individuals with a high risk family history may not benefit or respond to an increase in specific levels of physical activity compared to those without a low risk family history. The mechanisms underlying this familial clustering have not been firmly established, but may include an increased susceptibility to atherosclerosis (Gaeta et al., 2000), poor diet and lack of exercise (Hawe et al., 2003).

Race and ethnicity:

It has been indicated that the prevalence of high risk factors for CVD varied widely according to the race and ethnicity among both sexes and across all ages. For example, data from the third National Health and Examination Survey (NHANES-III) showed that non-Hispanic blacks have a 1.8-fold greater rate of fatal stroke, a 1.5-fold increase in heart disease deaths, and a 5-fold increase in end-stage renal disease compared with non-Hispanic whites (The Joint National Committee on High Blood Pressure, 1993). It has been found that significant racial differences are influential in the distribution of lean tissue (Weinsier et al., 2000). Compared to white women, black women have been found to have a lower amount of trunk lean mass, which contains organ tissue, and lower energy requirements during sleep, at rest, during exercise, and throughout the day. These racial differences in energy requirements may have been due, in part, to a reduced amount of metabolically active organ mass relative to muscle mass in the black women. Taken together, these contributors may underestimate the actual benefit of physical activity on CVD.

Genetic/genotype:

A beneficial association between physical activity and CHD morbidity/mortality has been established and that genetic factors may explain this association (An et al., 2005; Blair et al., 1995; Paffenbarger et al., 1993-1). For example, An et al., (2005) has shown that the potential for physical activity to improve insulin sensitivity may be affected by genetic variations or differential gene expression on exercise. Several candidate genes or genotypes, including PPARGC1A, have been identified that appear to influence $\dot{V}O_{2\ max}$ (Rankinen et al., 2004; Lucia et al., 2005) (Russell et al., 2003; Short et al., 2003; Tunstall et al., 2002). PPARGC1A transiently controls glucose transportation and regulation, lipid and glucose oxidation, and modulates muscle oxidative capacity (Attie and Kendziorski, 2003). A single 2-minutes bout of exhaustive exercise is associated with increased PPARGC1A expression (Pilegaard et al., 2003). Russell et al., (2003) has further reported that there are 1.5-2.7 fold increases in PPARGC1A levels in men and women after a 6-16-week exercise training programme.

In addition, hepatic lipase gene is a key rate-limiting enzyme in lipid and lipoprotein metabolism (Auwerx et al., 1989; Couillard et al., 2001; Zambon et al., 2000) which can be modified by physical exercise (Giada et al., 1991; Mendoza et al., 1991). Variations in the hepatic lipase gene are associated with higher levels of intermediate density lipoprotein (Zambon et al., 2000), endothelial dysfunction (Fan et al., 2001) and coronary artery calcification (Hokanson et al., 2002). Therefore, a common promoter polymorphism in the hepatic lipase gene may responsible for differential effects of physical activity on CVD risk factors (Carr et al., 1999; Hokanson et al., 2001). In addition, the maximal aerobic power (in which one part is skeletal muscle property) is strongly genotype-dependent (Prud'homme et al., 1984). These studies may provide an important role of the gene-environment on the relationship between physical activity and CVD and, therefore, functional genetic variation could result in differential levels of expression after exercise, which would depend on genotype.

<u>Hormonal function:</u>

There are many studies have shown that hormonal function is associated with risk factors for CVD. Among these hormones is Leptin, an adipocyte-derived hormone which plays an integral role in endocrine regulation of metabolism (Zhang et al., 1994; Halaas et al., 1995; Masuzaki et al., 1997). Leptin released into peripheral circulation is thought to regulate fat mass and to reduce food intake and stimulate thermogenesis (Halaas et al., 1995). Independent of BMI, leptin has been proposed as a risk factor for CHD (Wallace el al., 2001; Soderberg el al., 1999; Guagnano et al., 2003). For example, hypertension is associated with an increase in the serum levels of leptin (Guagnano et al., 2003), and mutations in the leptin gene resulting in leptin deficiency cause morbid obesity and hyperinsulinemia in humans (Montague et al., 1997). Lakka el al., (2004) has suggested that leptin and leptin receptor genes are associated with the magnitude of the effects of regular physical activity on glucose homeostasis in non-diabetic individuals. Franks et al., (2003), Ruige et al., (1999) and Donahue et al., (1999), have reported that plasma leptin concentrations were significantly inversely ($P<0.001$) associated with self-reported habitual physical activity after adjustment for BMI.

There are several postulated biological mechanisms for the observed inverse association between physical activity and plasma leptin concentrations (Bornstein, 1997; Considine, 1997). Some investigators (Kosaki et al., 1996; Trayhurn et a.,l 1998; Scriba et al., 2000) have noted that exercise-induced modifications of the sympathetic nervous system results in increased concentrations of catecholamines which may attenuate leptin synthesis and release.

Other hormones such as estrogen and testosterone have diffuse effects on the cardiovascular system, including favourable effects on lipid profiles and fibrinolytic proteins (Mendelsohn and Karas, 1999), hypertension (Phillips et al., 1997), and inflammatory and thrombotic markers (Cushman et al., 1999). In a cross-sectional study by Gannage-Yared et al., (2006) showed that adiponectin is related to insulin sensitivity, TG and HDL-C independent of age and BMI. Another two prospective studies have examined the relationships between sex hormone-binding globulin (SHBG) and cardiovascular outcomes. In the Gyllenborg et al., (2001) study, it has been found that the SHBG was the main predictive variable of HDL, VLDL, and TG explaining 12%, 17%, and 17% of the variation after adjustment for age, BMI and smoking in healthy adult men. In the Lapidus et al., (1986) study, low SHBG concentrations have been found to be associated with increased overall cardiovascular mortality during 12 years of follow-up but were not adjusted for BMI. These studies suggested that conflicting results of cross-sectional and intervention studies of the risk factors for CVD, in part, may be explained by inter-individual differences or changes in hormone function. Therefore, the relationships between physical activity and risk factors for CVD may modified by hormonal function l (Adlercreutz et al., 1986; Wheeler et al., 1984).

<u>Skeletal muscle properties:</u>

Multiple lines of evidence have suggested that skeletal muscle properties may at least partly explain individual differences in health-related physical activity phenotypes and the effects of exercise training on various health-related variables. Skeletal muscle metabolism and enzyme activities have been shown to be modified by training (Saltin et al., 1983) and is estimated about 45 % of the variance in the proportion of skeletal muscle fibres is associated with inherited factors, and about 40 % is influenced by environmental factors (Simoneau and Bouchard, 1995). Storlien et al., (1996) has shown that the properties of the skeletal muscle play a major role in insulin-stimulated glucose disposal. In addition, studies observed a significant positive correlation between properties of the skeletal muscle and HDL-C and a negative correlation with serum total TG concentration (Tikkanen et al., 1991) and body-fat content (Wade et al., 1990). Tikkanen et al., (1998) has studied the associations of physical fitness and physical activity with serum lipids and lipoproteins in healthy men. They have found that heredity and genes of skeletal muscle fibre properties are important determinants of CHD risk profiles, and clearly have effects on both fitness level and physical activity.

Cardiovascular and nervous systems:

The cardiovascular system supports physical activity primarily by ensuring adequate delivery of blood carrying oxygen, substrates, and hormones to the exercising muscles. The removal of metabolic waste products from muscle, as well as the dissipation of heat from the body is other important cardiovascular functions during physical activity. The most functional cardiovascular responses involve the generation of the appropriate arterial blood pressure and blood flow to various organs (Rowell, 1993; Waldrop et al., 1996).

The central nervous system responds immediately to physical activity by increasing the efferent activity of the sympathetic nervous system to the heart and blood vessels while withdrawing parasympathetic activity (Kajiura et al., 1995; Rowell, 1993). For example, Sensory (e.g. afferent) nerves monitor the metabolic status of exercising muscles, as well as blood pressure and other factors (e.g. oxygen content, pH, and temperature) in several areas of the circulation, thus providing feedback to the central nervous system regarding the adequacy of cardiovascular responses (Waldrop et al., 1996). The nervous system responds to this challenge by increasing activity in the sympathetic nerves that release norepinephrine in the heart, thereby increasing the heart rate. Therefore, the basic pattern of response is an increase in heart rate, cardiac output and muscle blood flow with increased exercise intensity (Rowell, 1993). Therefore, disturbances in these systems may limit the response of the CVD risk factors to physical activity or exercising muscle.

2.7. Physical activity guidelines and recommendations:

There are at least 20 national and international consensus reports on physical activity which have been published over the past 15 years. Many of these reports have looked at specific outcomes such as hypertension (Fagard, 1991), obesity (Bouchard and Blair, 1999), or CHD (Smith and Blair, 1995), but most have taken a global approach to health (Bouchard et al., 1990).

2.7.1. ***THREE*** days/week of at least moderate physical activity for 30 minutes or more:

Morris J was one of the first to undertake a scientific study of the role of exercise in protection against CVD. By the 1950s, Morris et al., has shown that physical activity can protect against heart attack through studies of men engaged in a variety of occupations.

They reported that conductors working on London's double-decker buses experienced less than half the incidence of heart attacks as the sedentary drivers (Morris et al., 1953 and 1956). In 1958, Morris and Crawford, (1958) have embarked on a new prospective study of physical activity and other lifestyle characteristics in 18 000 men in sedentary jobs in the civil service. They have shown that men who engaged in regular aerobic exercise (e.g. fast walking) were only half as likely to have a heart attack as other men. In addition, the occupation descriptions were classified in terms of physical activity, by three scales: light jobs (e.g. bus-driver), active jobs (e.g. postman), and heavy jobs (e.g. dock labourer). They have also found that men physically active and heavy jobs have a lower incidence of CHD than men with light physically jobs.

However, based on these observations, the frequency, intensity, and duration for physical activity were not defined. In evaluating these factors, investigators have made considerable progress in quantifying physical activity threshold and their effects on certain risk factors for CVD. In many studies, it has been revealed that a programme of three days per week of at least moderate physical activity (equivalent to brisk walking, which might be expected to leave the participant feeling warm or slightly out of breath) for 30 minutes or more is the threshold level against the risk of CVD (Gwinup, 1975; Pollock et al., 1975; Milesis et al., 1976; Pollock and Jackson, 1977).

2.7.2. ***FIVE*** days/week of at least moderate physical activity for 30 minutes or more:

Britain's physical activity guidelines have long been indistinguishable from those of the Centres for Disease Control and Prevention (CDC) and the American College of Sports Medicine (ACSM) (Pate et al., 1995; DHHS-US, 1996). Since 1996, the Department of Health's advice for physical activity has been that adults should aim to take five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996). This recommended level of activity can be achieved either by doing all the daily activity in one session, or through several shorter bouts of activity of 10 minutes or more. The rationale being that the evidence indicates that episodes or bouts of at least 10 minutes are required to achieve health benefits (DeBusk et al., 1990; Ebisu, 1985). The activity can be lifestyle activity, or structured exercise or sport, or a combination of these.

The recommendation has been developed as an option for those who get little or no exercise and was originally formulated by a review of existing evidence concerning exercise in Expert Consensus in 1994 (Health Education Authority, 1994). About 45 experts from the UK and overseas participated in the three-day consensus to develop policies and strategies for promoting physical activity at national and local levels. From different population-based studies, the experts assessed the inverse gradient of different physical activity doses on blood pressure, blood lipids, diabetes, and body weight. They indicated that at least 30 minutes of at least 5 days a week can provide substantial health benefits. In addition, they have acknowledged that there are some experimental studies suggesting that two or three bouts of shorter duration may together be as effective as a continuous bout of half an hour.

2.7.3. Metabolic equivalent (MET) scores recommendations:

A shorthand method for estimating the amount EE during physical activity is the metabolic equivalent (MET). Each activity can be assigned a MET value which represents the ratio of the EE of the activity to the resting metabolic rate (RMR) (Blair et al., 1985; Ainsworth et al., 2000), which can be taken as numerically equivalent to EE using the following equation: MET*hr x (weight in kilograms/60). On the basis of 1 MET being equivalent to 60 kcal/hr for an adult with a body weight of 60 kg (Blair et al., 1985). Therefore, MET*time score can be used to quantify, in units of kcal and independent of body size, the amount of physical activity reported by an individual.

The MET values are usually multiplied by the time spent in a specific activity, and the results are summed to give a MET score in units of MET*minutes or MET*hours per day or week. The MET*hr per day value describes a daily average of total activity that takes into account different intensities of activity and is not limited by a minimum weekly frequency of activity. In addition, the MET*hr per day can comprise physical activity in multiple domains: leisure-time, occupation, commuting, household and gardening. This, therefore, may provide a different description of activity to the at least 3 or 5 days per week of moderate activity and may provide a different basis to explain the relationship between activity and CVD risk factors.

<u>At least 40 MET*hr/day of total physical activity:</u> The cut-off point of 40 MET*hr/day was based on a study by the Stanford Heart Disease Prevention Program conducted between 1979 and 1980. The study included random samples of more than 2000 men and women (aged 20-74 years) from four California towns in the US. The mean BMI was 24.0 and 25.0 for women and men, respectively. The self-reported assessment of total EE from a seven-day physical activity recall of work and leisure activities was used. Participants responded on a seven-point scale labeled extremely inactive = 1 to extremely

active = 7. This data were used by Blair et al., (1984 and 1985) to calculate the daily EE of participants in terms of MET*hr using averaged MET values for each activity level. They have found that individuals who have relatively active lifestyles have energy expenditures of at least 40 MET*hr/day, which is equivalent to 40 kcal/kg/day. This value is relatively constant for men and women across the age range.

Table 2.1 (below) illustrates how to calculate MET scores for one day. The MET*hr/day can be calculated as follows: [(hours of sleeping * 1 MET) + (hours of light activity * 1.5 METs) + (hours of moderate activity * 4 METs) + (hours of hard activity * 6 METs) + (hours of very hard activity * 10 METs)]. Converting the 40 MET*hr/day criterion to EE kcal/day is simply achieved by multiplying the 40 MET*hr/day by weight in kilograms/60 kilograms. Therefore, the 40 MET*hr/day was based on calculating the total daily MET scores spent in sleep, light, moderate, hard, and very hard activities. The assumption underlying the calculation of the total activity score is that most adults spend most of their waking hours in light activity. However, the relationship between selecting this level of activity and chronic diseases is not fully known.

450-750 MET*min/week (7.5-12.5 MET*hr) of at least moderate activity: Recently, the US has updated guidelines (Haskell et al., 2007) which specifies that adults should achieve a minimal range of 450 to 750 MET*min/week (7.5-12.5 MET*hr) of at least moderate activity. These values are based on the MET range of 3 to 6 for moderate-intensity activity and 150 minutes/week (3 days * 150 minutes = 450 and 5 days * 150 minutes = 750). The MET values are based on the Compendium of Physical Activities (Ainsworth et al., 2000). Thus, if a man or women briskly walked at 4 mph (5 METs) for 30 minutes 5 days a week, they would accumulate 750 MET*min/week of activity [(5 MET * 30 minutes) * 5 days = 750 MET*min/week], but if they jogged (8 METs) for 20 minutes 3 days a week, they would accumulate 480 MET*min/week [(8 MET * 20 minutes) * 3 days = 480 MET*min/week]. This guideline was developed by reviewing advances in pertinent physiologic, epidemiologic, and clinical scientific data, including primary research articles about new scientific evidence relating physical activity to health, and physical activity recommendations by various organizations. However, the recommended range of 450 to 750 MET*min/week is based on calculating the total MET*min scores spent in at least moderate physical activity only, but not other activities such as sleeping, sitting, and light activities.

Table 2.2: Calculation example for MET score for one day assuming that 1 MET*hr was equivalent to 60 kcal/hr for an adult with a body weight of 60 kg (Blair et al., 1985).

Type of activity	Total time spent (hour)	MET value for activity	Total MET*hr/day	EE (kcal/day)
Active person				
Sleep	8.0	1.0	8.0	480
Light activity	12.5	1.5	18.75	1125
Moderate activities	2.0	4.0	8.0	480
Hard activities	0.5	6.0	3.0	180
Very hard activities	1.0	10.0	10.0	600
Total	**24.0**		**47.75 MET*hr**	2865 kcal
Inactive person				
Sleep	9.0	1.0	9.0	540
Light activity	14.0	1.5	21.0	1260
Moderate activities	1.0	4.0	4.0	240
Hard activities	0.0	6.0	0.0	0.0
Very hard activities	0.0	10.0	0.0	0.0
Total	**24.0**		**34.0 MET*hr**	2040 kcal

2.8. Summary of the literature:

The purpose of this section was to summarize the existing evidence from the literature on the role of physical activity and fitness in mortality or death, active disease (e.g. CHD), and CHD risk factors (e.g. TC). After reviewing the epidemiologic and clinical evidence, a clear association is found between physical fitness and CVD/CHD. Indeed, many cross-sectional, follow-up, and intervention studies have shown that there is a greater longevity, a reduction in the risks of CHD and all-cause mortality in more fit individuals. While the importance of physical fitness is well-established, the association level of physical activity with CHD risk factorsand CHD risk is inconsistent across the different studies that have addressed this matter. In general, the current literature suggested that if people deemed active based on the methods of categorization for physical activity, approximately one quarter of deaths related to CHD could be prevented.

In the last 15 years much effort has been put into the development of physical activity guidelines for adults. Most international physical activity guidelines advocate moderate-intensity physical activity on most days of the week (e.g. Department of Health, 1996, ACSM 1996). However, the literature review has revealed that it is not quite clear why moderate activity is favourable to improve the risk of CHD. For example, Leon (page 21) has shown that there were 63 % higher fatal CHD events in Multiple Risk Factor Intervention Trial in men (aged 35 to 57 years) with lower levels of LTPA compared to those with a moderate level of LTPA. In contrast, Sesso (page 23) has concluded that only vigorous activities (expressed as kilojoules), but not moderate and light activities, are inversely associated with CHD risk in men (averaged age 57.7 years).

There is still considerable debate regarding the least amount of activity, in terms of duration, intensity and frequency that would provide health benefits. For example, early work by Paffenbarger and associates (Paffenbarger et al., 1986) revealed that regular physical activity (expending > 2000 kcal per week) was associated with an average increase in life expectancy of 1 to 2 years by the age of 80. Subsequent studies have shown that an average EE of about 1000 kcal per week is associated with a 20 % to 30 % reduction in all-cause mortality (Lee and Skerrett, 2001b; Paffenbarger et al., 1986 and 1993b). A value of 10000 steps/day is emerging documenting the health benefits for apparently healthy adults (Tudor-Locke C and Bassett DR, 2004). However, a goal of 10000 steps/day may not be sustainable for some groups, including older adults and those living with chronic diseases. A 40 MET*h per day has been recommended to differentiate between the inactive and active groups (Blair, 1985). However, recently, the US has updated guideline (Haskell et al., 2007) which specifies that adults should achieve a minimal range of 450 to 750 MET*min/week (7.5-12.5 MET*hr) of at least moderate activity. It is therefore difficult to provide clear public health guidelines solely in terms of physical activity.

The conflicting evidence presented in the literature may be due to limitations associated with the characterisation of physical activity and other methodological limitations of the studies. The different possible limitations can be summarized as follows.

Firstly, the complexity of physical activity which is assessed in various combinations of dimensions (e.g. fitness or EE) is an important limitation. While each dimension on its own is an important component of physical activity, no single dimension is sufficient to describe all aspects of physical activity. In addition, the most appropriate dimension of physical activity behaviour that best predicts CHD risk factors remains to be unclear.

Secondly, based upon the population being studied and the research objectives, each instrument of physical activity (e.g. questionnaire or pedometer) has different strengths and weaknesses. It is obvious that most cross-sectional studies have used self-reported questionnaires or diaries to measure levels of physical activity which may or may not be appropriate under different circumstance. In addition, they may also not provide sufficient information even in a single dimension.

Thirdly, variations between the studies in defining different physical activity measures (e.g. number of days/week of moderate activity or total MET scores), intensities (e.g. average walking can be defined as light or moderate intensity), programme durations, and or types of physical activity (LTPA or occupational activity), may influence the association between physical activity and the CHD risk factors. In addition, the best measure of physical activity that used to establish physical activity guidelines remains to be clarified. For example, Tanasescu (page 22) has concluded that total physical activity, running, weight training, and walking are associated with reduced CHD risk in US adult men, and the average exercise intensity is associated with reduced risk independently from the number of MET spent in physical activity. In contrast, another follow-up study by Siscovick (page 23) has found no association between regular vigorous activity (assessed by self-perception questionnaire) and the incidence of CHD death in men (aged 35-59 years).

Fourthly, the cited literature on the same health outcome as revealed by many studies is also controversial. For example, Dey (page 34) has shown that active former athletes have significant lower mean TC levels after adjustment for age, BMI and body fat % in 162 people aged 46.5 years than age-matched older non-athletes. In this study, total physical activity was expressed as mega joules/kg of body weight. However, Young (page 35) has found that the improvement in the total MET scores was not significantly decreased the TC levels in 807 men between the ages of 18 and 74 years.

Finally, while the characteristics of the population being studied are of great importance, the benefits of physical activity or fitness vary based on the health status, body composition, culture, gender, age, and ethnicity. Therefore, the physical activity dimensions of men and women have traditionally been different; with men engaging in more intense physical activity than women (DHHS-US, 1996). In contrast, women are engaged in substantial amounts of child care and household activities, each of which is difficult to assess. This suggests that the intensity of moderate or vigorous activity may not be generalised to some people.

Such limitations and discrepancies between studies may have important implications and lead to conflicting interpretations of the quantitative effect of physical activity on the risk of CHD. This may hinder the development of a coherent evidence-based approach to policy relating to physical activity. Consequently, data on physical activity presented in the literature may demonstrate the hazards of misinterpretation when monitoring population adherence to the Department of Health guidelines for physical activity. Therefore, there is a need to have a better understanding regarding this growing body of literature and to have a clearer image of future research regarding physical activity at the level of policy making and individual behaviours.

Although some of the previous studies have compared different physical activity dimensions or instruments between each other, no study to date, has conducted research comparing the relative importance of different categorization methods for physical activity as estimated by diverse physical activity measures (e.g. MET) on CHD risk factors within the same population. In addition, no study, to date, has conducted research on estimating different physical activity guidelines using different systems obtained from different physical activity instruments within the same population. This concern is shown in *Figure* 3.1. Therefore, without a clear understanding of the relationship between physical activity and CHD risk factors, it is difficult to adequately advise the public health authorities on the level of physical activity which can bring improvements in health.

Chapter 3: Hypothesis and structure of the thesis

Chapter 3 Hypothesis and structure of the thesis

3.1. Hypothesis:

The level of physical activity deemed to be sufficient to achieve good health as expressed by the different public health guidelines varies. Individuals can be described as being active if they achieve 30 minutes or more of at least moderate physical activity on at least 5 days of the week (Department of Health, 1996), if they achieve 30 minutes or more of at least moderate physical activity on at least 3 days of the week (Gwinup, 1975; Pollock et al., 1975), or if they accumulate more than 40 MET*h/day (Blair et al., 1984 and 1985). Examination of the published literature revealed that little is known regarding the extent to which the agreement between the categorisation of activity, using each of these methods, is consistent or coherent, and how they in turn, relate to ill-health within the same group of individuals. It is self-evident that categorisation according to whether an individual does or does not achieve 30 minutes of activity on 3 or 5 days each week would be likely to result in differences in the distribution between levels of activity. This mainly because individuals who achieve 30 minutes of activity on 4 days of the week would be categorised as 'inactive' by one method and 'active' by the other. Given that inactivity is often associated with increasing BMI, as well as age, smoking and ill-health, there is a need to determine the extent to which differences in the level of physical activity continue to account for differences in CHD risk after controlling for differences in BMI and other confounding factors.

The central hypothesis examined in this thesis was that *subjects who are categorised as physically inactive (or with lower levels of activity) would exhibit a phenotype with greater risk of CHD, than those who are categorised as active (or with higher levels of physical activity), an effect that persists after adjustment for differences in age, BMI and smoking. The magnitude of this effect is influenced by the method used to categorise physical activity.*

To explore this central hypothesis, three inter-related and testable hypotheses were established:

1. *Individuals deemed inactive/less active by one method of categorisation would not necessarily be deemed inactive/less active by another method.* In other words, the identification of inactivity, and distribution of individuals between different levels of

activity, is not consistent, but dependent on the guideline used as the basis for describing activity behaviour.

This hypothesis was initially tested in a secondary analysis of data from the NDNS (Adults 19-64 years) where the level of agreement between three methods of categorisation of subjects into inactive and active groups [see 5.3] was explored. One possible source of discrepancy between levels of agreement could be the coding system used to describe differences in the intensity of different tasks. This possibility was examined using data from a group of subjects who completed the same diary as used in the NDNS. In this regard, while activity was expressed as both continuous (MET scores) and categorical (inactive/active) variables, three different coding systems for assigning the energy cost of different types of activity (NDNS, Blair and IPAQ) were examined [see 12.3]. Finally, as the NDNS diary has not been previously validated against any other method of characterising physical activity, the level of activity obtained from the diary was compared against that derived from the IPAQ questionnaire [see 12.3].

2. *Inactivity, or less activity, is associated with a more adverse phenotype and greater estimated risk of CHD than those who are active in each of the three methods of categorisation. This effect also persists even after controlling for differences in BMI and adjustment for age, smoking and established ill-health.* In other words, differences in the level of physical activity can be shown to directly contribute to differences in the adverse phenotype and risk of CHD over and above that which could be otherwise explained by differences in BMI as well as age, smoking and established ill-health.

This hypothesis was tested by examining the effect of different levels of activity on blood pressure (SBP and DBP), TC, HDL-C and estimated CHD risk in men and women within a secondary analysis of the NDNS dataset using each of the three methods of categorisation where subjects were deemed either inactive or active [see 6.3]. The effect was expressed in terms of the size and statistical significance of the overall group effect as well as the proportion of the variance that could be directly attributed to differences in activity (partial eta squared). Having demonstrated the effect of BMI, age, smoking on these outcome variables [see 6.3], the analysis was repeated controlling for these confounding factors [see 6.3]. As the presence of pre-existing ill-health would also influence these relationships, the analysis was further repeated after excluding those individuals who were taking prescribed medicines [see 7.3]. The effect of using a new method of categorisation based on combining two of the established methods of categorisation (days/week and MET score) on CHD risk factors and estimated CHD risk was then explored [see 8.3]. The dose-response relationship between levels of activity and risk factors and estimated CHD risk was explored ever further by expressing the level of activity as categorical and continuous variables as days of activity per week, minutes per day of moderate physical activity and total MET*h per day [see 9.3]. Finally, the effect of physical activity on CHD risk factors and estimated CHD risk was determined where activity level was categorised according to self-perceived levels of overall activity or job activity [see 10.3].

3. *The benefit of being active, relative to inactive, in terms of estimated CHD risk depends on the method of categorisation*. In other words, if the distribution of individuals between different categories of physical activity varies with the method of categorisation, then this, in turn, will influence the magnitude of the difference between inactive and active groups.

This hypothesis was tested by first categorising the subjects into active and inactive groups using the three different methods and then examining whether there were significant differences in the estimated CHD risk between a) the three inactive groups, b) the three active groups and c) the size of the difference between the three sets of inactive and active groups [see 11.3].

3.2. Structure of the thesis:

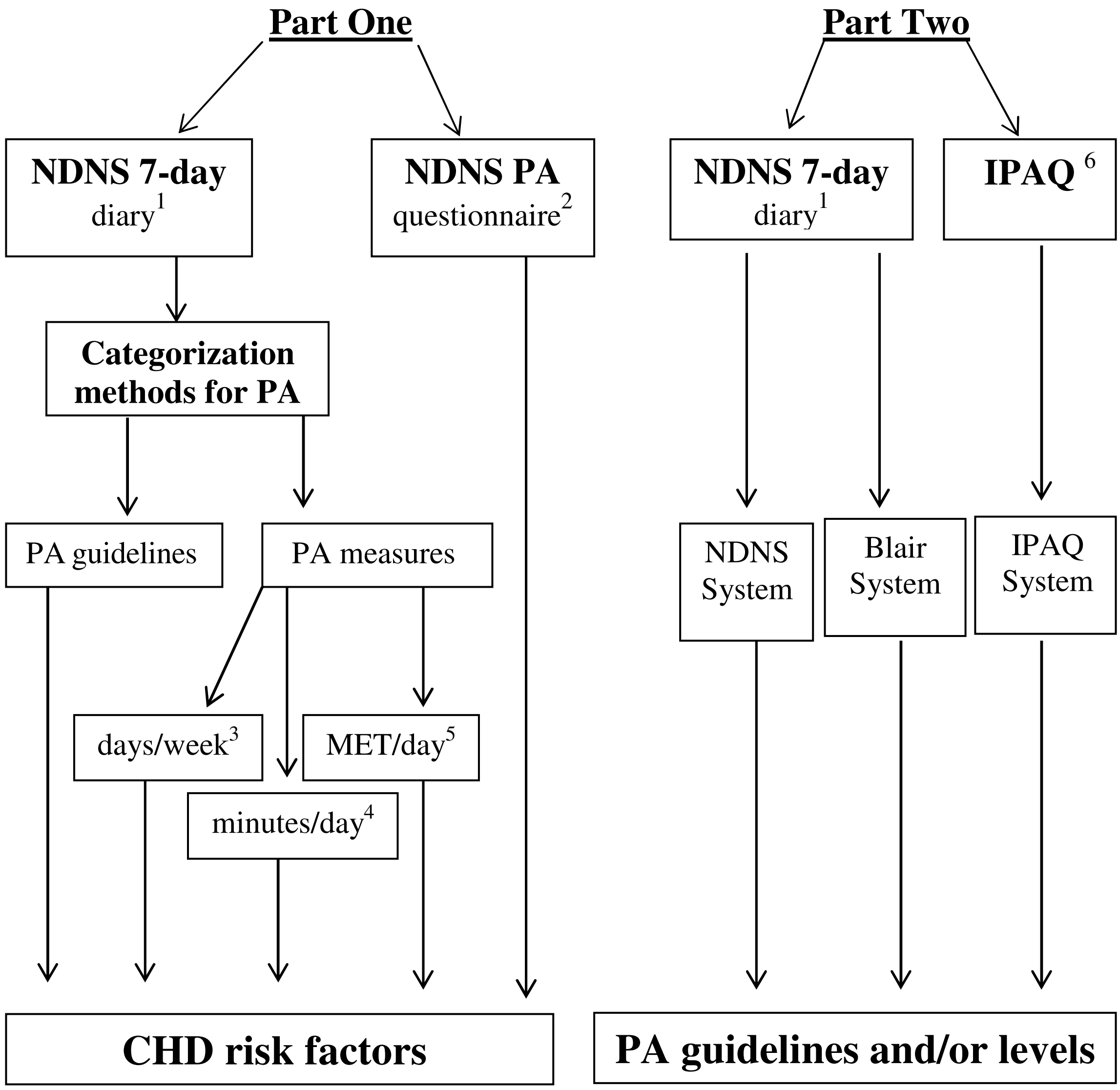


Figure 3.1: Schematic illustration of the thesis aim. This chart explains the influence of different physical activity (PA) guidelines and measures on the risk factors for coronary heart disease (CHD). In addition, it demonstrates the degree of agreement among the different physical activity guidelines and levels using different physical activity systems.

[1] NDNS: National Diet and Nutrition Survey
[2] the NDNS self-perception physical activity questionnaire
[3] days/week refers to the number of days/week of at least moderate activity for ≥ 30 minutes
[4] minutes/day refers to the number of minutes/day of at least moderate activity
[5] MET/day refers to total MET*h/day (MET : Metabolic equivalent)
[6] IPAQ: International Physical Activity Questionnaire

While physical fitness has been shown in the literature review to be an important factor in the modulation of the risk of CHD, there is no clear consensus regarding the levels of the optimal physical activity that is needed by adults to maintain good cardiovascular health. In addition, the most appropriate measure of physical activity that best used to establish physical activity guidelines remains to be unclear. The findings of this thesis will provide the literature and the public health authorities with data regarding the assessment of physical activity levels that may be influenced by using different methods (levels, measures or systems) for physical activity within the same population. Addressing this issue has important implications for the policy determination, interpretation and implementation, whereby different guidelines of physical activity are used to predict the CHD risk factors in both research and clinical settings. This data will also help in illustrating the relationship between physical activity and CHD risk factors more accurately. This in its turn will have substantial benefits for public health policies, as well as improving the overall quality of life in the society. The next *Chapter* (Methodological) describes the methods used to examine the hypothesis of this thesis in details.

Part One

Chapter 4: Methodology

Chapter 4 Methodology

This is an observational study in which physical activity behaviour, SBP, DBP, TC, HDL-C and BMI were determined in a group of volunteers aged 19-64 years who previously participated in the National Diet and Nutrition Survey (NDNS) programme. While there were some preliminary analyses conducted by the Food Standards Agency for the NDNS 2004, there was no attempt to investigate how physical activity behaviour maps against the different physical activity guidelines. There were also no studies that have investigated how the different methods affect the relationship between physical activity and risk factors for CHD. Furthermore, the single method (Department of Health guideline) used in the NDNS analysis was only examined in relation to dietary habits, blood pressure and BMI (without adjustments for confounding factors such as smoking) and not to an estimate of combined risk for CHD. The Food Standards Agency encourages scientists to have access to the NDNS data-set in order to investigate further secondary analyses. Therefore, this thesis was designed to use the NDNS data-set to address the effects that the use of different methods for distinguishing between activity and inactivity may have on the outcome of the analyses of the relationships between activity and CHD risk factors (such as SBP, DBP, TC, and HDL-C) in general and CHD risk in particular. This analysis has, to our knowledge, never been used to examine these relationships in the same individuals.

4.1 The National Diet and Nutrition Survey Programme:

The NDNS 2004 was commissioned and funded by the Departments of Health and the Food Standards Agency (in England, Wales and Scotland). It was carried out between July 2000 and June 2001 by the Social Survey Division of the Office for National Statistics in collaboration with the Medical Research Council Human Nutrition Research, Cambridge. Its aim is to provide a comprehensive cross-sectional picture of the dietary habits and the nutritional status of the population of Great Britain. The survey gives valuable information on adults aged 19 to 64 years and provides a sound basis for future food policy as it affects this group, and for the development of nutrition education programmes. In addition, the survey includes information on physical activity levels. This information helps to investigate the relationships between physical activity levels with CHD risk factors.

4.1.1. The sample design and selection:

The survey design included an interview to provide information about the socio-demographic circumstances of the respondent and their eating and drinking habits; a record of bowel movements, anthropometric measurements of the respondent (height, weight, waist and hip circumferences); health risk factor measurements (e.g. blood pressure); health status; smoking habits; socio-economic characteristics; and, for women in defined age groups, the use of the contraceptive pill, menopausal state and use of hormone replacement therapy, and a request for a sample of blood and a 24-hour urine collection. There was also a short interview conducted at the end of day seven (post-dietary and physical activity record interview) in which the respondents were asked about any problems they experienced or whether their behaviour had changed during the seven days, for example, if they had been unwell.

Explicit formal consent was required for taking the blood pressure and lipid samples from respondents. Respondents were given time to consider whether they wished to participate in the survey or not. Respondents were told that they were free to withdraw their consent to any procedure at any point, even after the consent form had been signed. In addition, consent to notify the respondent's General Practiceners (GP) of their participation in the NDNS survey and signed consent to send a record of the blood pressure and lipids measurements to the respondent's GP was sought. However, if the respondent was not registered with a GP and the blood pressure and lipids measurements were taken, duty of care passed to the survey doctor. If the respondent did not consent to informing their GP or the survey doctor then blood pressure and lipids measurements were not taken.

A nationally representative sample of adults aged 19 to 64 years living in private households was required. The sample was selected using a multistage random probability design with postal sectors. The sampling frame included all postal sectors within the mainland of Great Britain. A total of 152 postal sectors, divided into four fieldwork waves (each of three months duration) were selected as first stage units. With probability proportional to the number of postal delivery points, 38 sectors were allocated to each of the four fieldwork waves. These waves were required to cover a 12-month period in order to cover any seasonal behaviour changes, for example, potential reduction in the consumption of salad vegetables or decrease in physical activity level during the winter months. The 12-month fieldwork period was divided as follow:

- Wave 1: July to September 2000

- Wave 2: October to December 2000
- Wave 3: January to March 2001
- Wave 4: April to June 2001

The allocation took in the account the need to have approximately equal numbers of households in each wave of fieldwork and for each wave to be nationally representative. From each postal sector, 40 addresses were randomly selected. A letter was sent to each household in the sample in advance of the interviewer calling, telling them briefly about the survey.

Eligibility was defined as being aged between 19 and 64. Respondent volunteers with HIV or hepatitis B positive were excluded. Pregnant or breastfeeding women were excluded because their diet and physiology are likely to be sufficiently different from those of other similarly aged women as to possibly distort the results. In addition, if there was more than one adult between the ages of 19 and 64 years living in the same household, only one was selected at random to take part in the survey.

A token of appreciation a gift voucher for £10 was given to the respondent if the dietary and physical activity records were kept for the full seven days. Each respondent was also given a record of his or her anthropometric and blood pressure measurements.

4.1.2. Respondents and non-respondents:

Of the 5,673 addresses issued to the interviewers, 35 % (n = 1985) were not eligible for the survey. This high rate of ineligibility is mainly due to the exclusion of those aged under 19 years and those aged 65 or over. Just over one-third of the eligible sample (37 %; n 1364) refused outright to take part in the survey. Only 2 % (n = 73) of the eligible individuals were not contacted. Overall, 61 % (n = 2251) of the eligible sample completed the dietary interview (responding sample), including 45 % (n = 1,658 respondents, 741 men and 917 women) who completed a full seven-day physical activity diary (diary sample). For the anthropometric and blood pressure measurements, at least 93 % of the diary sample had the measurement taken, whereas 74 % of the diary sample consented to having a blood sample taken. *Appendix 2* shows the respondents and non-respondents in more details.

The potential for bias in any dataset increases as the level of non-response increases. Skinner and Holmes (2001) examined the potential impact of response and non-response bias to determine the implications of response and non-response for survey estimates within the NDNS in order to control for responders/non-responders. Without weighting to these differential response effects would lead to biased estimates because they will lead to under-representation of a particular group (estimates for different groups, for example, mean daily intake of energy in different age groups). The data presented in the NDNS have been weighted Skinner and Holmes (2001) for sex, age and region. Weighting factors were derived to compensate for differential non-response to compare the proportions, by sex, age and region, taking part in the survey with the corresponding proportion in the population using population estimates. It has been concluded that there was no evidence to suggest serious non-response bias in the NDNS data. However, the finding of this study should be interpreted with caution as the bias estimates were based upon assumptions about the total refusals and non-contacts for which only age, sex and region were known. Further weighting for non-response were not available for any other variables.

4.1.3. Fieldwork preparation:

Over the fieldwork period, a total of 88 interviewers from Office for National Statistics worked on the survey, the majority of working was accomplished in at least two waves. All the interviewers working on the survey had been fully trained by the Social Survey Division of Office for National Statistics and most had experience of working in other surveys in the NDNS programme, or of other surveys involving record keeping, such as the National Food Survey. Each interviewer attended a five-day residential briefing before starting the fieldwork. The briefing was conducted by researchers and other professional staff from the Social Survey Division of Office for National Statistics, from Human Nutrition Research, and from the Food Standards Agency and Department of Health. Phlebotomists attended for the last two days of the residential briefings.

Because this survey included invasive procedures such as venepuncture to take a blood sample, Ethics approval was gained for the feasibility and main stage survey from a Multi-centre Research Ethics Committee (MREC) and National Health Service Local Research Ethics Committees (LRECs).

Prior to the start of fieldwork, letters explaining the nature of the survey were sent by Office for National Statistics to Chief Constables of Police, Directors of Social Services and Public Health and to Chief Executives in Health Authorities who are responsible for one or more of the selected fieldwork areas (postal sectors). The letters also gave information on when and where the survey would take place and what is involved in the survey.

4.1.4. Health risk factor measurements:

The protocols for measuring blood pressure, blood lipids, weight and height are presented in *Appendix 3* at the end of this thesis.

Blood pressure measurement:

Of all the respondents who consented to blood pressure measurements, 119 (7 %) participants were taking prescribed anti-hypertensive medication at the time of measurement. For men and women in all age groups, the exclusion of those subjects taking anti-hypertensive prescriptions had a slight but insignificant effect (less than 1 %) on the mean values of SBP and DBP. Therefore, all respondents were included in the NDNS dataset. The main outcomes to be measured were SBP and DBP. Blood pressure was measured using the Dinamap 8100 oscillometric monitor. This device was previously used to measure blood pressure on the NDNS of young people aged 4 to 18 years (Gregory et al., 2000) and the Health Survey for England (Erens et al., 2001).

Blood lipids measurement:

The lipid profile included TC and HDL-C. In this survey, unlike in some of the previous NDNS surveys, the respondent was not asked to provide a fasting blood sample nor was the blood sample necessarily collected in the early morning. From clinical point of view, fasting and non-fasting TC and HDL-C values have been found to be equally acceptable for screening (Wilder et al., 1995; Desmeules et al., 2005). However, measurement of TG and glucose concentrations were not attempted in this survey because a fasting blood sample is required for these analytes and results from non-fasting samples would not have been interpretable. Blood samples were taken by a phlebotomist in the respondent's home in a non-fasting state. The blood samples were delivered to a local processing laboratory in the region of the fieldwork typically within 5 hours of collection. Ethics approval allowed for a maximum of two attempts to obtain the blood sample (maximum 30ml).

BMI measurement:

Measurements of standing height and weight were taken to calculate the BMI (weight [kg] /height [m]). Respondents unable to keep the correct posture for measurement of standing height, or with hair arranged in a 'permanent' style which affected the measurement of standing height were excluded. Each measurement was made twice, using the same protocol.

4.1.5. Subjective physical activity measurements:

The NDNS seven-day diary and the NDNS physical activity questionnaire can be found in the *Appendix* 4 and are available online at www.food.gov.uk.

1. *Seven-day diary physical activity:*

In this survey, the NDNS seven-day diary for physical activity was used. This diary has previously been used in the NDNS of young people aged 4 to 18 years (Gregory et al., 2000) and the Health Survey for England (Erens et al., 2001). Respondents were asked to record their physical activity over a period of seven days. The feasibility study has shown that the seven-day physical activity method was considered sufficient to collect information which would allow adults to be classified into broad bands of activity level, for example, very inactive, inactive or active (NDNS, 2004).

The first page of the NDNS seven-day diary, for each day collects information regarding the time spent in bed asleep (including napping), time spent at work or college on that day (including paid and unpaid work), and an opinion question asking them to assess whether they were more active, or as active or less active than usual that day. The second page for each day collects information about time spent in walking at an average pace, time spent in walking briskly, time spent in a range of listed activities, such as light and heavy housework, gardening, DIY (do it yourself) jobs and active caring, and time spent on any similar activities. The third page for each day collects information about time spent on a range of listed sports and leisure activities. The questions graded activity based on the intensity so that**,** for example, cycling leisurely along a flat road (moderate intensity) is recorded separately from cycling off road or up a hill (vigorous activity). The questions also asked about whether the respondent had got ‘out of breath or sweaty’ doing the activity, to help establish the intensity of the activity. In addition, the respondent was asked to report any time spent on any other similar activities and whether they had become ‘out of breath or sweaty’.

Respondents were told to record only activities that were not part of their everyday work. For example, a gardener should not record heavy gardening activities that he or she did as part of his/her everyday job because these were counted as part of the time he/she spent working that day. Respondents were asked to record only activities they had done for at least 10 minutes. Values of 10 or less minutes of activity were recorded as “zero” of activity; the rationale being that the evidence indicates that episodes or bouts of at least 10 minutes are required to achieve health benefits (DeBusk et al., 1990; Ebisu, 1985).

As part of the physical activity diary, all respondents were asked in a post- physical activity record interview to describe the kind of tasks they did in their work or college, for example, whether the work/college involved mainly sitting, standing, walking, lifting, carrying light loads, or hard physical labour. Then, the interviewer multiplied the time (hours) spent at work or college, obtained from the seven-day physical activity diary, by the intensity of 2 MET*hr values.

Information on duration, intensity and frequency of physical activity was required. With this information, the times spent in activities of moderate and vigorous intensity during the seven-day recording period were calculated and added together to give the total time spent in activities of "*at least moderate intensity*". Therefore, this measure was applied to all tested subjects even those who were classified to the vigorous physical activity group. In addition, the total periods of time spent in sleeping, sitting, work/college, household activities and leisure time physical activities were accumulated and calculated to represent a full one day of activity expressed in MET*hr (described below). This method has the advantage to recall about the time spent in sleep and in light, moderate, hard, and very hard activities. The assumption underlying the calculation of the total MET score is that most of the adults spend most of their waking hours in light activity.

2. *Physical activity questionnaire:*

As part of the NDNS survey, all respondents were given a short self-perception physical activity questionnaire. This questionnaire included only two questions to describe the perception of the respondents about their activity levels. These questions are:

1. Thinking about your (main) job in general, and including voluntary work, would you say that you are……
   1. very physically active,
   2. fairly physically active,
   3. not very physically active,
   4. or not at all physically active in your job?
2. In general and including things you do in your free time, compared to other people of your age would you describe yourself as……
   - very physically active,
   - fairly physically active,
   - not very physically active,
   - or not at all physically active?

4.1.6. Calculating the total physical activity scores (MET*hr/day):

The MET*hours per day (MET*hr/day) value describes a daily average of total activity that takes into account different intensities of activity and is not limited by a minimum weekly frequency of activity. In addition, the MET*hr per day can comprise physical activity in multiple domains: leisure-time, occupation, commuting, household and gardening. This, therefore, may provide a different description of activity to the at least 3 or 5 days per week of moderate activity and may provide a different basis to explain the relationship between activity and CHD risk factors.

Data from existing research (Blair, 1984) were used to develop the Physical Activity Diary Coding Guide by the NDNS. This new developed Coding Guide was used to calculate a total physical activity measured in MET*hr value for each activity on the prompt list derived from the NDNS diary.

The MET*hr value for each activity category was calculated as an average for the activities corresponding to that category. For example, vigorous/very vigorous activities have MET values ranging from 6.0 to 10.00. An average of 7.5 was taken based on the type of activities that could be coded as vigorous/very vigorous. Light activities were obtained by subtracting 24-hour minus times spent in sleep, moderate, hard, and very hard activities. The time (hours) spent in the light activities (including time spent at work or college) was multiplied by the intensity of 2 METs. Consequently, all activities (sleep, very light/light, moderate or hard/very hard) were grouped into different MET values. The total MET*hr score was derived by multiplying the duration of each activity (hours) by the average MET*hr score for the intensity of the activity. An example of how to calculate the total MET score for one day is given below in *Table* 4.1.

Table 4.1: Calculation of MET*h per one day based on the NDNS system.

Type of activity	**MET value for the type of activity**	**Total time spent (hour)**	**Total MET*hr scores**
Sleep	1.0	9.0	9.0
Very light/light activities (e.g. watching TV, cooking)	2.0	13.5	27.0
Moderate activities (e.g. brisk walking, light swimming)	4.0	1.0	4.0
Vigorous/very vigorous activities (e.g. football, weight lifting)	7.5	0.5	3.75
Total		24.0	**43.75 MET*hr**

Adopted from the NDNS 2004 (volume 4).

4.2. Data processing and analysis:

To address the above hypothesis (page 64) the first part of this thesis was designed to use the NDNS dataset. Three sets of subjective measures of physical activity (number of *"days/week of moderate activity of at least 30 minutes"*, *"minutes/day of moderate activity"* and "*MET*hr/day"*), obtained from the NDNS 7-day diary, and several risk factors for CHD (SBP, DBP, TC, HDL-C and BMI), were used. In addition, the NDNS self-perceived physical activity questionnaire was obtained from the same data-set. In this thesis, the British Hypertension Society (BHS) equation was also used to estimate the risk of CHD. These physical activity measures, CHD risk factors and estimated CHD risk were assessed in each individual in order to control any confounding factors that may exist between the different measurements.

The present data analysis included all men and women aged 19–64 years who had completed the CHD risk factors and seven-day diary physical activity. In analysing the findings of the thesis, the descriptive statistics were performed on all the variables to calculate the mean values for the entire of the sample. This sample included the proportion of subjects meeting the three days per week of at least moderate physical activity for 30 minutes or more (Gwinup, 1975; Pollock et al., 1975), five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996), and accumulative of at least total 40 MET*hr per day (Blair, 1984 and 1985). While there are two recommendations for MET scores, we have used in this Part of the study only the "≥ 40 MET*hr/day". The accumulative of 450-750 MET*min per week of at least moderate activity (Haskell et al., 2007) is considered in the Second Part of the thesis. In fact, while the NDNS data-set in this Part was secondarily analysed, the 450-750 MET*min was difficult to be determined. For simplicity, the following abbreviations for the categorization methods for physical activity (used in the guidelines) were used consistently all through this thesis:

- **30/3 guideline:** Three days per week of at least moderate physical activity for 30 minutes or more.
- **30/5 guideline:** Five days per week of at least moderate physical activity for 30 minutes or more.
- **MET40*h guideline:** Accumulative of at least total 40 MET*hr per day.
- **MET750*m guideline:** Accumulative of 450-750 MET*min per week of at least moderate activity.

On the basis of the physical activity guidelines, categorical variables (e.g. 30/5 guideline) were illustrated by using cross-tabulation to obtain the proportion of subjects reporting the same category consistently. In addition, Cohen's kappa statistic was used to assess the agreement of categorical of activity scores, in a table, after excluding the component which would be expected to occur from chance alone (Cohen, 1960). The value of kappa is usually between 0 and 1. If the results were made by chance, the value would be zero. The value of kappa is defined as

$$\kappa = \frac{p_0 - p_6}{1 - p_6}$$

If the results were in perfect agreement, the number of agreements would be equal to 1. The values of the kappa were classified as follow (Altman, 1991):

- very poor agreement = Less than 0.20
- fair agreement = 0.20 to 0.40
- moderate agreement = 0.40 to 0.60
- good agreement = 0.60 to 0.80
- very good agreement = 0.80 to 1.00

A number of studies have shown that the traditional risk factors such as SBP, DBP, TC and HDL-C levels have a potent impact on the overall risk of CHD (Lewis, B., 1984). In this thesis, these risk factors (SBP, DBP, TC and HDL-C) were treated as continuous outcomes and checked for normality by using histogram before the analyses. Consistently, the WHO guidelines (WHO, 1999) was used to indicate that high blood pressure, as defined below, passes a threat to health: normal systolic $\leq$ 139 mm Hg whereas high is $\geq$ 140; and normal diastolic $\leq$ 89 mm Hg whereas high is $\geq$ 90. In addition, the British Diabetic Association, (1998) was used which shows that a plasma TC concentration above 5.2 mmol/L, and HDL-C < 1.04 mmol/L for men and < 1.20 mmol/L for women represents an increase in health risk.

In this thesis, the British Hypertension Society (BHS) (Anderson et al., 1990) equation was used to estimate CHD risk (e.g. angina, non-fatal myocardial infarction, and death) as the percentage of the likelihood of an event over a period of 10 years. For example, a risk of 30 means that there is a 30 in 100 chance of an event in the next 10 years. The BHS provides a medical and scientific research forum to enable sharing of cutting edge research in order to understand the origin of high blood pressure and improve its treatment. An annual scientific meeting is held every September at a University Campus in the UK and Ireland. Importantly, one of the aims of the BHS is to calculate the risk of CHD. The risk factors included in this equation calculation are age, TC, HDL-C, SBP, DBP, treatment for hypertension, and cigarette smoking. BMI is not included in the equation assessment.

Several different approaches to predict the consequences of these adverse phenotypic traits have been developed to estimate the risk of ill-heath or death (i.e. CHD risk, CVD risk and the risk of all cause mortality). Each uses a common approach but not necessarily applies the same components or cut-offs. When this work started, the decision was taken to use the risk engine to predict CHD risk (BHS). This decision was largely determined by the nature of the data available within the NDNS dataset. Other risk engines were considered which have estimated a person's risk of having a CVD or CHD event over 5 to 10 years. Some equations (Assmann et al., 2002; Benetos et al., 2003) require other information that is not available in the NDNS database. For example the equation emerging from the IPC cohort (Benetos et al., 2003) requires information on heart rate, erythrocyte sedimentation rate, presence or absence of diabetes, and presence CVD disease and family history of cardiovascular disease, and pulse pressure, none of which were available in the NDNS database. Some of the equations were derived in populations outside the UK and would not necessarily reflect risk for a UK population (e.g. Benetos et al., 2003; ERICA Research Group, 1991; Grundy et al., 1999). The Framingham study (Grundy et al., 1999) is based on a population of men and women in another country (e.g. USA) and only over the age of 30 years. Some studies only provide equations for men (Benetos et al., 2003; Menotti et al., 2000; Tunstall-Pedoe, 1991). If the NDNS database were to used to predict outcomes by eliminating one sex or individuals outside a certain age range the power of the study would be reduced.

During the study, various groups proposed extending CHD risk to CVD risk which came together as the new 2005 Joint British Societies' (JBS-2) guidelines (JBS2, 2005) which also uses risk factors that are available in the NDNS database (blood pressure, smoking, TC, HDL-C and age category). There are advantages to estimating CVD, as opposed to CHD, risk as it embraces a broader range of disease outcomes. However, as so much of the analysis had been completed before the author became aware of the JBS-2 guidelines, the decision was taken to continue using the original CHD risk engine.

Again, for simplicity, the following abbreviations were used consistently all through this thesis:

- **CHD risk factors:** refers to SBP, DBP, TC and HDL-C.
- **eCHD risk:** refers to estimated of CHD risk.

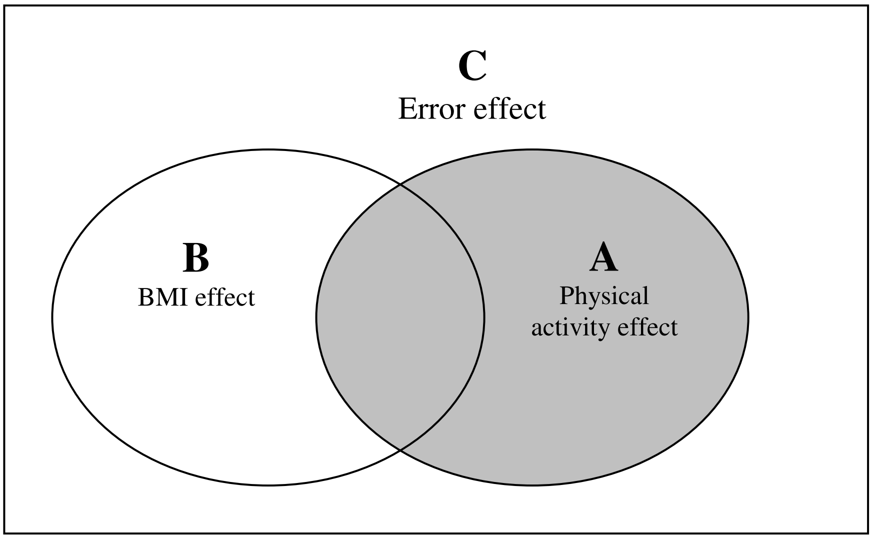
To test the above hypothesis, the General Linear Model (Univariate) was conducted to compare the values of the CHD risk factors (SBP, DBP, TC, HDL) and eCHD risk in subjects defined as active or inactive by 30/3, 30/5, and MET40*h guidelines. Participants achieving the 30/3, 30/5, and MET40*h guideline were considered active level. These guidelines are discussed in more detail in the *Chapter* 2 (Literature Review). The differences between the active and inactive groups were analysed separately for each guideline.

In addition, three different measures for physical activity were adopted to characterize physical activity in each subject. This reflects the measures which may give different results to characterize physical activity guidelines and levels.

The analysis was first carried out without any adjustment. Afterwards, to control for potential confounding factors, the relationships were adjusted for age, BMI and cigarette smoking. A growing body of evidence in the literature has demonstrated that the non-modifiable factors of age and gender, and the modifiable factors of smoking and BMI are the primary determinants of the SBP, DBP, TC and HDL-C levels, which collectively lead to an increase in the CHD risk (Smith et al., 2001; Yeo et al., 2001). For that reason, this thesis sought to examine the relative effects of physical activity on the CHD risk factors and eCHD risk after adjustments for age, smoking and BMI. In addition, it has been suggested that the gender might be an important modifier for the association between physical activity and the CHD risk factors and eCHD risk. Therefore, in this thesis, men and women were analyzed separately. Moreover, to address the possibility of the effect of medications, analysis was repeated with excluding those subjects who have been taking medications.

General Linear Model was also used to establish the variability in CHD risk factors and eCHD risk that is attributable to physical activity. It was used to analyse the data, because it allows regression analysis to be carried in the presence of fixed factors such as smoking, gender and categories of physical activity. It also allows physical activity to be analysed as an ordinal and as a continuous variable. Two commonly used measures of effect size in models involving fixed factors are 1) eta squared and 2) partial eta squared. They are equivalent to r squared values in regression analysis carried out without fixed factors.

Eta squared can be calculated as the ratio of the effect variance to the total variance. Thus, it is the proportion of the total variance that is attributed to a variable In contrast, the denominator of the partial eta squared formula is not the total variance, but the variance due to the effect variable plus error (Kirk, 1982; Tabachnick and Fidell, 1989): it excludes the variance due to the independent effects of other variables (see footnote to Figure 4.1). Omega squared, not used in the present thesis, is another statistic that can be used to examine the proportion of the variance in the population for a fixed effects model (Kirk, 1982; Tabachnick and Fidell, 1989).



For physical activity,

$$\text{Eta squared} = \frac{A}{\text{Total }(A+B+C)} \qquad \text{Partial eta squared} = \frac{A}{A + C}$$

C (error) represents the other factors that can not be explained in the model formula.

Figure 4 .1: Proportion of the variance that is attributable to each effect and the values used in the calculations of eta squared and partial eta squared.

Eta squared is more easily understood since it is the proportion of total variance attributed to the variable (physical activity in this study). The calculation of partial eta squared involves the same numerator by a smaller denominator (except when only one variable is used when eta and partial eta are the same). This is because the sum of squares associated with variables that overlap with physical activity are excluded from the denominator (see *Figure* 4.1) with the result that partial eta squared has a higher value than eta squared. Partial eta squared gives the contribution of each variable or interaction as if it were the only variable so that it is not masked by other variables. In addition the elimination from the denominator of variables that cannot be influenced (e.g. age and sex) can be seen as an advantage. A detailed discussion of the advantages and disadvantages of eta and eta squared is given in Keppel & Wickens 2004. SPSS prefers to display only partial eta squared.

In order to determine the dose-response relationships between physical activity and CHD risk factors and eCHD risk, applying dichotomous variables of physical activity defined from these guidelines does not provide any information illustrating any specific dose-response relationship. Therefore, the effects of the number of days/week of moderate activity, minutes/day of moderate activity and MET*hr/day were examined separately as categorical and continuous variables on the CHD risk factors and eCHD risk. These relationships were examined using the same analysis tests (General Linear Model) followed by multiple comparisons with Post Hoc Tests (Bonferroni). Trend analysis was checked by using the linear regression. In examining the relationship between physical activity and CHD risk factors and eCHD risk, three different types of analyses were undertaken:

1) Physical activity was used as a categorical variable (fixed factor) in the General Linear Model. This was particularly suitable for examining issues that related to central hypothesis of this thesis, which involved categorisation of subjects into active and inactive groups, according to physical activity guidelines. It is recognised that dichotomization of a continuous variable results in loss of power (equivalent to a loss of about 30% of data when continuous variable is used in the analysis). The loss of power is considerably less when 4 or more categories are used (and in some cases power may be increased - see below). Information was also available to allow categorisation of subjects into more than two categories. Thus physical activity was categorised into 4-5 categories for two reasons. First, this is helpful for presentation purposes. For example, it allows visual inspection of the dose response relationship in a simple way. This may not be obvious from examining a regression graph involving continuous variables, where deviations from certain parts of the regression line may be missed. Second, since the categorisation specifically included the cut-off points used to address the main hypothesis of this thesis, it is valuable for further evaluation of the data, in ways that may not be obvious when using continuous data in multiple regression analysis.

Three possible strategies were undertaken to define further categorical data for physical activity which would be more helpful in illustrating any dose-response or threshold in CHD risk factors and eCHD risk by physical activity:

1. Four categories measured in days/week (classified and used routinely by the NDNS).
    - none day/week (less active)
    - 1-2 days/week
    - 3-4 days/week
    - ≥ 5 days/week (more active)
2. Four categories measured in MET*hr/day scores:
    - < 40 MET/day (less active)
    - 40-45 MET/day
    - 45-50 MET/day
    - ≥ 50 MET/day (more active)
3. Five categories measured in number of minutes/day:

    For men:
    - Zero minute (less active)
    - 1.0-21.9 minutes
    - 22.0-54.9 minutes
    - 55.0.0-289.9 minutes
    - > 290.0 minutes (more active)

    For women:
    - Zero minute (less active)
    - 1.0-16.9 minutes
    - 17.0-39.9 minutes
    - 40.0-98.9 minutes
    - > 99.0 minutes (more active)

The rationale behind the cut-offs for categorisation was to achieve approximately equal numbers in each group without losing the cut-off point used in the guidelines. By doing this, it would enable an examination of any dose-response relative to existing guidelines and aid identification of any effects which might account for differences between guideline.

2) In addition to using physical activity as a categorical variable (fixed factor), it was used as an ordinal variable (covariate) in the General Linear Model. In this way, the total variability attributed to categories of physical activity can be partitioned into linear and non linear components (e.g. by examining the changes in partial eta squared). There is an

additional advantage in using ordinal data, which have to do with non-normal distribution of a continuous variable. Sometimes transformations are used to change a non-linear distribution to a normal or near normal distribution with the result that the power of the analysis is increased. The use of ordinal categorisation of continuous data can be regarded as a type of transformation, which can sometimes improve the power of the study (resulting in a higher partial eta squared) compared to the use of a continuous variable.

3) *Physical activity was used as a continuous variable in the General Linear Model.*

In order to examine the nature of the possible dose-response relationship, the NDNS data-set were explored using different curve fitting models (e.g. logarithmic, inverse, cubic, quadratic, S, and exponential) and linear model. The correlation coefficients generated by each model were compared to identify possible advantages of one model over another.

4.3. Power calculation:

Power calculations were undertaken using Sample Power 2.0 (Statistical Package for Social Sciences, Illinois, USA). Preliminary analysis of the NDNS dataset revealed the following variation in risk factors and eCHD risk, after adjusting for age and sex. eCHD risk was calculated by applying data from the NDNS to the prediction equation supplied by the British Hypertension Society .

	Mean ± sd
Systolic bp (mmHg)	125 ± 14
Diatolic BP (mmHg)	72 ± 10
Total Cholesterol (mmol/L)	5.3 ±1.0
CHD risk (in next 10 years)	6.5 ± 4.0

The NDNS database included measurements made on over 1600 individuals, but if it had complete data on risk factors on only half the subjects this would reduce the sample size to 800. Therefore the sample size calculations assumed that there were only 800 subjects and that these were equally distributed between active and inactive groups (400 per group). The possibility was considered at the outset that the risk factors or CHD risk could be affected differently by physical activity in men and women. If it was deemed necessary to analyse the data separately according to sex, then this would reduce the sample size to only 200 per group.

The Table below (4.2) shows the difference in risk factors and CHD between active and inactive groups that would be detected with 80% power and P = 0.05 (2 tailed) with a total sample size of 800 (400 per group) and 400 (200 per group) (equal variances assumed in each group).

Table 4.2: Power calculations.

	Mean ± sd*	Effect size**	
		200/group	400/group
Systolic bp (mmHg)	125 ± 14	3.9	2.8
Diastolic bp (mmHg)	72 ± 10	2.8	2.0
Total Cholesterol (mmol/L)	5.3 ± 1.0	0.3	0.2
CHD risk (in next 10 years)	6.5 ± 4.0	1.1	0.8

* Adjusted for age and sex
** The sample size is sufficiently large to detect the tabulated difference between the groups with 80% power and a P value of 0.05 (2 tailed)

Cohen J (1988) expressed effect size as a fraction of sd, for classification into small (0.2), moderate (0.5) and large (0.8) effect size. For a study population of 800 subjects (400/group) the standardised effect size is 0.2 indicating that the sample size is sufficiently large to detect a small effect size. This is consistent with clinical judgement: the sample size is adequate to detect a small and clinically relevant effect. Should it be deemed necessary to analyse men and women separately the power would still be adequate to detect relatively small effects (standardised effect size = 0.28).

Data are expressed as means and partial eta squared. A *P* value of less than 0.05 was considered statistically significant. Data analysis was performed on a personal computer with the statistical software package SPSS version 14.0 and 15.0.

Part One

Chapter 5: Distribution activity status according to different categorization methods for physical activity

Chapter 5 Activity status distribution according to different categorization methods for physical activity

5.1. Introduction:

Physical activity guidelines use different methods to categorize subjects into inactive and active. A literature review provides little or no information as to whether individuals deemed inactive by one method are also deemed inactive by another (i.e. little evidence of coherence and consistent "labelling"). Therefore, the aim of this *Chapter* was to investigate the hypothesis that individuals deemed inactive/less active by one method of categorization would not necessarily be deemed inactive/less active by another method. This also implies that those deemed active/more active by one method would not necessarily be deemed active/more active by another.

5.2. Methods:

To address the above hypothesis, three sets of statistics were used to compare different methods of categorizing subjects into inactive and active groups. A comparison of the followings was made:

a) Proportion of subjects categorized into inactive and active groups
b) Degree of agreement between different methods of categorization (the proportion categorized into inactive or active groups does not mean the methods agree in categorizing individual subjects into the same group)
c) Agreement between different methods of categorization after correction for chance. Cohen's kappa statistic (Cohen 1960) used as a measure of agreement beyond chance (i.e. it is chance corrected measure of agreement). The method is described in more detail in *Chapter* 4 (Methodology).

The following three methods of categorization were also compared:

1. 30/3 guideline: three days per week of at least moderate physical activity for 30 minutes or more (Pollock and Jackson, 1977).
2. 30/5 guideline: five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996)
3. MET40*h guideline: accumulation of at least total 40 MET*hr per day (Blair et al., 1984 and 1985)

5.3. Results:

a) *Activity status distribution according to three different categorization methods:*

A total of 1,658 adults (741 males and 917 females) completed the NDNS physical activity 7-day diary. *Table* 5.1 shows the distribution of the activity status according to different categorization methods of physical activity used in guidelines. The proportion of men deemed to be active by the 30/5 guideline (Department of Health guideline for physical activity) was approximately one third (34 %), and in women it was one quarter (25 %) of women. The proportion was higher when categorization was undertaken using the 30/3 (Men: 53 %, Women: 49 %) or the MET40*h guidelines (Men: 83 %, Women 72 %).

b) *Degree of the agreement between different methods of categorization:*

A cross tabulation of results obtained in men when the 30/5 and MET40*h methods of categorization were compared is shown in Table 5.2. The diagonals (top left and bottom right) indicate agreement. Therefore, the total agreement between the two methods is the sum of results in these cells (% + % = %). The off diagonals represent disagreement between methods (bottom left and top right). For example, interpreting the results from *Table* 5.2 indicate that the proportion of men (top right) who deemed active by the MET40*h guideline but inactive by the 30/5 guideline was 47 %. The results of all three comparisons are summarized in Table 5.3. It can be seen that agreement between methods agreed from 51 % (30/5 compared with MET40*h in men) to 81 % (30/3 compared with 30/5 in men).

c) *Cohen's kappa (agreement beyond chance):*

Table 5.3 also indicates Cohen's kappa (kappa = 0.18) for the comparison between 30/5 and MET40*h guidelines in men. The value of kappa = 0.18 means that there was only 18 % agreement in categorization beyond chance. This is substantially lower than the agreement of 51 % which was obtained without allowing for correcting categorization according to chance (there was a 50 % chance of correct categorization into active or inactive groups). The results of Cohen's kappa for all the other comparisons were shown in *Table* 5.3. In each case, the percentage agreement beyond chance (18-63 %) substantially lower than the agreement obtained without the chance correction (51-81 %).

Table 5.1: Distribution activity status according to different categorization methods for physical activity used in guidelines.

Categorization methods (used in guidelines)		Men	Women
3 days/week of moderate activity for 30 minutes or more	Inactive n (%)	348 (47)	467 (51)
	Active n (%)	393 (53)	450 (49)
5 days/week of moderate activity for 30 minutes or more	Inactive n (%)	488 (66)	684 (75)
	Active n (%)	253 (34)	233 (25)
Accumulative of at least total 40 MET*hr/day	Inactive n (%)	126 (17)	254 (28)
	Active n (%)	615 (83)	663 (72)
Total (n)		741	917

Table 5.2: A cross tabulation of results obtained in men when the 30/5 and MET40*h methods of categorization.

Methods of categorization		MET40*h guideline	
		Inactive (%)	Active n (%)
30/5 guideline	Inactive n (%)	**17**	47
	Active n (%)	< 1	**34**

Table 5.3: Degree of the agreement between different categorization methods for physical activity (used in guidelines).

% of agreement between guidelines	**a) 30/3 b) 30/5**		**a) 30/3 b) MET40*h**		**a) 30/5 b) MET40*h**	
	Men	women	Men	women	Men	women
% of inactive by both [1]	47	51	16	26	17	27
% of active by both [2]	34	25	52	47	34	25
% of active by a/ inactive by b [3]	19	24	< 1	< 1	< 1	< 1
% of active by b/ inactive by a [4]	0	0	31	25	49	47
% of agreement	81	76	68	73	51	52
Kappa	0.63	0.52	0.31	0.45	0.18	0.22

[1] % of inactive by both: if the subjects deemed inactive by either guidelines
[2] % of active by both: if the subjects deemed active by both guidelines
[3] % of active by a/ inactive by b: if the subjects deemed active by one guideline (a) but considered inactive by the other guideline (b)
[4] % of active by b/ inactive by a: if the subjects deemed active by one guideline (b) but considered inactive by the other guideline (a)

5.4. Discussion:

This thesis raised three issues for discussion. *Firstly*, using the 30/5 guideline, the overall results of this *Chapter* showed a similar proportion of subjects as active (34 % of men and 25 % of women) as those obtained using the same guideline (30/5) in the Food Standards Agency analysis of NDNS 2004 (36 % of men and 26 % of women). The small discrepancy was due to the slight difference in the number of subjects included in the analysis. *Secondly*, and more importantly with respect to hypothesis testing, this thesis generally showed substantial discrepancies between different methods of categorizing subjects who are inactive and active groups. Thus, the proportion of subjects deemed to be active varied from 51-81 % in men (49-19 % deemed to be inactive). The agreement between methods was not good so that, for example, only about half of the subjects would be classified as active by 30/5 and MET40*h methods of categorization. And the chance corrected measures of agreement was generally poor or fair. *Thirdly*, the discrepancy between different methods of categorization could have major implications in the effect of physical activity on CHD risk factors and eCHD risk. However, this depends on the extent to which physical activity contributes to these CHD risk factors and eCHD risk. This issue is dealt with in the next *Chapter* (6).

5.5. Conclusion:

There was a major discrepancy between methods of categorization as the proportion of men deemed to be active (51-81 %) and inactive (49-19 %), and the agreement between methods was generally poor or fair (18 to 63 % beyond chance). This thesis supported the examined hypothesis that subjects deemed to be active by one method of categorization were not necessary deemed to be active by another. Conversely, subjects deemed to be inactive by one method of categorization were not necessarily deemed to be inactive by another method. The effect of different methods of categorization of physical activity on CHD risk factors and eCHD risk is dealt with in the next *Chapter*.

<u>Part One</u>

Chapter 6: The impact of different categorization methods for physical activity on CHD risk factors and eCHD risk

Chapter 6 Impact of different categorization methods for physical activity on CHD risk factors and eCHD risk

6.1. Introduction:

Although there is a general consensus among public health and medical authorities that physical activity has beneficial effects on CHD risk factors and eCHD risk, the level of physical activity deemed to be sufficient to achieve good health (expressed as public health guidelines) is still variable. Therefore, the aim of this *Chapter* was to compare the values of the CHD risk factors (SBP and DBP, TC and HDL-C) and eCHD risk in inactive versus active within each categorization method for physical activity (used in guidelines) before and after adjustments for age, BMI and smoking.

6.2. Methods:

This *Chapter* compares the levels of SBP, DBP, TC, and HDL-C individually and then combines these CHD risk factors to estimate the risk of CHD (eCHD) in subjects classified as active or inactive according to three different categorization methods for physical activity. The differences between the active and inactive groups were analysed for each method separately. The subjects were categorized based on the following methods used in the guidelines:

a) 30/3 guideline: Three days per week of at least moderate physical activity for 30 minutes or more (Pollock and Jackson, 1977).
b) 30/5 guideline: Five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996)
c) MET40*h guideline: Accumulative of at least total 40 MET*hr per day (Blair et al., 1984 and 1985)

The data were analysed using the General Linear Model, both before and after adjustment for the confounding variables: age, BMI and smoking. Partial eta squared was used as a measure of effect size (proportion of the variance in the outcome that is attributable to physical activity): the ratio of physical activity variance to physical activity plus error. The method is described in more details in *Chapter* 4 (Methodology).

6.3. Results:

1. <u>Gender interaction:</u>

Table 6.1 shows the characteristics of the participants. Only those subjects who completed the NDNS physical activity 7-day diary and CHD risk factors were used in this thesis. In a preliminary study, the General Linear Model showed significant differences between men and women in eCHD risk and all CHD risk factors (except TC, P = 0.705). Therefore, men and women were analysed separately. The below *Table* 6.2 and *Figure* 6.1 provide information about differences and possible mechanisms according to gender interaction.

Before any formal statistical analysis was undertaken the NDNS data were examined for possible gender*physical activity interactions using the General Linear Model. An interaction was considered to be present when the homogeneity of regression could not be established (P value for gender*physical activity interaction < 0.05). The Table below (6.2) shows that there were a number of significant interactions involving categorical, ordinal and continuous variable analysis of physical activity. These occurred when lipids and eCHD risk were the dependent variables and not when blood pressure was the dependent variable. *Figure* 6.1 shows two examples of the way in which physical activity affected men and women differently with respect to TC and eCHD. For consistency it was decided to analyse the data for men and women separately (especially since the loss of power would not be great). However, these interactions were considered to be important and worthy of further discussion.

Table 6.1: The characteristics of the participants.

Health outcomes		Male	Female
SBP (mm Hg)	Mean (SD)	130.3 (14.9)	122.7 (16.5)
	≤ 139 n (%)	572 (77.9)	793 (86.8)
	≥ 140 n (%)	162 (22.1)	121 (13.2)
DBP (mm Hg)	Mean (SD)	74.2 (11.4)	69.0 (10.6)
	≤ 89 n (%)	682 (92.4)	885 (96.8)
	≥ 90 n (%)	56 (7.6)	29 (3.2)
TC (mmol/L)	Mean (SD)	5.3 (1.2)	5.3 (1.2)
	< 5.2 n (%)	269 (49.5)	326 (49.4)
	≥ 5.2 n (%)	274 (50.5)	334 (50.6)
HDL (mmol /L)	Mean (SD)	1.1 (0.32)	1.3 (0.38)
	High [1] n (%)	281 (52.5)	287 (43.5)
	Low [1] n (%)	254 (47.5)	373 (56.5)
eCHD risk [2]	Mean (SD)	9.2 (7.6)	4.3 (5.7)
Total (n)		**741**	**917**

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] High HDL: in men ≥1.04; in women ≥ 1.20. Low HDL: in men < 1.04; in women < 1.20

[2] eCHD risk: Estimation the percent likelihood of developing CHD over a period of 10 years

Table 6.2: P value for a gender interaction in the effect of physical activity on the CHD risk factors and estimated CHD risk, according to different criteria for physical activity, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

Physical activity (different methods)	**CHD risk factors**				**eCHD risk**
	SBP P value	**DBP** P value	**TC** P value	**HDL-C** P value	P value
Categorical					
30/3 guideline [1] (2 categories)	0.318	0.641	0.051	0.249	0.031 *
30/5 guideline [1] (2 categories)	0.594	0.990	0.472	0.300	0.113
MET*hr/day guideline [2] (2 categories)	0.925	0.989	0.014 *	0.057	0.029 *
30/3 + MET*hr/day [3] (3 categories)	0.849	0.991	0.022 *	0.123	0.026 *
30/5 + MET*hr/day [4] (3 categories)	0.956	0.981	0.067	0.125	0.055
days/week [5] (4 categories)	0.665	0.831	0.208	0.676	0.149
MET*hr/day (4 categories)	0.803	0.997	0.027 *	0.076	0.093
minutes/day [6] (5 categories)	0.948	0.988	0.108	0.512	0.104
Ordinal					
30/3 + MET*hr/day [3] (3 categories)	0.519	0.797	0.007 *	0.052	0.007 *
30/5+ MET*hr/day [4] (3 categories)	0.682	0.948	0.080	0.063	0.019 *
days/week [5] (4 categories)	0.267	0.572	0.109	0.237	0.026 *
MET*hr/day (4 categories)	0.212	0.649	0.113	0.109	0.135
minutes/day [6] (5 categories)	0.260	0.712	0.025 *	0.161	0.035 *
Continuous					
day/week [5]	0.506	0.984	0.172	0.128	0.016 *
MET*hr/day	0.164	0.520	0.258	0.962	0.391
minute/day [6]	0.207	0.761	0.111	0.763	0.267

* Significantly different due to gender interaction $P < 0.05$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; HDL-C: high density lipoprotein-cholesterol; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for ≥ 3 or 5 days per week, respectively

[2] Accumulative of at least total 40 MET*hr/day

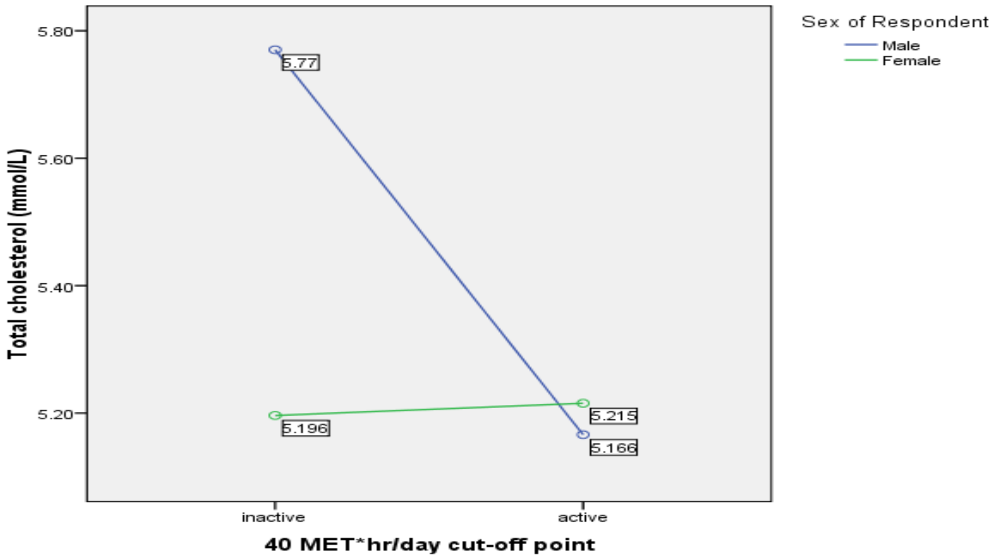
[3] Combined 30/3+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥ 3 days/week of moderate activity for ≥ 30 minutes" guidelines

[4] Combined 30/5+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥5 days/week of moderate activity for ≥ 30 minutes" guidelines

[5] day/week refers to the number of days/week of at least moderate activity for ≥ 30 minutes

[6] minute/day refers to the number of minutes/day of at least moderate activity

(**A**)



(**B**)

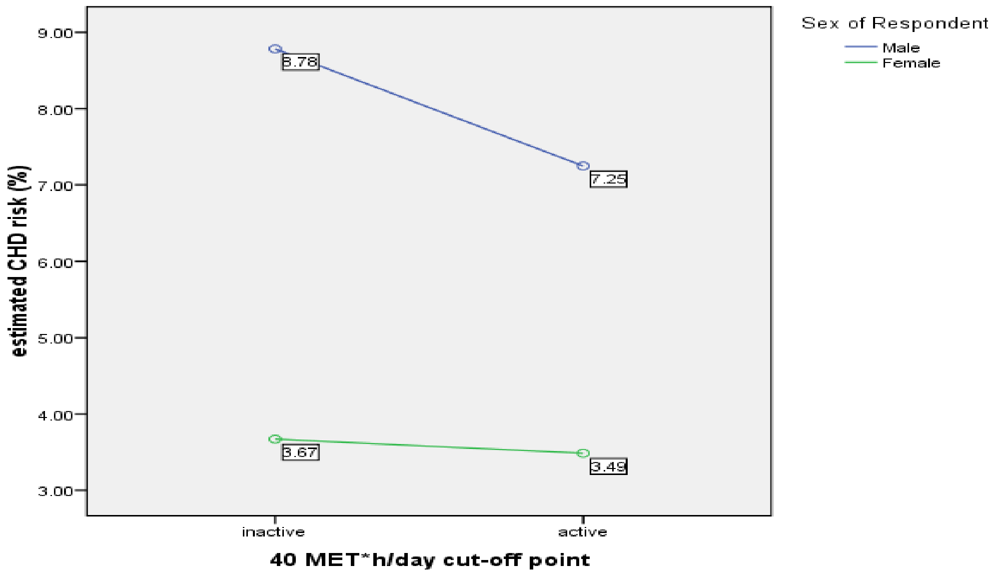


Figure 6.1: Gender interaction in total cholesterol (A) and estimated CHD (B) using the 40 MET*hr/day cut-off point, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

2. <u>*Association of different methods of categorization for physical activity with CHD risk factors and eCHD risk before adjustment for the confounding factors:*</u>

The results of this initial analysis are presented in *Table* 6.3. Analysing this data have shown that men who considered as active by the 30/5 guideline had significantly greater values of HDL-C and lower values of TC and eCHD risk ($P < 0.05$) compared to the inactive group. However, the values of SBP and DBP were not significantly different among the two groups. In women, while the levels of SBP, DBP and eCHD risk were significantly lower ($P < 0.05$) in the active group compared to the inactive group, the TC and HDL values were not significantly different.

Men who would be considered active by the 30/3 guideline had significantly lower values of DBP, TC, HDL-C and eCHD risk ($P < 0.05$) compared to the inactive group. On the contrary, the SBP values were not significantly different between the two groups. In women, the values of SBP and eCHD were significantly lower ($P < 0.05$) in the active group whereas the DBP, TC and HDL-C values were not significantly different.

Men defined as active using the MET40*h guideline had significantly higher and lower values of HDL-C and eCHD risk ($P < 0.05$), respectively. Other factors were not significantly different. In women, while the values of SBP and eCHD risk were significantly higher in the active group ($P< 0.05$) compared to the inactive women, the other CHD risk factors were not significantly different.

On the other hand, although some of the significant differences were found in these CHD risk factors and eCHD risk between the active and inactive groups defined by each physical activity guideline, the proportion of the variance was small. For example, in the men using the 30/3 guideline, the partial eta squared values showed that physical activity explains < 2 % variations for SBP and DBP, < 3 % variations for TC and HDL-C, and < 5 % variation for eCHD risk. In women, the partial eta squared values showed that < 1 % variations for SBP and DBP, < 2 % variations for TC and HDL-C, and < 3 % variation for eCHD risk were determined by physical activity. Same proportions were also found when eta squared was applied in both men and women.

In addition, this chapter indicated that the eCHD risk for the active groups defined by each of these physical activity guidelines appeared to be different in both genders, but not the CHD risk factors levels. For example, the eCHD risk of the active men defined by the 30/3, 30/5 and MET40*h guidelines were 7.6 %, 7.3 and and 8.8 %, respectively.

Table 6.3: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk between inactive and active groups of men (a) and women (b) as defined according to different categorization methods that are used in the physical activity guidelines.

(a)

Categorization methods (used in guidelines)		**CHD risk factors**				**eCHD risk** %
		SBP mmHg	**DBP** mmHg	**TC** Mmol/L	**HDL-C** mmol/L	
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	131.4 (*242*)	75.7 (*242*)	5.5 (*252*)	1.02 (*252*)	11.0 (*180*)
	Active: Mean value (n)	129.3 (*271*)	72.9 (*271*)	5.1 (*281*)	1.11 (*281*)	7.6 (*210*)
	P value	***0.056***	***0.001***	***0.001***	***0.001***	***0.000***
	Eta squared	***0.005***	***0.015***	***0.023***	***0.020***	***0.050***
	Partial eta Squared	***0.005***	***0.015***	***0.023***	***0.020***	***0.050***
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	130.9 (*338*)	74.7 (*338*)	5.4 (*351*)	1.04 (*351*)	10.2 (*254*)
	Active: Mean value (n)	129.1 (*175*)	73.2 (*175*)	5.1 (*182*)	1.11 (*182*)	7.3 (*136*)
	P value	***0.123***	***0.094***	***0.033***	***0.016***	***0.000***
	Eta squared	***0.003***	***0.004***	***0.009***	***0.011***	***0.034***
	Partial eta Squared	***0.003***	***0.004***	***0.009***	***0.011***	***0.034***
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	132.5 (*84*)	75.5 (*84*)	5.4 (*86*)	1.00 (*86*)	11.5 (*59*)
	Active: Mean value (n)	129.8 (*429*)	73.9 (*429*)	5.3 (*447*)	1.08 (*447*)	8.8 (*331*)
	P value	***0.080***	***0.175***	***0.165***	***0.044***	***0.011***
	Eta squared	***0.004***	***0.003***	***0.004***	***0.008***	***0.017***
	Partial eta Squared	***0.004***	***0.003***	***0.004***	***0.008***	***0.017***

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Categorization methods (used in guidelines)		CHD risk factors SBP mmHg	DBP mmHg	TC mmol/L	HDL-C mmol/L	eCHD risk %
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	124.9 (*288*)	69.6 (*288*)	5.4 (*313*)	1.27 (*313*)	5.3 (*212*)
	Active: Mean value (n)	120.5 (*279*)	68.4 (*279*)	5.3 (*336*)	1.31 (*336*)	3.4 (*220*)
	P value	***0.000***	***0.085***	***0.160***	***0.171***	***0.000***
	Eta squared	***0.018***	***0.004***	***0.003***	***0.003***	***0.030***
	Partial eta squared	***0.018***	***0.004***	***0.003***	***0.003***	***0.030***
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	123.6 (*416*)	69.4 (*416*)	5.4 (*475*)	1.28 (*475*)	4.8 (*313*)
	Active: Mean value (n)	119.9 (*151*)	67.6 (*151*)	5.2 (*174*)	1.30 (*174*)	3.1 (*119*)
	P value	***0.004***	***0.031***	***0.143***	***0.647***	***0.007***
	Eta squared	***0.010***	***0.006***	***0.003***	***0.000***	***0.017***
	Partial eta squared	***0.010***	***0.006***	***0.003***	***0.000***	***0.017***
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	125.1 (*146*)	70.1 (*146*)	5.4 (*161*)	1.27 (*161*)	5.5 (*105*)
	Active: Mean value (n)	121.8 (*421*)	68.6 (*421*)	5.3 (*488*)	1.29 (*488*)	4.0 (*327*)
	P value	***0.010***	***0.068***	***0.520***	***0.496***	***0.015***
	Eta squared	***0.008***	***0.004***	***0.001***	***0.001***	***0.014***
	Partial eta squared	***0.008***	***0.004***	***0.001***	***0.001***	***0.014***

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: estimation of the percent likelihood of developing CHD over a period of 10 years

3. <u>*The associations of the CHD risk factors and eCHD risk with age, BMI and smoking:*</u>

In this *Chapter*, the effects of age groups, BMI categories and smoking habits on the CHD risk factors and eCHD risk were examined. Because there was small number of subjects in the first BMI category (BMI < 20), BMI quartiles were also applied and examined. The mean age was 42 years (12.2 SD) for both genders. The BMI means were 27.2 and 26.5 for men and women, respectively.

The age categories used in the thesis were pre-specified by the original NDNS dataset. *Tables* 6.4-6.6 present the extent to which CHD risk factors and eCHD risk are explained by different age groups, BMI and smoking habits. For instance, the results indicated that the eCHD risk associated with age was significantly ($P < 0.001$) higher for older age groups (50-64 years old) compared to younger age groups (19-24 years). In addition, the results showed that women in the quartile 1 group (BMI mean = 21) had significant lower ($P < 0.001$) in the levels of SBP (120 mm Hg) compared to women in the quartile 4 (BMI mean = 34) (128 mm Hg). Based on the smoking habits, the smoking groups of men and women had significantly lower HDL-C levels ($P < 0.05$) compared to those who do not smoke. Since age, BMI and smoking habits within each gender influenced the CHD risk factors and eCHD risk (main effects), it is important to adjust for these variables when examining the relationship between different methods of categorization of physical activity and CHD risk factors and eCHD risk.

Table 6.4: CHD risk factors and estimated CHD risk in men (a) and women (b) according to age of men (a) and women (b). P values and partial eta squared are shown for analysis using age as a categorical, ordinal and continuous variable, after adjustment for physical activity, BMI and smoking.

(a)

Age groups [1]	**CHD risk factors**				**eCHD risk %**
	SBP mmHg	**DBP mmHg**	**TC mmol/L**	**HDL-C mmol/L**	
19-24 years old Mean value (n)	 128 * (40)	 65.0 ** (40)	 4.5 ** (32)	 1.00 (32)	 0.3 ** (32)
25-34 years old Mean value (n)	 125 ** (105)	 67.4 ** (105)	 5.1 * (78)	 1.02 (78)	 2.7 ** (78)
35-49 years old Mean value (n)	 130 * (205)	 77.7 (205)	 5.3 (152)	 1.03 (152)	 8.3 ** (152)
50-64 years old Mean value (n)	 135 (163)	 78.4 (163)	 5.6 (129)	 1.12 (128)	 16.5 (127)
P value (categorical)	***< 0.001***	***< 0.001***	***< 0.001***	***0.046***	***< 0.001***
Partial eta squared	***0.066***	***0.196***	***0.069***	***0.021***	***0.581***
P value (ordinal (Ptrend))	***< 0.001***	***< 0.001***	***< 0.001***	***0.011***	***< 0.001***
Partial eta squared	***0.049***	***0.155***	***0.065***	***0.017***	***0.549***
P value (continuous)	***< 0.001***	***< 0.001***	***< 0.001***	***0.016***	***< 0.001***
Partial eta squared	***0.065***	***0.140***	***0.067***	***0.015***	***0.677***

(b)

Age groups [1]	CHD risk factors				eCHD risk %
	SBP mmHg	DBP mmHg	TC Mmol/L	HDL-C mmol/L	
19-24 years old Mean value (n)	117 ** (57)	63.4 ** (57)	4.5 ** (42)	1.16 * (42)	-0.4 ** (42)
25-34 years old Mean value (n)	116 ** (131)	66.8 ** (131)	4.9 ** (95)	1.21 (95)	0.3 ** (95)
35-49 years old Mean value (n)	120 ** (212)	69.9 (212)	5.2 ** (165)	1.27 (165)	3.1 ** (165)
50-64 years old Mean value (n)	134 (167)	71.9 (167)	6.1 (127)	135 (127)	10.5 (126)
P value (categorical)	***< 0.001***	***< 0.001***	***< 0.001***	***0.005***	***< 0.001***
Partial eta squared	***0.198***	***0.058***	***0.181***	***0.030***	***0.561***
P value (ordinal (Ptrend))	***< 0.001***	***< 0.001***	***< 0.001***	***< 0.001***	***< 0.001***
Partial eta squared	***0.149***	***0.057***	***0.161***	***0.029***	***0.467***
P value (continuous)	***< 0.001***	***< 0.001***	***< 0.001***	***< 0.001***	***< 0.001***
Partial eta squared	***0.194***	***0.057***	***0.188***	***0.026***	***0.586***

Significantly different from older age group (50-64 years old) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] These age groups were classified and used routinely by the NDNS

Table 6.5: CHD risk factors and estimated CHD risk in men (a) and women (b) according to BMI in men (a) and women (b). P values and partial eta squared are shown for analysis using BMI as a categorical, ordinal and continuous variable, after adjustment for physical activity, age and smoking.

(a)

BMI category [1] (range)	**CHD risk factors**				**eCHD risk %**
	SBP mmHg	**DBP mmHg**	**TC Mmol/L**	**HDL-C mmol/L**	
Underweight (< 20)					
Mean value	125 *	70.9	4.7	1.16	6.5 *
(n)	(16)	(16)	(13)	(13)	(12)
Normal weight (20-25)					
Mean value	126 **	72.4 *	5.2	1.11 *	8.3 **
(n)	(144)	(144)	(108)	(107)	(107)
Overweight (25-30)					
Mean value	131	75.2	5.3	1.06 *	9.1 *
(n)	(229)	(229)	(179)	(179)	(178)
Obese (> 30)					
Mean value	135	77.5	5.4	0.96	10.9
(n)	(127)	(127)	(93)	(93)	(93)
P value (categorical)	***< 0.001***	***0.001***	***0.237***	***0.003***	***< 0.001***
Partial eta squared	***0.053***	***0.033***	***0.011***	***0.035***	***0.058***
P value (ordinal (Ptrend))	***< 0.001***	***< 0.001***	***0.105***	***< 0.001***	***< 0.001***
Partial eta squared	***0.052***	***0.032***	***0.007***	***0.033***	***0.055***
P value (continuous)	***< 0.001***	***< 0.001***	***0.130***	***< 0.001***	***< 0.001***
Partial eta squared	***0.042***	***0.026***	***0.006***	***0.049***	***0.063***

(b)

BMI category [1] (range)	CHD risk factors				eCHD risk %
	SBP mmHg	**DBP mmHg**	**TC mmol/L**	**HDL-C mmol/L**	
Underweight (< 20)					
Mean value	122 *	67.7	5.1	1.35 *	5.5
(n)	(46)	(46)	(40)	(40)	(38)
Normal weight (20-25)					
Mean value	120 **	68.1 *	5.1	1.36 **	3.7 *
(n)	(232)	(232)	(173)	(173)	(173)
Overweight (25-30)					
Mean value	123 **	68.8 *	5.5	1.23	4.4
(n)	(183)	(183)	(142)	(142)	(142)
Obese (> 30)					
Mean value	130	72.4	5.4	1.13	5.1
(n)	(115)	(115)	(80)	(80)	(79)
P value (categorical)	***< 0.001***	***0.002***	***0.005***	***< 0.001***	***0.005***
Partial eta squared	***0.059***	***0.025***	***0.030***	***0.050***	***0.030***
P value (ordinal (Ptrend))	***< 0.001***	***< 0.001***	***0.003***	***< 0.001***	***0.166***
Partial eta squared	***0.044***	***0.020***	***0.020***	***0.050***	***0.004***
P value (continuous)	***< 0.001***	***< 0.001***	***0.036***	***< 0.001***	***0.015***
Partial eta squared	***0.070***	***0.026***	***0.010***	***0.067***	***0.014***

Significantly different from highest BMI category (BMI > 30) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 6.6: CHD risk factors and estimated CHD risk in men (a) and women (b) according to BMI in men (a) and women (b). P values and partial eta squared are shown for analysis using BMI as a quartile, ordinal and continuous variable, after adjustment for physical activity, age and smoking.

(a)

BMI quartile (mean)	**CHD risk factors**				**eCHD risk %**
	SBP mmHg	**DBP mmHg**	**TC mmol/L**	**HDL-C mmol/L**	
Quartile 1 (22) Mean value (n)	125 ** (128)	71.6 ** (128)	5.1 (95)	1.10 * (95)	8.1 ** (95)
Quartile 2 (26) Mean value (n)	128 ** (119)	74.7 (119)	5.5 (92)	1.15 ** (91)	8.1 ** (91)
Quartile 3 (28) Mean value (n)	133 (131)	75.0 (131)	5.3 (104)	1.02 (104)	9.7 (103)
Quartile 4 (33) Mean value (n)	135 (133)	77.6 (133)	5.4 (99)	0.96 (99)	10.8 (99)
P value (categorical)	***< 0.001***	***< 0.001***	***0.072***	***< 0.001***	***< 0.001***
Partial eta squared	***0.079***	***0.039***	***0.018***	***0.057***	***0.072***
P value (ordinal (Ptrend))	***< 0.001***	***< 0.001***	***0.115***	***< 0.001***	***< 0.001***
Partial eta squared	***0.075***	***0.036***	***0.006***	***0.041***	***0.064***
P value (continuous)	***< 0.001***	***< 0.001***	***0.130***	***< 0.001***	***< 0.001***
Partial eta squared	***0.042***	***0.026***	***0.006***	***0.049***	***0.063***

Significantly different from highest BMI quartile (Quartile 4) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

BMI quartile (mean)	CHD risk factors				eCHD risk %
	SBP mmHg	**DBP mmHg**	**TC mmol/L**	**HDL-C mmol/L**	
Quartile 1 (21) Mean value (n)	120 ** (139)	68.9 * (139)	5.0 * (109)	1.38 ** (109)	3.9 (109)
Quartile 2 (24) Mean value (n)	120 ** (148)	67.9 ** (148)	5.2 (110)	1.33 ** (110)	3.9 (110)
Quartile 3 (27) Mean value (n)	124 (139)	68.4 * (139)	5.5 (112)	1.21 (112)	4.6 (112)
Quartile 4 (34) Mean value (n)	128 (139)	72.4 (139)	5.5 (97)	1.15 (97)	4.9 (96)
P value (categorical)	***< 0.001***	***< 0.001***	***0.002***	***< 0.001***	***0.097***
Partial eta squared	***0.055***	***0.036***	***0.036***	***0.062***	***0.015***
P value (ordinal (Ptrend))	***< 0.001***	***0.003***	***< 0.001***	***< 0.001***	***0.018***
Partial eta squared	***0.044***	***0.016***	***0.030***	***0.060***	***0.013***
P value (continuous)	***< 0.001***	***< 0.001***	***0.036***	***< 0.001***	***0.015***
Partial eta squared	***0.070***	***0.026***	***0.010***	***0.067***	***0.014***

Significantly different from highest BMI quartile (Quartile 4) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 6.7: CHD risk factors and estimated CHD risk in men (a) and women (b) according to smoking habits in men (a) and women (b), after adjustment for physical activity, age and BMI.

(a)

Smoking habits	CHD risk factors				eCHD risk %
	SBP mmHg	DBP mmHg	TC mmol/L	HDL-C mmol/L	
Smoke					
Mean value	132	75.7	5.3	1.01	12.1
(n)	(215)	(215)	(155)	(154)	(154)
Do not smoke					
Mean value	130	74.1	5.3	1.09	7.3
(n)	(298)	(298)	(236)	(236)	(235)
P value	***0.098***	***0.092***	***0.857***	***0.016***	***< 0.001***
Partial eta squared	***0.005***	***0.006***	***0.000***	***0.015***	***0.229***

(b)

Smoking habits	CHD risk factors				eCHD risk %
	SBP mmHg	DBP mmHg	TC mmol/L	HDL-C mmol/L	
Smoke					
Mean value	123	68.6	5.4	1.22	5.9
(n)	(278)	(278)	(207)	(207)	(207)
Do not smoke					
Mean value	123	69.6	5.2	1.32	2.8
(n)	(289)	(289)	(222)	(222)	(221)
P value	***0.759***	***0.251***	***0.079***	***0.003***	***< 0.001***
Partial eta squared	***0.000***	***0.002***	***0.007***	***0.020***	***0.156***

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

3. *Association of different categorization methods for physical activity with CHD risk factors and eCHD risk after adjustment for the confounding factors:*

The results are presented in *Table* 6.8. After adjusting for these confounding factors (e.g. age), the data analysis has shown that some of the significant relationships disappeared between the active and inactive groups (as defined by the three guidelines). For example, using the 30/5 guideline, there were insignificant differences between the active and inactive groups in relation to TC (in men) and SBP and DBP (in women). In addition, the results showed that the proportion of the variance in the CHD risk factors and eCHD risk between the active and inactive groups defined by each guideline was smaller once adjustments for age, BMI and smoking were done, particularly in women. For instance, the range of the partial eta squared values in the eCHD risk (explained by these guidelines) was 1.4-3.1 % (in men) and 0.4-1.3 % (in women) compared to 1.7-5.0 % in men and 1.4-3.0 % in women before the adjustments. *Figures* 6.2 and 6.3 illustrate the differences in the levels of the TC and eCHD risk between active and inactive groups as defined by the different categorization methods used in the guidelines for physical activity, after adjustment for age, BMI and smoking.

Overall, after adjustment for age, BMI and smoking status, those men considered active using the 30/5 guideline had significantly greater HDL-C than those considered inactive whilst blood pressure (SBP and DBP) and TC were comparable. Using the 30/3 guideline, significantly lower DBP and TC and higher HDL-C were evident in active men, whilst SBP was not different from those considered inactive. Using the MET40*h guideline, being active was only associated with a significantly lower SBP – the opposite of that seen using the 30/3 guideline. The proportion of the variance (partial eta squared) in these CHD risk factors that could be directly attributable to activity status was generally low. The highest partial eta squared was 2.3% of the variance in HDL when categorised using the 30/3 guideline. There were no significant differences in the CHD risk factors in the women according to activity status.

In the men using all three guidelines, those who were considered active exhibited a significantly lower eCHD risk than those considered inactive with similar values observed using each of the three guidelines. The eCHD risk was generally less in the women and was only associated with a significantly lower eCHD risk when considered active using the 30/3 guideline such that 3.1 % of the variance in eCHD risk could be directly attributed to differences in activity status. Similar trends were observed using other guidelines but the difference did not attain statistical significance where differences in activity status could account for 1.4 % and 1.6 % of the variance in eCHD risk using either the 30/5 or MET40*h guidelines, respectively. Only those women who were considered active using the 30/3 guideline were found to have a lower eCHD risk than inactive women; no differences in eCHD risk were evident using either the 30/5 or MET40*h categorisations. *Figure* 6.4 shows the proportions of variance in the CHD risk factors and eCHD risk explain by different categorization methods used in the guidelines for physical activity, after adjustment for age, BMI and smoking.

Figure 6.5 shows the comparison between the use of eta squared and partial eta squared to express the proportions of variance of the CHD risk factors and eCHD risk. Whilst the same proportions in CHD risk factors were found when using the partial eta squared and eta squared, the results showed that the proportion of variance in eCHD expressed in partial eta squared gave a greater value as compared to the eta squared. For example, the eCHD of the men using the 30/3 guideline, partial eta squared was 3.1 % compared to 0.09 % obtained by eta squared. The same trends were also found in women.

Table 6.8: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk between inactive and active groups of men (a) and women (b) as defined according to different categorization methods used in the guidelines for physical activity, after adjustment for the age, BMI and smoking.

(a)

Categorization methods (used in guidelines)		**CHD risk factors**				**eCHD risk** %
		SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	131.1 (*242*)	75.8 (*242*)	5.5 (*252*)	1.00 (*252*)	10.0 (*180*)
	Active: Mean value (n)	129.9 (*271*)	73.9 (*271*)	5.2 (*281*)	1.10 (*281*)	8.5 (*210*)
	P value	***0.309***	***0.043***	***0.011***	***0.003***	***0.000***
	Eta squared	***0.002***	***0.006***	***0.015***	***0.022***	***0.009***
	Partial eta squared	***0.002***	***0.008***	***0.017***	***0.023***	***0.031***
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	130.6 (*338*)	75.1 (*338*)	5.3 (*351*)	1.03 (*351*)	9.6 (*254*)
	Active: Mean value (n)	130.2 (*175*)	74.3 (*175*)	5.2 (*182*)	1.10 (*182*)	8.5 (*136*)
	P value	***0.758***	***0.411***	***0.400***	***0.016***	***0.021***
	Eta squared	***0.000***	***0.001***	***0.001***	***0.014***	***0.004***
	Partial eta squared	***0.000***	***0.001***	***0.002***	***0.015***	***0.014***
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	133.9 (*84*)	76.8 (*84*)	5.5 (*86*)	1.00 (*86*)	10.4 (*59*)
	Active: Mean value (n)	129.8 (*429*)	74.4 (*429*)	5.3 (*447*)	1.06 (*447*)	9.0 (*331*)
	P value	***0.013***	***0.051***	***0.080***	***0.161***	***0.014***
	Eta squared	***0.010***	***0.006***	***0.007***	***0.004***	***0.004***
	Partial eta squared	***0.012***	***0.007***	***0.008***	***0.005***	***0.016***

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Categorization methods (used in guidelines)		CHD risk factors SBP mmHg	DBP mmHg	TC mmol/L	HDL-C mmol/L	eCHD risk %
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	123.8 (*288*)	69.7 (*288*)	5.4 (*313*)	1.25 (*313*)	4.7 (*212*)
	Active: Mean value (n)	121.8 (*279*)	68.6 (*279*)	5.2 (*336*)	1.29 (*336*)	3.9 (*220*)
	P value	***0.098***	***0.227***	***0.306***	***0.302***	***0.020***
	Eta squared	***0.003***	***0.002***	***0.002***	***0.002***	***0.005***
	Partial eta squared	***0.005***	***0.003***	***0.002***	***0.003***	***0.013***
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	123.0 (*416*)	69.3 (*416*)	5.3 (*475*)	1.27 (*475*)	4.4 (*313*)
	Active: Mean value (n)	122.2 (*151*)	68.6 (*151*)	5.2 (*174*)	1.27 (*174*)	3.9 (*119*)
	P value	***0.558***	***0.471***	***0.244***	***0.977***	***0.202***
	Eta squared	***0.000***	***0.000***	***0.002***	***0.000***	***0.001***
	Partial eta squared	***0.001***	***0.001***	***0.003***	***0.000***	***0.004***
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	124.4 (*146*)	70.3 (*146*)	5.4 (*161*)	1.27 (*161*)	4.7 (*105*)
	Active: Mean value (n)	122.3 (*421*)	68.7 (*421*)	5.3 (*488*)	1.27 (*488*)	4.1 (*327*)
	P value	***0.120***	***0.114***	***0.290***	***0.901***	***0.142***
	Eta squared	***0.003***	***0.004***	***0.002***	***0.000***	***0.002***
	Partial eta squared	***0.004***	***0.004***	***0.003***	***0.000***	***0.005***

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

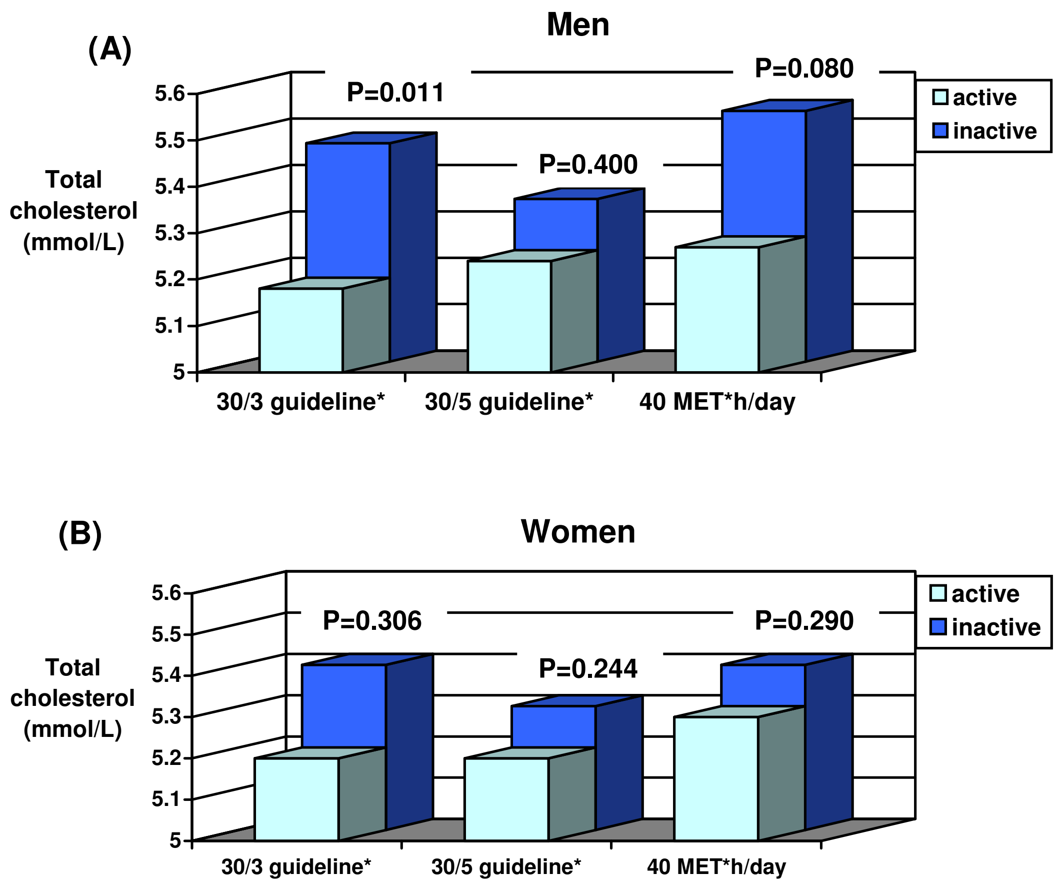


Figure 6.2: The differences in the levels of total cholesterol in men (A) and in women (B) between active and inactive groups as defined by the different categorization methods used in physical activity guidelines, after adjustment for age, BMI and smoking.

* 30/3 and G-30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively.

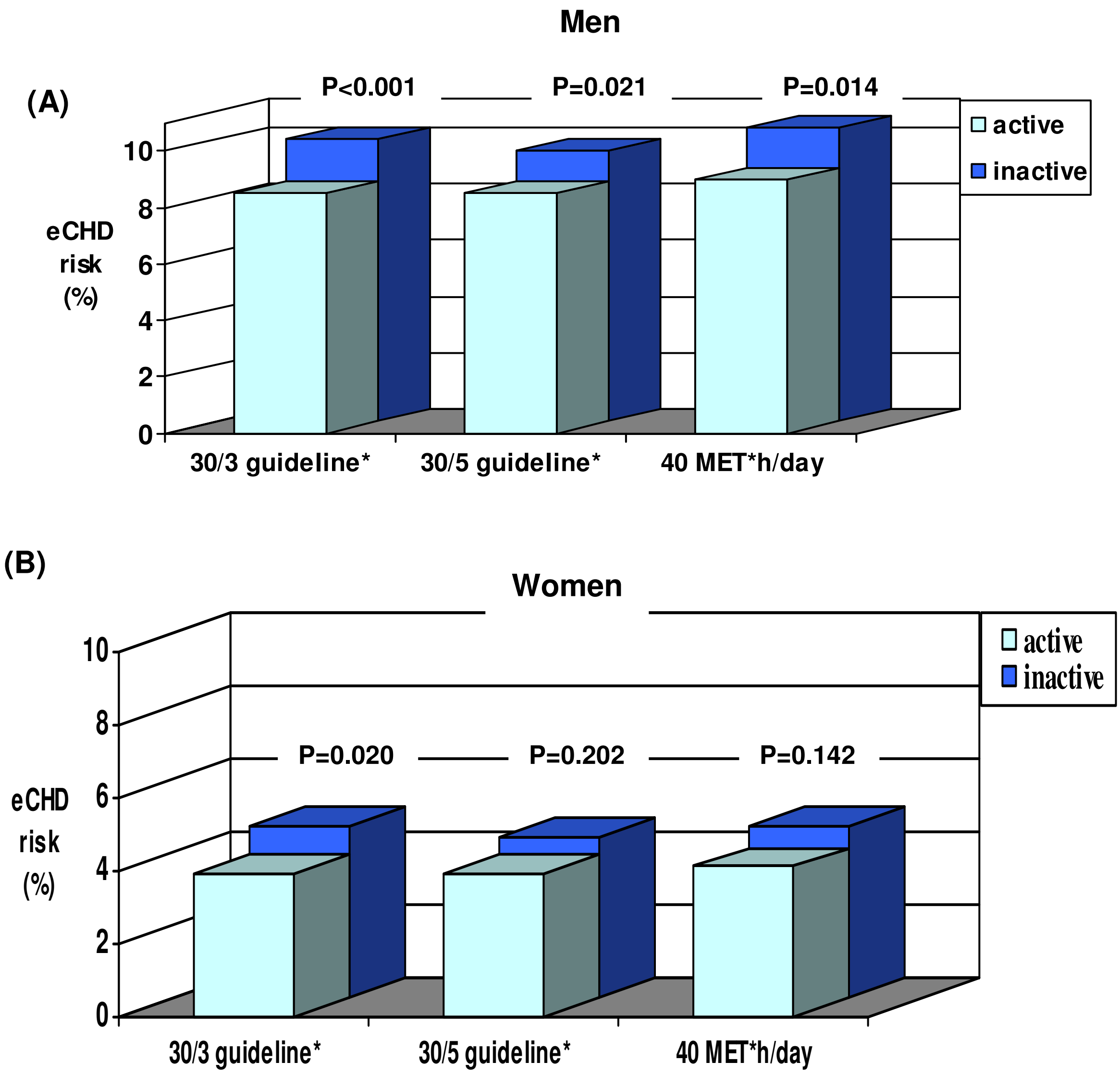


Figure 6.3: The differences in the estimation of the percentage of the likelihood of developing coronary heart disease (eCHD) over a period of 10 years between active and inactive groups of men (A) and women (B) as defined by the different categorization methods used in physical activity guidelines, after adjustment for age, BMI and smoking. The P values refer to differences between active and inactive groups within each method of categorization.

* 30/3 and G-30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively.

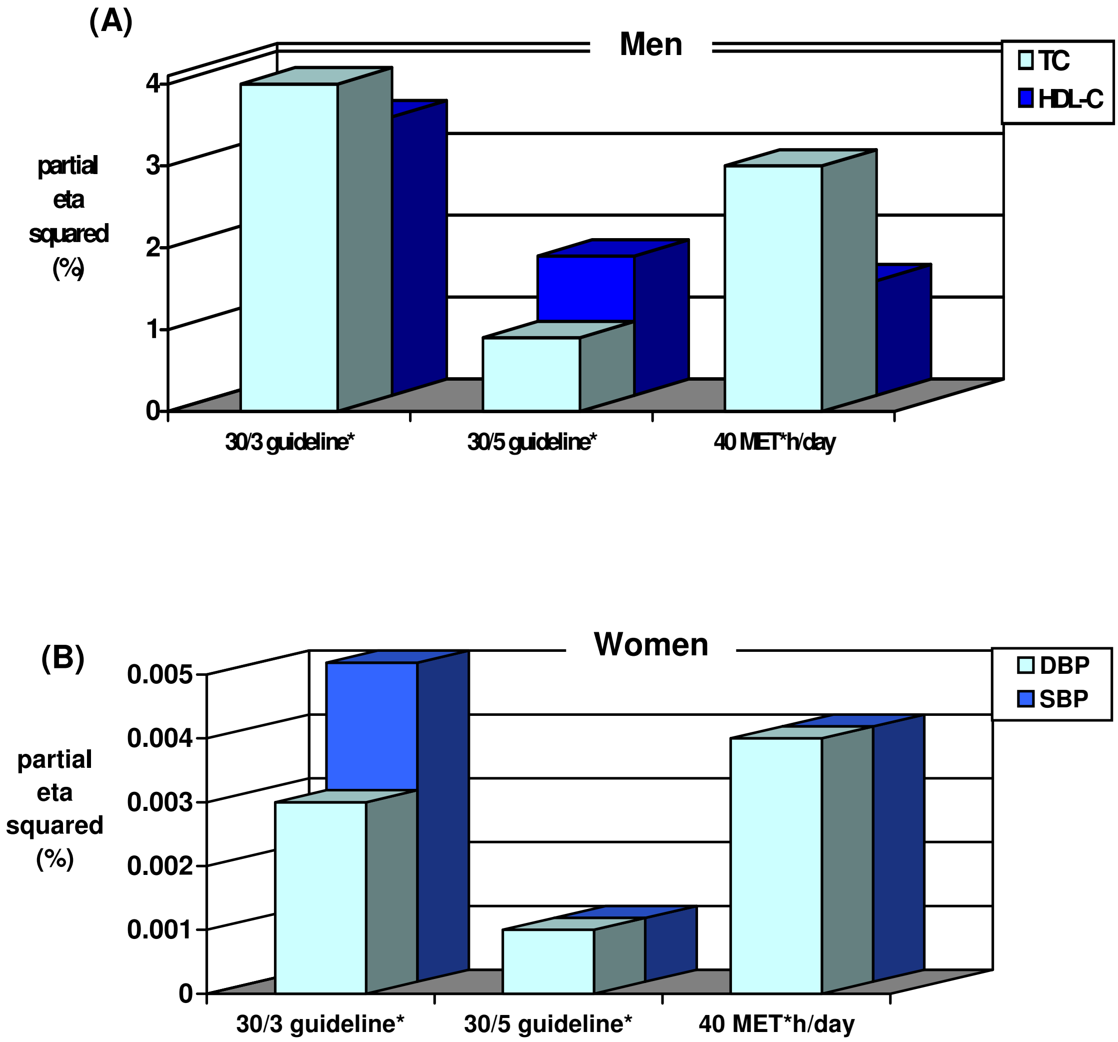


Figure 6.4: The proportions of variance in the levels of total cholesterol (TC) and HDL cholesterol in men (A) and systolic BP and diastolic BP in women (B) as explain by different categorization methods used in physical activity guidelines, after adjustment for age, BMI and smoking.

* 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 days or 5 days per week, respectively.

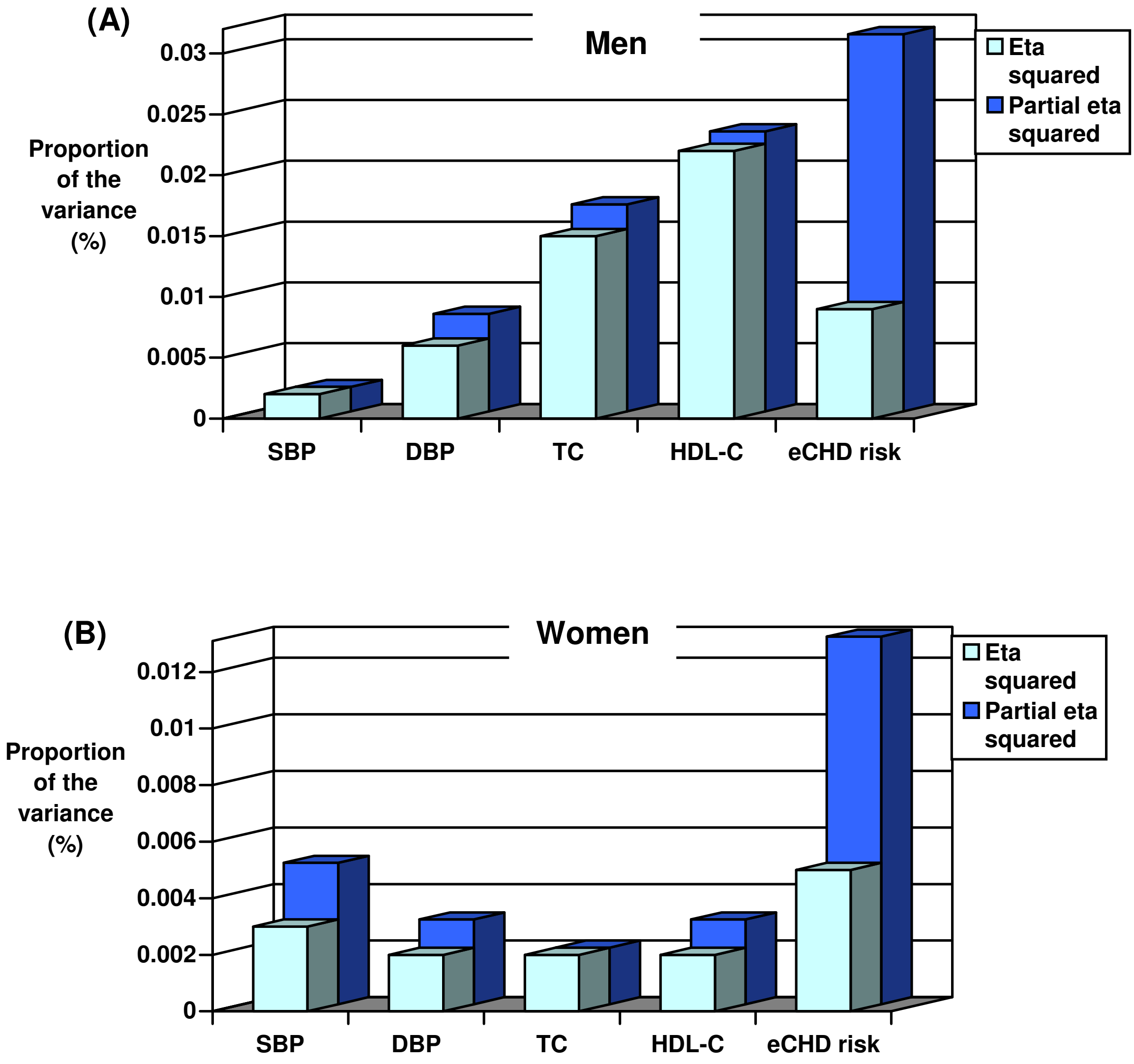


Figure 6.5: Comparison between the use of eta squared and partial eta squared in men (A) and women (B) in order to express the proportions of variance of the CHD risk factors and the estimation of coronary heart disease (eCHD) risk, explain by the adherence to the 3 days/week of at least moderate activity, after adjustment for age, BMI and smoking.

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

6.4. Discussion:

In this data-set, the apparent health benefits of being considered active men across all physical activity categorizations were evident and consistent for TC, HDL-C and eCHD risk, but not for SBP and DBP. In contrast, the analysis failed to indicate any significant association between these methods of categorization and CHD risk factors and eCHD risk in women. There is no clear explanation for this finding in women. However, the lack of the association between physical activity and lipid profiles and eCHD risk among women may be related to the changes in sex hormones, lower VO2max, smaller muscle mass, and lower haemoglobin and blood volume compared with men. In addition, this may be because the reported physical activity in women is more focused on household and child care activities than on sport and LTPA. A recent cross-sectional study in England, by Stamakis (2007), has found that men and women who achieved the recommended levels of physical activity, mainly because of heavy household activities, are more likely to be obese and to have poorer health compared to those who achieved the recommended levels mainly from walking or sport activities. Therefore, household activities may not reach the lowest level of intensity required to improve the CHD risk factors irrespective of the duration.

Since the range of the age in the NDNS data (19 to 64 years) is quite wide, the current analysis was carried out within the four age groups which were defined by the Food Standards Agency (e.g. 19-24 years, 25-34 years, 35-49 years and 50-64 years). The age was found to be a dominant factor influencing the risk analysis. The eCHD risk associated with age is found to be higher for older age groups compared to younger age groups (see *Table* 6.4). Likewise, subjects with high BMI or those who smoke cigarette have higher risk than those individuals with normal BMI and don't smoke. Therefore, this *Chapter* suggested that it is important for any association between physical activity and health outcomes to include differential risk across age groups, BMI and smoking habits.

While the data presented by the Food Standards Agency do not take into account any of the confounding factors, the analysis of this *Chapter* has clarified how some of these factors (e.g. smoking, age and BMI) interfere with the relationship between CHD risk factors and physical activity. The analysis by the Food Standards Agency (NDNS, 2004) was primarily performed to assess the correlation coefficients for the relationships between the time (hours) spent in activities of at least moderate activity and dietary intake, body size and blood pressure, without any adjustment for confounding factors (e.g.

smoking). In this current *Chapter*, the findings were similar to those findings obtained from the Food Standards Agency. However, when age, BMI, and smoking adjusted in this current *Chapter*, the significant associations with the SBP and DBP disappeared. In addition, while BMI was not significantly correlated to the time spent in at least moderate activity according to the Food Standards Agency analysis, this current *Chapter* showed that the associations was significant ($P < 0.041$) only in women after adjustment for age and smoking.

Moreover, beyond the analysis conducted by the Food Standards Agency, this current *Chapter* showed that men who deemed activity had generally significantly lower TC, Higher HDL-C and lower eCHD risk compared to those who considered inactive. This was consistent across three different categorization methods for physical activity (30/3, 30/5 and MET40*h). Therefore, this *Chapter* indicated that inactive men had worse blood lipids profiles (TC and HDL-C), but not blood pressure, and greater estimated risk of CHD than those men who are active in each of the three methods of categorisation and that this effect persists even after controlling for differences in BMI and adjustment for age, smoking.

Overall, after the adjustments for age, smoking and BMI, the proportions of variance of this effect was modest with less than 3.1 % of eCHD risk associated with activity status. These proportions were expressed in terms partial eta squared. When the proportion of variance expressed in eta squared was used, there were similar effects with the partial eta squared in the individual CHD risk factors, except for the eCHD risk. These findings indicated that the partial eta squared accounted for a greater proportion of the variance (3 folds) in the eCHD risk compared to the eta squared. This was because the large variability in eCHD risk due to age (67 %) was excluded from the calculation of partial eta squared but not the calculation of eta squared. In contrast, the discrepancy between partial eta squared and eta squared for the individual CHD risk factors was small because the age and other predictive variable (e.g. BMI) accounted for a small proportion of the variability (< 6 %). *Figure* 4.1 (page 82) shows difference in the procedures used to calculate eta squared and partial eta squared.

In the light of the previously established strong effects of physical activity on both CHD incidence and risk factors for CHD, it is not quite clear why such a weak association has been found in this *Chapter*. However, the following possible explanations may be considered:

1. Physical activity might not improve the specific risk factors of this data-set to a significant degree.
2. Physical activity might reduce the risk of CHD through other risk factors that might be involved in the causal pathway but are not available in this data-set. These risk factors extend to include insulin resistance, inflammation, endothelial function, haemostatic function and plasma concentration of factors such as triglycerides and protein kinase C. In addition, other confounding factors such as foetal growth, genetic inheritance, hormonal function, and ethnicity are also directly related to the CHD.
3. Effects might have been masked by concurrent medications.
4. The effects might be weakened by methodological aspects of the measurement of physical activity. For example, the measures (number of days/week of moderate activity or MET*hr/day) used in this study to assess physical activity might not be as effective as fitness (the ability to perform physical activity). In addition, physical activity level might estimate mainly the duration of the activity while the effect on CHD may be related more to the intensity.
5. The type of the NDNS diary used in this data-set may not be valid or sufficiently well designed to measure physical activity.
6. Although the above guidelines have been used as reference recommendations for physical activity, the use of a dichotomous method (inactive/active) may mask the dose-response relationship of activity required to see a difference between the active and inactive groups.

6.4.1. Physical activity may not be important:

Although there is now a consensus among public health and medical authorities that physical activity has beneficial effect on the levels of SBP, DBP, TC, HDL-C and eCHD risk, the associations are highly variable among the different studies. While the majority of the studies have found an inverse association between physical activity and risk factors for CVD, including CHD (Crespo et al., 2002; Ricardo et al., 2002; Franks et al., 2004), others have shown only a weak or no association (Sesso et al., 2000; Yu et al., 2003; Kirk et al., 2003; Brage et al., 2004; Tully et al., 2005).

Therefore, it is possible that physical activity has small proportion of variance on the CHD risk factors and eCHD risk investigated in this *Chapter*. For example, Sesso et al., (2000) and Yu et al., (2003) have shown that there are no significant associations between a record of leisure activity questionnaire (number of blocks walked, flights climbed, and participation in sports or recreational activities) and CHD risk in men. However, they have found that the total physical activity score and vigorous activity score have stronger effects on the reduction in CHD mortality. In addition, Brage et al., (2004) has observed that habitual physical activity (assessed by accelerometer) is not associated with HDL-C, SBP and DBP in children after adjusting for gender, ages, BMI, ethnicity, socioeconomic status, parental smoking. Moreover, a 30 years follow-up study by Bijnen et al., (1996) and a cross-sectional study by Young et al., (1993) have indicated that improving the total physical activity score is not associated with TC and blood pressure in adult and elderly men and women after correcting for age, cohort, smoking, BMI, and alcohol intake. Only HDL-C was significantly increased. However, Danielson et al., (1993) have found no significant differences in HDL-C and TC across tertiles of the total physical activity score or walking (measured by questionnaire) in 634 elderly women after adjusting for age, BMI, education, and oral oestrogen use.

One possible explanation for these findings is that most of the observational-based prospective studies have relied largely on questionnaire or self-reporting methods to assess physical activity level. These are particularly susceptible to measurement bias which may affect its relationship with CHD risk factors (Sallis and Saelens, 2000). In addition, each of these studies may have other limitations as discussed below.

6.4.2. Physical activity and other risk factors:

It should be noted that only a limited number of CHD risk factors are analyzed in this data-set. Therefore, it is possible that the effect of physical activity on CHD risk may be predominantly mediated by other risk factors that are not included in this data-set. These risk factors are briefly described below. *Figure* 6.6 (below) shows the potential mechanisms by which physical activity can influence eCHD risk.

Other risk factors exist in the pathway:

After controlling the traditional risk factors for CHD (including blood pressure, TC, HDL-C and body fatness) physical activity has still been found to be an independent risk factor for CHD (DHHS-US, 1996). This may indicate that while physical activity influences these traditional risk factors, it influences CHD risk through other mechanisms.

One possible mechanism that links physical activity with CHD risk is insulin resistance. Briefly, the mechanism by which regular physical activity may improve insulin sensitivity is by increasing skeletal muscle oxidative capacity and glucose uptake (Bruce et al., 2003; Christ-Roberts and Mandarino, 2004; Gill and Malkova, 2006; Holloszy, 2005;

Wojtaszewski et al., 2003; Zierath, 2002). Therefore, it is likely that the effects of physical activity on insulin sensitivity are link to its effects on SBP, DBP, TC and HDL-C. In addition, it seems that physical activity also reduces plasma TG concentrations. A combination of increased lipoprotein-lipase-mediated TG, clearance by exercised skeletal muscle and reduced hepatic production of VLDL are responsible for this TG-lowering effect (Gill and Hardman, 2003). Thus, regular physical activity is also likely to improve lipid profile (HDL-C, LDL and VLDL) through TG metabolism.

This effect while it may be related to additional factors that are independently related to the CVD risk, it may have little direct effect on CHD risk factors examined in this *Chapter* (see *Figure* 6.5). There is increasing evidence that inflammation (Reuben et al., 2003), disturbance in the haemostatic factors (Ciampricotti et al., 1990), endothelial dysfunction (Ghiadoni et al., 2001), and PKC (Thong et al., 2003) are predictors of CVD including CHD and have an inverse relationship on the levels of SBP, DBP, TC and HDL-C. Previous studies have indicated that regular physical activity is associated with improved endothelial function (Rinder et al., 2000; Franzoni et al., 2005), inflammatory markers (Wannamethee et al., 2002; Reuben et al., 2003), PKC (Thong et al., 2003), and haemostatic function (Smith, 2003). Therefore, the clinical importance of these factors to CHD supports the theory that these factors might be related to the mechanisms linking physical activity to the levels of the SBP, DBP, TC and HDL-C.

<u>*Other confounding factors:*</u>

The magnitude of the relationship between these physical activity guidelines and the CHD risk factors may also be modified by characteristics of the people that are not recorded by the questionnaire such as birth weight, family history, genetic profile, hormonal function, and skeletal muscle properties. Data from a large number of epidemiological studies in a wide range of populations suggest that these confounding factors affect the relationship between physical activity and CHD risk factors (Barker, 2004; Margaglione et al., 2000; Burt et al., 1995; An et al., 2005; Storlien et al., 1996; Masuzaki et al., 1997; Waldrop et al., 1996). There is conflicting evidence that the relative importance of metabolic syndrome (including SBP, DBP, TC and HDL-C) as compared to these confounding factors (Malik et al., 2004; Sundstrom et al., 2006). For example, Stern et al., (2004) have suggested that the Framingham risk assessment tool is a better predictor of short-term (10-year) cardiovascular risk compared to the metabolic syndrome. This is not surprising, as it includes potent cardiovascular risk factors that are not included in the metabolic syndrome definition, such as age and smoking. It should be noted that the age, BMI and smoking are adjusted in this thesis.

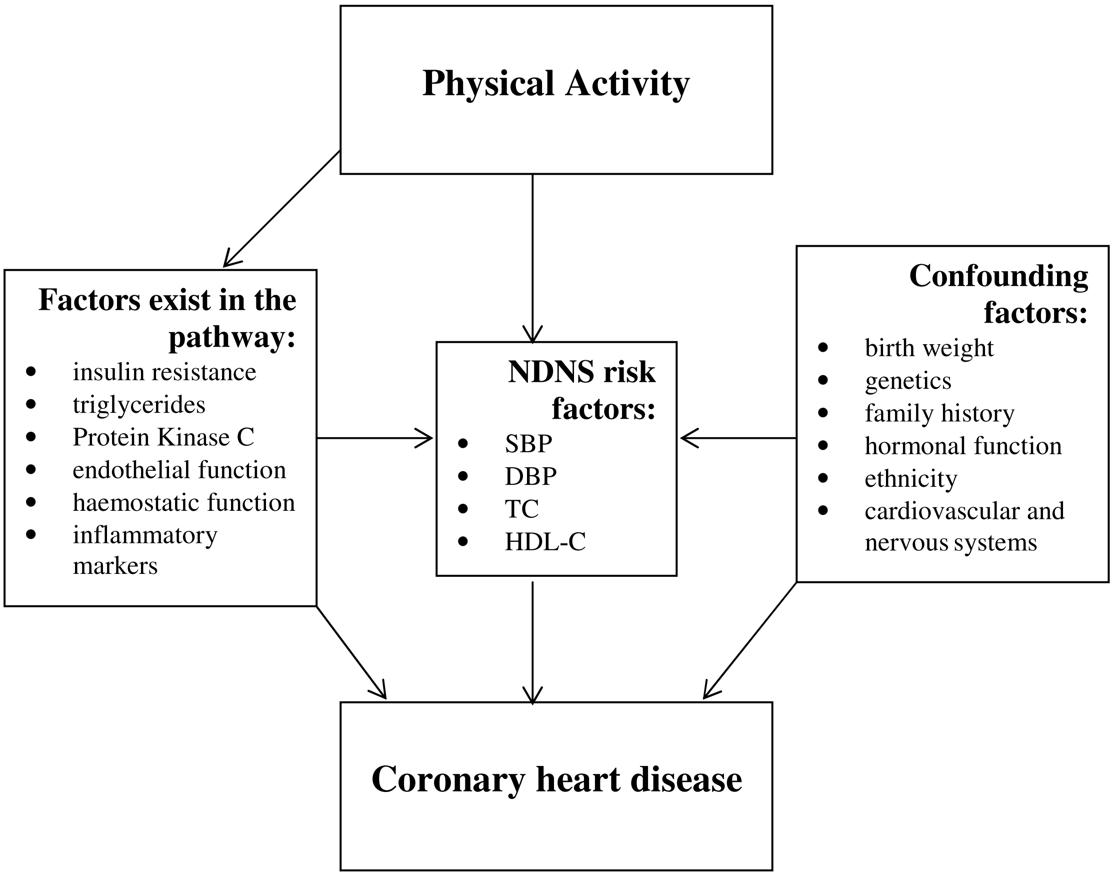


Figure 6.6: Mechanisms by which physical activity is likely to influence CVD risk.

6.4.3. Methodological implications of measuring physical activity:

Dimensions, instruments, and measures of physical activity:

In this thesis, measuring one dimension of physical activity (subjective) may limit the ability to find a strong association between physical activity and CHD risk factors and eCHD risk. This is because the actual physical activity level is a complex entity comprising numerous diverse dimensions that present a challenge in terms of accurate and reliable measurement.

In this regard, it is worth noting that physical activity refers to a behaviour, specifically a body movements that are carried out by skeletal muscle contractions and result in increased EE above RMR. Exercise, or "exercise training," is a specific type of physical activity that is performed with the intention of enhancing components of physical fitness. The major component of physical fitness is aerobic power or "cardiorespiratory fitness" (DHHS-US, 1996). Cardiorespiratory fitness, an objective measure of recent physical activity patterns (Paffenbarger et al., 1993-2), has been found to be a stronger predictor of several health outcomes compared to physical activity as measured by self-reported and accelerometer (Blair et al., 2001; Suzuki et al., 1998). This may be due to the fact that fitness exposures are less prone to misclassification than physical activity. Although determinants of cardiorespiratory fitness include age, sex, health status, and genetic factors, the principal determinant is habitual physical activity levels (DHHS-US, 1996).

In addition, there is a range of different instruments that can be used to characterise any given dimensions and/ or measures may not necessarily relate to the measures obtained by another instrument despite the fact that, they are both intended to describe the same dimension. Thus, the method of choice will depend on how the measurement will be used. For example, if a rough estimate of the physical activity level of a population in an epidemiological study is the desired outcome, then the use of a simple pedometer may be sufficient (Wasserman and Zinman, 1995). However, if patterns and intensity of activity are needed, then an accelerometer may be more suitable for the study. Therefore, each instrument and measure is limited by assumptions which may or may not be applicable under different circumstances.

Moreover, the number of physical activity measures (e.g. number of days or minutes of moderate activity, MET scores, total EE) used in the literature are large and result in some difficulty in selecting the most appropriate dimension to best predict CHD risk factors. Therefore, understanding the effects of different measures of the physical activity in the aetiology of the CHD risk is difficult.

Duration versus intensity:

Duration and intensity are components of physical activity. These components may explain the failure to show a strong association between physical activity and CHD risk factors and eCHD risk in this *Chapter*. For example, the habitual activities reported in this thesis, such as household chores and walking may not have been recalled correctly or not reached the minimum intensity required to improve the CHD risk factors irrespective of the duration. It is not known whether more health benefits are gained with activity of greater intensity or longer duration. Krauss et al., (2002) has suggested in a 6-month study of 111 overweight men and women that EE is more important than exercise intensity, and the most marked effects were observed at an EE of 2000 kcal with strenuous intensity. In the same study, it has also been suggested that the length of training period might be very important. However, a study by Asikainen et al., (2002) has questioned the lack of evidence with respect to the effectiveness of different exercise practices that are less intense than those recommended by the American College of Sports Medicine (ACSM) (1998), since the data on the real benefits of less intense exercise are sparse and contradictory.

By contrast, many studies have indicated that intensity is more important than duration. Reports in the literature have shown that the more intense the practice of physical activity, the better the indices of physical fitness; thereby implying improvements in CVD including CHD, diabetes, arterial hypertension, dyslipidemia, obesity and other factors (Guedes and Guedes, 2001; Thune et al., 1998; Heuvellen et al., 1998).

It has been suggested that chronic adaptations to the acute stress of exercise (intensity) promotes better health than normal levels of physical activity such as walking (duration) (Pate et al., 1995). For example, while prolonged walking at low intensity represents a reasonable metabolic rate and/or induces small lipid oxidization by skeletal muscle, the greatest effect of the intensity of exercise (e.g. jogging or running) appears to enhance oxidation of fat compared to walking. This effect has been linked to weight gain and the propensity towards obesity (Zurlo et al., 1990), which may be a critical risk of CVD.

To achieve positive effects, the ACSM (1998) has recommended that an adult should exercise 3–5 days a week with an intensity of 50–80 % of maximum VO_2, continuously or accumulatively for 20–60 minutes per day, expending 700–2000 kcal a week. It is possible that the failure to show a strong association in this *Chapter* may, at least in part, be due to the physical activity level being evaluated more in terms of duration rather than intensity of the exercise. The NDNS diary used in this thesis was directed towards assessing habitual activity. Therefore, the lack of information related to the prescribed exercise programmes may have contributed to the lack of an effect of the measured physical activity on the CHD risk factors and eCHD risk.

6.4.4. Validity of the NDNS 7-day diary:

The 2004 NDNS 7-day diary (volume 4) has also been used previously in other volumes for children and elderly. However, there is no information about the validity. Therefore, although the number of days or MET have been validated to measure physical activity (Gulati et al., 2003; Myers et al., 2002), the way in which the physical activity information was collected in this data-set may not be optimal or valid. In addition, this diary may not have been reliable because the subjects may not have understood it. Frequency and duration of activity can usually be recalled and estimated with reasonable precision through self-report (Chasan-Taber et al., 2002). However, the intensity is difficult to ascertain through self-report as it depends on subjects' interpretation of their effort. For example, brisk walking has been suggested as one of the easiest forms of exercise that can be used to meet the recommendations, but a brisk walk for some may be a more of a leisurely walk for others. Thus, it is possible that some questions in the NDNS diary may have been interpreted in different ways by different people.

Furthermore, the process of self-reported physical activity used in this data-set may also influence the ranking or estimated level of physical activity. Thus, the magnitude of error in the accuracy of recall of particular types of activity or questions in the NDNS diary may reduce the overall estimates of validity. Many questionnaires, which have been used previously to measure physical activity, may differ in their applications. However, there is no information about the ranking order using the NDNS diary compared to the other diaries or questionnaires. Therefore, differences in the overall scores and ranking orders behind these diaries and questionnaires may also partly influence the relationship between physical activity and the CHD risk factors and eCHD risk.

There is some evidence from other studies showing different scores or ranking orders about the level of physical activity using different physical activity questionnaires. For example, Ainsworth et al., (2006) has compared physical activity prevalence estimated from the Behavioural Risk Factor Surveillance System surveys (BRFSS) and the International Physical Activity Questionnaire (IPAQ). Although these instruments were validated, the findings indicated that the prevalence estimates for physical activity were higher on the IPAQ than the BRFSS for the lowest category (inactive) and for the highest category (attain recommendation). In another study that has compared activity levels in different European Union countries, German respondents generally showed higher scores for physical activity using IPAQ than the Finns and the Dutch (Rutten et al., 2003). However, when different physical activity questionnaires were used to estimate physical activity levels, Finland ranked before the Netherlands and Germany. Therefore, the ranking for light, moderate and vigorous activities measured by different types of physical activity questionnaires may give varied estimation or ranking for physical activity.

In addition, in another study, Brown et al., (2004a) has compared the level of agreement in results obtained from four physical activity questionnaires: physical activity questions by telephone, Active Australia Survey (AAS), BRFSS, and IPAQ. They have demonstrated that there were large differences between these questionnaires in reported physical activity times and, hence, in prevalence estimates of those meeting the guidelines for physical activity. Despite these differences, the same author in a similar study (Brown, 2004b) showed that four self-report physical activity measures (the AAS, IPAQ, BRFSS and Australian National Health Survey) provided acceptable levels of test-retest reliability for assessing activity status and moderate reliability for assessing total minutes of activity.

6.4.5. The dose response effect of activity:

Although these methods of categorization have been used as reference guidelines for physical activity, they do not provide any detailed information about trends between physical activity and the CHD risk factors and eCHD risk. For this reason, using a single cut-off point loses information about the dose response effect of activity required to see a difference between the active and inactive groups. In addition, shifting subjects (combing groups) from one group of physical activity to another group will dilute and change the result of each group. For example, the participation of 4 days/week is considered as inactive level by the " 30/5 guideline", whereas it is active level by the "30/3 guideline". This topic is further discussed in *Chapter 9*.

6.5. Conclusion:

In agreement with the second part of the hypothesis, the health benefits of being considered active, across all methods of categorization were evident and consistent with the levels of TC, HDL-C and eCHD risk, in men, but not women. By contrast, SBP and DBP were not significantly different between the inactive and active groups of both men and women. In general, the methods of categorization examined in this *Chapter* explain only small proportion of variations (less than 2 % of variability) in the levels of SBP, DBP, TC, HDL-C and eCHD risk (less than 3 % of variability). This may, in part, be explained by inter-individual differences or changes in levels of other risk and confounding factors discussed in *Chapter* 2. Unfortunately, these risk and confounding factors are not available in this data-set. Although the number of days/week of moderate activity and MET*hr/day have been validated to show a relationship between physical activity and CHD risk factors and eCHD risk, the findings in this chapter did not indicate a strong association using the same measures. Therefore, using one instrument to measure one dimension of physical activity (subjective), interpreting the NDNS diary in different ways by different people and evaluating the levels of physical activity in terms of duration and intensity may have limited the ability to find a strong association between physical activity and CHD risk factors and eCHD risk.

Taking these factors together, the results of this study may underestimate the actual benefit of physical activity guidelines (accumulation of at least 30 minutes activity 3 or 5 days/week of moderate activity or total 40 MET*hr/day). Although the lack of data in the NDNS limits further explanation of some of these issues, specific effects can be examined by:

1. Excluding subjects who are taking prescribed medical drugs.
2. Establishing a new categorization method by combining the measures of the activity (days/week of moderate activity and MET) based on those who meet the guidelines for physical activity.
3. Defining further categories and continuous variables for physical activity expressed in number of days/week of moderate activity, number of minutes/day of moderate activity, and total MET*hr/day.
4. Exploring the effects of physical activity level estimated by the NDNS self-perception questionnaire on the same health outcomes (CHD risk factors and eCHD risk).

These issues were examined and discussed in the following *Chapters* (7-10). In this *Chapter*, both the eta squared and partial eta squared were used. For simplicity and consistency, only partial eta squared is used in the subsequent *Chapters*.

Part One

Chapter 7: Excluding Subjects on Medications

Chapter 7 Excluding Subjects on Medications

7.1. Introduction:

The interpretation of the analysis reported in the previous *Chapter* (6) is constrained by the possible confounding effects of concurrent illness and medications. Criteria for exclusion from the NDNS data-set include HIV, hepatitis B positive, pregnant or breastfeeding, but do not exclude those with hypertension, hypercholesterolemia, diabetes nor obesity. Therefore, the pervious analysis may include those with both known and unknown conditions and/or any prescribed medication (used to improve blood pressure, TC, LDL, and HDL-C) that might bias or confound the association of physical activity with the CHD risk factors and eCHD risk. For example, some medicines, such as β-blocking agents have been shown to alter levels of physical activity, probably due to their effect on muscle blood flow (Bertoldi et al., 2006). Unfortunately, the NDNS data-set do not indicate either the presence of such conditions, nor the type of medication prescribed to the individuals. For these reasons, in attempt to control for such effects, those subjects who were taking medications were excluded from the data-set and the analysis in *Chapter* 6 was then repeated.

7.2. Methods:

In the previous *Chapter* (6), the analysis was intended to remove the confounding effects of age, BMI and smoking. In this *Chapter*, those subjects reported as taking prescribed medical drugs were excluded from the data-set and the previous analysis using the General Linear Model (Univariate) was repeated. Partial eta squared was used as a measure of effect size (proportion of the variance in the outcome that is attributable to physical activity): the ratio of physical activity variance to physical activity plus error.

7.3. Results:

Table 7.1 presents the summary of these findings. Exclusion of subjects who were taking prescribed medications omitted about one third of the subjects from the analysis. In general, after adjustment for the age, BMI and smoking, active men had significantly higher HDL-C than inactive men using all the three categorization methods and lower TC using both 30/3 and MET40*h guidelines, but not that based on the 30/5. There were no significant differences in both SBP and DBP with activity status. Men considered active using all three methods had significantly lower eCHD risk than those who were considered as inactive such that 1.4 – 2.9 % of the variance in eCHD risk could be attributable to differences in activity status. There were no significant activity-related effects evident in the women.

The results showed that the proportion of the variance (expressed in partial eta squared) was generally higher than in the previous analysis (in *Chapter* 6), but still accounted for a maximum of 4 % of the variance in TC and 3.4 % of HDL-C (see *Table 7.2*).

Table 7.1: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk between inactive and active groups of men (a) and women (b), as defined according to different categorization methods for physical activity, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Categorization methods (used in guidelines)		**CHD risk factors**				**eCHD risk** %
		SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	129.3 (*163*)	74.3 (*163*)	5.5 (*121*)	1.00 (*120*)	8.6 (*119*)
	Active: Mean value (n)	128.6 (*218*)	72.9 (*218*)	5.1 (*169*)	1.09 (*169*)	7.3 (*169*)
	P value	**0.587**	**0.190**	**0.001**	**0.002**	**0.004**
	Partial eta squared	**0.001**	**0.005**	**0.040**	**0.034**	**0.029**
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	129.1 (*240*)	73.8 (*240*)	5.3 (*180*)	1.03 (*179*)	8.2 (*178*)
	Active: Mean value (n)	128.6 (*141*)	72.9 (*141*)	5.1 (*110*)	1.10 (*110*)	7.3 (*110*)
	P value	**0.693**	**0.376**	**0.111**	**0.027**	**0.044**
	Partial eta squared	**0.000**	**0.002**	**0.009**	**0.017**	**0.014**
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	131.1 (*48*)	75.6 (*48*)	5.8 (*31*)	0.97 (*31*)	9.5 (*31*)
	Active: Mean value (n)	128.6 (*333*)	73.2 (*333*)	5.2 (*259*)	1.06 (*258*)	7.6 (*257*)
	P value	**0.218**	**0.110**	**0.003**	**0.043**	**0.010**
	Partial eta squared	**0.004**	**0.007**	**0.030**	**0.014**	**0.023**

(b)

Categorization methods (used in guidelines)		CHD risk factors SBP mmHg	DBP mmHg	TC mmol/L	HDL-C mmol/L	eCHD risk %
3 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	122.3 (*166*)	70.2 (*166*)	5.2 (*118*)	1.26 (*118*)	3.6 (*118*)
	Active: Mean value (n)	120.1 (*177*)	67.8 (*177*)	5.2 (*139*)	1.30 (*139*)	3.2 (*139*)
	P value	**0.105**	**0.024**	**0.696**	**0.358**	**0.304**
	Partial eta squared	**0.008**	**0.015**	**0.001**	**0.003**	**0.004**
5 days/week of moderate activity for 30 minutes or more	Inactive: Mean value (n)	121.5 (*243*)	69.3 (*243*)	5.2 (*178*)	1.27 (*178*)	3.5 (*178*)
	Active: Mean value (n)	120.4 (*100*)	68.6 (*100*)	5.2 (*79*)	1.29 (*80*)	3.1 (*79*)
	P value	**0.452**	**0.254**	**0.809**	**0.674**	**0.398**
	Partial eta squared	**0.002**	**0.004**	**0.000**	**0.001**	**0.003**
Accumulative of at least total 40 MET*hr/day	Inactive: Mean value (n)	123.0 (*77*)	70.8 (*77*)	5.2 (*54*)	1.31 (*54*)	3.4 (*54*)
	Active: Mean value (n)	120.6 (*266*)	68.5 (*266*)	5.2 (*203*)	1.27 (*203*)	3.4 (*203*)
	P value	**0.129**	**0.066**	**0.902**	**0.455**	**0.964**
	Partial eta squared	**0.007**	**0.010**	**0.000**	**0.002**	**0.000**

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 7.2: The extent to which CHD risk factors and estimated coronary heart disease (eCHD) risk in men (a) and women (b) are explained by categorization methods used in the guidelines for physical activity, before and after exclusion of subjects on medications, and after adjustment for age, BMI and BMI.

(a)

Categorization methods (used in guidelines)			**CHD risk factors**				**eCHD risk**
			SBP	**DBP**	**TC**	**HDL-C**	
Before excluding Medications	30/3 Guideline [1]	***P value***	0.309	0.043	0.011	0.003	0.000
		Partial eta squared	0.002	0.008	0.017	0.023	0.031
	30/5 Guideline [1]	***P value***	0.758	0.411	0.400	0.016	0.021
		Partial eta squared	0.000	0.001	0.002	0.015	0.014
	MET40*h [2]	***P value***	0.013	0.051	0.080	0.161	0.014
		Partial eta squared	0.012	0.007	0.008	0.005	0.016
After excluding Medications	30/3 Guideline [1]	***P value***	0.587	0.190	0.001	0.002	0.004
		Partial eta squared	0.001	0.005	0.040	0.034	0.029
	30/5 Guideline [1]	***P value***	0.693	0.376	0.111	0.027	0.004
		Partial eta squared	0.000	0.002	0.009	0.017	0.014
	MET40*h [2]	***P value***	0.218	0.110	0.003	0.043	0.010
		Partial eta squared	0.004	0.007	0.030	0.014	0.023

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively

[2] Accumulative of at least total 40 MET*hr/day

(b)

Categorization methods (used in guidelines)			Health risk factors				eCHD risk
			SBP	DBP	TC	HDL-C	
Before excluding Medications	30/3 Guideline [1]	***P value***	0.098	0.227	0.306	0.302	0.020
		Partial eta squared	0.005	0.003	0.002	0.003	0.013
	30/5 Guideline [1]	***P value***	0.558	0.471	0.244	0.977	0.202
		Partial eta squared	0.001	0.001	0.003	0.000	0.004
	MET40*h [2]	***P value***	0.120	0.114	0.290	0.901	0.142
		Partial eta squared	0.004	0.004	0.003	0.000	0.005
After excluding Medications	30/3 Guideline [1]	***P value***	0.105	0.024	0.696	0.358	0.304
		Partial eta squared	0.008	0.015	0.001	0.003	0.004
	30/5 Guideline [1]	***P value***	0.452	0.254	0.809	0.674	0.398
		Partial eta squared	0.002	0.004	0.000	0.001	0.003
	MET40*h [2]	***P value***	0.129	0.066	0.902	0.455	0.964
		Partial eta squared	0.007	0.010	0.000	0.002	0.000

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively

[2] Accumulative of at least total 40 MET*hr/day

7.4. Discussion:

Although exclusion of those receiving prescribed medication caused a reduction in the power of the statistical analysis, this was designed to remove some of the possible biases related to the therapeutic effects of the medications on the levels of the CHD risk factors and eCHD risk. Removing the subjects taking prescribed medications from the analysis may also help correct for some cases of underlying disease. However, participation in physical activity has been associated with lower use of medication and, consequently, inactive individuals may be more likely to use medicines and excluded from the analysis than active individuals (Bardel et al., 2000; Bertoldi et al., 2006). For example, a Swedish study (Bardel et al., 2000) has indicated that sedentary middle-aged (35–65 years) women have 39 % higher medicine use in comparison to very active women.

This *Chapter* indicated that inactive men were found to have higher levels of blood lipids (TC and HDL-C), and greater estimated risk of CHD, but not blood pressure, compared to active individuals in each of the three methods of categorisation. This effect was evident even after controlling for differences in BMI and adjustment for age, smoking and exclusion of subjects on medications. However, the findings failed to indicate any association of being considered active across these categorization methods with the CHD risk factors and eCHD risk in women.

Overall, after excluding those who were taking medications and adjustment for age, BMI and smoking, the proportion of the variance (partial eta squared) appeared to be increased, which could be attributed to activity status. For example, the findings indicated that the partial eta squared values of the TC, HDL-C and eCHD risk were increased, across the three guidelines, only in men. This may affect the analysis because the improving in the levels of TC and HDL-C by a drug might have an extra effect other than that of physical activity. It has been indicated that drugs used regularly are probably reported more often than those taken sporadically when asking for drug use during the preceding 14 days (Kelly et al., 1990).

Therefore, it is worth noting that the potential effect for the interaction between physical activity and medical drugs in the preceding days on these CHD risk factors may exist, especially for lipid-lowering drugs. Unfortunately, it is not possible to further examine this matter because the self-reported health status and medical drugs used in the preceding days is not available in this data-set. This may have a confounding effect on the levels of these CHD risk factors. For example, if someone is classified as inactive in one of these methods (guidelines), but is taking medications to lower blood lipids, this would confound these related results.

In general, after excluding those who are taking medications and adjustment for age, BMI and smoking, the analysis indicated that achieving the physical activity guidelines accounted for only small proportions of the variability of CHD risk factors and eCHD risk. The possible mechanisms behind the lack of a strong association between physical activity and CHD risk factors are discussed in *Chapter 2*.

7.5. Conclusion:

In conclusion, while in keeping with the second part of the hypothesis, the findings of this *Chapter* agreed with the findings of the previous *Chapter* (i.e. after adjustment for age, BMI and smoking but before excluding those on medications). After excluding those on medications and adjustment for age, BMI and smoking, being physically active by all three categorization methods accounted for only a small proportion of the variability of CHD risk factors and eCHD risk in both genders. However, the above analyses were based on the use of different cut-off points and measures of activity whivh may separately capture different activity components, e.g. occupational, leisure-time, and household tasks, of the overall physical activity profile. Consequently, the different measures may not be sufficiently inclusive to capture the size of the effect of physical activity on the CHD risk factors and eCHD risk. This issue is further evaluated and discussed in the following *Chapter*.

Part One

Chapter 8: Combination of physical activity guidelines using different measures

Chapter 8 Combination of physical activity guidelines using different measures

8.1. Introduction:

The findings described in the previous two *Chapters* (6 and 7) showed that proportion of the variance in the CHD risk factors and eCHD risk were only very weakly related to the three different categorization methods for physical activity (used in guidelines). However, it is well known that many variables of physical activity such as occupation, leisure-time and sports activities, and household tasks may influence the assessment of the level of physical activity to different degrees. Each instrument and measure of physical activity may capture these to different extents. Some studies have indicated that a substantial amount of the total daily walking occurs in non-leisure activity (e.g. occupation, transportation, and household tasks) and may be underestimated. It is recognized as a gap in physical activity surveys (CDC, 2000; Ford et al., 1991; Oja, 2001; Troiano et al., 2001; Whitt et al., 2004) that may affect the activity relationship with CHD risk.

It should be noted that two different measures, days/week of moderate activity and MET*hr/day, are used in the guidelines examined in this chapter. These may capture components of activity, such as total walking, to different extents. Thus, the choice of measure may affect the relationship between physical activity and the CHD risk factors and eCHD risk. It is also important to point out that the 30/3 and 30/5 guidelines do not relate to MET40*h guideline (expressed in total physical activity scores). The 30/3 and 30/5 guidelines focus more on measuring the number of days of participation in at least moderate physical activity (such as brisk walking for at least 30 minutes) rather than the total physical activity behaviour. For example, when physical activity is expressed as the number of days of at least moderate activity per week, the contribution of non-leisure activity (e.g. light or household activities) is ignored. Likewise, when physical activity is expressed as average MET*hr per day, the frequency of moderate or vigorous activity is not captured.

Therefore, the aim of this *Chapter* was to create a new categorization method that combines the physical activity expressed in number of days of at least 30 minutes of moderate physical activity with the total physical activity expressed in MET*hr/day. This will combine the different components of these measures which may affect the relationship between physical activity guidelines and CHD risk factors and eCHD risk.

8.2. Methods:

The statistical analysis carried out here is described in *Chapter* 4. To address the above aim, the MET40*h guideline proposed by Blair and other scores derived from the "30/3 or 30/5 guidelines" using different measure (number of days) is combined. Based on this combination, the subjects were classified into three different physical activity categories:

1. Not meeting either guideline (inactive): if the subjects do not meet either guidelines ("30/3 or 30/5 guidelines" and "MET40*h guideline")
2. Meeting only one guideline (possibly active): if the subjects meet either the "30/3 or 30/5 guidelines" OR "MET40*h guideline"
3. Meeting both guidelines (active): if the subjects meet both guidelines

8.3. Results:

I. <u>*Adjustment for age, BMI and smoking:*</u>

Using this method, relatively few men and women would fail to meet the criteria for either of the 30/3 plus MET40*h (approx 15 % and 23 %, respectively) or 30/5 plus MET40*h (approx 16 % and 26 %, respectively) guidelines and be considered inactive. More men and women would meet the both combined 30/3 + MET40*h (approx 52% and 47 %, respectively) than 30/5 + MET40*h (approx 38 % and 26 %, respectively) guidelines.

Tables 8.1 and 8.2 show the comparison of the CHD risk factors and eCHD risk between different activity groups as define by the combinations of the 30/3 + MET40*h guidelines and 30/5 + MET40*h guidelines, after adjustment for the age, BMI, and smoking. In general, there was a consistent significant trend relationship across activity status whereby the highest DBP and TC, lowest HDL-C and highest eCHD risk were evident in men who did not meet the criteria for 30/3 + MET40*h guidelines, but not SBP. For example, compared against those who failed to meet the criteria for of the 30/3 plus MET40*h, the Bonferroni test (which is derived from the General Linear Model) showed that men who met both guidelines had significantly lower eCHD risk (10.7 % versus 8.6 %, $P < 0.05$) (approximately 2.1 % absolute value). According to the 30/5 + MET40*h guidelines, the significant differences in the DBP and TC levels were no longer evident between those men who did not meet either and those who meet both guidelines. In women, the trend relationships of the CHD risk factors and eCHD risk across activity status were not significant using either combinations of 30/3 + MET40*h guidelines or 30/5 + MET40*h guidelines.

In men, the results show that the combination of the 30/3 + MET40*h guidelines also explains small proportions of the variance (partial eta squared) in the CHD risk factors and eCHD risk with a range of 1.1 % in SBP and 3.4 % in eCHD risk. The combination of the 30/5 + MET40*h guidelines explained less partial eta squared than observed with the combination of the 30/3 + MET40*h guidelines.

Table 8.1: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk between different activity groups of men (a) and women (b) as defined by the combination of the "3 days/week of moderate activity" and "40 MET*hr/day" guidelines. P values and partial eta squared are shown for analysis using physical activity as a categorical and ordinal variable, after adjustment for the age, BMI, and smoking.

(a)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1] Mean value (n)	133.8 (78)	77.3 (78)	5.5 (56)	0.98 (56)	10.7 (56)
Meeting only one [2] Mean value (n)	130.1 (170)	74.9 (170)	5.4 (128)	1.03 (127)	9.6 (126)
Meeting both [3] Mean value (n)	129.8 (265)	74.0 * (265)	5.2 * (207)	1.09 * (207)	8.6 % * (207)
P value (categorical)	***0.069***	***0.047***	***0.028***	***0.021***	***0.001***
Partial eta squared	***0.011***	***0.012***	***0.018***	***0.020***	***0.034***
P value (ordinal (Ptrend))	***0.051***	***0.018***	***0.009***	***0.006***	***< 0.001***
Partial eta squared	***0.007***	***0.011***	***0.018***	***0.020***	***0.034***

(b)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1] Mean value (n)	125.0 (133)	70.5 (133)	5.4 (95)	1.27 (95)	4.9 (95)
Meeting only one [2] Mean value (n)	122.4 (168)	68.8 (168)	5.3 (124)	1.25 (124)	4.4 (124)
Meeting both [3] Mean value (n)	122.0 (266)	68.6 (266)	5.3 (210)	1.29 (210)	3.9 (209)
P value (categorical)	***0.127***	***0.203***	***0.386***	***0.592***	***0.079***
Partial eta squared	***0.007***	***0.006***	***0.004***	***0.002***	***0.012***
P value (ordinal (Ptrend))	***0.061***	***0.107***	***0.226***	***0.564***	***0.025***
Partial eta squared	***0.006***	***0.005***	***0.003***	***0.001***	***0.012***

Significantly different from lowest physical activity category (Not meeting either) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] Not meeting either: if the subjects do not meet the 30/3 and MET40*h guidelines

[2] Meeting only one: if the subjects meet either the 30/3 or MET40*h guidelines

[3] Meeting both: if the subjects meet both guidelines

Table 8.2: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk in men (a) and women (b) between different activity groups as defined by the combination of the "5 days/week of moderate activity" and "40 MET*hr/day" guidelines. P values and partial eta squared are shown for analysis using physical activity as a categorical and ordinal variable, after adjustment for the age, BMI, and smoking.

(a)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1]					
Mean value	133.8	76.7	5.5	0.99	10.6
(n)	(83)	(83)	(58)	(58)	(58)
Meeting only one [2]					
Mean value	129.6	74.6	5.3	1.04	9.3
(n)	(256)	(256)	(198)	(197)	(196)
Meeting both [3]					
Mean value	130.2	74.2	5.2	1.10 *	8.6 *
(n)	(174)	(174)	(135)	(135)	(135)
P value (categorical)	***0.051***	***0.168***	***0.242***	***0.049***	***0.010***
Partial eta squared	***0.012***	***0.007***	***0.007***	***0.016***	***0.024***
P value (ordinal (Ptrend))	***0.120***	***0.104***	***0.126***	***0.014***	***0.003***
Partial eta squared	***0.005***	***0.005***	***0.006***	***0.016***	***0.024***

(b)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1]					
Mean value	124.5	70.3	5.4	1.28	4.7
(n)	(145)	(145)	(103)	(103)	(103)
Meeting only one [2]					
Mean value	122.2	68.8	5.3	1.26	4.3
(n)	(272)	(272)	(209)	(209)	(208)
Meeting both [3]					
Mean value	122.3	68.6	5.2	1.27	3.9
(n)	(150)	(150)	(117)	(117)	(117)
P value (categorical)	***0.254***	***0.267***	***0.391***	***0.941***	***0.240***
Partial eta squared	***0.005***	***0.005***	***0.004***	***0.000***	***0.007***
P value (ordinal (Ptrend))	***0.192***	***0.161***	***0.172***	***0.926***	***0.093***
Partial eta squared	***0.003***	***0.004***	***0.004***	***0.000***	***0.007***

Significantly different from lowest physical activity category (Not meeting either) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] Not meeting either: if the subjects do not meet the 30/5 and MET40*h guidelines

[2] Meeting only one: if the subjects meet either the 30/5 or MET40*h guidelines

[3] Meeting both: if the subjects meet both guidelines

I. *Exclusion of subjects on medications:*

Tables 8.3 and 8.4 showed the comparison of the CHD risk factors and eCHD risk between different activity groups as define by the combination of the 30/3 + MET40*h guidelines and 30/5 + MET40*h guidelines, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications. Using the 30/3 + MET40*h guidelines, the highest HDL-C, and lowest TC and eCHD risk were seen in those meeting both guidelines. For example, the Bonferroni test showed that men who met both guidelines had significantly higher HDL-C level (1.09 mmol/L) compared to those who did not meet either guidelines (0.95 mmol/L) (P = 0.007). There were no significant trend effects evident in SBP and DBP. Similar trend relationships were evident when using the 30/5 + MET40*h guidelines. In women, using the 30/3 + MET40*h guidelines (but not 30/5 + MET40*h guidelines), only DBP was significantly different between meeting both (67.9 mm Hg) and neither (71.5 mm Hg) guidelines (P = 0.013). Figure 8.1 and 8.2 demonstrate these relationships.

Tables 8.5 and 8.6 show the extent to which CHD risk factors and eCHD risk are explained by physical activity according to different methods, before and after exclusion of subjects on medications, and after adjustment for age, BMI and smoking. In men, taking this approach tended to double the partial eta squared values (compared to before excluding those on medications) so that the proportion of the variance in TC, HDL-C and eCHD risk increased to 5.2 %, 3.6 % and 4.0 %, respectively, particularly when categorized using the combined 30/3+MET40*h classification. The combination of the 30/5 + MET40*h guidelines explained slightly less partial eta squared values than observed with the combination of the 30/3 + MET40*h guidelines. In women, using the 30/3 + MET40*h guidelines, the partial eta squared value was only increase in DBP (1.8 %) compared to before excluding those on medications (0.6 %). In general, more of the variance in CHD risk factors and eCHD risk could be attributed to activity status when guidelines were combined as compared to single measures and when those on medication were excluded from the analysis. *Figure* 8.3 shows the extent to which eCHD risk are explained by physical activity according to different categorization methods after adjustment for age, BMI, smoking and exclusion of subjects on medications.

Table 8.3: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk in men (a) and women (b) between different activity groups as defined by the combination of the "3 days/week of moderate activity" and "40 MET*hr/day" guidelines. P values and partial eta squared are shown for analysis using physical activity as a categorical and ordinal variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1]					
Mean value	130.8	76.3	5.9	0.95	9.8
(n)	(44)	(44)	(29)	(29)	(29)
Meeting only one [2]					
Mean value	129.0	73.3	5.4 *	1.01	8.2
(n)	(123)	(123)	(94)	(93)	(92)
Meeting both [3]					
Mean value	128.5	73.0	5.1 *	1.09 *	7.3 *
(n)	(214)	(214)	(167)	(167)	(167)
P value (categorical)	***0.570***	***0.133***	***0.001***	***0.005***	***0.003***
Partial eta squared	***0.003***	***0.011***	***0.052***	***0.036***	***0.040***
P value (ordinal (Ptrend))	***0.327***	***0.089***	***< 0.001***	***0.001***	***0.001***
Partial eta squared	***0.003***	***0.008***	***0.051***	***0.036***	***0.038***

(b)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Not meeting either [1]					
Mean value	123.6	71.5	5.2	1.31	3.4
(n)	(68)	(68)	(48)	(48)	(48)
Meeting only one [2]					
Mean value	121.0	69.1	5.2	1.23	3.7
(n)	(107)	(107)	(76)	(76)	(76)
Meeting both [3]					
Mean value	120.2	67.9 *	5.2	1.30	3.2
(n)	(168)	(168)	(133)	(133)	(133)
P value (categorical)	***0.148***	***0.044***	***0.967***	***0.248***	***0.552***
Partial eta squared	***0.011***	***0.018***	***0.000***	***0.011***	***0.005***
P value (ordinal (Ptrend))	***0.063***	***0.015***	***0.852***	***0.845***	***0.525***
Partial eta squared	***0.010***	***0.017***	***0.000***	***0.000***	***0.002***

Significantly different from lowest physical activity category (Not meeting either) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] Not meeting either: if the subjects do not meet the 30/3 and MET40*h guidelines

[2] Meeting only one: if the subjects meet either the 30/3 or MET40*h guidelines

[3] Meeting both: if the subjects meet both guidelines

Table 8.4: Comparison of the CHD risk factors and estimated coronary heart disease (eCHD) risk in men (a) and women (b) between different activity groups as defined by the combination of the "5 days/week of moderate activity" and "40 MET*hr/day" guidelines. P values and partial eta squared are shown for analysis using physical activity as a categorical and ordinal variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	%
Not meeting either [1]					
Mean value	131.1	75.6	5.8	0.97	9.5
(n)	(48)	(48)	(31)	(31)	(31)
Meeting only one [2]					
Mean value	128.6	73.4	5.2 *	1.04	7.9 *
(n)	(192)	(192)	(149)	(148)	(147)
Meeting both [3]					
Mean value	128.6	82.9	5.1 *	1.10 *	7.3 *
(n)	(141)	(141)	(110)	(110)	(110)
P value (categorical)	***0.468***	***0.255***	***0.010***	***0.029***	***0.014***
Partial eta squared	***0.004***	***0.007***	***0.032***	***0.025***	***0.030***
P value (ordinal (Ptrend))	***0.364***	***0.147***	***0.009***	***0.008***	***0.006***
Partial eta squared	***0.002***	***0.006***	***0.024***	***0.024***	***0.027***

(b)

Physical activity category (combination of guidelines)	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	%
Not meeting either [1]					
Mean value	123.2	70.9	5.2	1.32	3.4
(n)	(76)	(76)	(53)	(53)	(53)
Meeting only one [2]					
Mean value	120.6	68.7	5.2	1.25	3.5
(n)	(168)	(168)	(126)	(126)	(126)
Meeting both [3]					
Mean value	120.5	68.1	5.2	1.30	3.2
(n)	(99)	(99)	(67)	(67)	(78)
P value (categorical)	***0.241***	***0.146***	***0.996***	***0.394***	***0.703***
Partial eta squared	***0.008***	***0.011***	***0.000***	***0.007***	***0.003***
P value (ordinal (Ptrend))	***0.170***	***0.071***	***0.931***	***0.876***	***0.600***
Partial eta squared	***0.006***	***0.010***	***0.000***	***0.000***	***0.001***

Significantly different from lowest physical activity category (Not meeting either) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] Not meeting either: if the subjects do not meet the 30/5 and MET40*h guidelines

[2] Meeting only one: if the subjects meet either the 30/5 or MET40*h guidelines

[3] Meeting both: if the subjects meet both guidelines

Table 8.5: The extent to which CHD risk factors and estimated coronary heart disease (eCHD) risk in men (a) and women (b) are explained by different categorization methods for physical activity (as categorical variable), before and after exclusion of subjects on medications, and after adjustment for age, BMI and smoking.

(a)

Categorization methods (as categorical variable)			**CHD risk factors**				**eCHD risk**
			SBP	**DBP**	**TC**	**HDL-C**	
Before excluding Medications	30/3 Guideline [1]	***P value***	0.309	0.043	0.011	0.003	0.000
		Partial eta squared	0.002	0.008	0.017	0.023	0.031
	30/5 Guideline [1]	***P value***	0.758	0.411	0.400	0.016	0.021
		Partial eta squared	0.000	0.001	0.002	0.015	0.014
	MET40*h [2]	***P value***	0.013	0.051	0.080	0.161	0.014
		Partial eta squared	0.012	0.007	0.008	0.005	0.016
	Combined 30/3 with MET40*h [3]	***P value***	0.069	0.047	0.028	0.021	0.001
		Partial eta squared	0.011	0.012	0.018	0.020	0.034
	Combined 30/5 with MET40*h [4]	***P value***	0.051	0.168	0.242	0.049	0.010
		Partial eta squared	0.012	0.007	0.007	0.016	0.024
After excluding Medications	30/3 Guideline [1]	***P value***	0.587	0.190	0.001	0.002	0.004
		Partial eta squared	0.001	0.005	0.040	0.034	0.029
	30/5 Guideline [1]	***P value***	0.693	0.376	0.111	0.027	0.004
		Partial eta squared	0.000	0.002	0.009	0.017	0.014
	MET40*h [2]	***P value***	0.218	0.110	0.003	0.043	0.010
		Partial eta squared	0.004	0.007	0.030	0.014	0.023
	Combined [3] 30/3 with MET40*h	***P value***	0.570	0.133	0.001	0.005	0.003
		Partial eta squared	0.003	0.011	0.052	0.036	0.040
	Combined [4] 30/5 with MET40*h	***P value***	0.468	0.255	0.010	0.029	0.014
		Partial eta squared	0.004	0.007	0.032	0.025	0.030

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively

[2] Accumulative of at least total 40 MET*hr/day

[3] Combined 30/3+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥ 3 days/week of moderate activity for ≥ 30 minutes" guidelines

[4] Combined 30/5+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥5 days/week of moderate activity for ≥ 30 minutes" guidelines

(b)

Categorization methods (as categorical variable)			Health risk factors SBP	DBP	TC	HDL-C	eCHD risk
Before excluding Medications	30/3 Guideline [1]	***P value***	0.098	0.227	0.306	0.302	0.020
		Partial eta squared	0.005	0.003	0.002	0.003	0.013
	30/5 Guideline [1]	***P value***	0.558	0.471	0.244	0.977	0.202
		Partial eta squared	0.001	0.001	0.003	0.000	0.004
	MET40*h [2]	***P value***	0.120	0.114	0.290	0.901	0.142
		Partial eta squared	0.004	0.004	0.003	0.000	0.005
	Combined 30/3 with MET40*h [3]	***P value***	0.127	0.203	0.386	0.592	0.079
		Partial eta squared	0.007	0.006	0.004	0.002	0.012
	Combined 30/5 with MET40*h [4]	***P value***	0.254	0.267	0.391	0.941	0.240
		Partial eta squared	0.005	0.005	0.004	0.000	0.007
After excluding Medications	30/3 Guideline [1]	***P value***	0.105	0.024	0.696	0.358	0.304
		Partial eta squared	0.008	0.015	0.001	0.003	0.004
	30/5 Guideline [1]	***P value***	0.452	0.254	0.809	0.674	0.398
		Partial eta squared	0.002	0.004	0.000	0.001	0.003
	MET40*h [2]	***P value***	0.129	0.066	0.902	0.455	0.964
		Partial eta squared	0.007	0.010	0.000	0.002	0.000
	Combined 30/3 with MET40*h [3]	***P value***	0.148	0.044	0.967	0.248	0.552
		Partial eta squared	0.011	0.018	0.000	0.011	0.005
	Combined 30/5 with MET40*h [4]	***P value***	0.241	0.146	0.996	0.394	0.703
		Partial eta squared	0.008	0.011	0.000	0.007	0.003

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] 30/3 and 30/5 guidelines refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively

[2] Accumulative of at least total 40 MET*hr/day

[3] Combined 30/3+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥ 3 days/week of moderate activity for ≥ 30 minutes" guidelines

[4] Combined 30/5+MET40*h guidelines: if the subjects meet both the "≥ 40 MET*hr/day" and "≥5 days/week of moderate activity for ≥ 30 minutes" guidelines

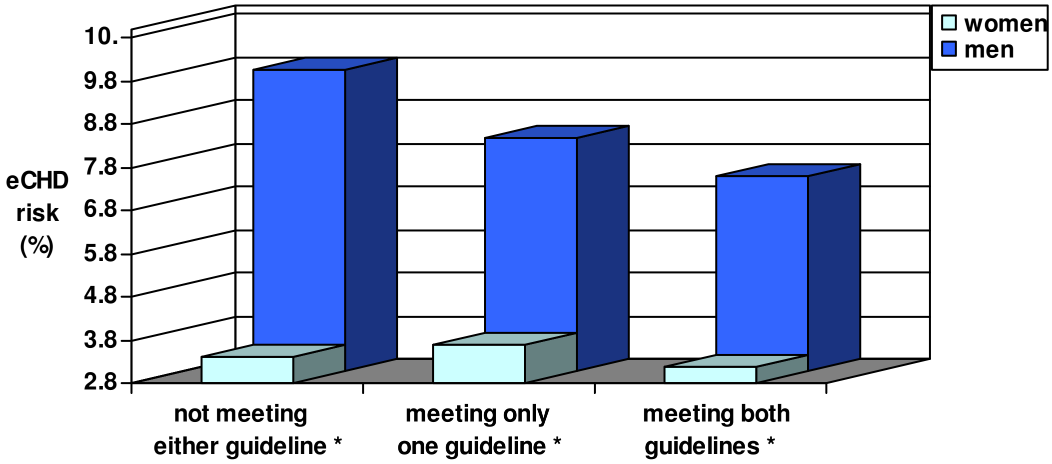


Figure 8.1: The estimation of the percentage of the likelihood of developing coronary heart disease (eCHD) according to the combination (as categorical) of at least 40 MET*hr/day and the at least 3 days/week of at least moderate activity for ≥ 30 minutes, after adjustment for age, BMI, smoking and excluding subjects on medications.

* Not meeting either guideline refers to not meeting the 30/3 and MET40*h guidelines. Meeting only one guideline: if the subjects meet either the 30/3 OR MET40*h guidelines. Meeting both guidelines: if the subjects meet both guidelines

The eCHD risk changes in men were significant [(P values were =0.003 for categorical and = 0.001 for ordinal (trend)], but not significant in women.

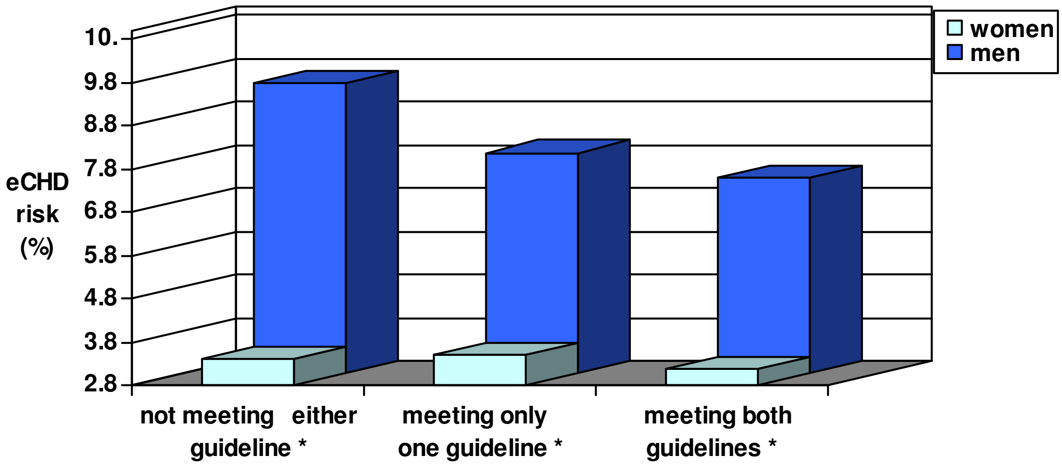


Figure 8.2: The estimation of the percentage of the likelihood of developing coronary heart disease (eCHD) according to the combination (as categorical) of ≥40 MET*hr/day and the ≥ 5 days/week of at least moderate activity for ≥ 30 minutes, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

* Not meeting either guideline refers to not meeting the 30/5 and MET40*h guidelines. Meeting only one guideline: if the subjects meet either the 30/5 OR MET40*h guidelines. Meeting both guidelines: if the subjects meet both guidelines

The eCHD risk changes in men were significant [(P values were =0.014 for categorical and = 0.006 for ordinal (trend)], but not significant in women.

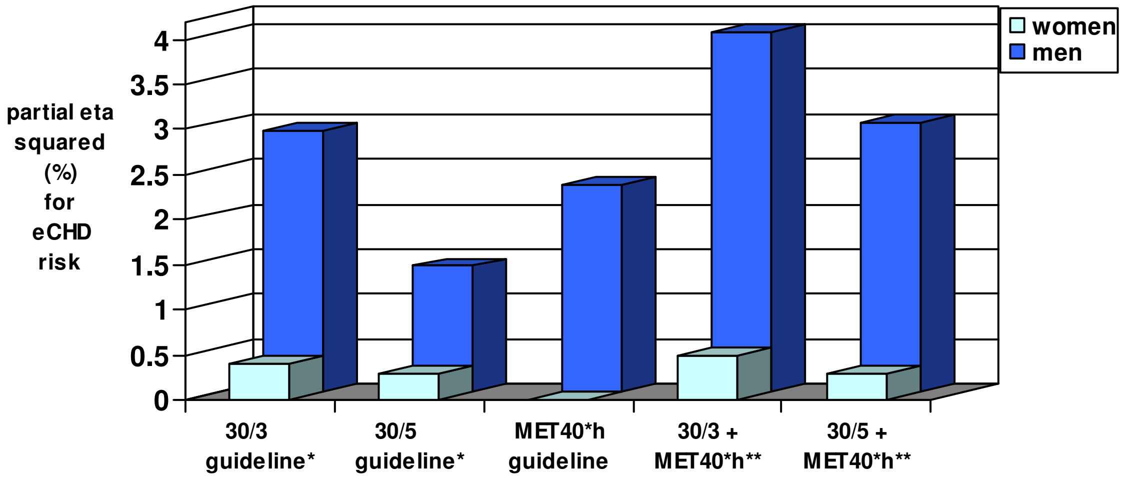


Figure 8.3: Percentages of the variation (express in partial eta squared) in the estimation of the coronary heart disease (eCHD) risk explain by different categorization methods for physical activity, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

* G-30/3 and G-30/5 refer to ≥ 30 minutes of at least moderate activity for at least 3 or 5 days per week, respectively

** 30/3+MET40*h: if the subjects meet both the "≥ 40 MET*hr/day" and "≥ 3 days/week of moderate activity for ≥ 30 minutes" guidelines. 30/5+MET40*h: if the subjects meet both the "≥ 40 MET*hr/day" and "≥5 days/week of moderate activity for ≥ 30 minutes" guidelines

8.4. Discussion:

In this chapter, the combined guidelines and measures, both aspects of at least moderate and total activities are captured. This mainly due to the fact that the 30/3 and 30/5 guidelines measure continuity of moderate physical activity rather than the average level of all activity assessed used for the MET40*h guideline. The re-categorization of subjects into activity groups using the combination of two different physical activity guidelines may have helped to reduce some of the uncertainty in classification when using the three guidelines individually. In addition, this combination method may help to interpret the results of this chapter more clearly by reducing the errors that are associated with physical activity guidelines. These errors may tend to classify one subject as inactive based on one guideline, but as active according to other guideline.

Using the combination of two different guidelines for physical activity (i.e. using different measures), this *Chapter* indicated that inactive men had unfavourable CHD risk factors and greater eCHD risk than those who were active in each of the three methods of categorisation. This effect persisted even after controlling for differences in BMI and adjustment for age, smoking and exclusion of subjects on medications. However, the findings failed to indicate any association of being considered active across these categorization methods with the CHD risk factors and eCHD risk in women.

This *Chapter* also provided further evidence that these guidelines explain only small proportions of variance in the CHD risk factors and eCHD risk after adjustment for the age, BMI and smoking. In women, the proportions of variance in the CHD risk factors and eCHD risk were even less than what observed in men. However, after excluding those who were taking prescribed medications and adjustment for the age, BMI, and smoking, the effects were found to be increased in men only and mainly for the levels of TC, HDL-C and eCHD risk (ranges from 3.6 to 5.2 % variations) compared to before the exclusion (ranges from 1.1 to 3.4 % of variations). Thus, correction for prescribed medicine appears to affect the relationship between physical activity and lipid profile. However, the cause of this effect cannot be examined because the type of medication is not known.

In general, when the combinations of the 30/5 + MET40*h guidelines was used, the proportions of the variance in the CHD risk factors and eCHD risk, expressed as partial eta squared, were less than the combinations of the 30/3 + MET40*h guidelines. The explanation for this is not clear, but, it is likely that the re-categorisation between 30/3 and 30/5 guidelines, which shifts some subjects from one group of activity to another group, may affect the findings of this study. However, taken together, more of the variance in CHD risk factors and eCHD risk could be attributed to activity status when guidelines were combined as compared to single measures and when those on medication were excluded from the analysis.

8.5. Conclusion:

This *Chapter* indicated that, using a new method of categorisation (combination of two different guidelines), inactive men had more unfavourable blood lipids and greater eCHD risk than those who were active. While this agreed with the second part of the hypothesis, there is still marginal evidence that using this combination method of categorization was related to reduction in adult CHD risk factors. The possible mechanisms behind these findings are addressed in *Chapter* 2. There is a little evidence from this *Chapter* for a dose-response relationship or a particular threshold value from which guidelines can be obtained. Therefore, it can be suggested that, although the value of physical activity in adults for public health purposes is beyond doubt, the guidelines should be further tested by breaking them down into a greater number of categories, not simply active/inactive. This issue is the main focus in the next *Chapter*.

Part One

Chapter 9: Physical activity dose-response relationship with the CHD risk factors and eCHD risk

Chapter 9 Physical activity dose-response relationship with the CHD risk factors and eCHD risk

9.1. Introduction:

The results shown in last three *Chapters* (6-8) have not supported a strong relationship between the adherence to different physical activity guidelines and the improvements in the CHD risk factors and eCHD risk as recorded in this NDNS database. These physical activity guidelines incorporate a dichotomous categorical approach (a single cut-off point) which does not allow for the investigation of a more complex dose-response relationship between physical activity and CHD risk factors. An alternative approach is to use a greater number of categories of physical activity so that the extremes of activity may be clearly differentiated. In this *Chapter*, the nature of the dose response relationship of expressing physical activity, using different measures, in terms of a) increasing the number of categories within each guideline approach, and b) expressing the absolute values as a continuous variable on the CHD risk factors and eCHD risk was examined.

9.2. Methods:

In order to address this aim, this *Chapter* sought to examine the effect of several categories and continuous variable of physical activity on the CHD risk factors and eCHD risk in the same subjects. Physical activity was expressed in:

1. number of days/week of moderate activity of 30 minutes or more
2. total MET*hr/day, and
3. number of minutes/day of moderate activity

Applying different categories for physical activity measures (number of days/week, minutes/day and MET*hr/day), would be expected to show one or more of the five possible "dose-response" relationships (see Figure 2.2, page 20) between physical activity and CHD risk factors and CHD risk. In examining the dose-response relationship between physical activity and CHD risk factors and eCHD risk, three different types of analyses were undertaken:

1) *Physical activity was used as a categorical variable (fixed factor)*
2) *Physical activity was used as an ordinal variable (as covariates)*
3) *Physical activity was used as a continuous variable*

The advantages and disadvantages of categorical, ordinal and continuous analysis of data have been addressed in the Methodology (page 84). Three different possible strategies were undertaken to define further categorical data for physical activity which would be more helpful in illustrating any dose-response or threshold in CHD risk factors and eCHD risk by physical activity:

1. Four categories expressed in number of days/week of moderate activity for 30 minutes or more (classified and used routinely by the NDNS):
   - zero day/week (less active)
   - 1-2 days/week
   - 3-4 days/week
   - ≥ 5 days/week (more active)
2. Four categories expressed in MET*hr/day scores:
   - < 40 MET/day (less active)
   - 40-45 MET/day
   - 45-50 MET/day
   - ≥ 50 MET/day (more active)
3. Five categories expressed in number of minutes/day of moderate activity:

   For men:
   - Zero minute (less active)
   - 1.0-21.9 minutes
   - 22.0-54.9 minutes
   - 55.0.0-289.9 minutes
   - > 290.0 minutes (more active)

   For women:
   - Zero minute (less active)
   - 1.0-16.9 minutes
   - 17.0-39.9 minutes
   - 40.0-98.9 minutes
   - > 99.0 minutes (more active)

The rationale behind the cut-offs for categorisation was to achieve equal numbers in each group without losing the cut-off point used in the guidelines. By doing this, it would enable an examination of any dose-response, allow comparisons relative to existing guidelines and aid communication and recognition of any effects which might lead to a difference in guideline.

In order to examine the nature of the possible dose-response relationship, the NDNS data-set were explored using different curve fitting models (e.g. logarithmic, inverse, cubic, quadratic, S, and exponential) and linear model. The correlation coefficients generated by each model were compared to identify possible advantages of one model over another. Partial eta squared was used as a measure of effect size (proportion of the variance in the outcome that is attributable to physical activity): the ratio of physical activity variance to physical activity plus error. The method is described in more details in *Chapter* 4 (Methodology).

9.3. Results:

9.3.1. Comparison between different curve fitting models and linear model:

In a linear regression model in which eCHD risk was the dependent variable and MET*h/day, age, BMI and smoking as independent variables, the following results were obtained a) for men, the r squared was 0.713 with significant independent effects of MET*h/day (P = 0.002) and b) for women, the r squared was 0.614 with no significant effects of MET*h/day.

Using the curvilinear models, the quadratic and cubic terms for MET*h/day did not improve significantly the model (r squared = 0.716 and 0.615 in men and women, respectively) and neither these terms were significant in either men or women. To give a visual appreciation of the lack of significant advantages of using curvilinear models over linear model, a bivariate curve fitting models (in TC, HDL-C and eCHD risk) were used in age groups defined by the NDNS data-set. Figure 9.1 shows the results of various curve fitting models. It is clear that the curves were generally similar to each other. The associated r squared values were also similar and not significant different from the r squared value obtained using the linear model. Therefore, all the subsequent statistical analysis was carried out using the General Linear Model (GLM).

MEN **WOMEN**

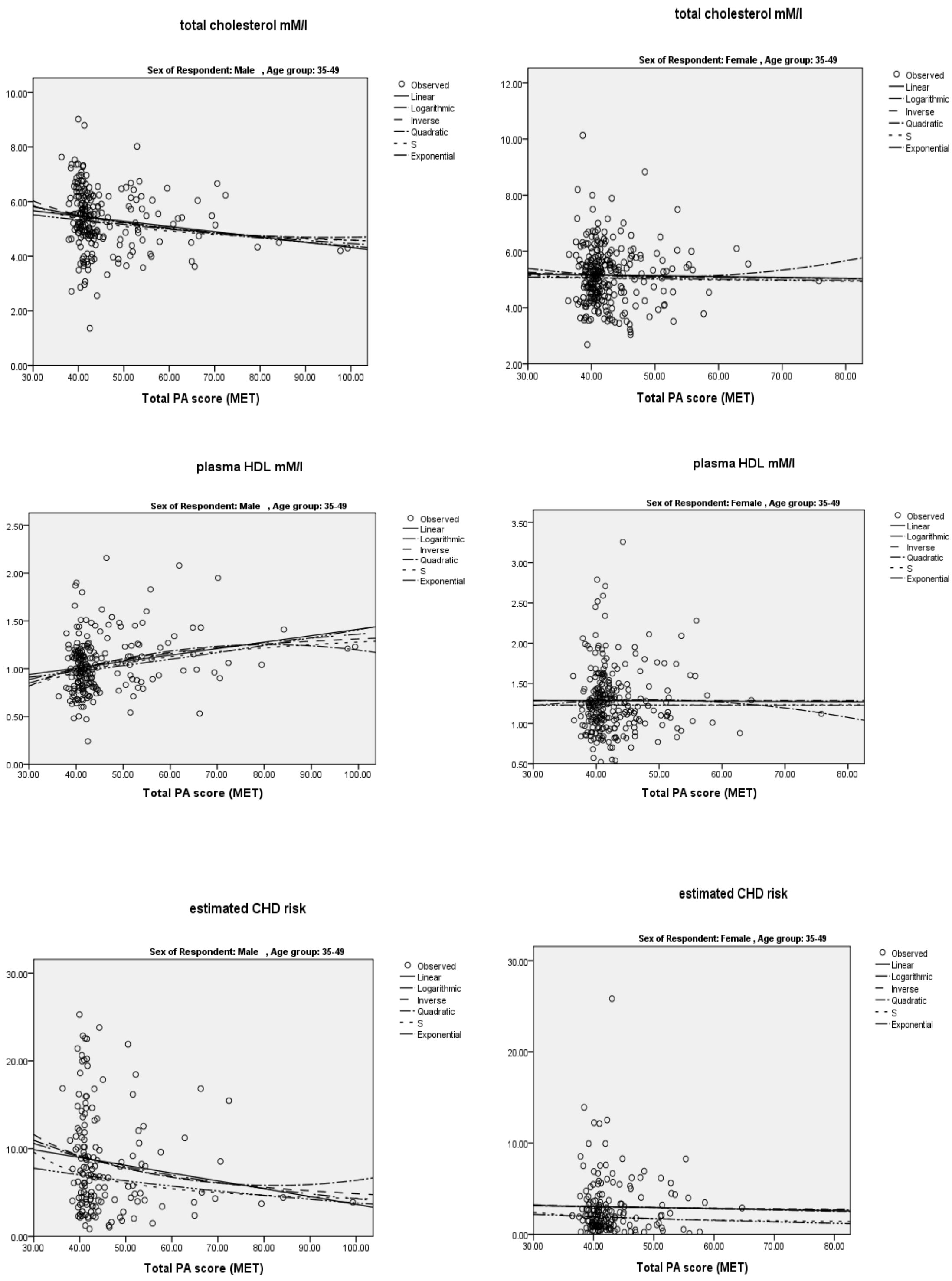


Figure 9.1: Comparison between various curve fitting models (e.g. logarithmic, inverse, quadratic, S, and exponential) and linear model obtained from the association of physical activity (expressed MET*h/day) with TC, HDL-C and eCHD risk in subjects aged 35-49 years.

9.3.2. Physical activity as categorical and continuous variables (before exclusion of subjects on medication):

All three types of analyses (categorical, ordinal and continuous variables) are included in *Tables* 9.1-9.3 (below) which summarise the association between physical activity and CHD risk factors and eCHD risk, after adjustment for the age, BMI and smoking. Since the overall conclusions of using these analyses remained unchanged, for simplicity and to reduce overload with statistical analyses, only categorical and continuous variables were interpreted in this *Chapter*.

Categories for the number of days/week: Using the number of days/week categories, there were approximately 23 % of men and 21 % of women failed to report any days/week of at least moderate activity. The proportion of men and women who reported at least five days/week was approximately 34 % and 26 %, respectively (see *Table* 9.1). In men, the GLM showed significant dose-response relationships between the number of days/week and all CHD risk factors (but not SBP) and eCHD risk. For example, the 3-4 days/week group had significantly (P = 0.046) lower level of TC (5.0 mmol/L) compared to the men in the zero day/week group (5.5 mmol/L), but did not fall further when activity levels exceed 5 days/week. In women, there were no clear dose-response relationship between the number of days per week of moderate activity and the CHD risk factors and eCHD risk. Although there was a consistent significant trend relationship across activity status, the GLM revealed that the proportion of the variance (partial eta squared) in the CHD risk factors and eCHD risk explained by physical activity was very small (ranges from 0.3 % to 4.6 % in men and 0.3 % to 1.6 % in women).

*Categories for the total MET*h/day:* Using the total MET*h/day categories, approximately 16 % of men and 26 % of women achieved 40 MET*h/day or less, whereas the majority of the men (53 %) and women (57 %) categorized in the 40-45 MET*h/day group (see *Table* 9.2). Using these categories, the GLM showed only significant dose-response relationships with HDL-C and eCHD risk. For example, the 40-45 MET*h/day group of men had significantly (P = 0.003) higher level of HDL-C (1.19 mmol/L) compared to those men in the < 40 MET*h/day group (1.00 mmol/L). In women, there were no clear dose-response relationship between the total MET*h/day and the CHD risk factors and eCHD risk. The proportion of the variance (partial eta squared) in the CHD risk factors and eCHD risk explained by physical activity was very small (ranges from 1.0 % to 3.6 % in men and < 1.0 % in women).

Categories for the number of minutes/day: In men, the results showed that there was no clear graded linear and dose–response relationship between physical activity expressed in the number of minutes/day and any of the CHD risk factors, except eCHD risk (Table 9.3). For instance, men in the > 290 minutes/day group of moderate activity (average 427 minutes/day) had significantly (P = 0.014) lower eCHD risk (8.4 %) compared to those who did not report any number of minutes/day (10.4 %). In women, only DBP was significantly decreased with increasing the number of minutes/day of moderate activity such that women in > 99 minutes/day group (242 min/d) had significantly lower DBP compared to those who did not report any number of minutes/day (67.5 mmHg versus 70.2 mmHg, P < 0.05). The proportion of the variance (partial eta squared) in the CHD risk factors and eCHD risk explained by these categories was also very small (ranges from 0.5 % to 5.5 % in men and 0.2 % to 2.4 % in women).

Physical activity as continuous variable: In men, after adjustment for age, BMI and smoking, significant dose-response relationships was found between physical activity (whether expressed in days/week, minutes/day and MET*h/day) and eCHD risk (see Tables 9.1 – 9.3). Less consistent relationships were observed for the individual risk factors. In women, significant relationships between physical activity and eCHD risk was only found when physical activity was expressed in MET*hr/d; no relationships were found with individual risk factors (see Table 9.1 – 9.3).

Table 9.1: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in number of days/week of at least moderate activity for ≥ 30 minutes. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI and smoking.

(a)

Physical activity category (days/week) [1]	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero day/week Mean value (n)	 131.5 (117)	 74.4 (117)	 5.5 (85)	 1.02 (84)	 10.0 (83)
1-2 days/week Mean value (n)	 130.8 (125)	 76.1 (125)	 5.4 (96)	 0.99 (96)	 10.0 (96)
3-4 days/week Mean value (n)	 129.3 (96)	 73.3 (96)	 5.0 * (74)	 1.08 (74)	 8.5 * (74)
> 5 days/week Mean value (n)	 130.2 (175)	 74.2 (175)	 5.2 (136)	 1.10 (136)	 8.5 * (136)
P value (categorical)	***0.702***	***0.177***	***0.046***	***0.018***	***0.007***
Partial eta squared	***0.003***	***0.010***	***0.021***	***0.026***	***0.31***
P value (ordinal (Ptrend))	***0.383***	***0.148***	***0.039***	***0.008***	***0.002***
Partial eta squared	***0.001***	***0.004***	***0.011***	***0.018***	***0.025***
P value (continuous)	***0.209***	***0.046***	***0.044***	***0.005***	***0.001***
Partial eta squared	***0.003***	***0.008***	***0.010***	***0.021***	***0.026***

Significantly different from lowest physical activity category (zero day/week) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] days/week refers to the number of days per week of at least moderate activity for ≥ 30 minutes

(b)

Categorical methods (days/week) [1]	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero day/week Mean value (n)	125.5 (119)	70.1 (119)	5.4 (82)	1.29 (82)	4.4 (82)
1-2 days/week Mean value (n)	122.6 (169)	69.4 (169)	5.4 (128)	1.23 (128)	4.9 (128)
3-4 days/week Mean value (n)	121.3 (128)	68.6 (128)	5.3 (101)	1.31 (101)	3.9 (100)
> 5 days/week Mean value (n)	122.2 (151)	68.6 (151)	5.2 (118)	1.27 (118)	3.9 (118)
P value (categorical)	***0.111***	***0.623***	***0.676***	***0.346***	***0.084***
Partial eta squared	***0.011***	***0.003***	***0.004***	***0.008***	***0.016***
P value (ordinal (Ptrend))	***0.063***	***0.212***	***0.246***	***0.807***	***0.098***
Partial eta squared	***0.006***	***0.003***	***0.003***	***0.000***	***0.006***
P value (continuous)	***0.205***	***0.304***	***0.151***	***0.839***	***0.146***
Partial eta squared	***0.003***	***0.002***	***0.005***	***0.000***	***0.005***

Significantly different from lowest physical activity category (zero day/week) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] days/week refers to the number of days per week of at least moderate activity for ≥ 30 minutes

Table 9.2: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in total MET*hr/day. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI and smoking.

(a)

Physical activity category (total MET*hr/day)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
< 40 (group mean = 39)					
Mean value	133.9	76.8	5.5	1.00	10.5
(n)	(84)	(84)	(59)	(59)	(59)
40-45 (group mean = 42)					
Mean value	129.7	74.8	5.3	1.02	9.5
(n)	(270)	(270)	(207)	(206)	(205)
45-50 (group mean = 47)					
Mean value	128.1	73.1	5.0	1.19 *	8.1 *
(n)	(46)	(46)	(40)	(40)	(40)
< 50 (group mean = 61)					
Mean value	130.9	74.0	5.3	1.10	8.3 *
(n)	(113)	(113)	(85)	(85)	(85)
P value (categorical)	***0.056***	***0.172***	***0.111***	***0.003***	***0.005***
Partial eta squared	***0.015***	***0.010***	***0.016***	***0.036***	***0.033***
P value (ordinal (Ptrend))	***0.322***	***0.071***	***0.107***	***0.006***	***0.001***
Partial eta squared	***0.002***	***0.006***	***0.007***	***0.020***	***0.029***
P value (continuous)	***0.991***	***0.220***	***0.085***	***0.030***	***0.002***
Partial eta squared	***0.000***	***0.003***	***0.008***	***0.012***	***0.025***

Significantly different from lowest physical activity category (< 40 MET*h/day) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Physical activity category (total MET*hr/day)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
< 40 (group mean = 39)					
Mean value	124.4	70.3	5.4	1.27	4.7
(n)	(146)	(146)	(104)	(104)	(104)
40-45 (group mean = 42)					
Mean value	122.5	68.9	5.3	1.27	4.2
(n)	(325)	(325)	(250)	(250)	(250)
45-50 (group mean = 47)					
Mean value	119.7	67.3	5.4	1.26	4.0
(n)	(51)	(51)	(40)	(40)	(40)
< 50 (group mean = 61)					
Mean value	123.1	69.4	5.2	1.30	4.1
(n)	(45)	(45)	(35)	(35)	(35)
P value (categorical)	***0.230***	***0.285***	***0.711***	***0.962***	***0.522***
Partial eta squared	***0.008***	***0.007***	***0.003***	***0.001***	***0.005***
P value (ordinal (Ptrend))	***0.192***	***0.230***	***0.487***	***0.828***	***0.243***
Partial eta squared	***0.003***	***0.003***	***0.001***	***0.000***	***0.003***
P value (continuous)	***0.312***	***0.390***	***0.496***	***0.527***	***0.035***
Partial eta squared	***0.002***	***0.001***	***0.001***	***0.001***	***0.002***

Significantly different from lowest physical activity category (< 40 MET*h/day) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 9.3: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in number of minutes/day of at least moderate activity. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI and smoking.

(a)

Physical activity category (minutes/day) [1]	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	%
Zero min/d (0 min/d) Mean (n)	130.4 (96)	74.6 (96)	5.5 (67)	1.00 (67)	10.4 (66)
1-21 min/d (11 min/d) Mean (n)	132.6 (103)	77.6 (103)	5.5 (84)	1.03 (84)	9.8 (83)
22-54 min/d (35 min/d) Mean (n)	129.5 (101)	74.2 (101)	5.2 (77)	1.04 (77)	9.1 (77)
55-289 min/d (123 min/d) Mean (n)	128.9 (109)	73.2 (109)	5.1 (83)	1.09 (83)	8.5 * (83)
≥ 290 (427 min/d) Mean (n)	131.0 (104)	74.4 (104)	5.2 (80)	1.09 (80)	8.4 * (80)
P value (categorical)	***0.337***	***0.032***	***0.078***	***0.302***	***0.014***
Partial eta squared	***0.009***	***0.021***	***0.022***	***0.013***	***0.032***
P value (ordinal (Ptrend))	***0.538***	***0.123***	***0.017***	***0.034***	***0.001***
Partial eta squared	***0.001***	***0.005***	***0.015***	***0.012***	***0.030***
P value (continuous)	***0.900***	***0.201***	***0.125***	***0.042***	***0.003***
Partial eta squared	***0.000***	***0.003***	***0.006***	***0.011***	***0.022***

Significantly different from lowest physical activity category (zero min/d) - * P < 0.05, ** P < 0.001.

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Physical activity category (minutes/day)	CHD risk factors				eCHD risk %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero min/d (0 min/d)					
Mean	125.5	70.2	5.4	1.29	4.6
(n)	(97)	(97)	(67)	(67)	(67)
1-16 min/d (9 min/d)					
Mean	123.7	69.6	5.4	1.22	4.8
(n)	(109)	(109)	(83)	(83)	(83)
17-39 (27 min/d)					
Mean	120.6	67.5	5.3	1.34	3.9
(n)	(118)	(118)	(92)	(92)	(92)
40-98 (62 min/d)					
Mean	123.6	71.2	5.3	1.24	4.4
(n)	(122)	(122)	(91)	(91)	(91)
≥ 99 (242 min/d)					
Mean	121.1	67.5 *	5.2	1.26	3.9
(n)	(121)	(121)	(96)	(96)	(95)
P value (categorical)	***0.064***	***0.016***	***0.792***	***0.221***	***0.380***
Partial eta squared	***0.016***	***0.022***	***0.004***	***0.013***	***0.010***
P value (ordinal (Ptrend))	***0.049***	***0.253***	***0.244***	***0.645***	***0.210***
Partial eta squared	***0.007***	***0.002***	***0.003***	***0.001***	***0.004***
P value (continuous)	***0.380***	***0.680***	***0.980***	***0.636***	***0.512***
Partial eta squared	***0.001***	***0.000***	***0.000***	***0.001***	***0.001***

Significantly different from lowest physical activity category (zero min/d) - * P < 0.05, ** P < 0.001.

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

9.3.3. Physical activity as categorical and continuous variables (after exclusion of subjects on medication):

All analysis was repeated after excluding those who had been taking prescribed medical drugs. *Tables* 9.4-9.6 present the CHD risk factors and eCHD risk, according to different categorization methods for physical activity, after adjustment for the age, BMI smoking and after the exclusion of subjects on medications. In addition, *Figures* 9.2-9.4 demonstrate the dose-response relationships of different categorization methods for physical activity with the CHD risk factors and eCHD risk.

Categories for the number of days/week: There was a statistically significant group effect of activity level expressed in days/week with TC, HDL-C and eCHD risk with risk falling with increasing physical activity, but not SBP and DBP (*Table* 9.4). For example, compared against the men in the zero day/week group, significant differences in eCHD risk was evident when activity levels exceeded 5 days/week (8.6 % versus 7.3 %, P < 0.05). The eCHD risk decreased by approximately 1.3 % (absolute values) across the least to most active groups (8.6 % versus 7.3 %, P < 0.05). Again, in women, there were no clear dose-response relationship between the number of days per week of moderate activity and the CHD risk factors and eCHD risk. GLM analysis revealed that 4.5 %, 3.4 % and 3.0 % of the variance in TC, HDL-C and eCHD risk, respectively, could be directly attributed to differences in physical activity level expressed in number of days/week of moderate activity, after adjustment for age, BMI and smoking in those subjects who were not on medication (see *Figure* 9.2).

*Categories for the total MET*h/day:* There was a statistically significant group effect of activity level expressed in MET*h/day with TC, HDL-C and eCHD risk with risk falling with increasing physical activity, but not SBP and DBP (*Table* 9.5). For example, compared against the most inactive group (< 40 MET*h/d), significant differences in HDL-C were only evident when activity levels exceeded 45 MET*h/d (0.97 mmol/L versus 1.21 mmo/L, P < 0.01). The HDL-C value increased by approximately 0.21 mmol/L (absolute values) across the least to most active groups (0.97 mmol/L to 1.21 mmol/L, P < 0.01). Nevertheless, the results showed that there was no obvious direct linear relationship between activity level expressed in total MET*h/day and the CHD risk factors and eCHD risk, in both men and women (see *Figure* 9.3). For example, men in 45-50 MET*h/d group had the highest HDL-C. However, there was no further increasing in HDL-C as activity increased beyond 50 MET*h/d (e.g. HDL-C on 50 MET*h/d was not significantly different from that on 45-50 MET*h/d group). GLM analysis revealed that 6.3 % of the variance in HDL-C could be directly attributed to differences in physical activity level expressed in MET*h/d after adjustment for age, BMI and smoking in those subjects who were not on medication. In women, there were no clear dose-response relationship between the total MET*h/day and the CHD risk factors and eCHD risk.

Categories for the number of minutes/day: The results showed that there was only graded linear and dose–response relationship between physical activity expressed in the number of minutes/day and TC (Table 9.6). For instance, men in the 22-54 minutes/day of moderate activity (average 35 minutes/day) had significantly (P < 0.05) lower TC (5.1 mmol/L) compared to those who did not report any number of minutes/day (5.7 mmol/L). In women, only DBP was significantly decreased with increasing the number of minutes/day of moderate activity such that women in > 99 minutes/day group (242 minutes/day) had significantly lower DBP compared to those who did not report any number of minutes/day (66.3 mmHg versus 69.8 mmHg, $P < 0.05$). The proportion of the variance (partial eta squared) in the CHD risk factors and eCHD risk explained by these categories was also very small (ranges from 0.5 % to 5.5 % in men and 0.2 % to 2.4 % in women) (see *Figure* 9.4).

Physical activity as continuous variable: All the analyses were repeated after excluding those individuals on medication. In men, significant dose-response relationships were found between physical activity (whether expressed in days/week, minutes/day and MET*h/day) and eCHD risk as well as for total cholesterol and HDL (no relationship was found for SBP and DBP (see Tables 9.4 – 9.7). No relationships between physical activity and individual risk factors or eCHD risk were found (Tables 9.4 – 9.7).

Table 9.4: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in number of days/week of at least moderate activity for ≥ 30 minutes. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity category (days/week) [1]	**CHD risk factors**				**eCHD risk %**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero day/week Mean value (n)	129.3 (74)	73.8 (74)	5.6 (51)	1.00 (50)	8.6 (49)
1-2 days/week Mean value (n)	129.4 (89)	74.6 (89)	5.4 (70)	1.00 (70)	8.6 (70)
3-4 days/week Mean value (n)	128.6 (77)	72.9 (77)	5.0 * (59)	1.09 * (59)	7.4 (59)
> 5 days/week Mean value (n)	128.5 (141)	72.9 (141)	5.1 * (110)	1.10 * (110)	7.3 * (110)
P value (categorical)	***0.960***	***0.581***	***0.004***	***0.021***	***0.038***
Partial eta squared	***0.001***	***0.005***	***0.045***	***0.034***	***0.030***
P value (ordinal (Ptrend))	***0.617***	***0.292***	***0.002***	***0.004***	***0.008***
Partial eta squared	***0.001***	***0.003***	***0.033***	***0.029***	***0.025***
P value (continuous)	***0.390***	***0.136***	***0.003***	***0.002***	***0.005***
Partial eta squared	***0.002***	***0.006***	***0.031***	***0.034***	***0.027***

Significantly different from lowest physical activity category (zero day/week) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] days/week refers to the number of days/week of at least moderate activity for ≥ 30 minutes (4 categories)

(b)

Physical activity category (days/week) [1]	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	**%**
Zero day/week Mean value (n)	 123.4 (66)	 70.9 (66)	 5.2 (44)	 1.27 (44)	 3.2 (44)
1-2 days/week Mean value (n)	 121.5 (100)	 69.8 (100)	 5.2 (74)	 1.25 (74)	 3.8 (74)
3-4 days/week Mean value (n)	 119.7 (77)	 67.5 (77)	 5.1 (60)	 1.30 (60)	 3.3 (60)
> 5 days/week Mean value (n)	 120.4 (100)	 68.0 (100)	 5.1 (79)	 1.29 (79)	 3.1 (79)
P value (categorical)	***0.301***	***0.130***	***0.979***	***0.811***	***0.487***
Partial eta squared	***0.011***	***0.017***	***0.001***	***0.004***	***0.010***
P value (ordinal (Ptrend))	***0.101***	***0.034***	***0.681***	***0.502***	***0.509***
Partial eta squared	***0.008***	***0.013***	***0.001***	***0.002***	***0.002***
P value (continuous)	***0.201***	***0.064***	***0.497***	***0.601***	***0.507***
Partial eta squared	***0.005***	***0.010***	***0.002***	***0.001***	***0.002***

Significantly different from lowest physical activity category (zero day/week) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] days/week refers to the number of days/week of at least moderate activity for ≥ 30 minutes (4 categories)

Table 9.5: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in total MET*hr/day. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity category (total MET*hr/day)	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	%
< 40 (group mean = 39)					
Mean value	131.1	75.6	5.8	0.97	9.5
(n)	(48)	(48)	(31)	(31)	(31)
40-45 (group mean = 42)					
Mean value	128.6	73.5	5.3 *	1.02	8.1
(n)	(206)	(206)	(159)	(158)	(157)
45-50 (group mean = 47)					
Mean value	125.7	71.9	4.9 *	1.21 **	6.7 *
(n)	(35)	(35)	(31)	(31)	(31)
> 50 (group mean = 61)					
Mean value	129.7	73.0	5.2 *	1.09 *	7.1 *
(n)	(92)	(92)	(69)	(69)	(69)
P value (categorical)	***0.289***	***0.350***	***0.009***	***0.000***	***0.009***
Partial eta squared	***0.010***	***0.009***	***0.040***	***0.063***	***0.040***
P value (ordinal (Ptrend))	***0.749***	***0.200***	***0.021***	***0.004***	***0.003***
Partial eta squared	***0.000***	***0.004***	***0.019***	***0.030***	***0.031***
P value (continuous)	***0.529***	***0.305***	***0.025***	***0.019***	***0.005***
Partial eta squared	***0.001***	***0.003***	***0.018***	***0.019***	***0.027***

Significantly different from lowest physical activity category (< 40 MET*h/day) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Physical activity category (total MET*hr/day)	**CHD risk factors**				**eCHD risk**
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	%
< 40 (group mean = 39)					
Mean value	123.0	70.8	5.2	1.31	3.4
(n)	(77)	(77)	(54)	(54)	(54)
40-45 (group mean = 42)					
Mean value	121.2	68.8	5.2	1.26	3.5
(n)	(201)	(201)	(151)	(151)	(151)
45-50 (group mean = 47)					
Mean value	117.8	66.2	5.4	1.28	3.4
(n)	(32)	(32)	(24)	(24)	(24)
< 50 (group mean = 61)					
Mean value	119.6	68.4	5.1	1.32	2.6
(n)	(33)	(33)	(28)	(28)	(28)
P value (categorical)	***0.195***	***0.158***	***0.759***	***0.719***	***0.480***
Partial eta squared	***0.014***	***0.015***	***0.005***	***0.005***	***0.010***
P value (ordinal (Ptrend))	***0.064***	***0.082***	***0.888***	***0.872***	***0.287***
Partial eta squared	***0.010***	***0.009***	***0.000***	***0.000***	***0.005***
P value (continuous)	***0.239***	***0.185***	***0.837***	***0.376***	***0.368***
Partial eta squared	***0.004***	***0.005***	***0.000***	***0.003***	***0.003***

Significantly different from lowest physical activity category (< 40 MET*h/day) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 9.6: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity expressed in number of minutes/day of at least moderate activity. P values and partial eta squared are shown for analysis using physical activity as a categorical, ordinal and continuous variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity category (minutes/day)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero min/d (0 min/d)					
Mean	128.8	73.2	5.7	0.96	9.3
(n)	(60)	(60)	(38)	(38)	(37)
1-21 min/d (11 min/d)					
Mean	129.8	75.9	5.5	1.04	8.3
(n)	(72)	(72)	(60)	(59)	(59)
22-54 min/d (35 min/d)					
Mean	129.0	73.0	5.1 *	1.03	7.9
(n)	(78)	(78)	(60)	(60)	(60)
55-289 min/d (123 min/d)					
Mean	127.3	72.3	5.0 *	1.10	7.2
(n)	(86)	(86)	(67)	(67)	(67)
≥ 290 (427 min/d)					
Mean	129.8	73.3	5.1 *	1.09	7.2
(n)	(85)	(85)	(65)	(65)	(65)
P value (categorical)	***0.766***	***0.228***	***0.003***	***0.072***	***0.052***
Partial eta squared	***0.005***	***0.015***	***0.055***	***0.030***	***0.033***
P value (ordinal (Ptrend))	***0.919***	***0.330***	***0.001***	***0.011***	***0.004***
Partial eta squared	***0.000***	***0.003***	***0.040***	***0.023***	***0.030***
P value (continuous)	***0.801***	***0.382***	***0.035***	***0.038***	***0.011***
Partial eta squared	***0.000***	***0.002***	***0.015***	***0.015***	***0.022***

Significantly different from lowest physical activity category (zero min/d) - * P < 0.05,

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

(b)

Physical activity category (minutes/day)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero min/d (0 min/d)					
Mean	122.2	69.8	5.2	1.28	3.3
(n)	(55)	(55)	(37)	(37)	(37)
1-16 min/d (9 min/d)					
Mean	123.4	71.3	5.3	1.27	3.2
(n)	(60)	(60)	(43)	(43)	(43)
17-39 (27 min/d)					
Mean	119.4	67.1	5.1	1.31	3.5
(n)	(72)	(72)	(58)	(58)	(58)
40-98 (62 min/d)					
Mean	122.8	71.3	5.1	1.25	3.8
(n)	(74)	(74)	(54)	(54)	(54)
≥ 99 (242 min/d)					
Mean	118.8	66.3 *	5.2	1.28	3.1
(n)	(82)	(82)	(65)	(65)	(65)
P value (categorical)	***0.086***	***0.003***	***0.962***	***0.930***	***0.769***
Partial eta squared	***0.024***	***0.047***	***0.002***	***0.003***	***0.007***
P value (ordinal (Ptrend))	***0.105***	***0.058***	***0.653***	***0.881***	***0.917***
Partial eta squared	***0.008***	***0.011***	***0.001***	***0.000***	***0.000***
P value (continuous)	***0.217***	***0.244***	***0.592***	***0.363***	***0.342***
Partial eta squared	***0.005***	***0.004***	***0.001***	***0.003***	***0.004***

Significantly different from lowest physical activity category (zero min/d) - * $P < 0.05$,
Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

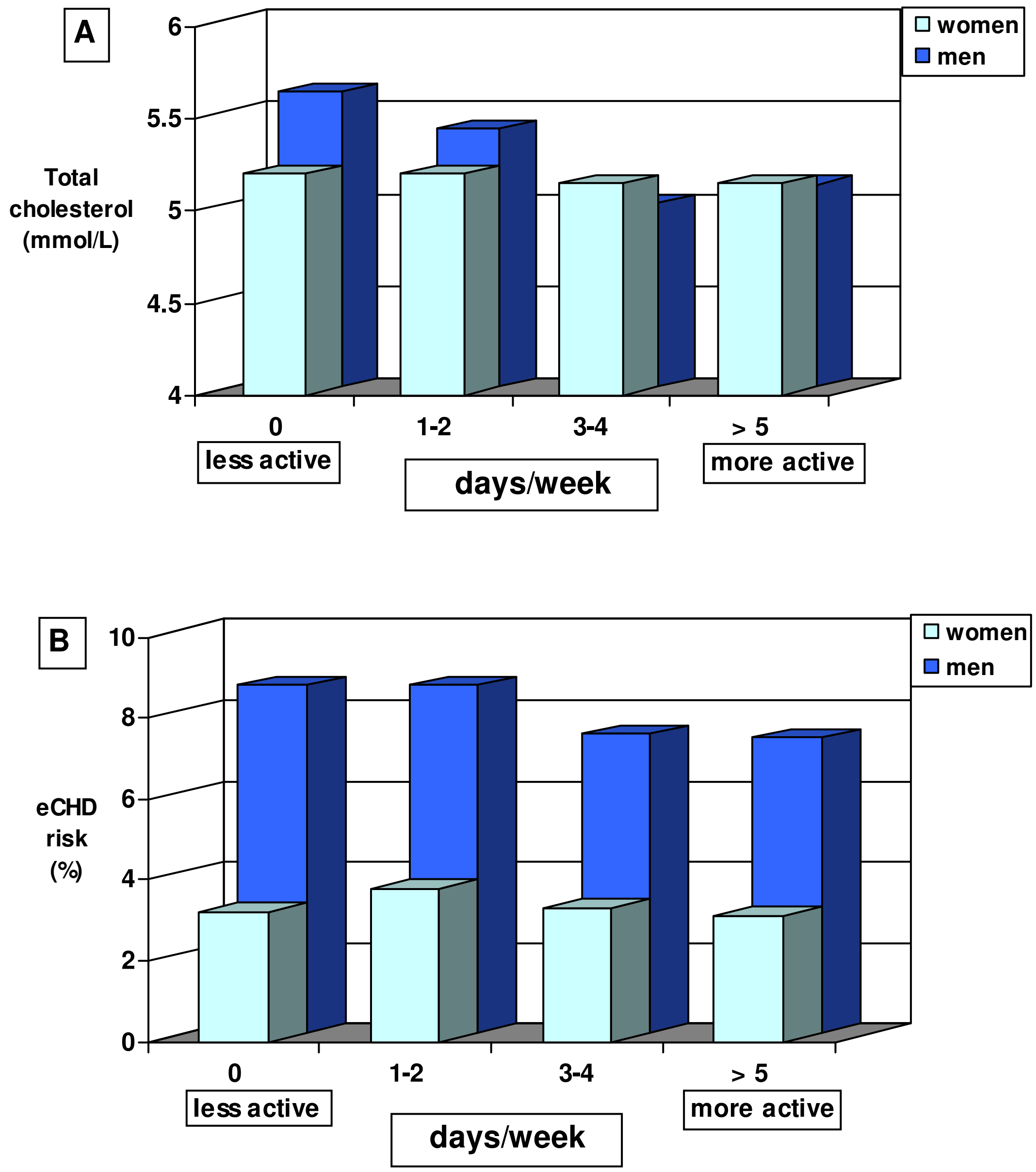
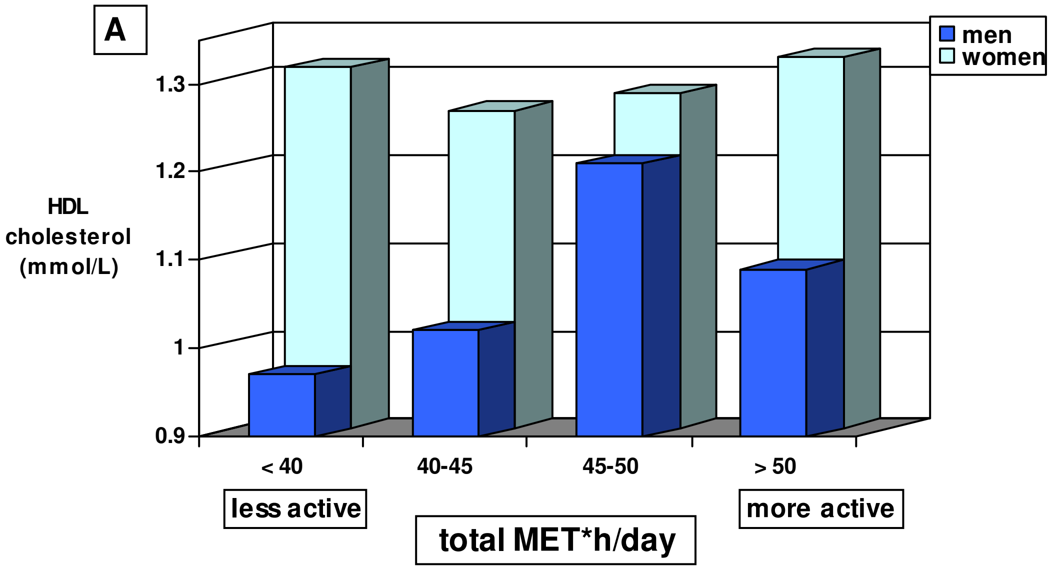


Figure 9.2: Total cholesterol (A) and the estimation of the percent likelihood of developing coronary heart disease (eCHD) risk over a period of 10 years (B), according to categorization method for physical activity expressed in number of days/week of at least moderate activity for ≥ 30 minutes, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

Total cholesterol changes in men were significant [(P values were 0.004, 0.002 and 0.003 for categorical, ordinal (trend) and continuous variables, respectively], but not significant in women. eCHD risk changes in men were significant [(P values were 0.038, 0.008 and 0.005 for categorical, ordinal (trend), and continuous variables, respectively], but not significant in women.



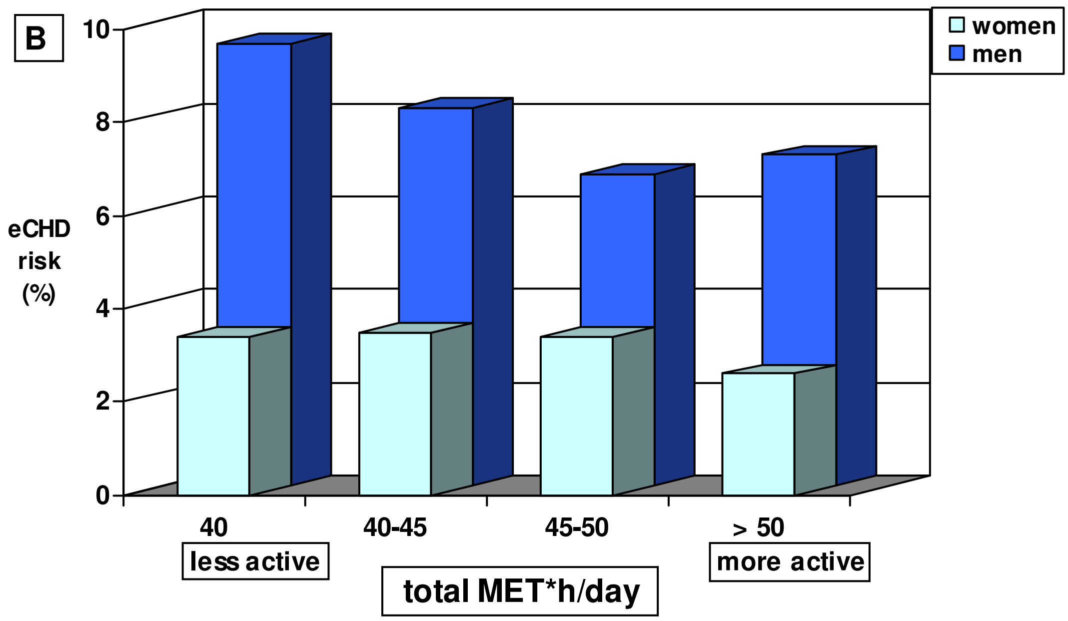
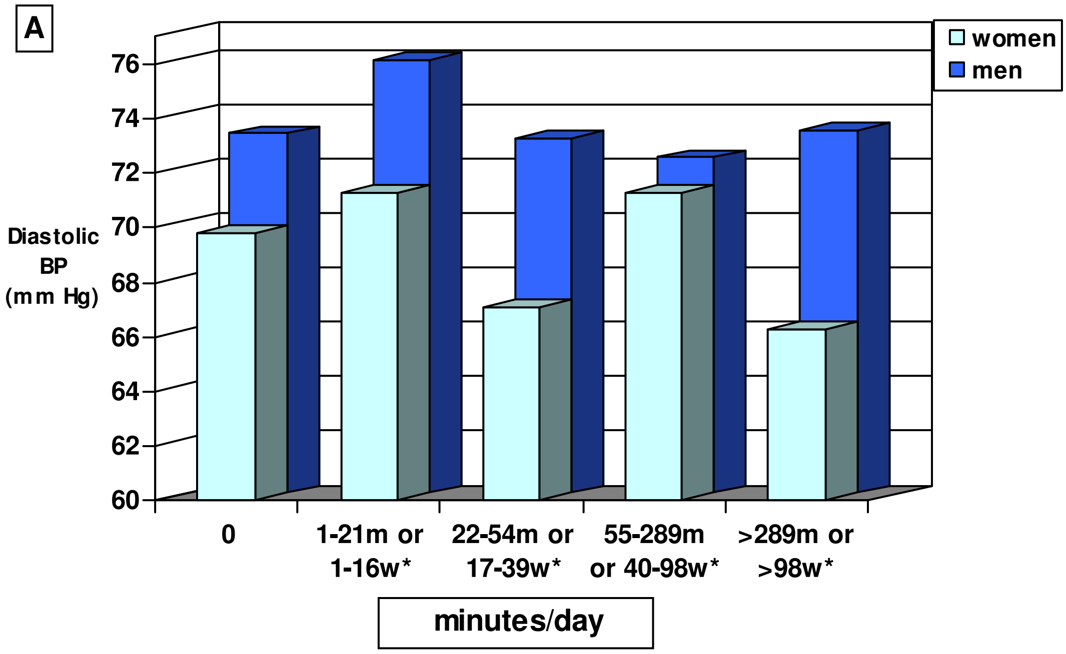


Figure 9.3: HDL cholesterol (A) and the percent likelihood of developing coronary heart disease (eCHD) risk over a period of 10 years (B), according to categorization method for physical activity expressed in MET*hr/day, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

HDL-cholesterol changes in men were significant [(P values were 0.000, 0.004 and 0.019 for categorical, ordinal (trend) and continuous variables, respectively], but not significant in women. eCHD risk changes in men were significant [(P values were 0.009, 0.003 and 0.005 for categorical, ordinal (trend) and continuous variables, respectively], but not significant in women.



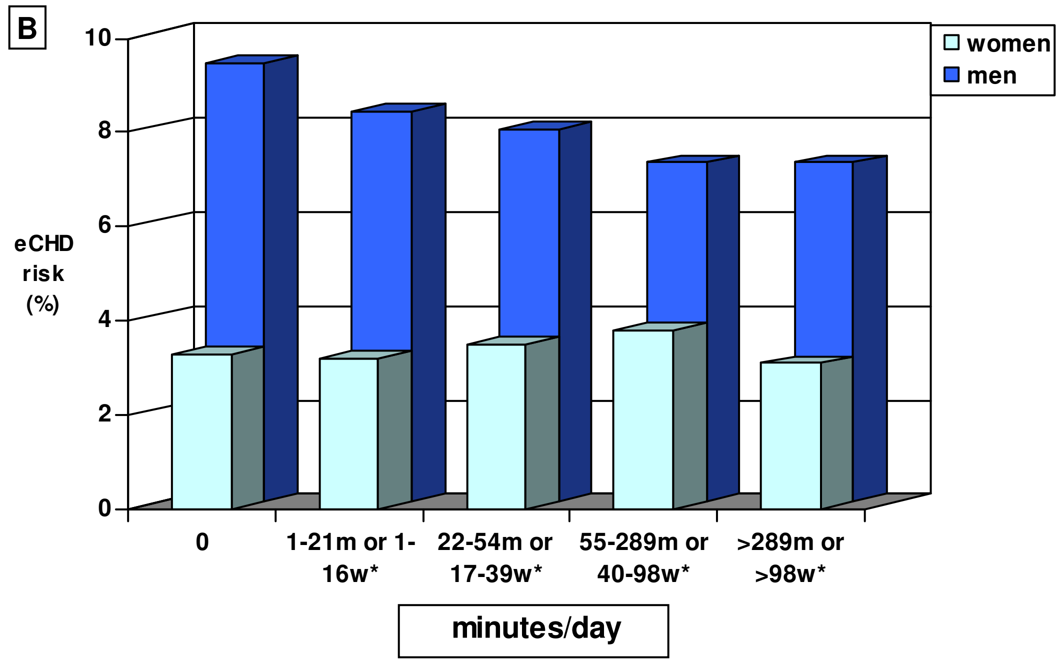


Figure 9.4: Diastolic BP (A) and the percent likelihood of developing coronary heart disease (CHD) risk over a period of 10 years (B), according to categorization method for physical activity expressed in number of minutes/day (d/w) of at least moderate activity, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

* These categories established based on an equal number of subjects in each category. Therefore, the number of minutes/day was categorized as follow: For men, 0, 1-21, 22-54, 55-289 and >289 minutes/day. For women, 0, 1-16, 17-39, 40-98 and >98 minutes/day.

Diastolic BP changes in women were significant only when using physical activity as categorical variable (P=0.003), but not significant in men. eCHD risk changes in men were significant only when using physical activity as ordinal and continuous variables, but not categorical [(P values were 0.008 and 0.005 ordinal (trend) and continuous variables, respectively]. In women, it is not significant.

Table 9.7: CHD risk factors and estimated CHD risk in men (a) and women (b) according to physical activity as continuous variable expressed in number of days/week of at least moderate activity for ≥ 30 minutes, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical Activity (days/week) [1]	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero day/week					
Mean value	129.4	73.9	5.6	1.00	8.6
(n)	(74)	(74)	(51)	(50)	(49)
1 day/week					
Mean value	131.4	75.9	5.6	0.98	9.1
(n)	(52)	(52)	(42)	(42)	(42)
2 days/week					
Mean value	126.6	72.8	5.3	1.02	8.0
(n)	(37)	(37)	(28)	(28)	(28)
3 days/week					
Mean value	131.2	74.4	5.1	1.07	7.5
(n)	(44)	(44)	(33)	(33)	(33)
4 days/week					
Mean value	125.2	71.0	4.8	1.10	7.2
(n)	(33)	(33)	(26)	(26)	(26)
5 days/week					
Mean value	128.8	73.9	5.0	1.06	7.3
(n)	(46)	(46)	(38)	(38)	(38)
6 days/week					
Mean value	128.5	72.4	5.3	1.10	7.5
(n)	(56)	(56)	(41)	(41)	(41)
7 days/week					
Mean value	128.2	72.2	5.0	1.14	6.9
(n)	(39)	(39)	(31)	(31)	(31)
P value (continuous)	***0.390***	***0.136***	***0.003***	***0.002***	***0.005***
Partial eta squared	***0.002***	***0.006***	***0.031***	***0.034***	***0.027***

Significantly different from lowest physical activity category (zero day/week) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] days/week refers to the number of days per week of at least moderate activity for ≥ 30 minutes

(b)

Physical Activity (days/week) [1]	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
Zero day/week					
Mean value	123.4	70.9	5.2	1.27	3.2
(n)	(66)	(66)	(44)	(44)	(44)
1 day/week					
Mean value	119.8	68.3	5.3	1.25	3.8
(n)	(54)	(54)	(38)	(38)	(38)
2 days/week					
Mean value	123.5	71.6	5.1	1.25	3.8
(n)	(46)	(46)	(36)	(36)	(36)
3 days/week					
Mean value	120.0	68.1	5.1	1.28	3.4
(n)	(41)	(41)	(33)	(33)	(33)
4 days/week					
Mean value	119.5	66.9	5.3	1.34	3.2
(n)	(36)	(36)	(27)	(27)	(27)
5 days/week					
Mean value	119.4	67.5	5.4	1.36	2.9
(n)	(38)	(38)	(26)	(26)	(26)
6 days/week					
Mean value	122.6	70.3	4.9	1.26	3.2
(n)	(25)	(25)	(21)	(21)	(21)
7 days/week					
Mean value	119.8	67.0	5.1	1.26	3.3
(n)	(37)	(37)	(32)	(32)	(32)
P value (continuous)	***0.201***	***0.064***	***0.497***	***0.601***	***0.507***
Partial eta squared	***0.005***	***0.010***	***0.002***	***0.001***	***0.002***

Significantly different from lowest physical activity category (zero day/week) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

1 days/week refers to the number of days per week of at least moderate activity for ≥ 30 minutes

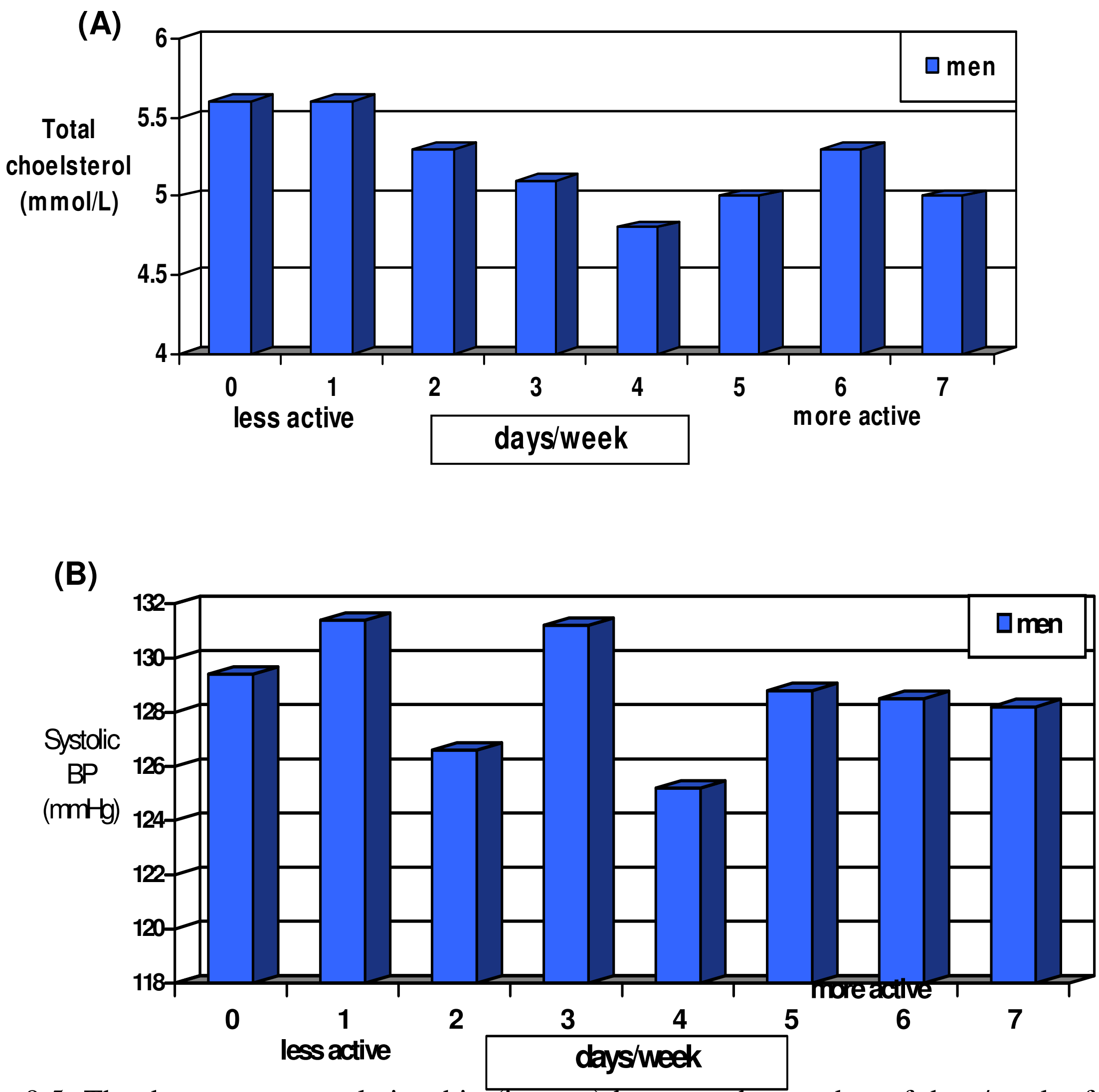


Figure 9.5: The dose-response relationship (in men) between the number of days/week of at least moderate physical activity for ≥ 30 minutes/day and (A) total cholesterol and (B) systolic BP, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

Total cholesterol changes in men were significant (P value = 0.003 for continuous variable), but not significant in Systolic BP.

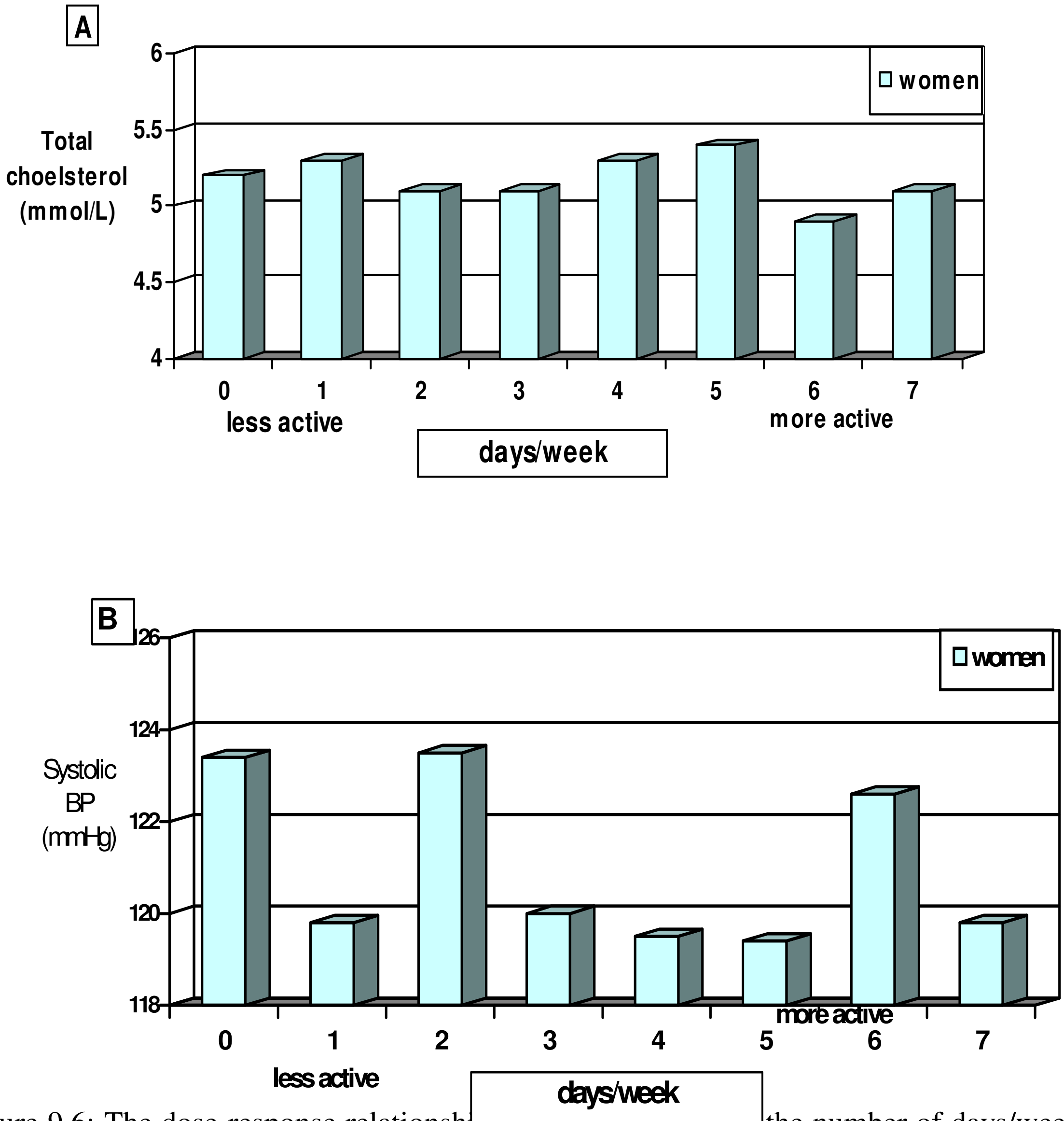


Figure 9.6: The dose-response relationship (in women) between the number of days/week of at least moderate physical activity for ≥ 30 minutes/day and (A) total cholesterol and (B) systolic BP, after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

Total cholesterol and systolic BP changes in women were not significant.

9.4. Discussion:

This chapter shows that, overall, there was no strong dose-response relationship between physical activity on the one hand and CHD risk factors and eCHD risk on the other hand. The relationships were generally stronger after exclusion of subjects on medications. This would be due to the elimination of disease related factors such as requiring treatment for heart failure, statins for hypercholesterolemia, and antihypertensive drugs for the treatment of high blood pressure. Even so, a dose-response relationship was obtained with categories of different measures for physical activity [e.g. days/week (4 categories), MET*h/day (4 categories) and minutes/day (5 categories)], and only some CHD risk factors. There was a significant dose-response relationship whereby the highest TC, low HDL-C and highest eCHD risk were evident in men who considered least active than those who were more active, after adjustment of age, BMI, smoking and exclusion of subjects on medications. There were no significant dose-response relationships between physical activity and SBP or DBP. In addition, there were no significant dose-response relationships in women.

When these measures (days/week. MET*h/day and minutes/day) were examined as continuous variables, the findings revealed that the dose-response relationships with the TC, HDL-C and eCHD risk were also significant in men, but not SBP and DBP. In women, there were no significant dose-response relationships. In agreement with this current findings, there has been a widespread agreement that the dose-response relationship between physical activity and health is a curvilinear relationship (Lee and Skerrett, 2001b; Blair and Connelly, 2001; Haennel and Lemire, 2002). For example, reviews by Lee and Skerrett (2001b), have shown a continuous dose-response gradient of morbidity and mortality across a wide range of physical activity levels (see *Figure* 2.1). Although this dose-response relationship is widely accepted, it is derived mainly from evidence on CHD and diabetes rather than the CHD risk factors. In addition, whilst the Department of Health guideline is based on a measure of physical activity, it is not clear from the *Figure* (2.1) whether the effect is related to physical activity or physical fitness.

The apparent benefits of physical activity on the eCHD risk appeared to be largely mediated by improvements in lipids profiles in men. The reason for the lack of demonstrable effect of physical activity on CHD risk factors and eCHD risk in women remained elusive. As discussed in previous *Chapters*, it may be related to the types of physical activity undertaken and the confounding effects of hormonal changes associated with menopause. It is also possible that more complete assessment of physical activity dimensions including physical fitness would have yielded different results. Finally, it is possible that physical activity provided beneficial effects in other risk factors that were not measured by the NDNS (e.g. coagulation, insulin).

9.5. Conclusion:

In support the hypothesis, when further categories were defined for each method of physical activity, a dose-response relationship was evident in TC, HDL-C and eCHD risk, in men only. The results of this *Chapter* confirmed those results obtained from previous *Chapter* that physical activity explains only small proportion of variance in the CHD risk factors and eCHD risk. However, the self-perception diary may have been a subject to reporting biases and misclassifications (less or more physical activity than the actual level) which may have been introduced into this chapter. Therefore, differences in the overall scores for physical activity as well as the ranking may partly be due to the way physical activity was perceived by the participants. This matter is the main focus of the next *Chapter*.

Part One

Chapter 10: NDNS self-perception physical activity questionnaire

Chapter 10 NDNS self-perception physical activity questionnaire

10.1. Introduction:

The results described in the previous *Chapters* (6-9) demonstrated that the differences in the CHD risk factors and eCHD risk were barely explained by the NDNS 7-day diary physical activity. Recently, more attention has been focused on how self-perceived diary and questionnaire are subject to reporting bias (less or more physical activity than actual level) and misclassification in adults. For example, Peate et al., (2002) has studied 101 fire-fighters who completed a questionnaire to rank their fitness level from 0 to 7 (level 0 was low fitness). It has been found that there was no association between the fire-fighters' self-perception of their level of fitness and their aerobic capacity measured by the sub-maximal treadmill test. Therefore, differences in the overall scores for physical activity as well as in the ranking may partly be due to the self-perception of physical activity. Therefore, there is a need to explore how self-perceived levels of physical activity may change the relationship between physical activity and CHD risk factors and eCHD risk. Addressing this issue may help us to explain the relationship between physical activity and CHD risk factors and eCHD risk.

The aim of this *Chapter* was to explore how subjects would describe their own activity behaviour in terms of overall and job activities. This *Chapter* also aimed to examine the effect of the overall and job activities with the CHD risk factors and eCHD risk, and to compare these outcomes with those measures of activity behaviour derived from the activity diary (e.g. number of days/week and minutes/day of at least moderate activity or total MET*h/day).

10.2. Method:

As part of the NDNS survey, all respondents were given a short self-perception physical activity questionnaire. This questionnaire included only two questions describing the perception of the respondents regarding their physical activity levels. These questions are:

1. In overall and including things you do in your free time, compared to other people of your age would you describe yourself as……
    - very physically active,
    - fairly physically active,

- not very physically active,
- or not at all physically active?

2. Thinking about your (main) job in general, and including voluntary work, would you say that you are……
    0. very physically active,
    1. fairly physically active,
    2. not very physically active,
    3. or not at all physically active in your job?

Partial eta squared was used as a measure of effect size (proportion of the variance in the outcome that is attributable to PA): the ratio of PA variance to PA plus error. The statistical analysis carried out in this *Chapter* is described in *Chapter* 4 (Methodology). All the analyses were conducted after adjustment for age, BMI, and cigarette smoking and after exclusion of subjects on medications.

10.3. Results:

A total of 381 men and 342 women indicated their perception of overall physical activity. Fewer men (306) and women (257) indicated their perception of job activity – those who were not in occupation did not complete this question and were excluded from the analysis. Most men described themselves as 'fairly' (54 %) or 'very' (19 %) physically active' as compared to others of the same age, with only 23 % and 5 % of men describing themselves as 'not very' or 'not at all' physically active respectively. The same distribution of perceived overall activity was evident for the women. Similar patterns of perception of job activity were also evident. Most men described their job activity as either 'fairly' (39 %) or 'very' (22 %) physically active with 23 % and 16 % describing their job activities as 'not very' or 'not at all' physically active. Once again, the same distribution of perceived job activity was evident in the women.

Table 10.1 shows the association between different categories for the self-perception of the overall activity and the CHD risk factors and eCHD risk (after adjustment for the age, BMI, and smoking and after exclusion of subjects on medications). In addition, *Figure* 10.1 illustrates the percent likelihood of developing CHD risk over a period of 10 years, according to four categories of overall activity. Compared to those who classified themselves as 'not at all physically active', the GLM showed that only those men who considered themselves to be 'very physically active' has significantly higher HDL-C (1.10 mmol/L versus 0.85 mmol/L, $P < 0.05$). Differences in perception of activity level accounted for 3.3 % of the variance in HDL-C. There were no significant group effects for SBP, DBP, TC or eCHD risk. In the women, only those women who considered themselves 'very physically active' has significantly lower SBP than those 'not at all physically active' (119.8 mmHg versus 128.9 mmHg, $P < 0.05$) with differences in activity level accounted for 2.6 % of the variance in SBP. No other significant group effects were evident in the women.

Table 10.2 shows the relationship between the self-perception of job activity and the CHD risk factors and eCHD risk. *Figure* 10.2 illustrates the percent likelihood of developing CHD risk over a period of 10 years, according to four categories of job activity. When activity was classified using job activity, there were no significant group effects in men. However, significant group effects of activity level on TC and HDL-C were evident in the women. For example, the lowest TC levels were evident in those women who considered themselves 'not very physically active' based on their job activity, values which were significantly lower than those observed in the women who considered themselves 'not at all physically active' (4.8 mmol/L versus 5.4 mmol/L, $P < 0.05$). TC levels did not continue to fall as activity levels increased further. Differences in perceived activity level by job activity accounted for 6.3 % of the variance in TC. There were no significant difference in HDL-C between the least active group and any other group – the only difference was evident between the 'fairly physically active' and 'very physically active' groups such that differences in perceived activity level by job accounted for 4.4 % of the variance in HDL-C.

Table 10.3 and *Figures* 10.3-10.7 represent the extent to which CHD risk factors and eCHD risk are explained by different categorization methods for physical activity, after adjustment for age, BIM and smoking and exclusion of subjects on medications. In men, the results presented in this *Chapter* showed that using the NDNS self-perception physical activity questionnaire explained less variation than those results obtained from the NDNS 7-day diary in *Chapter* 9. For example, the partial eta square showed that MET*hr/day categories measured by the NDNS 7-day diary explained 4.0 % of the variations in eCHD risk compared to 0.6 % explained by self-perception of job activity. However, in women, the results obtained from the NDNS questionnaire became stronger than those observed using the NDNS diary. For instance, the partial eta squared showed that self-perception of job activity explained 6.3 % of the variations in TC, whereas the number of days/week explained less than 1.0 % of the variations.

On the other hand, *Table* 10.4 shows the correlation between physical activity level assessed by the self-perception questionnaire with the physical activity measures obtained from the 7-day diary (number of days/week, minutes/day and MET*hr/day) was relatively small. The relationship between activity levels derived from the NDNS diary and the individual's perception of their physical activity level, both overall and based on job activity, were weak. Higher correlations between perceived activity and calculated activity were generally observed firstly, in the men compared to the women and secondly, when perceived activity level was based on job activity compared to that assessed overall. The strongest association was observed between perceived activity by job and activity expressed in minutes/day of moderate physical activity, where the correlation values were 31 % for the men and 13 % for the women. In contrast, when perceived activity level was assessed overall, the correlation values were only 5 % and 2 %. A similar, but weaker, pattern of association was evident when activity level was expressed as MET*h/d and the lowest associations were evident when activity was expressed in days/week.

Table 10.1: CHD risk factors and estimated CHD risk in men (a) and women (b) according to four categories of self-perception of overall activity (NDNS questionnaire), after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical Activity (overall activity)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
very physically active Mean value (n)	128.3 (74)	72.0 (74)	5.3 (60)	1.10 * (60)	8.7 (60)
fairly physically active Mean value (n)	129.0 (204)	73.6 (204)	5.2 (150)	1.05 (149)	7.9 (148)
not very physically active Mean value (n)	129.5 (88)	74.1 (88)	5.4 (68)	1.03 (68)	8.2 (68)
not at all physically active Mean value (n)	129.7 (15)	76.1 (15)	5.3 (12)	0.85 (12)	10.2 (12)
P value (categorical)	***0.956***	***0.393***	***0.402***	***0.022***	***0.158***
Partial eta squared	***0.001***	***0.008***	***0.010***	***0.033***	***0.018***
P value (ordinal (Ptrend))	***0.575***	***0.104***	***0.553***	***0.009***	***0.741***
Partial eta squared	***0.001***	***0.007***	***0.001***	***0.024***	***0.000***

(b)

Physical Activity (overall activity)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
very physically active Mean value (n)	119.8 * (62)	67.6 (62)	5.1 (46)	1.29 (46)	2.9 (46)
fairly physically active Mean value (n)	120.2 (183)	68.6 (183)	5.3 (140)	1.31 (140)	3.4 (140)
not very physically active Mean value (n)	122.4 (80)	70.6 (80)	5.1 (56)	1.22 (56)	2.9 (56)
not at all physically active Mean value (n)	128.9 (17)	72.4 (17)	4.9 (15)	1.23 (15)	4.8 (15)
P value (categorical)	***0.031***	***0.154***	***0.394***	***0.432***	***0.110***
Partial eta squared	***0.026***	***0.016***	***0.012***	***0.011***	***0.024***
P value (ordinal (Ptrend))	***0.014***	***0.025***	***0.532***	***0.220***	***0.286***
Partial eta squared	***0.018***	***0.015***	***0.002***	***0.006***	***0.005***

Significantly different from lowest physical activity category (not at all physically active) - * P < 0.05, ** P < 0.001

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

Table 10.2: CHD risk factors and estimated CHD risk in men (a) and women (b) according to four categories of self-perception of job activity (NDNS questionnaire), after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical Activity (job activity)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
very physically active Mean value (n)	130.7 (74)	72.6 (74)	5.2 (56)	1.05 (56)	8.6 (56)
fairly physically active Mean value (n)	127.7 (129)	73.9 (129)	5.2 (93)	1.06 (93)	7.9 (93)
not very physically active Mean value (n)	128.5 (77)	71.9 (77)	5.4 (61)	1.02 (60)	8.2 (59)
not at all physically active Mean value (n)	126.4 (53)	74.4 (53)	5.4 (40)	0.98 (40)	7.9 (40)
P value (categorical)	***0.263***	***0.401***	***0.563***	***0.273***	***0.713***
Partial eta squared	***0.012***	***0.009***	***0.008***	***0.016***	***0.006***
P value (ordinal (Ptrend))	***0.121***	***0.730***	***0.249***	***0.105***	***0.539***
Partial eta squared	***0.007***	***0.000***	***0.005***	***0.011***	***0.002***

(b)

Physical Activity (job activity)	**CHD risk factors**				**eCHD risk** %
	SBP mmHg	**DBP** mmHg	**TC** mmol/L	**HDL-C** mmol/L	
very physically active Mean value (n)	121.0 (57)	67.3 (57)	5.4 (42)	1.43 (42)	2.9 (42)
fairly physically active Mean value (n)	119.3 (111)	68.0 (111)	5.1 (84)	1.25 (84)	3.2 (84)
not very physically active Mean value (n)	122.8 (62)	71.5 (62)	4.8 * (47)	1.26 (47)	3.0 (47)
not at all physically active Mean value (n)	120.0 (27)	68.4 (27)	5.3 (21)	1.33 (21)	2.4 (21)
P value (categorical)	***0.350***	***0.085***	***0.007***	***0.038***	***0.714***
Partial eta squared	***0.013***	***0.026***	***0.063***	***0.044***	***0.007***
P value (ordinal (Ptrend))	***0.643***	***0.099***	***0.064***	***0.173***	***0.580***
Partial eta squared	***0.001***	***0.011***	***0.018***	***0.010***	***0.002***

Significantly different from lowest physical activity category (not at all physically active) - * $P < 0.05$, ** $P < 0.001$

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

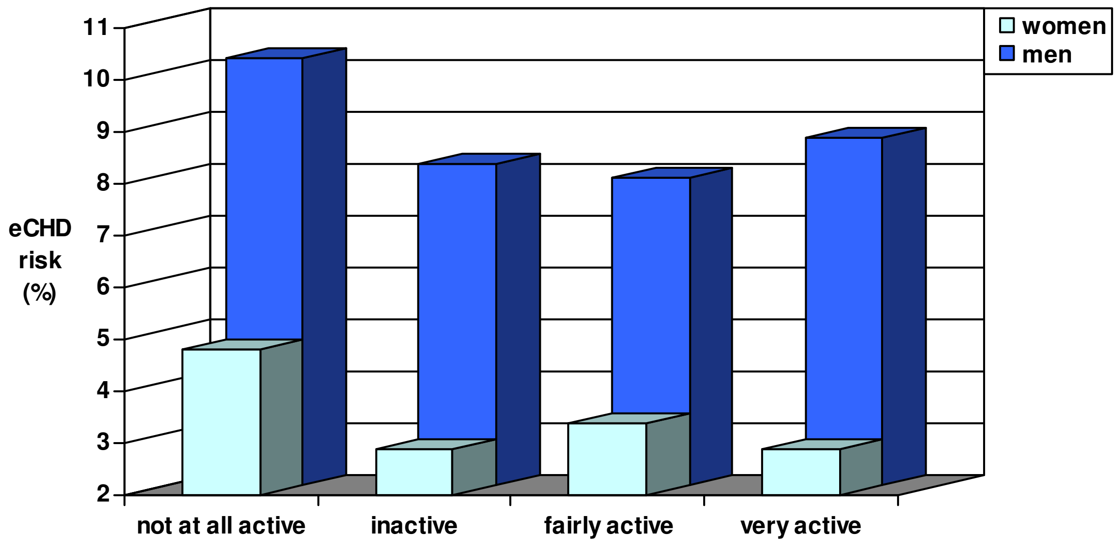


Figure 10.1: Estimation of the percent likelihood of developing coronary heart disease (eCHD) risk over a period of 10 years, according to four categories of overall activity (NDNS questionnaire), after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

The eCHD risk changes in men and women were not significant when using physical activity as categorical and ordinal (trend) variables.

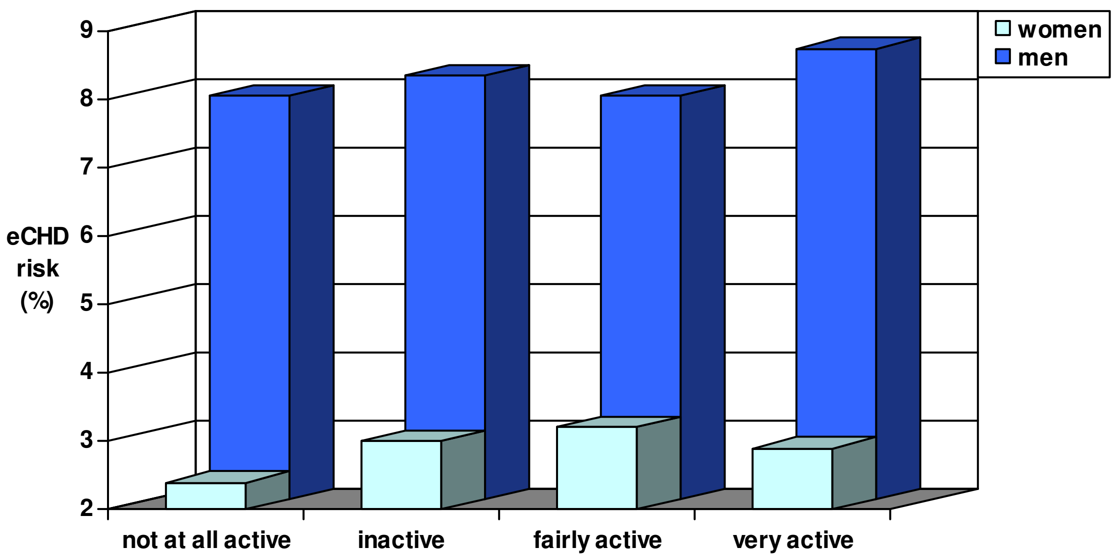


Figure 10.2: Estimation of the percent likelihood of developing coronary heart disease (eCHD) risk over a period of 10 years, according to four categories of job activity (NDNS questionnaire), after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

The eCHD risk changes in men and women were not significant when using physical activity as categorical and ordinal (trend) variables.

Table 10.3: The extent to which CHD risk factors and estimated CHD risk in men (a) and women (b) are explained by physical activity. P values and partial eta squared are shown for analysis using physical as a categorical variable, after adjustment for the age, BMI, smoking and after exclusion of subjects on medications.

(a)

Physical activity (category)		**CHD risk factors**				**eCHD risk**
		SBP	**DBP**	**TC**	**HDL-C**	
days/week [1] (4 categories)	***P value***	0.960	0.581	0.004	0.021	0.038
	Partial eta squared	0.001	0.005	0.045	0.034	0.030
minutes/day (5 categories)	***P value***	0.766	0.228	0.003	0.072	0.052
	Partial eta squared	0.005	0.015	0.055	0.030	0.033
40 MET*h/d (4 categories)	***P value***	0.289	0.350	0.009	0.000	0.009
	Partial eta squared	0.010	0.009	0.040	0.063	0.040
overall activity [2] (4 categories)	***P value***	0.956	0.393	0.402	0.022	0.158
	Partial eta squared	0.001	0.008	0.010	0.033	0.018
job activity [2] (4 categories)	***P value***	0.263	0.401	0.563	0.273	0.713
	Partial eta squared	0.012	0.009	0.008	0.016	0.006

(b)

Physical activity (category)		**CHD risk factors**				**eCHD risk**
		SBP	**DBP**	**TC**	**HDL-C**	
days/week [1] (4 categories)	***P value***	0.301	0.130	0.979	0.811	0.487
	Partial eta squared	0.011	0.017	0.001	0.004	0.010
minutes/day (5 categories)	***P value***	0.086	0.003	0.962	0.930	0.769
	Partial eta squared	0.024	0.047	0.002	0.003	0.007
40 MET*h/d (4 categories)	***P value***	0.195	0.158	0.759	0.719	0.480
	Partial eta squared	0.014	0.015	0.005	0.005	0.010
overall activity [2] (4 categories)	***P value***	0.031	0.154	0.394	0.432	0.110
	Partial eta squared	0.026	0.016	0.012	0.011	0.024
job activity [2] (4 categories)	***P value***	0.350	0.085	0.007	0.038	0.714
	Partial eta squared	0.013	0.026	0.063	0.044	0.007

Key: CHD: coronary heart disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC Total Cholesterol concentration; HDL-C: high density lipoprotein-cholesterol concentration; eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years

[1] These categories were obtained from the NDNS 7-day diary

[2] These categories of self-perception activity were obtained from the NDNS self- perception physical activity questionnaire

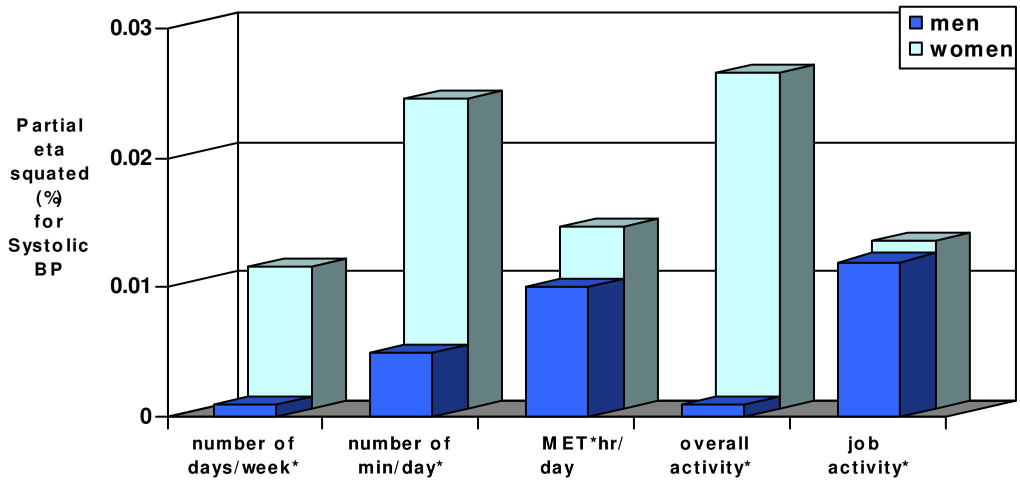


Figure 10.3: Partial eta squared for systolic BP, according to different categorization methods for physical activity.

* number of days/week: refers to the number of days per week of at least moderate activity for ≥ 30 minutes (4 categories); number minutes/day: refers to the number of minutes per day of at least moderate activity (5 categories); MET/d: refers to total MET*h per day (4 categories); overall (4 categories) and job (4 categories) activity were obtained from the NDNS self-perception physical activity questionnaire

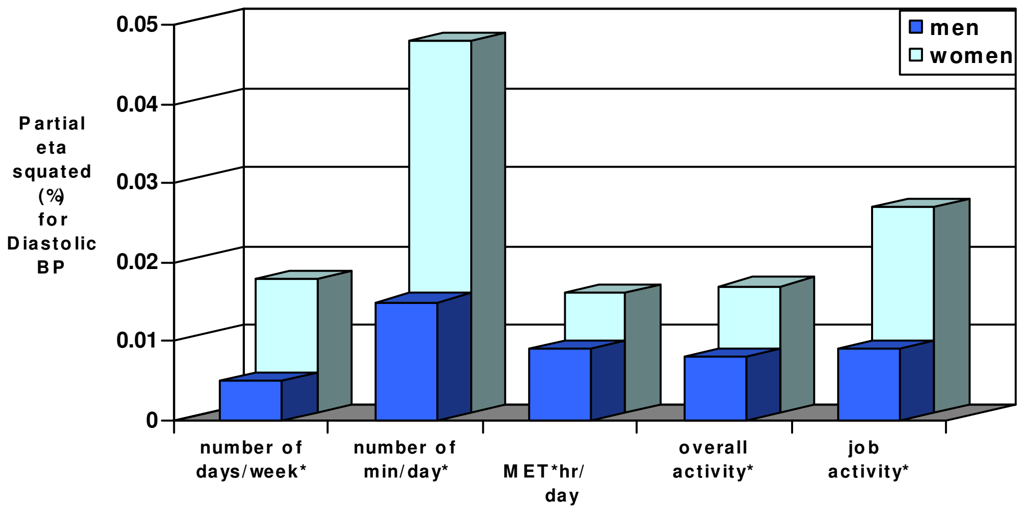


Figure 10.4: Partial eta squared for diastolic BP, according to different categorization methods for physical activity.

* number of days/week: refers to the number of days per week of at least moderate activity for ≥ 30 minutes (4 categories); number minutes/day: refers to the number of minutes per day of at least moderate activity (5 categories); MET/d: refers to total MET*h per day (4 categories); overall (4 categories) and job (4 categories) activity were obtained from the NDNS self-perception physical activity questionnaire

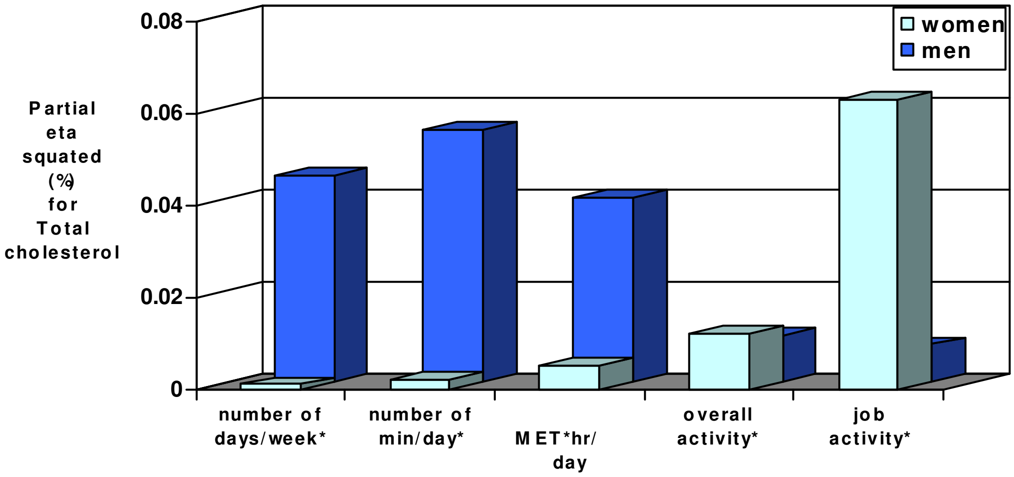


Figure 10.5: Partial eta squared for Total cholesterol, according to different categorization methods for physical activity.

* number of days/week: refers to the number of days per week of at least moderate activity for ≥ 30 minutes (4 categories); number minutes/day: refers to the number of minutes per day of at least moderate activity (5 categories); MET/d: refers to total MET*h per day (4 categories); overall (4 categories) and job (4 categories) activity were obtained from the NDNS self-perception physical activity questionnaire

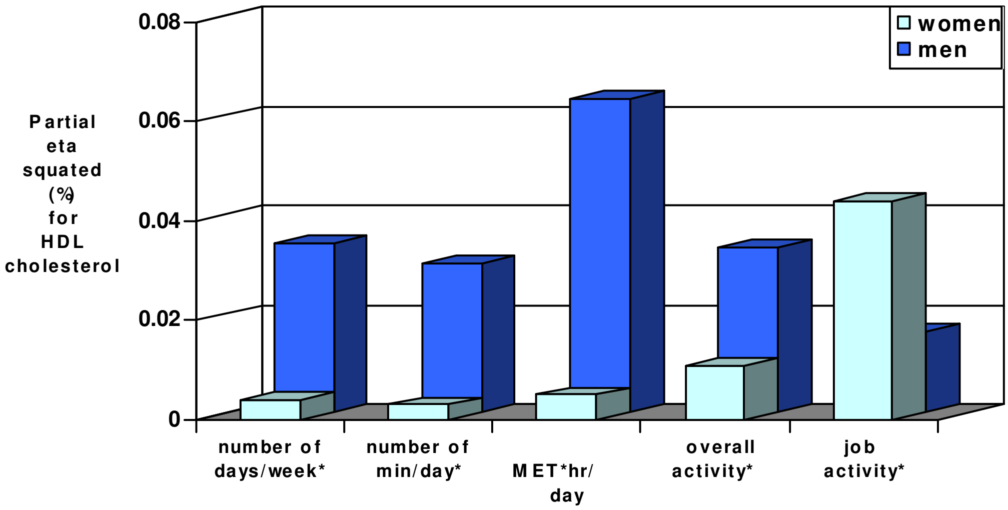


Figure 10.6: Partial eta squared for HDL cholesterol, according to different categorization methods for physical activity.

* number of days/week: refers to the number of days per week of at least moderate activity for ≥ 30 minutes (4 categories); number minutes/day: refers to the number of minutes per day of at least moderate activity (5 categories); MET/d: refers to total MET*h per day (4 categories); overall (4 categories) and job (4 categories) activity were obtained from the NDNS self-perception physical activity questionnaire

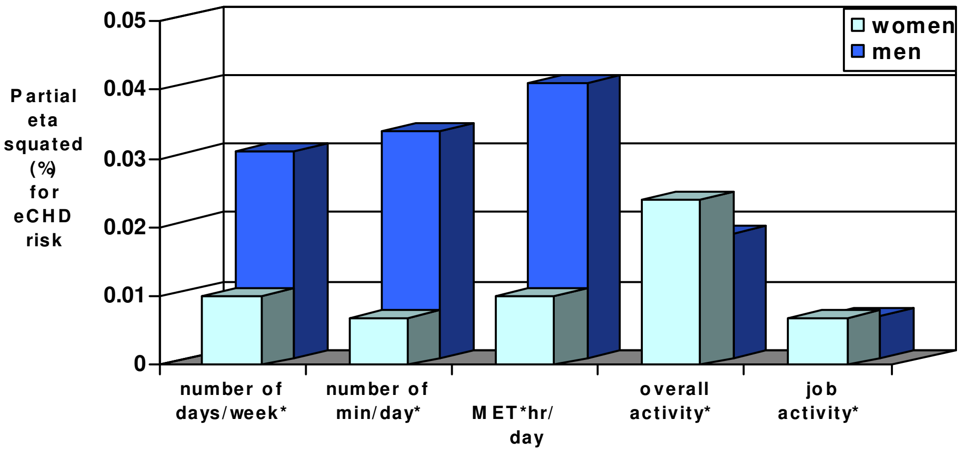


Figure 10.7: Partial eta squared for the estimated coronary heart disease (eCHD) risk as a percentage of the likelihood of developing CHD risk over a period of 10 years, according to different categorization methods for physical activity.

* number of days/week: refers to the number of days per week of at least moderate activity for ≥ 30 minutes (4 categories); number minutes/day: refers to the number of minutes per day of at least moderate activity (5 categories); MET/d: refers to total MET*h per day (4 categories); overall (4 categories) and job (4 categories) activity were obtained from the NDNS self-perception physical activity questionnaire

Table 10.4: The correlation between the physical activity measures of the NDNS physical activity self-perception questionnaire with the measures of physical activity obtained from the NDNS 7-day diary.

Gender	**NDNS questionnaire measures**	**NDNS 7-day diary measures**		
		Days/week [1] r square	Minutes/day [2] r square	MET*hr/day r square
Men	Job activity [3]	0.18	0.31	0.25
	Overall activity [3]	0.10	0.05	0.06
Women	Job activity [3]	0.06	0.13	0.11
	Overall activity [3]	0.07	0.02	0.04

[1] Days/week refers to the number of days/week of moderate activity.
[2] Minutes/day refers to the number of minutes/day of moderate activity.
[3] These measures of self-perception activity were obtained from the NDNS self- perception physical activity questionnaire

10.4. Discussion:

The findings of this *Chapter* suggested that most of the subjects would see themselves as at least fairly physically, based on both overall and in their occupational activity. More subjects perceived their job activity levels to be relatively low compared to their overall activity.

In disagreement with the hypothesis, using the overall categorisation method, the findings failed to show any significant difference between inactive and active men and women in relation to CHD risk factors and eCHD risk. However, according to the job categorisation method, the findings indicated that women, but not men, who would see themselves as not very physically active had higher TC level specifically when compared to those who were not at all very physically active. These effects persisted even after adjustment for age, BMI, smoking and exclusion of subjects on medications.

The set of results outlined in this *Chapter* provides further evidence that physical activity (estimated by the NDNS self-perception questionnaire) explains small proportion of variance in the CHD risk factors and eCHD risk (adjustment for the age, BMI, smoking and exclusion of subjects on medications). In addition, these findings demonstrate that the variations in the CHD risk factors and eCHD risk obtained from the NDNS questionnaire were less compared to those resulted by applying different physical activity measures obtained from the NDNS 7-day diary (*Chapter* 9). Interestingly, these results indicate that physical activity self-perception varies with sex. For example, in contrast to the findings of the previous *Chapters* using the NDNS 7-day diary, the findings of this *Chapter* show that the associations of self-perception physical activity with the CHD risk factors and eCHD risk were slightly stronger in women compared to men.

The mechanisms behind these findings are still unclear. However, one possible explanation for these variations is the fact that self-perception physical activity is prone to many psychological, health status and social problems. For example, people may have different self-perceptions of their physical activity or may feel ashamed about their levels of activity. In fact, it has been indicated that feeling "too fat" to engage in physical activity may overestimate the actual level of physical activity (Yancey et al., 2004a). In addition, data from another study (Yancey et al., 2004b) in Los Angeles County lends credence to the argument that social comparisons influence physical self-perception. Among a socioeconomically and ethnically diverse sample of county employees, sedentary individuals' ratings of their health and fitness statuses in the control group were similar to those of their more active peers. These ratings have also found to be unrelated to their level of physical activity or physical activity stage of change.

On the other hand, the findings show that the relationship between activity measures derived from the NDNS diary (number of days/week, minutes/day and MET*hr/day) and the individual's perception of their physical activity level, both overall and based on job activity, were weak. The correlations were better for job activity than overall activity in both genders. It should be noted that the process of self-perception physical activity questionnaire used in this *Chapter* does not provide information regarding the duration and types of activities.

Therefore, the magnitude of error in the accuracy of a particular activity classification in the NDNS questionnaire may influence the overall estimates of physical activity levels and, thus, may provide a potential source of bias that could affect the strength of association between physical activity and the CHD risk. If this interpretation is correct, the relationship between physical activity and CHD risk factors and eCHD risk would seem more likely to be affected by these problems.

10.5. Conclusion:

Using the NDNS questionnaire, in disagreement with the hypothesis, this *Chapter* failed to demonstrate a dose-response relationship between physical activity and CHD risk factors and eCHD risk, in both genders. In addition, the effects of physical activity assessed by the NDNS questionnaire on CHD risk factors and eCHD risk were also found to have a minor association. Importantly, this *Chapter* concluded that the physical activity levels measured by the NDNS self-perception questionnaire are not quite correlated with the measures of activity obtained from the NDNS 7-day diary. Whilst each set of categorization method was derived from the same subjects, the findings showed that there were different effects (expressed in partial eta squared) explained by physical activity on the CHD risk factors and eCHD risk. However, based on these inter-related sets of data, it was not possible to determine whether these differences were significant or not. Therefore, this matter is addressed in more details in *Chapter* 11.

Part One

Chapter 11: The eCHD risk and different categorization methods for physical activity

Chapter 11 The eCHD risk and different categorization methods for physical activity

11.1. Introduction:

Physical activity guidelines offered evidence-based behavioural benchmarks that are related to the reduction in the risk of morbidity and mortality, especially if people adhere to them (Warburton et al., 2007). In the last 15 years, much effort has been put into the development of physical activity guidelines for adults. However, there is still considerable debate in the current literature regarding the least amount of activity, in terms of duration, intensity and frequency that would provide health benefits (e.g. 30 minutes of moderate activity for at least 5 days/week, 10,000 steps, 40 MET*h/day). It is therefore difficult to provide clear public health guidelines solely in terms of physical activity. The aim of this *Chapter* was to examine whether those deemed inactive by which ever method of categorization for physical activity (used in guidelines) would have higher eCHD risk than those deemed active and that the magnitude of the difference between inactive and active groups varies depending on the method of categorization used.

11.2. Methods:

The aim was tested by first categorizing the men and women into inactive and active groups using three different methods of categorization and then examining whether there were significant differences in the estimated CHD risk between a) the three inactive groups, b) the three active groups and c) the magnitude of the difference between the three sets of inactive and active groups.

In order to examine whether the difference in eCHD risk is significant between these methods of categorization or not, the analysis was carried out by comparing a) the proportion of the variance (expressed in partial eta squared) and b) the predictive power of the total model (expressed in r squared) obtained using three different methods of categorizing individuals into inactive and active groups. Partial eta squared was used as a measure of effect size (proportion of the variance in the outcome that is attributable to physical activity): the ratio of physical activity variance to physical activity plus error. The data were analyzed first using the General Linear Model and then using the non-independent t-test, after adjustment for age, BMI and smoking and exclusion of subjects on medications. The following three methods of categorization were used in guidelines:

1. 30/3 guideline: Three days per week of at least moderate physical activity for 30 minutes or more (Pollock and Jackson, 1977).
2. 30/5 guideline: Five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996)
3. MET40*h guideline: Accumulative of at least total 40 MET*hr per day (Blair et al., 1984 and 1985)

11.3. Results:

Table 11.1 shows the comparisons between different methods of categorization for physical activity and its relation to the eCHD risk. Within all the three methods of categorization, men considered active had significantly ($P < 0.05$) lower eCHD risk than those who were considered as inactive such that 1.4 – 2.9 % of the variance in eCHD risk could be attributable to differences in activity status. There were no significant activity-related effects evident in the women. The results showed that the proportion of the variance (expressed in partial eta squared) of the CHD risk factors and eCHD risk explained by these categorization methods did not vary significantly between these methods. In addition, the analysis showed that there were no significant differences in the predictive power of the total model (expressed in total r squared) when the three different methods of categorization were used in the model. Finally, when subjects were categorized into active and inactive groups using the three methods, there were no significant differences in eCHD risk between any of the following:

- the three inactive groups
- the three active groups, and
- the magnitude of the differences between the three set of inactive and active groups.

Table 11.1: Estimation of CHD risk according to different methods of categorization for physical activity.

Gender	Categorization methods (guidelines)	eCHD risk % [1]				Partial eta squared3	R squared4
		Inactive (n)	Active (n)	Mean difference (SE) [2]	P value		
Men	30/3	8.635 (119)	7.293 (169)	1.342 (0.458)	0.004	0.029	0.725
	30/5	8.210 (178)	7.260 (110)	0.950 (0.468)	0.044	0.014	0.721
	MET40*h	9.521 (31)	7.645 (257)	1.876 (0.725)	0.010	0.023	0.723
Women	30/3	3.574 (118)	3.198 (139)	0.376 (0.365)	0.304	0.004	0.643
	30/5	3.473 (178)	3.141 (79)	0.332 (0.392)	0.398	0.003	0.642
	MET40*h	3.355 (54)	3.375 (203)	0.020 (0.444)	0.964	0.000	0.641

[1] eCHD risk: Estimation of the percent likelihood of developing CHD over a period of 10 years
[2] SE = Standard Error
3 Partial eta squared refers to physical activity
4 R squared refers to the whole regression model that includes the effects of age, BMI and smoking in subjects not taking medications.

11.4. Discussion:

After excluding those who are taking medications and adjustment for age, BMI and smoking, the findings indicated that all the three methods of categorization were able to identify a difference in eCHD risk between those deemed inactive with those deemed active (1.0 to 1.9 % higher risk in those men deemed active). In women, none of the three methods of categorization were able to identify a difference between those deemed to be inactive and active.

This thesis failed to support the hypothesis of this thesis (page 64) since no demonstrable difference in eCHD risk could be identified when the three methods of categorization were used for predict this risk. This conclusion was based on the lack of significant difference between methods in the overall r squared and partial eta squared for physical activity as well as lack of significant difference in the eCHD risk between the three sets of inactive and active groups. In other words, no one method of categorization gave a better prediction of eCHD risk over the other. Although this may be at first sight seem surprising, especially since more physical activity was to be undertaken to classify as active in one method of categorization than another.

On the other hand, since physical activity accounted for less than 1.0 and 3.0 % of the variability in the eCHD risk in women and men, respectively, it would be difficult to demonstrate a difference between the methods of categorization with the number of subjects involved. For example, if eta squatted is treated as r squared (as in some statistical packages), it can be shown that in men a sample size of 3011 will be required to detect a difference between r squared = 0.029 (r = 0.17) and r squared = 0.014 (r = 0.12) with 80 % power and a p value of 0.05.

11.5. Conclusion:

In men, but not in women, being physically active by all three methods of categorization was associated with lower eCHD risk compared to inactive groups. No one method of categorization gave a significantly better prediction of CHD risk over another. These methods accounted for only a small proportion of the variability in eCHD risk. This is the first study in which different methods of categorizing subjects into inactive and active have been used in a single common data-set. However, this data-set are based on the NDNS 7-day diary that does not appear to have adequately validated. This matter is addressed in more detail in Part Two of *Chapter* 12.

Part Two

Chapter 12: Comparison between estimated physical activity levels measured by the NDNS seven-day diary and IPAQ

Chapter 12 Comparison between estimated physical activity levels measured by the NDNS seven-day diary and IPAQ

12.1. Introduction:

There is a general agreement among public health and medical authorities that physical activity has beneficial effects on health (i.e. prevention of CHD and diabetes) (Blair and Connelly, 1996; Department of Health, 2004). However, just the level of physical activity that is needed to protect against ill-health remains to be undetermined (Lee and Skerrett, 2001b). This is due, at least in part, to limitations in the tools or instruments that can be used to assess activity exposure. For example, much of the evidence has been derived from epidemiological surveys where activity was assessed using a range of self-reported activity participation such as questionnaires and diaries. Differences between instruments in the aspects of physical activity, that are assessed, (e.g. recorded prospectively or recalled later; time spent when sleeping and sitting, intensity and duration of physical activity, total physical activity, and PAEE) may account for the heterogeneity in dose-response for physical activity on CVD risk (Sallis and Saelens, 2000).

A principal study of physical activity, diet and health of adults in the UK is the National Diet and Nutrition Survey (NDNS) has been conducted by HM Government (Food Standards Agency, 2004). In this survey, activity was assessed in a more detailed and complete way using a prospective NDNS 7-day diary and questionnaire. In a retrospective analysis, using this data-set, we have explored the relationship between the measures of physical activity and the factors known to be associated with CHD risk factors and eCHD risk (in the previous *Chapters*). In disagreement with other studies (Manson et al., 1999; Lee and Skerrett, 2001b), using simple diary and questionnaires, we found that the associations between physical activity, blood pressure and lipid profile are weak. Such observations do not directly support the current Department of Health recommendations about the amount of physical activity that is associated with good cardiovascular health (Department of Health, 2004).

There has been increasing evidence that the applying different physical activity questionnaires to the same groups of subjects results in different scores and individual ranking orders (Ainsworth et al., 2006). However, to our knowledge, there are no studies that have addressed the NDNS 7-day diary ranking order and compared it to other validated differently-structured questionnaires. Having shown in the first part of this thesis that there is a weak association between different categorization methods for physical activity with CHD risk factors and eCHD risk, there is a need to determine whether the differences in ascribing an activity score by the NDNS diary compared to those obtained from other questionnaires are present or not. In addition, the level of agreement in the overall scores and ranking order, using different coding and classifying systems for physical activity within the same type of instruments, has not been determined in the literature.

Therefore, the aim of this *Chapter* was to explore the agreement in MET scores assessed in a group of volunteers using three different systems for physical activity coding and classifications, measured by the NDNS 7-day diary and the International Physical Activity Questionnaire (IPAQ). In addition, this *Chapter* aimed to determine the extent to which different physical activity guidelines are met using different calculation systems in the same volunteers. The IPAQ questionnaire was selected as it is a widely accepted, validated questionnaire that encompasses the domains raised in earlier simple questionnaires together with the capacity to provide a quantitative statement as to the amount and intensity of activity exposure (Craig et al., 2003). The following questions were asked:

1) What is the agreement between the NDNS and modified Blair systems based on the "*total MET scores*" obtained from the NDNS diary? Is there a significant difference between these two systems?
2) What is the agreement between the NDNS and modified Blair systems based on the MET scores of "*at least moderate activities*" obtained from the NDNS diary? Is there a significant difference between these three systems?
3) What is the agreement between the NDNS and IPAQ systems obtained from the NDNS diary and IPAQ, respectively, based on the MET scores of "*at least moderate activities*"? Is there a significant difference between these three systems?
4) How good is the agreement of the individuals' adherence to the activity guidelines of "30/5" (Department of Health, 1996), "MET40*h" (Blair et al., 1985), and "MET750*m" (Haskell et al., 2007) based on the above mentioned systems?

12.2. Methodology:

This study was approved by the School Medicine Ethnics Committee. The Committee approval letter is enclosed in *Appendix* 5.

12.2.1. Study subjects and recruitment:

The first-year medical students at the University of Southampton were recruited in one of the lectures given by Dr S Wootton. The undergraduate first-year students group was selected as it was believed that a large group of subjects would be readily accessible and have the same occupational activity (student) but variable leisure time activity. The invitation to participate was linked to a class activity and governance approval from the School of Medicine Ethics Committee and Director of Education was granted to only approach these first-year students as it would be of benefit to their own learning experience linked to the class.

It was estimated that out of 250 students, at least 30% (80 students) would participate in the study (see page 186 189 for sample size calculation). However, the results indicate that out of 120 students attended the class, while 99 students had been interested to participate in the study, only 26 students returned the filled in diary and questionnaire. Only first-year medical students were eligible as a) they are readily available, b) they are a reasonably well defined study population and c) are likely to exhibit broad differences in leisure time pursuits whilst having a similar occupational activity. There were no exclusion criteria.

Details of the study were announced in one of the lectures given by Dr S Wootton to invite the students to participate in the study. The group results of the study were incorporated into the teaching materials for use with this group and in subsequent years. A spreadsheet of individual results were posted via email to the year group in an anonymized form such that those who participated could identify their own results and relate them to group norms.

12.2.2. Study design:

Participants Information Sheets, explaining the importance of this study and instructions on how to get involved in the study, were handed to the students (see *Appendix* 6). The students were briefly instructed how to complete the NDNS 7-day diary and the IPAQ. They were asked to record only activities they had done for at least 10 minutes. The rationale being that the evidence indicates that episodes or bouts of at least 10 minutes are required to achieve health benefits. The National Institutes of Health (National Institutes of Health, 1996) concluded that intermittent or shorter bouts of physical activity (at least 10 min) have similar CHD preventive effects and other health benefits if performed at a level of moderate intensity (such as brisk walking, cycling, swimming, home repair, and yard work) with an accumulated duration of at least 30 min/day.

The pilot studies have shown that the time taken to fill out the NDNS 7-day diary is less than 30 minutes/day, and approximately 10 minutes to complete the IPAQ. Then, participants were asked to record the amount of time they spend in specific categories of activity in their own time and return their data anonymously to the investigator in the class. The NDNS 7-day diary and IPAQ are found in the *Appendix* 4 and are available online at www.food.gov.uk (for NDNS diary) and www.ipaq.ki.se (for IPAQ). For each intensity category, a list of examples was given in the NDNS diary and IPAQ.

NDNS physical activity seven-day diary:

The physical activity 7-day diary was adapted from the NDNS of young people who are generally more active than most adults. Respondents were asked to record the total time that they spend on an activity during seven-day period. The first page of the diary collects information about the daily time spent in bed asleep (including napping), time spent at work (including paid and unpaid work) or college that day, and an opinion question asking them to assess whether they were more active, about as active or less active than usual that day. The second page for each day collects information about time spent in walking at an average pace and briskly, time spent on a range of listed activities (such as light and heavy housework, gardening, and active caring), and time spent on any similar activities. The third page for each day deals mainly with information regarding the time spent on a range of listed sports and leisure activities, whether the respondent had got 'out of breath or sweaty' doing the activity. The difference between 24 hours per day and the total duration of self-reported spent in sleep, moderate, and vigorous activities was considered as light activities. This correction was based on the assumption that these common activities are not asked for in the NDNS diary.

Data from existing research (Blair, 1984) have used to develop the NDNS Physical Activity Diary Coding Guide system for the NDNS diary. This newly developed NDNS system was used to calculate the MET*hr value for each activity derived from the NDNS diary (described below in the Coding and classification systems for physical activity levels). In addition to the developed NDNS system, the alternative MET system obtained from Blair (1984) was also used to calculate the total MET scores.

a. <u>International Physical Activity Questionnaire (IPAQ):</u>

The items in the long IPAQ form were structured to provide separate domain specific scores for walking, moderate-intensity and vigorous-intensity activity within each of the work, transportation, domestic chores and gardening (yard) and leisure-time domains. Using the IPAQ, the participants were first asked about their occupational physical activity (i.e. whether tasks were sedentary, moderate, or physically vigorous) during the last 7 days. The total number of minutes/hours per day or week spent during household tasks (including gardening and child care), walking or cycling for transportation, type of sports performed, and duration of sitting during weekdays and weekend, were asked next.

An overall physical activity level was computed as the sum of time spent in total for each of the three categories of activity: walking, moderate and vigorous activities. However, the IPAQ sitting question was an additional indicator variable of the time spent in sedentary activity and is not included as part of any summary score of the IPAQ physical activity level. The *Compendium of Physical Activities* was used to assign METs for each activity (Ainsworth et al., 2000).

12.2.3. Coding and classification systems for physical activity:

Table 12.1 presents different coding and classification systems for physical activity. In this study, we have modified applied the Blair system to analyse the NDNS diary data, as the Minnesota questionnaire for the Blairs' raw data were not used. This also applies to the IPAQ system when it was used to analyse the NDNS diary data. Briefly, the questions in the NDNS diary and IPAQ allowed for collecting the quantitative and qualitative data regarding the duration (number of minutes/hours per day), frequency (number of days per week) and categories (moderate or heavy intensity) of each activity types.

Calculation of MET scores based on the NDNS, Blair and IPAQ systems:

The information derived from the NDNS diary was used to calculate the MET scores of the "total" and "at least moderate activities" according to the NDNS and modified Blair systems. In addition, the information derived from the IPAQ was used to calculate the MET scores of the "at least moderate activities" according to IPAQ system.

The MET value for each activity category was calculated as an average for the activities corresponding to that category. For example, using the NDNS system, light activities have MET values ranging from 1.5 to 2.5, and an average of 2.0 was taken based on the type of activities that could be coded as light. Consequently, all activity categories (sleep, very light/light, moderate, vigorous/very vigorous) were grouped into different MET values.

This information that was obtained from the NDNS diary and IPAQ allowed calculating the MET score of "total" and "at least moderate activities" by multiplying the time (minutes or hours) spent in each activity by the corresponding MET value of each activity category. Examples of how to calculate the MET*hr/day and MET*min/week scores of the "total" and "at least moderate activities" are given in *Appendix* 7.

Five days per week of at least moderate physical activity for 30 minutes or more:

Physical activity level, expressed as number of minutes per day, was also calculated to determine the proportion of subjects who met the Department of Health physical activity guideline, which was interpreted as "≥ five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996).

Table 12.1: Comparison between different physical activity systems according to classifications, codings and examples of different types of physical activities.

Physical activity systems	Physical activity classifications	Average MET coding (range)	Example of activities
NDNS 2004 system	Sleep	1.0	Sleeping and napping.
	Very light/light activities	2.0 (1.5-2.5 METs)	Sitting; watching TV; reading; cooking; cleaning; bowling; table tennis; average walking; card playing; riding and driving a car; listening to music; light golf/ cricket; riding horse.
	Moderate activities	4.0	Brisk walking; light cycling/ aerobics/ badminton/swimming/ dancing; playing with children/child care; heavy cricket/ golf; general yoga/ gardening/canoeing.
	Vigorous/very vigorous activities	7.5 (6.0-10.0 METs)	Football; weight lifting; heavy dancing/ swimming/badminton/ softball/ netball; judo, karate; tennis.
Blair 1984 system	Sleep	1.0	Sleeping and napping.
	Very light/light Activities	1.5 (1.1-2.9 METs)	Mowing lawn with riding mower.
	Moderate Activities	4.0 (3.0-4.9 METs)	Brisk walking, walking/bicycling to and from work, and for pleasure; table tennis; bowling; general golf; light canoeing.
	Vigorous activities	6.0 (5.0-6.9 METs)	Jogging; tennis singles; general swimming/dancing.
	Very vigorous activities	10.0 (> 7.0 METs)	General badminton; squash; football; mountain climbing; tennis double; vigorous canoeing.
IPAQ	Walking	3.3	Average/leisure/brisk walking.
	Moderate	4.0	Bicycling/swimming at a regular pace; doubles tennis; moderate yard chores such as sweeping/ carrying light loads.
	Moderate inside chores	3.0	Washing windows, scrubbing floors and sweeping inside home.
	Vigorous yard chores	5.5	Heavy lifting, chopping wood, shoveling snow, or digging.
	Cycling	6.0	Travel from place to place.
	Vigorous	8.0	Aerobics, running, fast bicycling, or fast swimming; heavy lifting/construction, digging, or climbing up stairs.

12.2.4. Categorization methods for physical activity (used in guidelines):

The information derived from the NDNS diary and IPAQ was used to determine the proportion of subjects who met the level of the physical activity guidelines. In this study, the participants were categorized as active if they achieve the following guidelines:

1. 30/5 guideline: five days per week of at least moderate physical activity for 30 minutes or more (Department of Health, 1996).
2. MET40*h guideline: accumulative of at least total 40 MET*hr per day (Blair et al., 1985).
3. MET750*m guideline: accumulative of 450-750 MET*min per week of at least moderate activity (Haskell et al., et al 2007).

12.2.5. Data entering:

In analysing out data, time was recorded to the nearest 10 minutes. Values of 10 or less minutes of activity were recorded to “zero” of activity. In addition, the missing number of minutes or hours, for example in walking, was recorded to “zero”. However, the average hours of sleep was determined for the students based on the missing sleeping time. Only one participant did not record sleeping time for only one day of the period of 7 days. The data were entered anonymously into a computer, which involved the use of a password before the information was accessed. The internal consistency checks were applied to avoid mis-keying. For instance, checking that the time spent in all activities did not add up to more than 24 hours. In addition, entries were also checked where the students might have recorded an activity twice. For example, walking and pushing a child in a pushchair. This was recorded as active childcare and not also as time spent walking. Although there were no established rules for data cleaning on physical activity; data with unreasonable results were considered outliers and thus were excluded from the analysis. For example, all walking, moderate and vigorous time variables with the total of at least or greater than “16 hours” were excluded. The anonymous information forms were locked in a filing cabinet.

12.2.6. Statistical analyses:

The NDNS 7-day diary and IPAQ establish the time spent undertaking a range of physical activities, including moderate and vigorous intensities, as well as time spent in sleeping (only NDNS diary). Because the NDNS diary and IPAQ include a different set of questions and instructions which can calculate each activity score, they were treated in the way that they have been designed to be validated. With this information, the summation over a week allowed calculating the total number of minutes and MET scores spent in "total" (only NDNS diary) and "at least moderate" (both NDNS diary and IPAQ) activities. This summation was based on three different systems: 1) NDNS, 2) "modified Blair" and 3) IPAQ. Thereafter, the descriptive statistical analysis was used to determine the proportion of subjects meeting the guidelines for physical activity (e.g. 30/5, MET40*h and MET750*m guidelines) according to each systems.

According to the MET scores of the "total" as well as "at least moderate" activities, Paired t-tests were performed to identify if there is a significant difference between the NDNS, modified Blair and IPAQ systems. In order to illustrate the extent of agreement between these systems, Bland-Altman plots and the 95 % limits of agreement were calculated. These limits were defined as m ± 1.96 SD (where m = mean of the differences and SD = standard deviation of the differences).

In general, the use of the mean value and ± SD of the difference between two measures (e.g. NDNS and modified Blair systems) has been strongly advocated by Bland and Altman (Bland and Altman, 1986) to graphically illustrate the magnitude and pattern of agreement (including systematic differences), and allow for detection of outliers and trends. Bland-Altman Plot illustrates that if the vertical value departs from zero it represents the magnitude of bias of the test value. In addition, Pearson correlation was used to examine the associations of the mean value and difference between the paired systems with regard to the MET scores.

On the basis of the categorical variables (e.g. 30/5 guideline), the categorization methods for physical activity (used in guidelines) were illustrated by using cross-tabulation to obtain the proportion of subjects reporting the same category consistently. In addition, Cohen's kappa statistic was used to assess the agreement of categorical of activity scores calculated by the NDNS, modified Blair and IPAQ systems obtained from the NDNS diary and IPAQ. In general, kappa measures the agreement between categorical variables, in a table, after excluding the component which would be expected to occur from chance alone (Cohen, 1960). The value of kappa is defined as

$$\kappa = \frac{p_0 - p_6}{1 - p_6}$$

The value of kappa is usually between 0 and 1. If the results were made by chance, the value would be zero. If the results were in perfect agreement, the number of agreements would be equal to 1. The Cohen's kappa values were classified as follow (Altman, 1991):

- very poor agreement = Less than 0.20
- fair agreement = 0.20 to 0.40
- moderate agreement = 0.40 to 0.60
- good agreement = 0.60 to 0.80
- very good agreement = 0.80 to 1.00

The sample size calculation was performed to find out how large a sample is needed to enable statistical judgments that are accurate and reliable. Out of 250 students, it was estimated that at least a 30% (80 students) will participate in the study. A sample size of 80 is sufficient to detect a kappa value as low as 0.315 with 80 % power at a *P* value of 0.05 (two tailed). Even if only 50 or 25 students completed the study, the sample size would be sufficient to detect a kappa value of 0.400 or 0.565, respectively (with 80 % power and a *P* value of 0.05). Statistical analyses were performed by using SPSS version 15.0 for Windows software.

12.3. Results:

Since the IPAQ does not actually measure all domains of physical activity, such as sleeping and light activities (only at least moderate activities), the information derived from the NDNS diary was first used to calculate the "total daily activities" expressed in MET*min scores using the NDNS and modified Blair systems. Thereafter, the "at least moderate activities" derived from the NDNS diary and IPAQ were compared based on the NDNS, modified Blair and IPAQ systems. *Tables* 12.2-12.4 show the descriptive analysis and the calculation of the physical activity level using the NDNS, modified Blair and IPAQ systems. In general, the SPSS Explore test showed that the normality of the data was not significantly different from normal distribution.

Table 12.2: The level of total physical activity expressed in MET scores/day of the student group (n = 26) based on the NDNS calculation system.

Type of activity	MET value for the type of activity	Mean (SD) of total minutes spent	MET*min/day (MET*hr/day)
Sleep	1.0	479 (39)	479
Average walking	2.0	41 (31)	82
Light activities (e.g. cooking, ironing, light gardening)	2.0	25 (25)	50
Very light/light activities (unreported activities)	2.0	827 (71)	1654
Moderate activities [1] (e.g. brisk walking, light swimming)	4.0	37 (28)	148
Vigorous/very vigorous activities [1] (e.g. football, weight lifting)	7.5	31 (26)	233
Total MET*min/day (Total MET*hr/day)			**2646** (44.1)

[1] At least moderate activity = 381 MET*min/day (6.3 MET*hr/day)

Table 12.3: The level of total physical activity expressed in MET scores/day of the student group (n=26) based on the modified Blair calculation system.

Type of activity	MET value for the type of activity	Mean (SD) of total minutes spent	MET*min/day (MET*hr/day)
Sleep	1.0	479 (39)	479
Light activities (e.g. cooking, ironing)	1.5	831 (84)	1247
Moderate activities [1] (e.g. average & brisk walking, active caring)	4.0	78 (50)	312
Vigorous activities [1] (e.g. dancing, swimming)	6.0	43 (40)	258
Very vigorous activities [1] (e.g. football, weight lifting)	10.0	9 (11)	90
Total MET*min/day (Total MET*hr/day)			**2386** (39.8)

[1] At least moderate activity = 660 MET*min/day (11.0 MET*hr/day)

Table 12.4: The level of at least moderate physical activity expressed in MET scores/day of the student group (n = 26) based on the IPAQ calculation system.

Type of activity	**MET value for the type of activity**	**Mean (SD) of total minutes spent**	**MET*min/day** (MET*hr/day)
Walking (average and brisk)	3.3	77.0 (52)	254
Cycling (from place to place)	6.0	3.0 (10)	18
Moderate inside chores (e.g. washing windows)	3.0	6.8 (7.9)	20
Moderate activities (e.g. moderate work, leisure)	4.0	14.4 (15)	57
Vigorous yard chores (e.g. digging in yard)	5.5	0.2 (0.8)	1
Vigorous activities (e.g. running, heavy lifting)	8.0	20.4 (16)	162
MET*min/day of at least moderate activity (MET*hr/day of at least moderate activity)			**512.0** (8.5)

12.3.1. Total MET*min/day (NDNS and modified Blair systems):

In this study, we have modified the Blair system to analyse the NDNS diary data, as the Minnesota questionnaire used to establish the Blair system was not used. This also applies to the IPAQ system when it was used to analyse the NDNS diary data. The results showed a high Pearson correlation between the NDNS and modified Blair systems (r = 0.88) in regard to the total MET*min/day. However, the paired t-tests showed a significant difference ($P < 0.001$) between the NDNS (2646 MET*min/day) and modified Blair (2386 MET*min/day) systems.

Bland-Altman plots (*Figure* 12.1) revealed a good association between the difference in activity score derived from the two systems (activity score modified Blair – activity score NDNS) and the mean activity score value of these systems (activity score Blair + Activity score NDNS / 2) (r = 0.73; P < 0.001 for trend). However, there was a trend toward a bias effect whereby at lower activity levels, the activity score derived by the modified Blair system was less than that derived by the NDNS system. The mean difference in activity score between the two systems was -260 MET*min where the activity score of the modified Blair system was lower than that of the NDNS system. The 95 % confidence interval (difference ± 2 SD) of the limits of agreement ranged from -554 to 38 MET*min (the difference from zero on the Bland-Altman is equivalent to paired t-test). The difference in activity score between these systems decreased with rising activity levels. This Figure (12.1) shows that three of the group appeared to show a different relationship in that they clearly fell outside the 95 % confidence interval such that activity levels calculated by modified Blair system was comparable or greater than NDNS system. This trend was expected in that Blair codes light intensity activities at a lower MET value than NDNS whilst the reverse is true for higher intensity activities where Blair system uses higher MET values for high intensity activities.

In order to identify which other factors might have influenced the level of agreement, the calculation of total MET scores was repeated using the same MET value for a specific activity in both systems. Thus, when the light activities were multiplied by a 1.5 MET value in both systems, a very similar pattern as before but the scatter plot is shifted such that modified Blair system now exceeded the NDNS system. The mean difference between the two systems was significantly higher ($P < 0.001$) in modified Blair compared to the NDNS by 188 MET*min (the range of the 95 % of confidence interval of the limits of agreement was -74 to 450 MET*min for the individual values) (see *Figure* 12.2). Once again, three of the group fell outside the 95 % confidence interval.

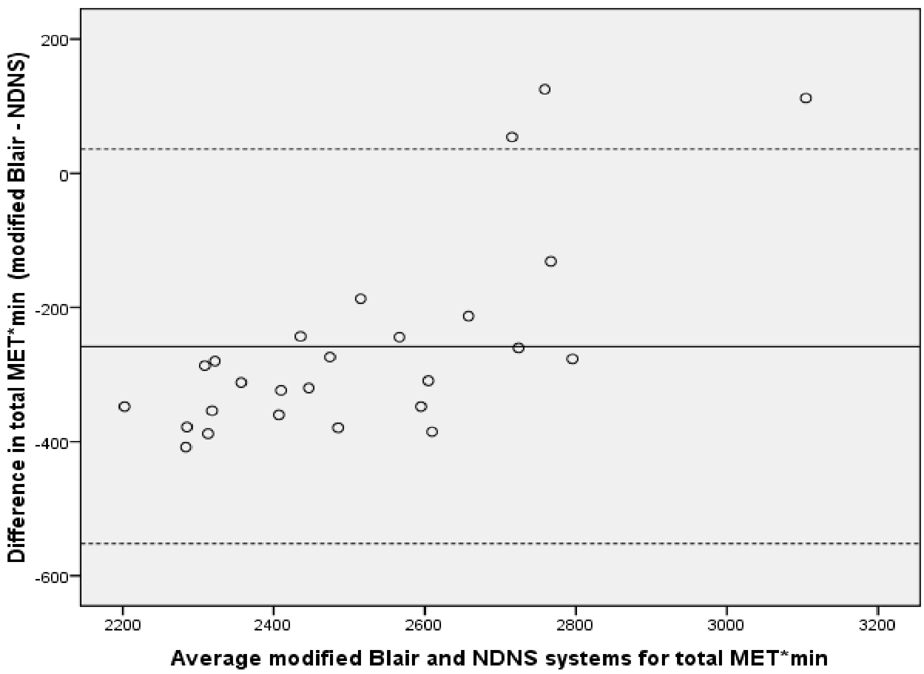


Figure 12.1: Bland-Altman plot between modified Blair and NDNS systems. Difference against average for <u>total daily MET*min</u> (n = 26). The solid line indicates the mean difference between the two systems; the dated lines represent the 95 % CI.

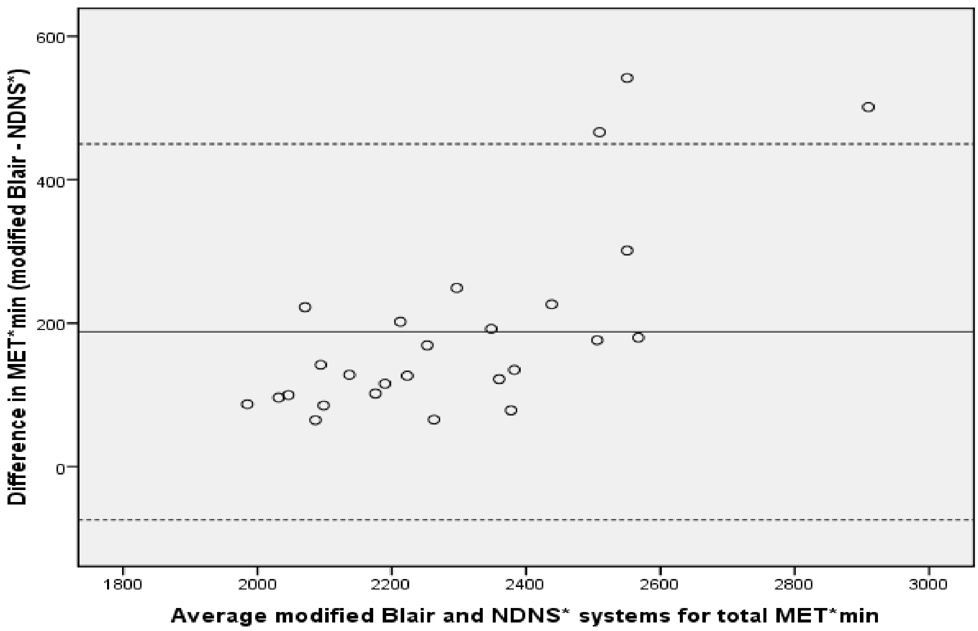


Figure 12.2: Bland-Altman plot between modified Blair and NDNS* systems. Difference against average for total daily MET*min (n = 26). The solid line indicates the mean difference between the two systems; the dated lines represent the 95 % CI.
* NDNS system; all light activities were multiplied by a 1.5 MET rather than 2 METs.

12.3.2. MET*min/day of at least moderate activity:

In this section, the NDNS, modified Blair, modified IPAQ (used to analyze the NDNS diary) and IPAQ (used to analyze the IPAQ questionnaire) systems were used to analyze the MET*min/day of at least moderate activity. The results showed a high Pearson correlation between the NDNS and modified Blair systems (r = 0.91) in regard to the MET*min/day of at least moderate activity. However, the paired t-tests showed a systematic significant difference ($P < 0.001$) between the NDNS (381 MET*min/day) and modified Blair (660 MET*min/day) systems.

Bland-Altman plots (*Figure* 12.3) revealed a good association between the difference in activity score derived from the two systems (activity score modified Blair – activity score NDNS) and the mean activity score value of these systems (activity score Blair + Activity score NDNS / 2) (r = 0.79; P < 0.001 for trend). However, there was a trend toward a bias effect whereby at lower activity levels, the activity score derived by the NDNS system was less than that derived by the modified Blair system. The mean difference in activity score between the two systems was 279 MET*min where the activity score of the modified Blair system was higher than that of the NDNS system. The 95 % confidence interval (difference ± 2SD) of the limits of agreement ranged from -108 to 672 MET*min for the individual values. The difference in activity score between these systems decreased with rising activity levels. Again, three of the group appeared to show a different relationship in that they clearly fell outside the 95 % confidence interval such that activity levels calculated by modified Blair system was comparable or greater than NDNS system. Similar pattern was found when modified IPAQ system when used to analyze the NDNS diary.

Whilst the results showed a moderate Pearson correlation between the NDNS and IPAQ systems (r = 0.58) in regard to the MET*min/day of at least moderate activity, the paired t-tests indicated a systematic significant difference ($P < 0.013$) between the NDNS (381 MET*min/day) and IPAQ (512 MET*min/day) systems. In addition, Bland-Altman Plot (*Figure* 12.4) revealed a poor level of agreement as well as a low association between the IPAQ and NDNS systems and the mean value of these systems ($r = 0.34$; $P = 0.088$ for trend). The mean difference between the two systems was 131 MET*min higher in the IPAQ compared to the NDNS system with 95 % confidence interval of the limits of agreement ranged from -109 to 671 for the individual values. This *Figure* (12.4) shows that the difference did not decrease with rising activity levels.

This trend was as expected in that NDNS codes moderate intensity activities at a lower MET value than Blair and IPAQ systems. When the number of minutes of the average walking activity was multiplied by a 4 MET value in the NDNS system, while the difference became smaller with modified Blair system (199 MET*min higher in modified Blair), it remained significantly different ($P < 0.001$). However, the difference between the IPAQ and NDNS systems was very close to zero and was not significantly different between the two systems (only 50 MET*min higher in IPAQ).

Whilst the results showed a moderate Pearson correlation between the modified Blair and IPAQ systems (r = 0.58) in regard to the MET*min/day of at least moderate activity, the paired t-tests indicated a systematic significant difference ($P < 0.013$) between the modified Blair (660 MET*min/day) and IPAQ (512 MET*min/day) systems. In addition, Bland-Altman Plot (*Figure* 12.5) revealed a poor level of agreement as well as a low association between the modified Blair and IPAQ systems and the mean value of these systems ($r = 0.27$; $P = 0.178$ for trend). The mean difference between the two systems was 148 MET*min higher in the modified Blair compared to the IPAQ with 95 % confidence interval of the limits of agreement ranged from -466 to 764 for the individual values.

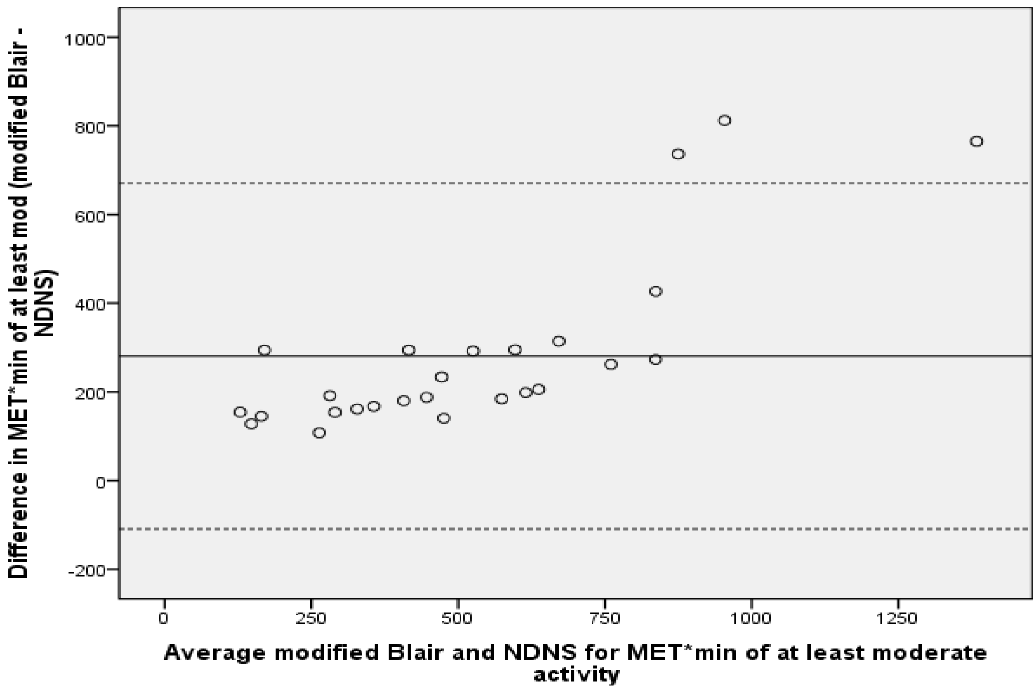


Figure 12.3: Bland-Altman plot between modified Blair and NDNS systems. Difference against average for MET*min of at least moderate activity (n = 26). The solid line indicates the mean difference between the two systems; the dated lines represent the 95 % CI.

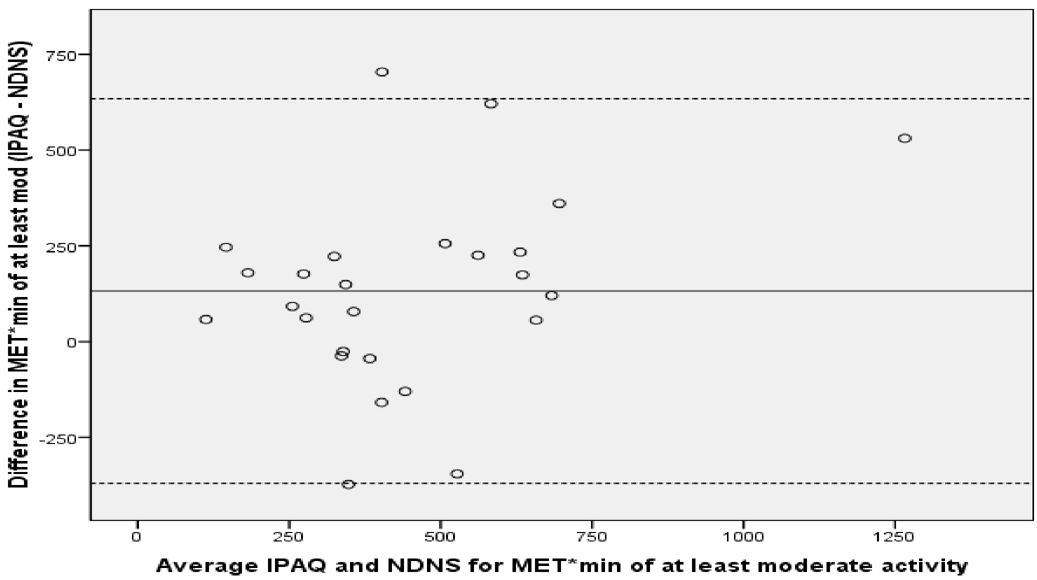


Figure 12.4: Bland-Altman plot between IPAQ and NDNS systems. Difference against average for MET*min of at least moderate activity (n = 26). The solid line indicates the mean difference between the two systems; the dated lines represent the 95 % CI.

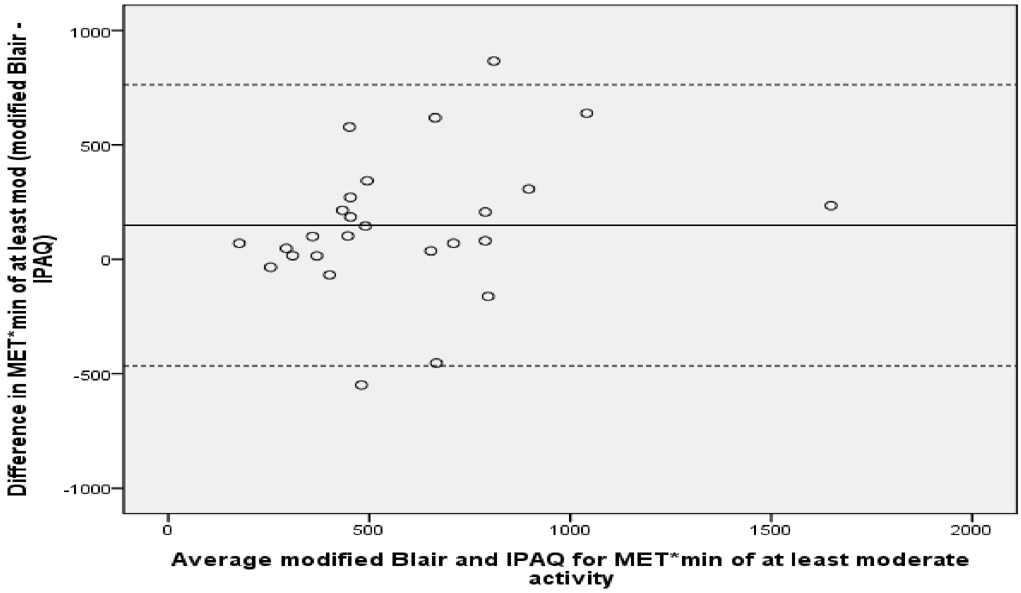


Figure 12.5: Bland-Altman plot between modified Blair and IPAQ systems. Difference against average for MET*min of at least moderate activity (n = 26). The solid line indicates the mean difference between the two systems; the dated lines represent the 95 % CI.

12.3.3. Physical activity guidelines:

The proportion of subjects meeting the guidelines for physical activity such as MET40*h guideline (using NDNS and modified Blair systems), and MET750*m guideline or 30/5 guideline "of at least moderate activities" (using NDNS, modified Blair and IPAQ systems) were identified. In this analysis, the descriptive statistics and kappa were used to examine the level of agreement between these systems.

The following *Tables* 12.5 and 12.6 represent the recommended total score of MET40*h and 30/5 guidelines calculated by the NDNS and modified Blair systems. The rows represent the NDNS system and the columns represent the modified Blair system. As far as the recommended total score of MET40*h and 30/5 guidelines are concerned, the values for kappa were 0.07 and 0.18 (not significantly different from zero) ($P < 0.345$; standard error = 0.07) and ($P < 0.112$; standard error = 0.12 respectively). This indicates a very poor level of agreement between these systems (which may be caused by chance). Out of the 26 participants, only one and two participants agreed between the NDNS and modified Blair systems according to the MET40*h and 30/5 guidelines, respectively.

Table 12.5: Agreement in physical activity categorization (MET40*h guideline) between the NDNS and modified Blair systems for calculating MET scores from the same activity diary.

Systems		**modified Blair system** (MET40*h guideline)		Total	*kappa*	SE [2]
		inactive	active		0.07	0.07
NDNS system [1] (MET40*h guideline)	inactive	1	0	1		
	active	13	12	25		
Total		14	12	26		

[1] Both systems used the same cut-off value (MET40*h guideline) to distinguish between activity (> 40 MET*hr/day) and inactive (< 40 MET*hr/day) individuals

[2] SE = Standard Error

Table 12.6: Agreement in physical activity categorization (30/5 guideline) between the NDNS and modified Blair systems for calculating number of days/week of at least moderate activity for ≥ 30 minutes from the same diary.

Systems		**modified Blair system** [1] (30/5 guideline)		Total	*Kappa*	SE [2]
		inactive	active		0.18	0.12
NDNS system [1] (30/5 guideline)	inactive	2	10	12		
	Active	0	14	14		
Total		2	24	26		

[1] Both systems used the same cut-off value (30/5 guideline) to distinguish between activity (> 5 days/week) and inactive (< 5 days/week) individuals

[2] SE = Standard Error

In addition, *Table* 12.7 represents the comparison between the NDNS and modified IPAQ systems regarding the MET750*m guideline, which also shows a very poor level of agreement between these systems. However, the comparison between these systems according to the 30/5 guideline was not applicable because all the participants were considered active (based on the modified IPAQ).

Table 12.7: Agreement in physical activity categorization (MET750*m guideline) between the NDNS and modified IPAQ systems for calculating MET scores from the same diary.

Systems		**modified IPAQ** [1] (MET750*m guideline)		Total	*Kappa*	SE [2]
		inactive	active		0.10	0.06
NDNS system [1] (MET750*m guideline)	Inactive	4	0	4		
	Active	16	6	22		
Total		20	6	26		

[1] Both systems used the same cut-off value (MET750*m guideline) to distinguish between activity (>750 MET*min/week) and inactive (<750 MET*min/week) individuals

[2] SE = Standard Error

However, the results showed a fair agreement with the NDNS and modified Blair systems; when these systems treated in the way they have been designed to be used and when their own scoring recommendations were applied. For example, when the 30/5 guideline (defined by NDNS system) and the MET40*h guideline (defined by the modified Blaire systems), the value for kappa was 0.39 and the difference was significant from zero (P < 0.045; standard error = 0.178) (see *Table* 11.8). However, according to the MET750*m guideline, the kappa was not applicable to compare between the NDNS and IPAQ systems because all participants were considered active (based on the IPAQ).

Table 12.8: Agreement between NDNS and Blair methods for categorizing physical activity (30/5 and MET40*h guidelines).

Methods		**Partial Blair method** [1] (MET40*h guideline)		Total	*Kappa*	SE [3]
		Inactive	Active		0.39	0.178
NDNS method [2] (30/5 guideline)	Inactive	9	3	12		
	Active	5	9	14		
Total		14	12	26		

* These methods were treated in the way by applying their own scoring recommendations

[1] Use of NDNS diary and Blair system for calculating MET*hr/day (inactive < 40 MET*hr/day; active > 40 MET*hr/day)

[2] Use of NDNS diary and NDNS system to calculate number of days/week of at least moderate activity for ≥ 30 minutes (inactive < 5 days/week; active > 5 days/week)

[3] SE = Standard Error

Descriptive results of subjects classified as being sufficiently active according to different physical activity recommendations defined by the NDNS, modified Blair and IPAQ systems are summarized in *Table* 12.9. There were 54 % of the participants met the 30/5 guideline estimated by the NDNS system, whereas 46 % of the participants classified as being sufficiently based on the MET40*h guideline estimated by the modified Blair system. Although the difference between the NDNS and modified Blair systems in regard to these recommendations was only 8 %, the kappa showed a very poor level of agreement between these systems. Based on the MET750*m guideline, all the participants (100 %) met this criterion when using the IPAQ systems.

Table 12.9: Numbers and percentages of subjects meeting recommended guidelines for physical activity, according to three different methods (IPAQ, Blair and NDNS).*

Methods	Achieving physical activity guidelines		Total
	No	Yes	
IPAQ method [1] (MET750*m guideline)	0 (0 %)	26 (100 %)	26 (100 %)
Modified Blair method [2] (MET40*h guideline)	14 (54 %)	12 (46 %)	26 (100 %)
NDNS method [3] (30/5 guideline)	12 (46 %)	14 (54 %)	26 (100 %)

* The same subjects (n=26) completed the IPAQ questionnaire and the NDNS 7-day diary.

[1] Use of IPAQ questionnaire and IPAQ system for calculating MET*min/week (inactive < 750 MET*min/week; active > 750 MET*min/week)

[2] Use of NDNS 7-day diary and Blair system for calculating MET*hr/day (inactive < 40 MET*hr/day; active > 40 MET*hr/day)

[3] Use of NDNS 7/day diary and NDNS system to calculate number of days/week of at least moderate activity for ≥ 30 minutes (inactive < 5 days/week; active > 5 days/week)

12.4. Discussion:

The main aim of this *Chapter* was to identify the level of agreement in MET scores and the extent to which different physical activity guidelines are met using three different physical activity systems (NDNS, modified Blair, and the IPAQ systems). These systems were assessed and analyzed in each individual in order to control for any confounding factors that may exist between the measurements. To our knowledge, none of the previous studies to date has estimated different physical activity guidelines (30/5, MET40*h and MET750*m guidelines) using different systems (NDNS, modified Blair, and/ or IPAQ) obtained from different physical activity instruments (NDNS diary and IPAQ) within the same population. Since the Pearson correlation only estimates the strength of the association and fails to detect agreement (Bland and Altman, 1986), the Bland-Altman and kappa were used as primary measures of agreement.

In this *Chapter*, the undergraduate first-year students group was selected as it was believed that a large group of subjects would be readily accessible and have the same occupational activity (student) but variable leisure time activity. The invitation to participate was linked to a class activity and governance approval from the School of Medicine Ethics Committee and Director of Education was granted to only approach these first-year students as it would be of benefit to their own learning experience linked to the class. The initial response rate in this group was disappointingly low. Repeated approaches to the students did not substantively increase the response rate. We were not permitted, under governance, to continue to approach students to further improve response. Equally, as Ethics approval was only for these first-year students, it was not possible to approach any other student group without re-applying to the Ethics Committee. Time pressures meant that this work could only be considered as preliminary observations as a pilot study. While this study could be considered as a pilot study investigating the level of physical activity based on different systems, it can be further used as a first step towards a larger population in trying to understand whether using different systems give similar or different results in the same individuals.

In this *Chapter*, a high degree of association (r squared = 0.88) was found between levels of physical activity derived using the NDNS and Blair systems. However, when examined using a Bland-Altman analysis, there was a significant difference between the mean level of physical activity expressed as total MET*day derived by the two systems with a wide limit of agreement. Similar relationships were evident when comparing physical activity derived using the NDNS and IPAQ systems where more moderate levels of association ($r = 0.58$) and significant difference and a wide limit of agreement.

The findings of this current study are similar with findings from past studies (Chasan-Taber et al., 1996; Norman et al., 2001; Aadahl and Jorgensen, 2003) in term of Pearson correlation. For example, a study performed by Chasan-Taber et al., (1996) showed that the correlations between diary-based and questionnaire-based activity scores were 0.28 and 0.58 for moderate and vigorous activities, respectively, in a prospective study of 51,529 men. In addition, in a study conducted in Sweden, Norman A et al (2001) has found a moderate correlation (r squared = 0.56) for MET*hr when comparing a questionnaire with the 7-day activity diary in 111 men (aged 44-78 yr). Aadahl and Jorgensen (2003) have found that the Spearman correlations for MET scores have been shown to be 0.74 ($P < 0.001$) and 0.20 (not significant) when comparing an activity scale with a diary and accelerometer, respectively, in 2500 Danish men and women (aged 20-60 years). Also, they found that the physical activity questionnaire overestimates the MET scores compared to physical activity diaries.

The majority of epidemiological studies have explored the associations between different physical activity instruments using the correlation coefficients. When 10 commonly used physical activity questionnaires were validated against five different reference methods, Jacobs et al., (1993) has indicated that the correlations differ considerably depending on which reference method was used. Schmidt and Steindorf (2006) revealed that correlation coefficients are still the common approach used in many studies to validate physical activity questionnaires, which has been criticized in the theoretically oriented literature for more than 20 years. In fact, they have shown that serious bias in questionnaires can be revealed by Bland-Altman plots, but they may remain undetected by correlation coefficients. Therefore, although there are some general principles, it is not quite clear what are the most appropriate statistical and interpretation of validation methods that can be used (e.g. the use of correlation approach can yield misleading conclusions in validation studies).

According to the at least moderate activity, the best agreements between these systems were obtained when data were analyzed assuming the average of walking as a moderate activity by the NDNS system, especially with the IPAQ system. Therefore, this study raised questions regarding the constituents of the moderate-intensity activities. For example, according to the NDNS system, the underestimation of the MET*min/day for the "at least moderate activities" could partly, but not completely, be explained by multiplying the time spent in average walking by a value of 2 METs. In addition, the Bland–Altman plots demonstrated that the difference depends on the extent of physical activity; as the MET*min scores increase, the difference between these systems becomes smaller. It should be noted that defining acceptable agreement between these systems is difficult because the criteria for a gold standard system do not exist.

These data were also used to compare the proportions of the participants who gave the same activity classification based on different guidelines for physical activity estimated by the NDNS, modified Blaire and IPAQ systems. These guidelines extended to include the MET40*h, MET750*m and 30/5 guidelines. While the first guideline (MET40*h) is derived from the NDNS diary, the latter two are derived from the NDNS diary and IPAQ. These findings further indicated that the kappa provided further evidence that there has been a very poor level of agreement between the NDNS, modified Blair, and modified IPAQ systems, and with regard to the physical activity guidelines (MET40*h, MET750*m and 30/5 guidelines) (see *Tables* 12.5-12.8)**.**

The findings also showed that when the NDNS and modified Blair systems treated in the way that have been designed to be validated and using their own guideline (30/5 for NDNS and MET40*h for Blair), the results showed a fair agreement (kappa = 0.39). Therefore, this current study indicated that the potential problem may arise when using one system and applying its results to a different guideline established by a different system. For example, a potential problem is more likely to arise if someone uses the NDNS system and then applies the results to the MET40*h guideline (established by modified Blair system). This is of particular importance when addressing the findings of the NDNS secondary analysis obtained from the NDNS data-set between physical activity and the CHD risk factors and eCHD risk. Hence, these results need to be interpreted with caution.

This data, which are detailed in the Results (*Table* 12.9), showed the individuals classification based on whether or not they meet physical activity guidelines. Based on the IPAQ system, all the participants were categorized as active based on the current MET750*m guideline. However, about half of the same participants were classified as active; based on the 30/5 guideline (estimated by NDNS system) and MET40*h guideline (estimated by modified Blair system), respectively.

In general, the results of this current study were, to some extent, in agreement with previous studies (Matthews et al., 2005; Ekelund et al., 2006; Meriwether et al., 2006; Mäder et al., 2006; Rose et al., 2008; Mayer et al., 2008). In one of these studies, Ekelund U et al (2006) indicated that the agreement of IPAQ to capture insufficiently active individuals was 45 %. They study also revealed that 77 % of those meeting the ACSM/CDC guidelines (at least 30 minutes/day) as determined by the accelerometer were captured by the IPAQ in 185 Swedish adults aged 20 to 69 years. In addition, according to the moderate and vigorous activities, they have found that the IPAQ is significantly different from the time measured by the accelerometer (mean difference: −25.9 minutes/day, 95 % limits of agreement: −172 to 120 minutes/day; $P < 0.001$). In another study, Meriwether et al., (2006) has found that the Physical Activity Assessment Tool (measures activities in the last 7 days) classified participants as "active" (≥ 150 minutes per week of at least moderate activities) concordantly with accelerometer for 69.8 % of participants and with IPAQ for 66.7 % in 68 adult volunteers. The strength of agreement was fair (kappa = 0.34 and 0.21 compared to the accelerometer and IPAQ, respectively), and markedly fewer participants were classified as active based on the IPAQ ($P < 0.001$). In addition, when Mayer et al., (2008) has compared the telephone assessment of physical activity with a written questionnaire in 34 adults, the kappa value was 0.48.

In this current study, the findings observed almost similar daily average of total MET*hr scores (44.1 MET*hr/day) compared to the findings of the NDNS secondary analysis (44.9 MET*hr/day) of the young adults aged 19-24 years old obtained from the 2004 NDNS data-set. However, when this data analyzed by using the modified Blair system, show that the average of the total MET*hr scores was 39.8 MET*hr/day. This indicates that the NDNS system has overestimated the level of activity, expressed as a total MET*hr score, when compared to the modified Blair system.

In comparison with other studies, a recent Danish study by Aadahl et al., (2007) has found that the mean of MET*hr/day obtained by self-report questionnaire is 45.3 and 49.7 for women and men, respectively (33–64 years of age; n = 1640). They corrected the missing time to the total 24-hour by multiplying with the intensity factor of 2.0 MET value. Other studies have found lower overall MET*hr/day scores of 40.6 (Schaller et al., 2005) with 40.8 (Norman et al., 2001) in men compared to 38.8 in women (Schaller et al., 2005). Norman et al (2001) multiplied the light activities by the intensity factor of 2.0. Whereas, a MET value of 1.75 is given to the difference between 24-hour per day and the total duration of self-reported activity/inactivity by Schaller et al., (2005). In these studies, the intensity of the activities was measured based on a compendium of physical activities (Ainsworth et al., 1993 and 2000). These findings confirm the fact that the total MET scores observed in this study may be overestimated when using the NDNS system.

In most if not all of the above mentioned studies, the main confusion found in this current study has been related to MET coding and classifications/categorizations of some activities (range and average), which are inconsistent between the systems of NDNS, modified Blair and IPAQ. For example, the NDNS system estimated the difference between 24 hours per day and the total duration of self-reported activities, which was considered as light/very light activities, corresponding to the mean of self-care/ walking at home (2.5 MET) and general sitting/watching TV (1.5 MET). These activities were multiplied by an estimated MET value of 2.0, which is between the suggested values of 1.5 MET and 2.5 METs. However, Blair system gives a lower MET value for light activities, which have an average of 1.5 METs (range from 1.1 to 2.9 METs). The MET-factor 1.5 was chosen by Blair system under the assumption that most of the light/very light activities are spent in sedentary activities or household tasks with an average of less than 2 MET values. Some studies have shown that the extent of these light-intensity activities is very difficult for most respondents to assess (Norman et al., 2001; Schaller et al., 2005; Aadahl and Jorgensen, 2003). *Table* 12.1, which is detailed in the Methods, shows the comparison between different codings, classifications and examples for physical activities established by different systems.

In addition one of the confusion found in this current study was related to the average and range of MET. For example, an average of 4.0 MET values (by both Blair and IPAQ systems) and ranges of 3.0-4.9 and 3.0-5.9 were assigned as moderate-intensity activities based on Blair and IPAQ systems, respectively. Based on the NDNS system, an average of 4.0 MET values was also used that could be classified as moderate-intensity activities; however, there was no clear range. In addition, the vigorous and very vigorous activities were combined, and averages of 7.5 and 8.0 MET values were chosen based on the NDNS and IPAQ systems, respectively. However, using the Blair system, averages of 6.0 and 10.0 were used for vigorous and very vigorous activities, respectively. Consequently, assigning different average MET values to the same type of activity may increase the difference between these systems. For example, if a person walks 10 minutes at an average speed, he/she should score 20 METs*min based on the NDNS compared to 40 or 33 METs*min when using Blair or IPAQ systems, respectively.

On the other hand, one other major limitation with the NDNS diary is the lack of clarity in the information regarding the light and occupational activities. These activities, occupy most of the time that we spend daily, were measured by subtracting the time spent in sleep, moderate, and vigorous activities from the 24-hrs. In addition, a primary reason why the NDNS system underestimated the "at least moderate activity" appears to be the inability of participants to distinguish between light and moderate (and a lesser extent to vigorous activity) activities based on the NDNS diary. An example could be average and brisk walking, which many people probably walk at an average intensity, but they believe walk briskly. Moreover, the answers in the NDNS diary and IPAQ might be associated with errors caused by, for example, difficulties in remembering the frequency and duration of the activities, especially the IPAQ.

12.5. Strengths and limitations of the study:

12.5.1. <u>Strengths</u>:

The strength of this study was to estimate the physical activity levels using three different coding and classification systems for physical activity obtained from different physical activity instruments. In addition, this study assessed the degree of agreement at which different physical activity guidelines are met, using a variety of systems obtained from two distinct physical activity instruments within the same population. For these reasons, this study investigated both continuous and categorical variables which may helped to explain the lack of association found in the 2004 NDNS secondary analysis between physical activity and CHD risk factors (blood pressure and blood lipid profile) and eCHD risk which was due, at least in part, to the differences in ascribing an activity score.

12.5.2. <u>Limitations</u>:

This study has had some limitations which may not be quite representative of the general population. This is mainly because the studied sample consisted of 1) small number of participants (only 26 students), which may have weakened the power of the study to present significant differences and agreements between different systems and guidelines, 2) low response rate (22 %) associated with this study's design (out of 120, only 26 students responded), 3) more educated volunteer students, and 4) non-random, convenient sampling in an effort to avoid low participation rates. As mentioned in the introduction section, and in interpreting and discussing the findings, one needs to be very clear about the objectives of this study. The intention was not to give estimates of the prevalence of physical activity in the population. However, the aim was rather to study the differences in the overall scores and ranking orders, using different coding and classifying systems for physical activity, which may have influenced the agreement between the amount of physical activity and the CHD risk factors and eCHD risk. Despite this obvious limitation, the average MET score obtained from the students was similar to those obtained from the same age group from the NDNS with a larger population. Therefore, this indicates that the small size of the second part of the study is of minor limitation.

12.5. Conclusion:

In conclusion, when measuring the same amount of physical activity on the same subjects using different systems for coding and classifying physical activities, a systematic difference and a poor agreement with the trend towards the difference getting smaller with increasing physical activity were found. Compared to the modified Blair and IPAQ systems, a closer examination revealed that the NDNS system underestimates the MET*min/day for the "at least moderate activities". This could partly, but not completely, be explained by classifying the duration of average walking as light rather than moderate activity and multiplying it by the 2 MET value. Kappa showed a very poor level of agreement between the NDNS, modified Blair and IPAQ systems according to the proportions of the participants who gave the same activity categorization based on different guidelines for physical activity. In addition, this study indicated that a potential problem might arise when using one system and applying its results to different guidelines established by different systems.

Therefore, this study would help in explaining why adults fulfilling the Department of Health recommendation for physical activity obtain trivial benefits in the CHD risk factors and eCHD risk, according to a secondary analysis of an NDNS survey that used an activity diary. It should be noted that a precise definition of the MET threshold is not possible because the gold standard system for coding and classifying physical activity does not exist yet.

Chapter 13: General discussion

Chapter 13 General discussion

The aim of this thesis was to (1) describe the extent of agreement between three different methods of categorisation of subjects into inactive and active groups, (2) examine the effect (expressed as partial eta squared) of different levels of activity on blood pressure (SBP and DBP), TC, HDL-C and estimated CHD risk in men and women (within a secondary analysis of the NDNS dataset) using each of the three methods of categorisation where subjects were deemed either inactive or active, and (3) categorize the subjects into active and inactive groups using the three methods and then examining whether there were significant differences in the estimated CHD risk between a) the three inactive groups, b) the three active groups and c) the size of the difference between the three sets of inactive and active groups

13.1. Summary and overview of the major findings:

13.1.1. Activity status distribution for the UK population:

This data-set analyzed in this thesis showed that the distribution of individuals between different levels of activity (inactive/active) was inconsistent, and depended on the guideline used as the basis of describing activity behaviour. At a population level (i.e. the NDNS dataset), this thesis showed that the proportion of individuals who deemed active varies widely from 34 to 83 % in men and 25 to 72 % in women. This variation depends on the method of categorization (i.e. which is dependent on the guideline). Kappa values (beyond chance) showed that the proportion of subjects categorized in the same categories (inactive and active categories) ranged from 18 to 63 % in men, and 22 to 52 % in women. Likewise, in the second part of the thesis (i.e. the students), in which different physical activity systems were compared, kappa showed that the degree of agreement in categorization was poor with a range of 0 to 39 % for the proportion of classified subjects. Therefore, this thesis generally indicated a poor level of agreement between the three methods of categorization.

The Department of Health (1996) has stated that adults need to accumulate at least 30 minutes of moderate physical activity for 5 or more days of the week. The data analyzed in this thesis revealed that the majority of men (66 %) and an even higher proportion of women (75 %) did not achieve the level of this guideline. According to the 30/3 and MET40*h guidelines, the findings of this thesis showed that 53 % of men and 49 % of women met the 30/3 guideline, and 83 % of men and 72 % of women fulfilled the

MET40*h recommendation. Therefore, most of the population achieved the total MET recommendation (lower target) but not the recommendation to undertake the at least 3 or 5 days/week of at least moderate activity for 30 minutes or more. One possible source of discrepancy between different coding system concerns different methods to classify the same activity. This issue is further discussed in section 13.2.

13.1.2. CHD risk factors and eCHD risk:

This thesis indicated that, in the three methods of categorisation (i.e. physical activity guidelines), inactive men were associated with increased levels of TC, reduced HDL-C and greater eCHD risk compared to the active individuals. This effect persisted even after controlling for differences in BMI and adjustment for age, smoking and after excluding individuals on medications. However, there was no significant difference in blood pressure between the two groups of men. By contrast, no relationships were found with CHD risk factors and eCHD risk in women, irrespectively of the method of categorization. After excluding individuals who were taking medications and adjusting the values for age, BMI and smoking, the proportion of variance in CHD risk factors and eCHD risk explained by physical activity was found to be small. These results are in agreement with a number of other studies (Fagard, 1999 and 2001; Whelton et al., 2002; Tully et al., 2005; Andersen and Jensen, 2007; Hardcastle, 2008; Krousel-Wood, 2008). The findings indicated that TC and HDL-C were reduced in men, but not in women. These results are consistent with the findings of many other studies (Mbalilaki, 2007; Thompson et al., 2001; Kraus et al., 2002; Jakes et al., 2003; Kelley et al., 2004; Barengo et al., 2006). However, in this thesis, being classified active did not significantly reduce the SBP and DBP levels in either men or women compared to inactive group. These findings were inconsistent with the results of many other studies (Kronenberg et al., 2000; Kelley et al., 2001; Whelton et al., 2002; Aires et al., 2003; O'donovan et al., 2005; Parker et al., 2007; Gilson et al., 2007). The explanation for this discrepancy is unclear although blood pressure is confounded by many other factors, such as stress.

This thesis also indicated that inactive men, but not in women, had higher estimated risk of CHD than those who deemed active in each of the three physical activity guidelines. In agreement with these findings, there is evidence that physical activity is associated with a reduced risk of CHD among men (Hakim et al., 1999; Sesso et al., 2000; Lee et al., 2000a; Tanasescu et al., 2002). Similarly, the effects of physical activity on eCHD risk seem to be less beneficial to women, again consistent with other studies (Fagard, 1999; Manson et al., 1999 and 2002; Lee., et al 2001a; Wilmore et al., 2001; Bassett et al., 2002; Jakes et al., 2003). In this thesis, despite the fact that these physical activity guidelines accounted for a small proportion of variance in the CHD risk factors, a UK study by McPherson et al., (2002) has estimated that the lowering of TC to less than 6.5 mmol/l could achieve an 11 % reduction in CHD (both sexes), and the lowering of DBP by 10 mmHg could result in a 12 % and 15 % reductions in CHD risk for women and men. In addition, a more recent study of 15 years of follow-up (Andersen and Jensen, 2007) has indicated that a 2 mmHg reduction in the SBP is associated with a 10 % drop in stroke-related mortality rate and about 7 % decrease in mortalities caused by ischemic heart disease or other vascular diseases in middle age population. This thesis showed that the reductions in eCHD risk explained by physical activity in men were mainly due to an improvement in TC and HDL-C levels. By contrast, changes in the levels of SBP, DBP, TC and HDL-C were found to play an equally important role in eCHD risk in women.

Interestingly, this thesis suggested that adherence to the current Department of Health guideline (30/5 guideline) is probably sufficient to reduce the risk of CHD in men, but not in women, for reasons that are unclear. Nevertheless, the lack of the association among women may be related to changes in sex hormones which can influence the CHD risk factors and eCHD risk (Donahue et al., 1988). In addition, it has been suggested that the physical activity assessment techniques are less accurate in women than in men (Blair et al., 1993). This is mainly because the focus on physical activity is more on self-reported traditional sport and LTPA, omitting other activities pertinent to women, such as housework and child care.

Some studies have suggested that the beneficial effects of physical activity on CHD risk factors appear to be mediated partially by the decrease in body weight and the maintenance of fat-free mass (Pate et al., 1995; Jakicic et al., 2001, Saris et al., 2003). This thesis showed that there were no significant differences in BMI between the active individuals who meet these physical activity guidelines compared to inactive groups who did not meet the guidelines (data not shown). Thus, it is important to note that the adherence to these guidelines is likely to be insufficient for the maintenance of a healthy body weight. However, the effects of fitness on CHD risk factors and eCHD risk may differ from activity. A recent study of a 7.7 years followed prospectively study of 29,139 men and 11,985 women by Williams, PT (2008) has indicated that a higher cardiorespiratory fitness reduced the odds for hypertension, hypercholesterolemia, and diabetes, independent of physical activity and was an important risk factor separate from physical activity. Despite the benefits of physical fitness are well evident in the literature review, the current physical activity guidelines (including the Department of Health guideline) are based on the measurement of physical activity rather than physical fitness. Although physical fitness is known to be a function of physical activity, the level of activity needed to attain the level of fitness that brings these health benefits is still not known.

On the other hand, although the above three physical activity guidelines serve as reference recommendations to define active and inactive levels, applying dichotomous variables is not optimal for establishing a dose-response relationship between physical activity and CHD risk factors and eCHD risk. Therefore, this may hinder the interpretation of real effects which could mask physiological alterations in CHD risk factors and eCHD risk. The nature of the dose-response relationships between physical activity and the CHD risk factors and eCHD risk would influence public perceptions regarding the extent of physical activity needed to improve general health.

Several others studies (Khaw et al., 2006; Blair et al 2001; Lee and Skerrett, 2001b; and Oja, 2001) have suggested that helping people to move from an inactive level to moderately active levels produces the greatest reduction in risk CHD, CVD or all-cause mortality. A suggested dose–response relationship by Lee and Skerrett (2001b) (see also *Figure* 2.1 in the Literature Review) has shown a continuous dose-response gradient of CHD and type 2 diabetes mellitus across a wide range of physical activity or fitness levels. Although this *Figure* (2.1) has been used by the Department of Health (Department of Health, 2004), it is derived mainly from evidence on CHD or type 2 diabetes, and it is not clear whether the effect is related to physical activity or fitness. In this thesis, when further categories of physical activity were redefined in terms of number of days/week (4 categories), number of minutes/day (quintiles), and MET*hr/day (4 categories)], the current findings agree with this Figure (2.1) in relation to TC, HDL-C and eCHD risk in men only. On the contrary, weak evidence was found by the same thesis for a dose-response of activity volume and blood pressure (SBP and DBP), in both men and women (see *Tables* 9.4-9.6 and *Figures* 9.2-9.4).

This thesis also demonstrated that the dose-response of the eCHD risk was stronger than the CHD risk factors. This is consistent with a review by Oja, (2001) that has shown a fairly strong evidence of a crude dose-response between the total volume of weekly physical activity and fitness with CHD. However, the current findings disagree with the results of other studies showing inverse relationships between a cluster of metabolic variables (including blood pressure) and reported physical activities during LTPA or objective measurements of fitness (Khaw et al., 2006; Blair et al., 2001; Kohl, 2001; Oja, 2001;Laaksonen et al., 2002; Lakka et al., 2003; Rennie et al., 2003; Lindstrom et al., 2003; Holme et al., 2007; Ekelund, 2007; Onat et al., 2007). For example, Ekelund, (2007) found a linear dose-response association between the total amounts of activity with clustered metabolic risks. Thus, sedentary individuals may have benefited from accumulating physical activity throughout the day, and more activity accumulated leads to the greater metabolic health benefits. In addition, a cross-sectional survey of 4,228 men and women (60 year-old) by Onat et al., (2007) has found a strong inverse dose–response relationship between LTPA and the metabolic syndrome. The adjusted odds ratio for having the metabolic syndrome in the high LTPA group was 0.33 using the low LTPA group as reference.

In addition, an attempt to increase the power of the analysis, the categories for each measure were collectively examined as a continuous variable. When physical activity was used as a continuous variable (using different measures), significant dose-response relationships with TC, HDL-C and eCHD risk were found in men, but not in women. SBP and DBP were not significant in either men or women. In this analysis, the General Linear Model was used to examine the dose-response relationship between these physical activity measures and the studied risk factors. In addition, when bivariate Curvilinear Models were used, they showed no significant advantage over the General Linear Model.

In contrast, using the NDNS self-perception questionnaire, the findings failed to show any significant difference between subjects who would see themselves as overall at least fairly physically and very active in relation to CHD risk factors and eCHD risk. This failed to support the hypothesis raised in this thesis. According to the job categorization, the findings indicated that women who would see themselves as not very physically active had higher TC level only than those women who were not at all very physically active. These effects, using the NDNS self-perception questionnaire, persist even after adjustment for age, BMI, smoking and after exclusion of subjects on medications.

The mechanism behind this inconsistency of the findings of this current thesis compared to other studies is not quite clear. However, the majority of epidemiological studies have explored the nature of the dose–response relationship between physical activity and disease outcomes using tertiles (Bijnen et al., 1998), quartiles (Aadahl et al., 2007; Church, 2007) and quintiles (Aadahl et al., 2007). Therefore, it is difficult to compare a dose-response relationship in this current thesis with findings from past studies which have met different distribution methods, different measures (e.g. MET), different types (e.g. LTPA), different dimensions (e.g. fitness) and different systems for physical activity. In addition, other factors such as insulin sensitivity and coagulation may affect the interpretation. Some of these issues are discussed in more details in section 13.2.

13.1.3. Methods of categorization and CHD (eCHD):

Although the distribution of individuals between different categories of physical activity varies with the method of categorisation, the use and interpretation of the 30/3, 30/5 and MET40*h guidelines appeared to identify a difference in eCHD risk between men who deemed inactive and those who considered active. However, the findings failed to demonstrate any significant advantage of physical activity on eCHD risk across these methods of categorization in women. Therefore, no one method of categorization gave a better prediction of CHD risk over another. Although all the three methods of categorization were consistent in showing that more active individuals had a lower eCHD risk, they accounted for only a small proportion of the variability in eCHD risk. This issue is discussed in more details below.

13.2. Exploration of the hypothesis and the results

Whilst some of the significant associations have been found between the above categorization methods used in the guidelines for physical activity and the CHD risk factors and eCHD risk, the nature of the relationship was weak. In the next sections, these inconsistencies are addressed by focusing on the mechanisms behind these discrepancies, and how these relate to the findings of this thesis and other studies.

13.2.1. The NDNS 7-day diary:

Since physical activity is a complex multidimensional behavior and can be defined in several ways, it is difficult to assess it in free-living populations, for which a gold standard or a single standard for measuring physical activity does not exist. In the current thesis, the level of physical activity was subjectively estimated by the NDNS physical activity diary during 7 days behaviour rather than more accurate instruments (e.g. accelerometers) or measures (e.g. fitness). It should also be noted that the assessment of physical activity in large-scale epidemiological studies (as with NDNS survey) is difficult because of its complicated nature (Wareham and Rennie, 1998). One problem with measuring physical activity in large population is the respondent burden. In some cases, the burden may be great enough to a degree that the participants will not comply with the measurement protocol. In other situations, while they may attempt to complete the diary, the effort required may cause them to alter their normal activities. This problem is particularly relevant to records keeping methods such as NDNS diary. Such differences in the accuracy of information about the duration and intensity of physical activity may have affected the current results.

Since the NDNS diary is based on self-reports, the inter-individual differences in the perception and reporting of the intensity of physical activities may also induce considerable error in the activity levels. Because of the differences in the aspects of physical activity assessed and the techniques (e.g. time spent when sleeping and sitting, intensity and duration of physical activity, total physical activity, TEE) may hinder a real association in the current results between the physical activity levels and the CHD risk factors. For example, it is suggested that light (e.g. home-related tasks) or moderate (e.g. walking) activities are recalled less readily or precisely compared to vigorous activities (Shephard, 2001).

In this thesis, it is not quite certain whether the activities reported by the NDNS 7-day diary were performed in single/continuous bouts or were accumulated in multiple episodes. In fact, it is more likely that the daily or weekly physical activities (e.g. walking, lawn work, and gardening) reflect accumulation of activity, most of which was performed intermittently and at a moderate intensity. In addition, the NDNS 7-diary counts in only activities of more than 10 minutes, and ignores those activities spent in less than 10 minutes which encompasses the larger proportion of activities during the day. It should be noted that a wide range of activities, spent in less than 10 minutes, were added up to complete a full one day of 24-hour, and then averaged out as light activities and before being scored as an intensity of 2 METs. Consequently, this may have caused errors and resulted in a considerable variability in the total MET scores as most of the time spent was in this period. For example, if someone briskly walks or takes the stairs everyday from place to place, most of the working hours (5 minutes each way) would be of a moderate rather than light intensity (as calculated by the NDNS). Therefore, the current results should be interpreted in context of all these considerations.

Since physical activity levels at work have been recently on the continuous decline in most industrialized countries (Powell, 1987), assessment of LTPA is often assumed to be the best representation of physical activity in the population. However, the MRFIT study (Leon et al., 1987) has shown that the most frequently reported activities are the domestic/household activities, including lawn and garden work (80 %), walking (65 %), and home repairs (60 %). These types of activities have been found to be associated with favourable health outcomes and are likely to be performed, at least partly, on an intermittent basis (Magnus et al., 1979; Leon et al., 1987). Most of these activities are invariably cited in public health recommendations (The Chief Medical Officer, 2004). As it has been estimated that energy cost is equivalent to a moderate intensity of 3.0 to 6.0 MET, the minimum intensity required to achieve a health benefit (Ainsworth et al., 2000).

For these reasons, while the NDNS diary may have been designed primarily to measure the leisure time and domestic/household activities, there is no clear information about work and transportation–related activities. However, it has been acknowledged that physical activity can occur across four domains, including work-related, leisure-time, transport-related and domestic/household. Each domain represents a sphere of daily life activities that are common to most populations regardless of culture or economic development. In addition, it is worth noting that it is possible to be more or less active within each domain by itself. Several studies have shown that regular walking or cycling to and from work and other work-related activities are related to lower levels of the risk factors for CHD (Andersen, 2000; Hu et al., 2001, 2002 and 2003; Khaw et al., 2006; Hu et al., 2007a, 2007b and 2007c). For example, Andersen et al, (2000) indicated that moderate LTPA is inversely associated with all-cause mortality in both men and women in all age groups. The benefits have been further observed from cycling as a modality of transportation to work even after adjustment for LTPA. In addition, three recent follow-ups of 18.9 years Finnish participants, aged 25-64 years, (Hu et al., 2007a, 2007b and 2007c) have indicated that moderate or high levels of work-related activities or LTPA are significantly associated with a reduction in the Framingham risk score (with the 10-year risk of CHD events) among both men ($P < 0.05$) and women ($P < 0.01$).

In addition, the concept of physical activity on an average weekday or weekend, which is required for respondents to describe as they answer a questionnaire or diary, involves a risk of information bias, especially in relation to LTPA (Howley, 2001). Therefore, because the LTPA was mainly assessed by the NDNS diary, which is typically performed during weekends (i.e. once or twice per week), the average week of physical activity may not be accurate. Moreover, because sporting activities, which may be performed at a range of skill levels and pace of any physical activity can vary (especially walking, jogging and cycling), the actual health benefits may differ considerably. Furthermore, domestic physical activity may not be intense enough to produce improvements in cardiovascular fitness at the level that is required to reduce the risk of disease. A recent cross-sectional study, by Stamakis et al., (2007), has determined the independent associations of domestic activity and other activity types (walking and sports) with multiple CVD risk factors (resting pulse rate, obesity, TC, HDL-C, blood pressure, C-reactive protein) in 14,836 adults (ages 16 years and over) live in households in England. They found that men and women who achieved the recommended levels of physical activity, mainly because of heavy domestic physical activity, are more likely to be obese and poor health compared to men who were active at the recommended levels which were mainly resulted from walking, sport and/or exercise participation.

Therefore, because there is unclear description or misidentification about transportation and work-related domains specified by the NDNS diary and limitations in the measurement of LTPA and domestic activities, some degree of error may have been introduced in this current thesis. This may lead to underestimate and misclassify physical activity levels obtained by the NDNS diary which in turn may have altered the relationship between physical activity and CHD risk factors and eCHD risk.

13.2.2. Moderate-intensity versus vigorous-intensity:

The focus shifting on "moderate-intensity" has raised questions regarding the activities that constitute moderate-intensity and how to measure the prevalence of this broader range of activities within populations. This confusion may be due, in part, to a disagreement on the clarity and consistency of physical activity intensities. *Table* 12.1 in *Chapter* 12 (Part Two) shows the comparison between different coding and classification systems and examples of physical activities classified by different systems.

The Department of Health, (1996) has suggested that health benefits occur at least with moderate intensity activities, which are generally equivalent to a brisk walk and noticeably accelerate the heart rate. These activities are considered optimal when done for at least 30 minutes for at least 5 days per week (this level is sufficient to expend about 150 calories of energy per session, or 750 calories per week). While the Surgeon General's report (DHHS-US, 1996) has defined moderate activity as a 30 minute of brisk walking, 15 minutes of running, 30 minutes of lawn mowing, or 45 minutes of playing volleyball (a level sufficient to expend about 150 calories of energy per day on most, if not all, days of the week, or 1000 calories per week). In addition, the current US updated guideline (Haskell et al., 2007) has defined moderate activity as a 30 minute of brisk walking, basketball for 15-20 minutes, or swimming laps for 20 minutes.

Therefore, the definition of physical activity intensities in different ways and the understanding of its roles in communication and clarification of health messages in physical activity guidelines are critical issues. Accordingly, it is still controversial whether high-intensity or moderate-intensity physical activity exerts better effects on CHD risk factors and eCHD risk. Whaley MH and Kaminsky, (2001) have hypothesized that the current guidelines have created a widespread belief that moderate activity offers greater health benefits than vigorous activity. In support of this hypothesis, a recent nationally representative survey of 1191 Britons aged 16–65 (O'Donovan and Shave, 2007) has shown that the about 56 % of men and 71 % of women think that moderate activity offered greater health benefits than vigorous activity and indicated that moderate activity is recommended.

In this current thesis, the term of "at least moderate physical activity" encompasses for both moderate and vigorous activities. When the moderate and vigorous levels of physical activity were separated from each other, no significant change in the studied CHD risk factorswas observed (data not shown). This is consistent with other studies which have suggested that low- to moderate-intensity leisure activity including domestic ones may be associated with decreased overall and CVD mortality (Leon et al., 1987; Wannamethee et al., 2002; Barengo et al., 2004; Bucksch, 2005). By contrast, other studies have found that only moderate or vigorous-intensity activity has an effect (Lee and Paffenbarger, 2000b; Yu et al., 2003).

This debate on the optimal pattern of health-enhancing physical activity has a long history. Since 1970s, enough information was available on the beneficial effects of vigorous exercise on cardiorespiratory fitness that the American College of Sports Medicine (ACSM) and the American Heart Association (AHA) began issuing as part of their physical activity recommendations to the public (DHHS-US, 1996). These recommendations generally were focused on endurance and specified sustained periods of vigorous physical activity. The Surgeon General's report (DHHS-US, 1996) also has acknowledged that greater health benefits can be obtained by the engaging in physical activity of more vigorous intensity or of longer duration performed three or more times per week. Recently, the US updated guidelines (Haskell et al., 2007) have specified that moderate and vigorous-intensity activities are complementary in the production of health benefits and that a vigorous physical activity level above the recommended (moderate) levels provides even greater health benefits.

In addition, many studies have found that vigorous activity offers greater health benefits than moderate activity (Lakka et al., 1994; Mensink et al., 1999; Sesso et al., 2000; Swain and Franklin, 2006; Sakuta and Suzuki, 2006). For example, Mensink et al., (1999) and Sesso et al., (2000) have indicated that vigorous activity (5–9 MET), but not moderate activity (3–5 MET), is associated with significantly lower health risk factors. Consistently, in a more recent study, it has been indicated that vigorous-intensity activities have greater benefit for reducing CVD and premature mortality than moderate-intensity physical activity, independently of the EE (Swain and Franklin, 2006). Therefore, people who can maintain a regular regimen of activity, which is of longer duration or of more vigorous intensity, are likely to derive greater benefits over moderate intensity.

Moreover, although moderate physical activity is widely endorsed by most of the organizations (e.g. Department of Health, AHA), the recommended 30 minutes of moderate activity per day is not a universal remedy. For many people, moderate physical activity is probably sufficient to reduce the risk of breast cancer (Monninkhof et al., 2007). However, regular participation in vigorous activity is probably required to reduce the risk of prostate cancer (Giovannucci et al., 2005) and colorectal cancer (Slattery, 2004). Brisk walking is sufficient to protect women from type 2 diabetes (Hu et al., 1999), whereas men probably require vigorous activity to get protection against chronic disease (Lee and Paffenbarger, 2000-2; Tanasescu et al., 2002). Furthermore, some studies suggested that the beneficial effects of physical activity on CHD risk factors appear to be mediated partially by a decreased in body composition. Several major organizations recommend moderate physical activity in the range of 60–90 minutes of moderate activity/day for weight-loss maintenance (Pate et al., 1995; Department of Health, 2004; Jakicic et al., 2001, Saris et al., 2003). Therefore, it is important to note that adherence to these guidelines is likely to be insufficient for the maintenance of a healthy body weight. In addition, health benefits appear to be proportional to the amount and intensity of activity; and every increase in activity adds some benefits.

13.2.3. Coding and classification systems for physical activity:

Regardless of the internationally accepted coding and classification systems by Blair, (1984) and Ainsworth et al., (2000) that have been created for physical activity, the new developed Physical Activity Diary Coding Guide by the NDNS was designed to analyze the physical activity information derived from the NDNS diary. In this current thesis, the new developed NDNS system was used to examine the relationship between physical activity CHD risk factors and eCHD risk.

Although there is a growing interest in physical activity, especially the total physical activity expressed in MET score, and its relation to various health outcomes, some degree of miscalculation related to the coding and classifications of different activities may be introduced in this current thesis. For example, when the same amount of physical activities on the same subjects was analysed and compared using the NDNS, modified Blair and IPAQ systems, the findings showed that the generated intervals of prediction using Bland Altman Plots were quite wide and variable. This resulted in a significant difference and a poor level of agreement with a wide limit of agreement between these systems.

In addition, the kappa provided further evidence that there has been a very poor level of agreement between the NDNS and modified Blair systems with regard to the MET40*h guideline (kappa = 0.07) and 30/5 guideline (kappa = 0.18). However, when using the scoring recommendations of NDNS and Blair systems and treating them in the way they have been designed to be validated and using their scoring recommendations, the results showed a fair agreement (kappa = 0.39). Therefore, a potential problem is more likely to arise if someone uses the NDNS system and then applies the results to, for example, the MET40*h guideline which is established by Blair system. This is of particular importance when addressing the findings of the NDNS secondary analysis obtained from the NDNS data-set between physical activity and the CHD risk factors and eCHD risk. Therefore, these results need to be interpreted with caution.

While there are similarities across the above systems, there are also differences that may limit the comparability of the results across studies and add confusion to the relationship between physical activity and CHD risk factors and eCHD risk. For example, the MET values of the average walking can be classified as a light-intensity and coded as 2.0 (by NDNS) or classified as a moderate-intensity and coded as 4.0 (by Blair and IPAQ) (see *Table* 12.1). In this current thesis, these changes in coding and classifications for selected activities between these systems showed that the difference within individual's MET score or activity level for the same activity was large. Therefore, the true relationship between physical activity levels obtained from the NDNS diary and the CHD risk factors and eCHD risk may have not been accurate.

13.2.4. Other factors:

There are other several factors that may have contributed to the limits and/or influenced the findings of this current thesis. *Firstly*, although the NDNS system was primarily based on previously published data, it may not reflect the exact intensity values of some physical activities (e.g. average walking). *Secondly*, depending on the intense of the activity, individual variations in movement patterns and differences in the way activity is reported (e.g. effort, pace, age, and gender differences) may influence the intensity values of activities. For example, one person may rate his or her walking pace as "brisk" while another classifies the same pace as "slow". *Thirdly*, there is a considerable uncertainly in assessing an intensity value to certain kinds of specific activities. For instance, the intensity of the light activities (that are not covered by the diary) might lead to underestimation in men who have a higher mean intensity value than the assumed 2.0 METs. Likewise, an overestimation may occur in women with lower intensity value than 2.0 MET. These common activities may lead to a lower strength of the NDNS diary.

Fourthly, while the Blair and Ainsworth systems use MET as a corresponding standard RMR when sitting or lying quietly only, this may give inaccurate scores. In healthy individuals, RMR accounts for approximately 65 % of the total daily EE and is largely determined by many factors (Compher et al., 2006), which may be responsible for many of the variations about total MET scores on any given day. These factors' list extends to include age, gender, fasting and non-fasting, nicotine or caffeine consumption, thyroid hormones, genetics, body and room temperature, exercise training, and time length of rest prior to the RMR test (Compher et al., 2006). In fact, these factors have been indicated to give wider set of results for RMR. For example, when a single measurement of RMR after a 4-hour fast was compared with RMR measured after a 12-hour fast, the 4-hour measure was 99 kcal/day higher (Haugen et al., 2003). It should be noted that the MET score is a way of expressing intensity in comparison to RMR with one MET is equal to the standard for RMR (roughly 1 kcal/kg of body weight/hour) (Taylor et al., 1978).

Finally, there have been concerns that the absolute MET intensities may be inaccurate for people of different body masses and body fat compositions (percentages). Howell et al., (1999) has shown that the energy cost (kcal) of activity is higher among heavier individuals. Therefore, using the MET intensities may underestimate the actual energy cost of weight bearing activity for heavier individuals. Moreover, individuals with greater lean body mass also tend to have a higher RMR than do otherwise comparable individuals whose body composition includes a greater proportion of adipose tissue (Tataranni and Ravussin, 1995). Other studies have shown that fat-free mass, fat mass, Vo2max and gender explains 70–85 % of the variation in RMR (Arcerio et al., 1993; Buchholz et al., 2001). In addition, a higher RMR has been found to persist in the trained men compared with the untrained ones when the groups were matched for fat-free mass and body fat (Poehlman et al., 1988).

In spite of the limitations in the calculations of MET, the MET score has some advantages. *Firstly*, as one MET*hr is approximately equivalent to 60 kcal/hour (1 kcal/minute) for an average adult with body weight of 60 kilogram (Blair et al., 1985, Brown and Bauman, 2000), MET value can be worked out as numerically equivalent to EE in kcal, independently of body weight. For example, to conversion of the MET40*h guideline to EE kcal/day is simply achieved by multiplying the "40 MET*hr/day" by (weight in kilograms/60 kilograms). *Secondly*, statistically, the continuous or the categorical MET scores permit the use of linear regression analyses that may help to observe if there is any association between the physical activity measured in MET and CHD risk factors and eCHD risk.

Therefore, this thesis would help in explaining why adults fulfilling the Department of Health guideline for physical activity obtain trivial benefits in CHD risk factors and eCHD risk (according to a secondary analysis of an NDNS survey that used an activity diary). For example, according to the NDNS system, a closer examination of the duration of the average walking revealed that underestimation of the MET*min/day for the "at least moderate activities" could partly, but not completely, be calculated by multiplying the values by a factor of 2 MET value. This thesis raised questions regarding the constituents of the moderate-intensity activities; an issue which is discussed in more details above.

13.3. Strengths and limitations:

13.3.1. Strength of the thesis:

The current thesis has some methodological strengths such as the fairly large size of the studied population (n = 1658) with a reasonable response rate (45 %), a quite representative population which included men and women of a wide range of age (19-64 yrs). The NDNS diary can capture the different guidelines for physical activity (e.g. 30.5 and MET40*h guidelines). The proportion of variance in the CHD risk factors and eCHD risk explained by physical activity were analysed separately for each guideline. In addition, in order to control any confounding factors that may exist between the measurements, the effects of the number of days/week and minutes/day of moderate activity and total MET*hr/day on the CHD risk factors and eCHD risk were examined separately for each individual as categorical and continuous variables. Moreover, because there is no consistent coding or classifying system for all activities, three different scoring systems for physical activity were used to investigate the proportion of subjects meeting the physical activity guidelines.

13.3.2. Limitations of the thesis:

This thesis is an observational study in which the estimation of causality between physical activity and CHD risk factors and eCHD risk cannot be addressed. Therefore, findings of this thesis were subject to a number of limitations associated with the characterization of physical activity or methodological limitations. *Firstly*, the NDNS generally focused on cross-sectional information as with regard to monitoring the dietary habits and the nutritional status of the British population (e.g. food composition and nutrients intakes) rather than collecting data on physical activity. This information includes 7-day diary for dietary habits and physical activities, physical measurements (e.g. height and weight), blood samples, a detailed interviews to collect information on socioeconomic status, demographic and lifestyle characteristics, and urine samples. Therefore, this may cause a potential burden to the participants and a decline in the response rate as they may have considered filling the survey a time-consuming process. This may raise some concerns regarding the representativeness of the data generated which may have given inaccurate information about physical activity levels.

Secondly, the NDNS 7-day diary was used to collect information on physical activity behaviours. It has been shown that most of the cross-sectional studies (Rütten, 2003; Brown, 2004-2) using diaries or questionnaires to measure physical activity levels gave discrepant data between and within individuals and populations. However, it should be noted that there is no golden standard system for measuring physical activity as behaviour.

Thirdly, there is no clear validation for the NDNS 7-day diary. One potential source of bias is that neither transportation nor occupational activities were clearly examined. This may have caused underestimation of the true effects of physical activity on the CHD risk factors and eCHD risk. Consistently, some studies have suggested that limitations in the measurement of physical activity behaviour have underestimated true relationships between physical activity and various health outcomes (Blair et al., 2001, Dishman et al., 2004).

Fourthly, the NDNS diary is generally focused on moderate and vigorous activities spent in at least 10 minutes (and ignores all activities spent in less than 10 minutes) rather than light activities. Basically, if the activities are not moderate or vigorous, the diary stated that all activities are classified as light activities and coded as a value of 2 METs. Because there is a wide range of activities spent in less than 10 minutes, this may have resulted in an error and/ or a large variability in the activity levels, especially when measuring the total MET*hr/day. For example, if someone briskly walks or takes the stairs everyday from place to place most of the working hours (5 minutes each way) would be a moderate rather than a light intensity (as might be calculated by the NDNS).

Fifthly, although the NDNS diary can be applied simply and quite easily, this may lead to a potential bias in the result analysis as the simplicity can lead to uncertainty and information loss. In addition, the NDNS diary is limited to a period of 7 days. Therefore, in this system, physical activity assessment over a short time period is less likely to reflect usual behaviour as activity levels may vary with seasons or as a result of illness or time constraints. It is also well-established that the health benefits of physical activity result from regular participation over a period of several weeks or months (ACSM, 1978).

Sixthly, it should be noted that only a small number of CHD risk factors has been analyzed in this thesis. However, physical activity has been reported to have a wider range of physiological effects apart from those analyzed in this study. These extend to include effects on insulin resistance, TG, endothelial function, inflammatory markers, and haemostatic function. Therefore, the apparent health benefits of physical activity are substantial and may have physiological benefits other than those CHD risk factors for eCHD risk analyzed in this study.

Lastly, although several potential confounding factors have been adjusted (sex, age, smoking, BMI, and excluding medications), it is possible that other uncontrolled confounders (such as diet, ethnicity, birth weight, family history, genetic, hormonal function, skeletal muscle properties, cardio-nervous systems, and socioeconomic profile) could have impact on the amount of activity required to improve the studied risk factors. For example, chronic stress induced by the different psychosocial and/or socioeconomic situations may activate the hypothalamic–pituitary–adrenal axis as well as the sympathetic nervous system, and therefore contribute to the development of the metabolic syndrome (Bjorntorp, 2001). Likewise, patients with genetic haemochromatosis, have been found to have lower exercise capacity independently of other covariates of exercise capacity (Davidsen et al., 2007). Therefore, some individuals might require more physical activity to maintain health than others. This is mainly due to the inter-individual differences in these confounder factors.

Taken these contributors together (which may be potential source of bias), the results of this thesis may have underestimated the actual benefits of physical activity recommendations on the CHD risk factors and eCHD risk. Therefore, misreporting of physical activity levels assessed by the NDNS diary (may be well-recognized problem in the NDNS data) may have caused errors in activity measurements and classifications with an associated decrease in statistical power.

Chapter 14: General Conclusion

Chapter 14 General conclusion

The results from this thesis using the NDNS 7-day diary supported the hypothesis that individuals deemed inactive by one method of categorisation would not necessarily be deemed inactive by another.

In addition, these findings clearly indicated that while the health benefits of being considered active, across all methods of categorization were evident and consistent for TC, HDL-C and eCHD risk in men but not women, SBP and DBP were not significantly different between the inactive and active groups of either men or women. The results further showed that when a new method of categorization (combination of two different guidelines) was used, inactive men had more unfavourable effects on blood lipids and greater eCHD risk than those who were active. When each measure of physical activity was expressed as a categorical, ordinal and continuous variable, a significant dose-response relationship was evident in TC, HDL-C and eCHD risk in men only. Interestingly, this thesis confirmed that only a small proportion of the variability in CHD risk factors and eCHD risk was explained by physical activity (based on all methods) in both genders after adjustment for age, BMI, smoking, and exclusion of those on medications. It was found that when the NDNS self-perception questionnaire was applied, there was no significant dose-response relationship between physical activity and CHD risk factors and eCHD risk in either gender. Notably, the physical activity levels assessed by the NDNS self-perception questionnaire were weakly correlated with the measures of activity (e.g. MET) obtained from the NDNS 7-day diary.

Furthermore, this thesis clearly indicated that in men, but not women, being physically active by any of the three methods of categorization was associated with lower eCHD risk compared to inactive groups and there was no one method of categorization that gave a better prediction of CHD risk than the others.

This thesis also provided us with important information about the consequences of using different systems for coding and classifying physical activities (NDNS, modified Blair and IPAQ) to measure the same amount of physical activity on the same subjects. It was conclusively shown that there was a systematic difference and a poor agreement between any two of the systems examined and that the bias decreased as the physical activity level increased. A close examination of the NDNS scoring system showed that, compared to the modified Blair and IPAQ systems, it underestimated the MET*min/day for the "at least moderate activities" component. The Kappa values (which are a chance corrected measure of the proportions of the subjects who are categorized in the same way) further suggested a very poor level of agreement between the three categorizing methods, each of which has been used in guidelines. This inconsistency between scoring systems may help explain why adults in the NDNS data set appear to have obtained only trivial benefits in the CHD risk factors and eCHD risk despite fulfilling the Department of Health recommendation for physical activity. Further, a potential problem may occur when applying the values from one system to guidelines established by different systems.

Finally, like other studies, the analyses carried out in this thesis are subject to a number of limitations inherent in the dataset. For example, the NDNS diary may not capture the full range of daily activities such as the transportation and occupational domains. In addition, all undefined activities are classified as light activities and this may lead to underestimation or overestimation. The questionnaire has been designed to be easily applied but this may result in the loss of important detail.

Chapter 15: Public health issues and recommendations

Chapter 15 Public health issues and recommendations

15.1. Message to the public health authorities:

Physical activity guidelines offer evidence-based behavioural benchmarks that are related to the reduction in the risk of morbidity and mortality, especially if people adhere to them. However, this may be constrained by different methods used to characterize activity behaviour. Although different physical activity dimensions or instruments have been compared with each other in many studies, there is, to date, no study that has conducted research addressing the relative importance of different methods of categorization for physical activity as estimated by different physical activity measures (i.e. number of days/week, MET) on CHD risk factors and eCHD risk within the same population. In addition, to our knowledge, assessing the degree of agreement at which different physical activity guidelines are met, using a variety of systems obtained from two distinct physical activity instruments within the same population, has not yet been determined. Therefore, without a clear understanding of the relationship between physical activity and CHD risk factors and eCHD risk, it is difficult to adequately advise the public health authorities on the level of physical activity which can bring improvements in health.

The findings of this thesis indicate that the achievement of 30/3, 30/5 or MET40*h guidelines for physical activity appears to explain small differences in the levels of CHD risk factors and eCHD risk. However, the MESSAGE of this thesis to the public health authorities is that while the level of agreement between the guidelines (inactive/active) was poor, a beneficial effect of activity on eCHD risk was found irrespective of the method of categorization. This MESSAGE is important and may be informative for policy and decision makers in public health as it may help in resolving the confusion in the literature that has resulted from the multiplicity of guidelines for physical activity by showing that there is benefit in eCHD risk associated with all three methods of categorization. Therefore, public health efforts should be focused on facilitating an active lifestyle and the public should be informed about the levels that produce a minimum benefit.

Essentially, the Department of Health guideline advises people to stay active in order to reduce the risk of CHD. However, the document recommends 5 days per week of moderate activity but does not clearly indicate whether there would be no benefit unless this target is fully achieved or if this recommendation relates to a maximum effect. The document illustration (Figure 2.1) appears to show a continuously increasing effect of activity but no time scale is displayed. While the current physical activity recommendations are based on a dose response pattern described by Curve E, one of the aims of this thesis was to examine critically the evidence in support of this dose-response pattern. In an attempt to increase the public awareness, the nature of the dose-response relationships between physical activity and the CHD risk factors and eCHD risk would influence public perceptions and about the extent of physical activity that is needed to improve general health. Before give a recommendation, the Department of Health should investigate the dose-response of different curve fitting models using several health outcomes. Ideally, information on frequency, duration (time) and intensity (light, moderate and vigorous) of activities should be available to investigate the dose (or volume) of activity.

In addition, the document does not indicate how individuals should perform the sufficient level of physical activity. For instance, whilst walking is a practical and fun way to change a sedentary life style and to improve the health of the nation, the public health do not fully recognize the value of brisk walking as a moderate-intensity physical activity. Thus, to motivate adherence to the physical activity guidelines, MESSAGES that translate guidelines should express not only how much physical activity one should attempt, but also how to achieve such a recommendation. O'Donovan G and Shave R, (2007) have suggested that British physical activity guidelines should be amended because most men and women erroneously believe that moderate activity offers greater health benefits than vigorous activity.

15.2. The Department of Health 1996 guideline versus the US 2007 ones:

There are at least 20 national and international guidelines that have been published over the past 15 years. Some of these documents have looked at specific outcomes such as hypertension (Fagard, 1991), obesity (Bouchard and Blair, 1999), and CHD (Smith and Blair, 1995). However, some of these studies have taken a global approach to health (Bouchard et al., 1990 and 1994). From a public health perspective, important recommendations for health-related physical activity were first introduced by Pate et al., (1995) and further emphasized in the benchmark report by the Surgeon General of the United States (DHHS-US, 1996). The Department of Health 1996 guideline has long been indistinguishable from those of the Center for Disease Control/American College of Sports Medicine (CDC/ACSM) 1995 guidelines (DHHS-US, 1996, Pate et al., 1995). It should be noted that these guidelines have been issued for more than 10 years.

Recently, the ACSM and the American Heart Association (AHA) (Haskell et al., 2007) have updated physical activity guidelines in the US. These guidelines outline exercise recommendations for healthy adults and older adults and are an update from the 1995 CDC/ACSM guidelines. Vigorous-intensity physical activity was not implied in the Department of Health 1996 guidelines. However, the explicitly of these guidelines is an integral part of the US 2007 updated guidelines. To acknowledge the preferences of some adults for vigorous-intensity physical activity, the US updated guidelines have been clarified to encourage participation in either moderate and/or vigorous-intensity physical activity.

The recent recommendations by the ACSM and AHA have acknowledged the importance of muscle contractions, muscular strength and endurance in relation to CVD. On the other hand, the Department of Health 1996 guidelines have mentioned the importance of muscular strength and endurance, but stopped short of making specific declarations in this area. Skeletal muscle is an endocrine organ, which produces hormone-like substances in response to contraction (Petersen and Pedersen, 2005). By muscle contraction, metabolism is changed not only in the working muscle, but in other organs as well (e.g. in fat tissue and the liver). Observational studies have suggested an inverse association between risk of all-cause mortality and muscle contractions (Fitzgerald, 2004; Katzmarzyk and Craig, 2002). Although the specific mechanisms for these associations are not known, muscle contraction is particularly important for enhancing glucose metabolism, lipid profile, and blood pressure (Ivy et al., 1999; Argiles et al., 2005).

Many activities (e.g., brisk walking to work, gardening with shovel, carpentry) in contemporary life are conducted routinely at a moderate intensity and last for at least 10 minutes. This concept was not effectively communicated in the 1996 guidelines. The US updated guidelines now clearly state that moderate- or vigorous-intensity activities performed as a part of daily life performed in bouts of 10 minutes or more can be counted towards the recommendation.

In addition, to meet the current US 2007 updated guidelines, the ACSM and the AHA (Haskell et al., 2007) have recommend a minimum goal that should be in the range of 450 to 750 MET*min/week. This recommendation is based on calculating the total MET*min spent in only the "at least moderate physical activities", but not any other activities (e.g.

sitting or light activities). This data are based on the 2000 compendium of physical activities (Ainsworth et al., 2000) which classifies brisk walking and jogging/running as 5 METs and 8 METs respectively. The concept of MET score is not clearly stated by the 1996 Department of Health guidelines.

On the other hand, the Department of Health guideline (1996) was originally formulated by a review of existing evidence concerning exercise in relation to different disease outcomes such as blood pressure, blood lipids, diabetes, and body weight. However, the panel of the 2007 US guidelines has summarized a diverse literature from the fields of epidemiology, exercise physiology, medicine, and the behavioural sciences with regard to the relationship between physical activity, CVD and many other diseases (e.g. hypertension, blood lipids, colon cancer, diabetes, obesity, mental health, muscles, bones, and joints health). In addition, the panel of the 2007 guidelines has further reviewed recent advances in clinical scientific data, including primary research articles and systematic reviews published in the literature since the original guidelines were issued in 1995. This additional evidence includes compelling new data on women, and more conclusive evidence on stroke, some cancers, and cognitive function. Therefore, the US 2007 panel has reviewed the recent literature and updated it by including studies using newer technological devices for measuring physical activity such as the Intelligent Device for Energy Expenditure and Physical Activity-IDEEA (Zhang and Sun, 2003).

15.3. Recommendations for future research:

In terms of public health measures, the Department of Health 1996 guidelines for physical activity remain fundamentally unchanged despite more than 12 years passing since it has been issued. Since the population perception of physical activity guidelines has changed gradually over the past two decades and reduced the credibility of the recommendations that are offered, the findings of this current thesis formulate a number recommendations for future research as follows:

Firstly, *developing the NDNS 7-day diary*, because the NDNS diary does not clearly capture the full range of activity in daily life (especially as patterns of transportation and occupational activities), further analysis should investigate if the range of physical activity estimated by the NDNS diary is appropriate to measure all relevant daily activities (total physical activity). The assumption underlying the calculation of the total physical activity is that most adults spend most of their time in light and occupational activities. Therefore, there is a need to develop the NDNS diary by classifying the activities based on their types (e.g. transportation, occupation) and intensities (e.g. light, moderate activities).

Secondly, *type of physical activity dimensions*, since measuring physical activity is a complex multidimensional behaviour and that a gold or single standard does not exist, caution must be taken when using subjective dimension (e.g. questionnaire) to quantify the amount of daily physical activity performed in free-living populations. Although physical fitness, direct observation of movement or the doubly labeled water technique can obtain accurate estimates of physical activity, such instruments are not feasible or practical to use in large population studies. However, on a practical basis, measures of physical activity and EE by using 24-hour heart rate monitors and motion sensors (e.g. pedometers and accelerometers) may be necessary to obtain more specific quantified estimates of different measures of physical activity, including frequency, intensity, duration, and total amount, as well as aerobic and resistance activity (Wareham et al., 2002; Shephard, 2003; Westerterp and Plasqui, 2004). Combining these instruments with diaries or questionnaires is recommended. In addition, it is important to understand the dimensions of activity that are most strongly associated with a particular outcome. Thus, targeting a wrong dimension or instrument may limit the potential benefits of physical activity predicted by surveys or observational studies.

Thirdly, as brisk walking is considered a moderate-intensity physical activity, future efforts should be directed at promoting the role of walking in promoting general health, particularly as an important aspect of CHD prevention. In addition, future research is required to determine whether expending as little as 40 MET*h per day or 3 days per week offers health benefits or not. If so, sedentary people may be more likely to engage in physical activity and maintain an active lifestyle. Moreover, Marquez DX et al., (2008) has indicated that most of the women (n=83) and men (n=65) met physical activity guidelines even when reporting low levels of LTPA. Therefore, future studies should determine whether equivalent health benefits are achieved by meeting guidelines through LTPA and non-LTPA.

Fourthly, *coding and classifications of physical activity*, regardless of the internationally accepted coding and classification systems by Blair (1984) and Ainsworth et al., (2000) as well as the new developed NDNS system, there are differences between these systems which add confusion to the relationship between physical activity and CHD risk factors and eCHD risk. This may cause a potential problem especially when using one system and applying its results to a different recommendation established by another different system. Therefore, physical activities need to be classified in consistent and standardized systems in terms of both coding and classification.

Fifthly, *physical activity and other risk factors for CHD*, because physical inactivity is a risk factor for many diseases and conditions, it remains to be determined how the interrelated characteristics of amount, intensity, duration, frequency, type, and pattern of physical activity are related to a range of specific risk factors for CHD (e.g. insulin, TG) across different ages, and gender, and those with a variety of health states. Therefore, it is necessary to define the types and required levels of physical activity that is recommended to reduce specific risk factors of CHD.

Sixthly, *the dose–response relation*, it has been suggested that, for instance, each 1-MET increase in exercise capacity is associated with a 12–16% reduction in CVD risk (Blair et al., 1995; Myers et al., 2002). Therefore, health benefits appear to be proportional to the amount of activity; thus, every increase in activity adds some benefits. In designing and analyzing future research, attention needs to be paid to evaluate the dose-response relationship of multiple measures of physical activity, such as the number of days/week and minutes/day of moderate activity, MET scores, and EE. Therefore, randomized controlled trials may be necessary to address the causal pathways underlying the effect of physical activity and to study how a specific risk factor for CHD could be reduced by different physical activity measures (e.g. days/week of moderate activity, MET scores) and levels (e.g. type, intensity, amount).

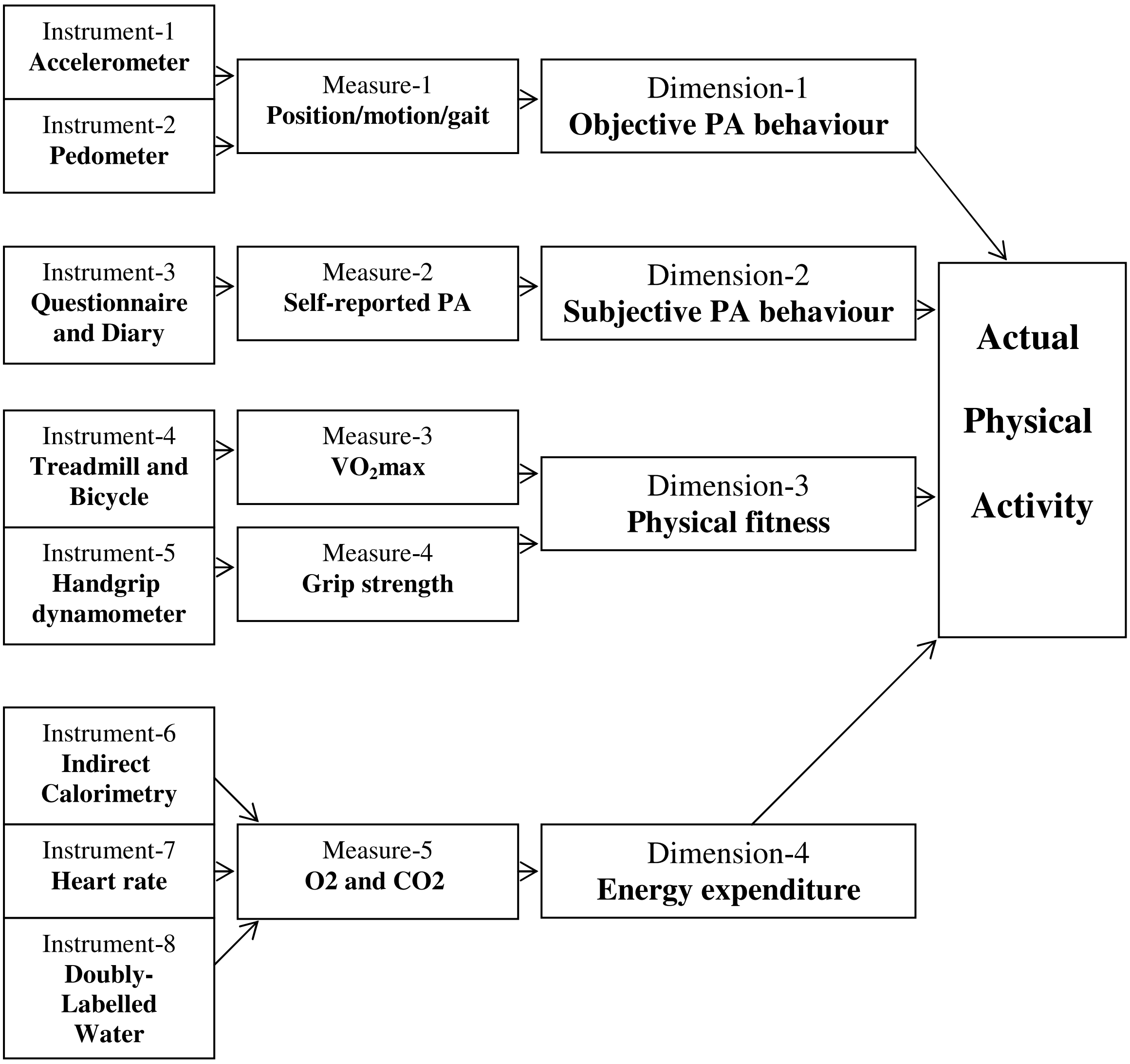
Finally, *for public health*, whilst the intensity of brisk walking is considered a moderate physical activity, information to motivate people to achieve the guidelines for physical activity should be translated into a set of MESSAGES that are informative, thought provoking, and persuasive. These MESSAGES should be disseminated to the public via multi-phase social-marketing campaigns that are carefully planned and thoroughly evaluated.

For future research, the aim of these recommendations is to understand the biological mechanisms by which physical activity measures and levels provide health benefits and better quality of life. This may also help to provide a more comprehensive and explicit public health recommendations for adults based on the available evidence of the health benefits of physical activity. Therefore, when exploring the inter-relationship between activity, fatness and health, there is a need to develop a more coherent approach to measure activity. These recommendations will also help in illustrating the relationship between physical activity and CHD risk more accurately. This in its turn will have substantial benefits for public health policies, as well as improving the overall quality of life in the society.

List of appendices

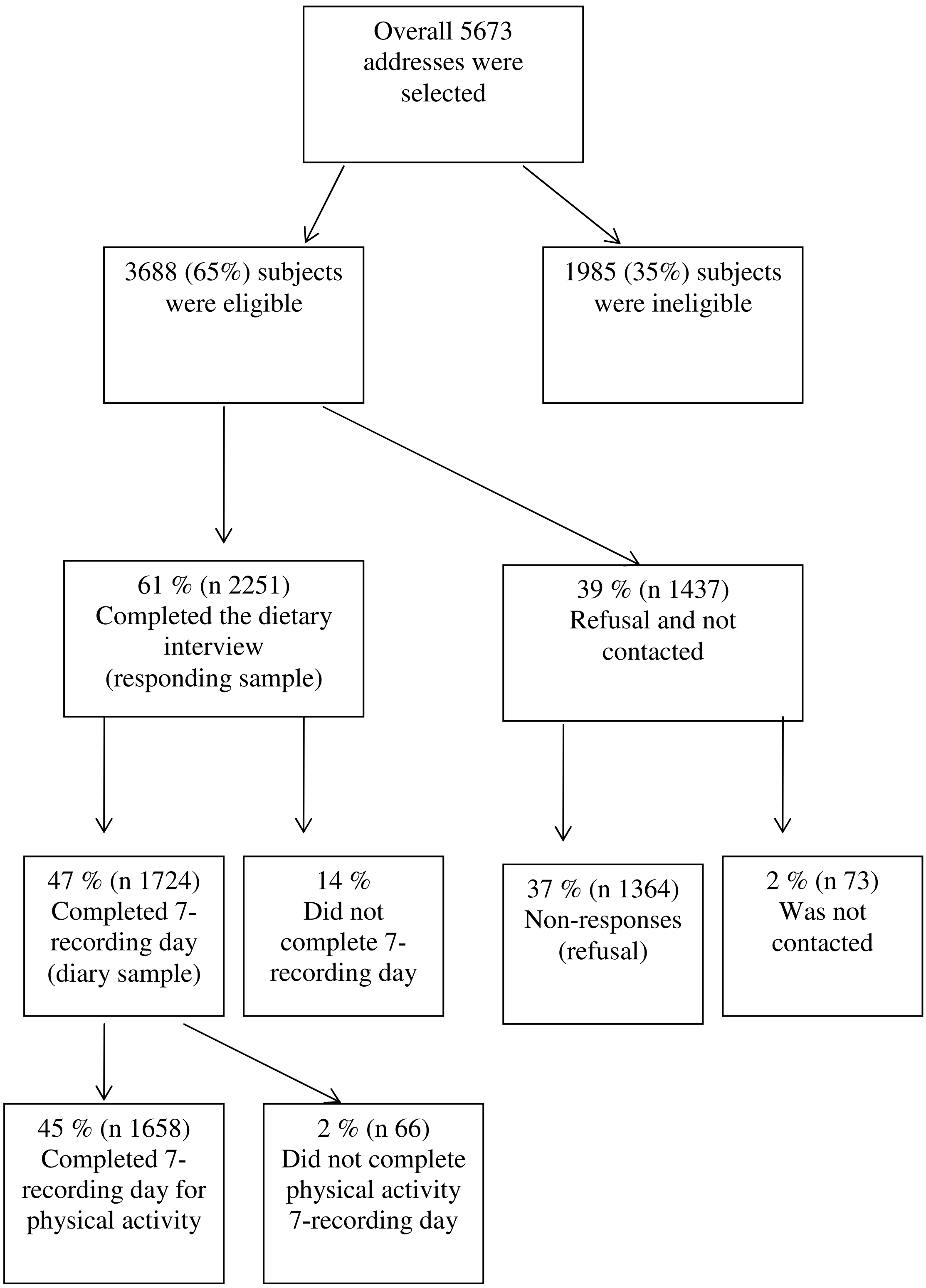
Appendix 1

Dimensions, instruments and measures of physical activity



Appendix 2

The respondents and non-respondents rate of the NDNS data



Appendix 3

<u>Protocols:</u>

a. *<u>Height Measurement:</u>*

1. Height will be measured by a portable standiometer to the nearest millimetre.
2. Shoes will be removed.
3. If the participants are wearing a temporary hairstyle, they will be asked if it is possible to alter their hairstyle.
4. Standiometer will be placed on a flat hard surface.
5. Participant will be stood facing forward with feet flat on the base-plate, heels against the rod, back as straight as possible and arms hanging at the sides.
6. The headplate will be lowered to just above the participant's head.
7. The head will be tilted forward until the top of the external ear canal and the top of the lower bone of the eye socket were on a plane parallel to the floor.
8. The participant will be instructed to focus on a point straight.
9. The positioning procedure will be repeated before lowering the headplate until it rested gently on the participant's head.

b. *<u>Weight Measurement:</u>*

1. Weight will be measured to the nearest 100 grams.
2. The scale will be placed on a hard level surface.
3. The participant will remove shoes, heavy outer garments, heavy jewellery and loose changes and keys.
4. When the scale turned on, and when a zero displayed, the participant will step onto the scales.

5. Then, the participant will stand facing forwards in the centre the scales with heels against the back edge, and arms hanging at the sides.
6. Posture will be adjusted so that the participant stood as straight as possible, looking directly ahead to ensure that the weight is evenly distributed.
7. Once the display reading stabilised, the measurement will be recorded.

c. *Blood Pressure:*

1. The blood pressure will be measured by using the Dinamap 8100.
2. Three readings will be taken at one minute intervals for systolic, diastolic and mean arterial pressure (mmHg) and heart rate (beats per minute).
3. Measurements were taken on the right arm.
4. Three different sizes will be available - small (17-25cm), standard (23-33 cm), and large (3140 cm)
5. The circumference of the upper right arm will be measured in order to select the correct sized cuff for the participant. Where the circumference will fell in the overlap between two sizes, the standard cuff will used.
6. The cuff will be connected via a pneumatic hose to the Dinamap, ensuring that the screw connectors is properly connected to avoid any air leak.
7. The measurements will be timed so that wherever possible, the participant had not eaten, smoked or drunk alcohol in the preceding 30 minutes.
8. If this is not possible, the participant's food and alcohol consumption or smoking in the previous 30 minutes will be recorded.
9. The participant will be asked to remove any outer garments (such as jackets) or roll up sleeves so that the arm is exposed and unconstricted.

10. The participant will be asked to sit on a chair with the right arm supported on a surface so that the elbow is at approximately heart level and legs uncrossed.
11. The brachial pulse medial will be located to the biceps tendon and positioned the cuff so that the arrow marked on the cuff rested over the brachial artery. The cuff will be secured so that two fingers could be inserted between it and the participant's arm.
12. Before taking the measurement, the participant will be explained that it necessary for to sit and rest for five minutes without talking.
13. After this interval, the monitor will be switched on, and the cuff inflated. After the first reading is displayed the Dinamap will take two further readings at one minute intervals.
14. Each reading will be recorded on the questionnaire as it is taken.
15. Any difficulties which may affect the measurements will be recorded, including if the measurements had be taken on the left arm.
16. If all three readings were classified as severely raised or severely low, the participant will be advised to contact his/her GP. The GP and survey doctor will be then informed.

d. *Cholesterol and HDL-C:*

1. The blood samples were collected by the phlebotomist using the Sarstedt Monovette blood collection system with butterfly or fixed needle, according to their preference.
2. The Monovette system of blood collection is an enclosed system which allows the safe, spill-free collection of blood which is critical in the home environment. It can also offer trace element contamination control and is manufactured from

plastic which allows the safe transport of the sample, inside an outer rigid plastic container, through the postal system.

3. Samples of the anti-coagulated blood sample were collected by centrifugation and stored in a cool box, at about 4°C.
4. The samples were delivered to a local processing laboratory in the region of the fieldwork typically within 5 hours of collection.
5. The local laboratories undertook the processing and initial stabilisation of the blood samples into whole blood, red cells, plasma and metaphosphoric acid stabilised plasma portions.
6. The blood sample sub-fractions were stored frozen, typically at -40°C at these laboratories until their removal on dry ice to Medical Research Council Human Nutrition Research (HNR) in Cambridge, where they were stored frozen, at -80°C, until further subdivided and analysed.
7. The colourimetric assays were performed on the Cobas Fara analyser for cholesterol and HDL-C. These assays were conducted at the HNR.
8. Cholesterol was measured by the oxidation of cholesterol (liberated by cholesterol esterase) and then by cholesterol oxidase to 7-hydroxy-cholesterol.
9. The cholesterol assay was calibrated by use of the Roche human calibrator.
10. HDL-C has been defined as that fraction of total cholesterol which remains in solution after precipitation of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol with the magnesium chloride plus phosphotungstic acid assay.
11. This assay was added to the plasma sample. The sample was then centrifuged, and the clear supernatant was assayed by the cholesterol assay. The HDL-C assay was calibrated by the use of Roche P human calibrator.

Appendix 4

University of Southampton

1. <u>The NDNS seven-day diary</u>

Code No. ☐

<u>How to complete the National Diet & Nutrition Survey (NDNS) 7-day activity diary</u>

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. There are four activity pages for each day, but, depending on what you are doing each day. <u>You only need to tell us about activities that you did for 10 minutes or longer</u>. In on some pages, if you did not do any of these activities on any particular day, then simply leave this page blank for that day. Please make sure you fill in one of these pages for each day, just before you go to bed. <u>Don't forget to enter the date and the day of the week and circle the recording day.</u>

<u>***The first page:***</u> The first page of the diary, for each day, collects information about time spent in bed asleep (including napping), time spent at work (including paid and unpaid work) or college, and an opinion question asking you to assess whether you were more active, about as active or less active than usual that day.

<u>***The second page:***</u> Column A shows a list of different household activities. In Column B, give a brief description of the activity. While in Column C, say how long you spent doing the activity, to the nearest 10 minutes. <u>Please do not tell us about any activities you have done as part of your job</u>. There is space at the bottom of the table for you to tell us about any similar activities that you have done that are not listed.

<u>***The third and fourth pages:***</u> Column A lists a range of listed sports and leisure activities. <u>If you did not do any of these activities on any particular day, then simply leave this page blank for that day</u>. In Column B, give a brief description of the activity. While in Column C, say how long you spent doing the activity, to the nearest 10 minutes. Again, <u>do not need to tell us about any activities you have done as part of your job</u>. There is space at the bottom of the table for you to tell us about any similar activities that you have done that are not listed.

Day 1 **Today's date is** [| |]

Code Number: [ ]

Recording day (ring one): 1 2 3 4 5 6 7

1. What time did you go to bed last night? [|] [|] *am / pm*
   Hours *Minutes*

2. What time did you get up today? [|] [|] *am / pm*
   Hours *Minutes*

3. Did you go to work today? (including unpaid work)
   Yes *Go to question 3a*
   No *Go to question 4*

3a. How long did you work today (including unpaid work), in your main job? (Please exclude any lunch break) [|] [|]
   Hours *Minutes*

3b. If you have a second job (including unpaid work), how long did you work today in your second job? (Please exclude any lunch break) [|] [|]
   Hours *Minutes*

4. Did you go to college today? (excluding evening classes)

Yes *Go to question 4a*

No *Go to question 5*

4a. How long were you at college today?

__ | __	__ | __
Hours	*Minutes*

5. Did you spend any other time sleeping during today? If so, how long?

__ | __	__ | __
Hours	*Minutes*

6. Thinking about the activities you have done today, would you say that today you have been...

(tick one box)

more active than usual ☐

about as active as usual ☐

or less active than usual? ☐

On this page please tell us how long you spent doing these activities today. Only count the activities you did for periods of 10 minutes or more. Please record only the time you spent actually doing the activity - try to be as accurate as possible and record to the nearest 10 minutes. **You do not need to tell us about any activities you did as part of your job.**

A	**B**	**C**	
How long did you spend today?	**Please give some details about the activity**	**Hours**	**Minutes**
Walking at an average pace			
Walking briskly			
Light housework, such as dusting, ironing, laundry, washing up, tidying up, cooking, light shopping			
Heavy housework, such as moving heavy furniture, spring cleaning, scrubbing floors, cleaning windows, carrying a heavy load			
Light gardening, such as pruning, watering, potting			
Heavy gardening, such as digging, clearing rough ground, chopping wood, mowing a large area with a hand mower			
Light DIY, such as wiring, plumbing, light carpentry			
Heavy DIY, such as refitting a kitchen or bathroom, laying concrete, sawing wood			
Active caring, such as pushing a pushchair/pram, lifting another person or child, active play with child. Please include only the time you were active			
Have you done any other activities like these? If so, please write them in the space below.	**Please give some details about the activity**	**Hours**	**Minutes**

On this page, please tell us how long you spend doing these activities today. Only count the activities you did for period of 10 minutes or more. Please record only the time you spent actually doing the activity – try to be as accurate as possible and record to the nearest 10 minutes. **You do not need to tell us about any activities you did as part of your job.**

A	B		C
How long did you actually spend doing this today?	**Hours**	**Minutes**	**Did doing this activity make you out of breath or sweaty?**
Yoga/Tai Chi			Yes / No
Football (soccer), including refereeing			Yes / No
Netball/Hockey/Ice-skating			Yes / No
Rugby			Yes / No
Cricket			Yes / No
Rounders/Softball			Yes / No
Judo/Jujitsu/Karate/Kick boxing/Tae kwan do			Yes / No
Yoga/Tai Chi			Yes / No
Football (soccer), including refereeing			Yes / No
Netball/Hockey/Ice-skating			Yes / No
Rugby			Yes / No
Cricket			Yes / No
Rounders/Softball			Yes / No
Judo/Jujitsu/Karate/Kick boxing/Tae kwan do			Yes / No
Have you done any other activities like these? If so, please write them in the space below.	**Hours**	**Minutes**	**Did doing this activity make you out of breath or sweaty?**
			Yes / No
			Yes / No
			Yes / No

"This is the end of day 1"

2. <u>International Physical Activity Questionnaire (IPAQ):</u>

University of Southampton

The School of Medicine

Code No. [ ]

Gender: [Male] [Female]

<u>How to complete the International Physical Activity Questionnaire (IPAQ)</u>

<u>Please answer each question</u> even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport. These activities are classified into 5 PARTS.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. <u>Do not</u> include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3. Example of question: <u>During the last 7 days</u>, on how many days did you do vigorous physical activities for at least 10 minutes at a time as part of your work?

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on in a motor vehicle (e.g. a train, bus, car), bicycle or walking. Example of question: <u>During the last 7 days</u>, on how many days did you bicycle for at least 10 minutes at a time to go from place to place?

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family. Example of question: <u>During the last 7 days</u>, on how many days did you do moderate activities for at least 10 minutes at a time?

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the last 7 days solely for recreation, sport, exercise or leisure. <u>Please do not include any activities you have already mentioned</u>. Example of question: <u>During the last 7 days</u>, on how many days did you walk for at least 10 minutes at a time in your leisure time?

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about. Example of question: <u>During the last 7 days</u>, how much time did you usually spend sitting on a weekday and weekend?

International Physical Activity Questionnaire (IPAQ)

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

☐ **Yes**

☐ **No** → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

_____ **days per week**

☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

_____ **hours per day**

_____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

_____ **days per week**

☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**

_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**

_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you travelled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No travelling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **travelling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**

_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**

_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days walking from place to place?

_____ **hours per day**

_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**

_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**

_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**

_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**

_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

    _____ **days per week**

    ☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

    _____ **days per week**

    ☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?

_____ **hours per day**

_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**

_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**

_____ **minutes per day**

Appendix 5

University of Southampton

[redacted]

School Ethics Committee

Chair: Dr Angela Fenwick
Administrator: Helen Flynn

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Ref: SOMSEC00005.07/AF/hmf

8th November 2007

Mr Ahmad Al-Haifi
Institute of Human Nutrition
Mailpoint 113, Level F
Centre Block
Southampton General Hospital

Ethics Approval Number: SOMSEC005.07

Dear Mr Al-Haifi

Re: Comparison between estimated physical activity levels measured by the NDNS seven-day diary and the IPAQ

Thank you for addressing the issues relating to the above project in the letter dated 5th November 2007 from Professor Elia. I am pleased to inform you that full approval is now granted for the project set out in your application form dated 6th September 2007. Approval is valid until March 2008, which is the end date specified in your application. We will be in touch with you again at this time to confirm that your project has been completed.

Please note the following points:

- In order to adhere to University Policy, you must have received notification of University insurance cover before you commence your study.
- The above ethics approval number must be quoted in all correspondence relating to your research, including emails.
- If you wish to make any substantive changes to your project you must inform the School of Medicine Ethics Committee as soon as possible.

We wish you well with your research.

Yours sincerely

Dr Angela Fenwick
Chair: School of Medicine Ethics Committee

Cc: Professor Marinos Elia, Institute of Human Nutrition, Southampton General Hospital
Dr Martina Prude, Legal Services, University of Southampton

Appendix 6

PARTICIPATION INFORMATION SHEET

TITLE OF THE STUDY: Comparison between estimated physical activity levels measured by the NDNS seven-day diary and the IPAQ

PURPOSE OF THE STUDY: This is an invitation to participate in a study conducted by researchers at the Institute of Human Nutrition (INH)-University of Southampton. The purpose of the research is to compare the agreement or classification consistency of estimated physical activity levels measured by the NDNS seven-day diary and the International Physical Activity Questionnaire (IPAQ). The results have relevance to the Department of Health's recommendation about the amount of physical activity that should be undertaken (see below).

INVESTIGATORS:

Prof M Elia (Main Supervisor)	Dr S Wootton (Sec. Supervisor)	Ahmad Al-Haifi
Faculty of IHN	Faculty of IHN	PhD student
02380794968	02380794968	02380794968
M.elia@soton.ac.uk	saw@soton.ac.uk	chsahmad@soton.ac.uk

INTRODUCTION: There is general agreement among public health and medical authorities that physical activity has a beneficial effect on health (ie prevention of cardiovascular disease and diabetes). However, just how much physical activity is needed in adults to protect against ill-health remains less clear. The principal study of physical activity, diet and health of adults in the UK is the National Diet and Nutrition Survey, conducted by HM Government. In this survey, physical activity was assessed by a prospective seven-day activity diary. Whilst undertaking a secondary analysis of this survey on the one hand, we found very weak associations between physical activity and blood pressure and lipid profile. Such observations undermine the current Department of Health recommendations about the amount of physical activity that is associated with good health. Therefore, there is a need to determine whether this lack of association may be due, at least in part, to differences in ascribing an activity score by the 7-day diary relative to that obtained by validated questionnaires, which have been found to relate to cardiovascular risk factors.

DESCRIPTION OF THE STUDY: We aim to compare the classification consistency or agreement of physical activity levels between the NDNS seven-day diary with that obtained using the International Physical Activity Questionnaire (IPAQ). To help us to achieve this aim, we are seeking the participation of all first year Medical Students in this research study. After a short group meeting to explain how to record and code the amount of time you spend in specific categories of activity, you will be required to:

1) complete the physical activity diary for 7 continuous days (less than 30 minutes/day), and
2) complete the IPAQ questionnaire at the beginning and end of the study (approximately 10 minutes).

CONFIDENTIALITY: All your answers to the survey questions will be completely confidential. Your replies will be coded so your name will not be used in the study.

REFUSAL OR WITHDRAWAL: This is a voluntary study and there will be no penalty if you decide not to be in the study. In addition, your choice to leave the study at any time will not be known to the investigators and affect your relationship with them.

RISKS AND DISCOMFORTS: You will not be at physical or psychological risk and will experience no discomfort resulting from the research procedures.

BENEFITS FOR PARTICIPATION: There are no direct benefits from participating in this research study. However, participants will receive the results of the physical activity levels of the group and their own score using anonymous identifier.

ETHICS REVIEW AND COMPLAINTS: This study has been reviewed by the School of Medicine- School Ethics Committee (SoM-SEC) of the University of Southampton. If you have any concerns or complaints regarding the way this research has been conducted, you can contact the SoM-SEC on 023 8079 6685 or mail to the following address:

School of Medicine Office
Mailpoint 801, Level B
South Academic Block
Southampton University Hospital Trust
SO16 6YD

Thank you for taking the time to read this information sheet and complete the attached consent form (if you have done so). I look forward to seeing you in the near future if you choose to participate in this study.

Appendix 7

Examples of calculating total physical activity scores

*Example 1: Calculation of MET score based on **the NDNS system** for one day:*

Type of activity	MET value for the type of activity	Total time spent (hour)	Total MET*h scores
Sleep	1.0	9.0	9.0
Very light/light activities (e.g. watching TV, cooking)	2.0	13.5	27.0
Moderate activities (e.g. brisk walking, light swimming)	4.0	1.0	4.0
Vigorous/very vigorous activities (e.g. football, weight lifting)	7.5	0.5	3.75
Total		24.0	**43.75**

*Example 2: Calculation of MET score based on **the Blair system** for one day:*

Type of activity	Total time spent (hour)	MET value for activity	Total MET-hour/day (kcal/kg/d)
Active person			
Sleep	8.0	1.0	8.0
Light activity	12.5	1.5	18.75
Moderate activities	2.0	4.0	8.0
Hard activities	0.5	6.0	3.0
Very hard activities	1.0	10.0	10.0
Total	**24.0**		**47.75**
Inactive person			
Sleep	9.0	1.0	9.0
Light activity	14.0	1.5	21.0
Moderate activities	1.0	4.0	4.0
Hard activities	0.0	6.0	0.0
Very hard activities	0.0	10.0	0.0
Total	**24.0**		**34.0**

*Example 3: Calculation of MET score based on **IPAQ system** for one week:*

Type of activity	MET value for the type of activity	Total time spent (minutes*day)	Total MET* min/week
General walking	3.3	20 * 5	330
Cycling from place to place	6.0	20 * 5	600
Moderate inside chores (e.g. washing windows)	3.0	20 * 5	300
Moderate activities (e.g. moderate work)	4.0	20 * 5	400
Vigorous yard chores (e.g. digging in the yard)	5.5	20 * 5	550
Vigorous activities (e.g. running, heavy lifting)	8.0	20 * 5	800
Total			**2980**

List of references

References:

Aadahl, M., Kjær, M. and Jørgensen, T. (2007) Associations between overall physical activity level and cardiovascular risk factors in an adult population. Eur J Epidemiol, 22:369–378.

Adlercreutz, H., Härkönen, M., Kuoppasalmi, K., Näveri, H., Huhtaniemi, I., Tikkanen, H., Remes, K., Dessypris, A. and Karvonen, J. (1986) Effect of training on plasma anabolic and catabolic steroid hormones and their response during physical exercise. Int J Sports Med, 1:27–28.

Aihie Sayer, A., Cooper, C. and Evans, J.R. (1998) Are rates of ageing determined in utero? Age Ageing, 27:579–83.

Ainsworth, B. E., Haskell, W. L. and Whitt, M. C. (2000) Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc, 32 (9): S498-516.

Ainsworth, B. E., Macera, C. A., Jones, D. A., Reis, J. P., Addy, C. L., Bowles, H. R. and Kohl, H. W. 3rd (2006) Comparison of the 2001 BRFSS and the IPAQ Physical Activity Questionnaires. Med Sci Sports Exerc, 38(9):1584-92.

Aires, N., Selmer, R.and Thelle, D. (2003) The validity of self-reported leisure time physical activity, and its relationship to serum cholesterol, blood pressure and body mass index. A population based study of 332,182 men and women aged 40–42 years. Eur J Epidemiol, 18: 479–85.

Altman, D. G (1991). Practical Statistics for Medical Research. London England: Chapman and Hall, pp. 404.

American College of Sports Medicine (ACSM) (1978). Position statement on the recommended quantity and quality of exercise for developing and maintaining fitness in healthy adults. Med Sci Sport Excer, vii-x.

American College of Sports Medicine (ACSM) (1998). Position Stand: the recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Med Sci Sports Exerc, 30: 975–991.

Andersen, L. B., Schnohr, P. and Schroll, M. (2000) All-cause mortality associated with physical activity during leisure time, work, sports, and cycling to work. Arch Intern Med, 160:1621-28.

Andersen, U. O. and Jensen, G. (2007) Decreasing population blood pressure is not mediated by changes in habitual physical activity. Results from 15 years of follow-up. Blood Press, 16(1):28-35.

An, P., Teran-Garcia, M. and Rice, T. (2005) Genome-wide linkage scans for prediabetes phenotypes in response to 20 weeks of endurance exercise training in non-diabetic whites and blacks: the HERITAGE Family Study. Diabetologia, 48: 1142–49.

Arcerio, P., Goran, M. and Poehlman, E. (1993) Resting metabolic rate is lower in women than in men. J Appl Physiol, 75:2514–20.

Arciero, P. J., Smith, D. L. and Calles-Escandon, J. (1998) Effects of short-term inactivity on glucose tolerance, energy expenditure, and blood flow in trained subjects. *J Appl Physiol,* 84(4): 1365-73.

Argiles, J. M., Lopez-Soriano, J., Almendro, V., Busquets, S. and Lopez-Soriano, F. J. (2005) Cross-talk between skeletal muscle and adipose tissue: a link with obesity? *Med Res Rev,* 25: 49–65.

Asikainen, T. M., Miilunpalo, S. and Oja, P. (2002) Randomised, controlled walking trials in postmenopausal women: the minimum dose to improve aerobic fitness? *Br J Sports Med,* 36: 189–194.

Assmann, G., Cullen, P. and Schulte, H. (2002) Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. *Circulation,* 105: 310– 5.

Attie, A. D. and C. M. Kendziorski (2003). PGC-1alpha at the crossroads of type 2 diabetes. *Nat Genet* 34: 244–245.

Auwerx, J. H., Marzetta, C. A. and Hokanson, J. E. (1989) Large buoyant LDL-like particles in hepatic lipase deficiency. *Arteriosclerosis,* 9:319–325.

Ballantyne, F. C., Clark, R. S., Simpson, H. S. and Ballantyne, D. (1982) The effect of moderate physical exercise on the plasma lipoprotein subfractions of male survivors of myocardial infarction. *Circulation,* 65(5):913-918.

Barengo, N. C., Hu, G. and Lakka, T. A. (2004) Low physical activity as a predictor for total and cardiovascular disease mortality in middle aged men and women in Finland. *Eur Heart J,* 25: 2204–2211.

Barengo, N. C., Kastarinen, M., Lakka, T., Nissinen, A. and Tuomilehto, J. (2006) Different forms of physical activity and cardiovascular risk factors among 24–64-year-old men and women in Finland. *Eur J Cardiovasc Prev Rehabil,* 13: 51–59.

Barker, D. J. (2004) The developmental origins of chronic adult disease. *Acta Paediatr. Suppl* 93: 26–33.

Bardel, A., Wallander. M. A. and Svardsudd, K. (2000) Reported current use of prescription drugs and some of its determinants among 35 to 65-year-old women in mid-Sweden: A population-based study. *J Clin Epidemiol,* 53:637–643.

Barengo, N. C., Hu, G., Kastarinen, M., Lakka, T. A., Pekkarinen, H., Nissinen, A. and Tuomilehto, J. (2005) Low physical activity as a predictor for antihypertensive drug treatment in 25-64-year-old populations in eastern and south-western Finland. J Hypertens, 23(2): 293-9.

Barold, S. S., Hannss, R. J., Ling Ong, S., Falkoff, M. D., Robert Heinle, A. and Sengupta, A. (1985) Exercise-induced myocardial infarction due to coronary thrombosis. *Am Heart J,* 109: 590-593.

Bassett, D. R., Fitzhugh, E. C., Crespo, C. J., King, G. A. and McLaughlin, J. E. (2002) Physical activity and ethnic differences in hypertension prevalence in the United States. Prev Med, 34(2): 179-86.

Baynard, T., Franklin, R. M., Goulopoulou, S., Carhart, R. and Kanaley, J. A. (2005) Effect of a single vs multiple bouts of exercise on glucose control in women with type 2 diabetes. Metabolism, 54(8):989-994.

Beeson, M., Sajan, M. P., Dizon, M., Grebenev, D., Gomez-Daspet, J., Miura, A., Kanoh, Y., Powe, J., Bandyopadhyay, G., Standaert, M. L. and Farese, R. V. (2003) Activation of protein kinase C-ζ by insulin and phosphatidylinositol-3,4,5-$(PO_4)_3$ is defective in muscle in type 2 diabetes and impaired glucose tolerance: amelioration by rosiglitazone and exercise. *Diabetes,* 52:1926–34.

Belardinelli, R., Georgiou, D., Cianci, G. and Purcaro, A. (1999) Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. *Circulation,* 9;99(9):1173-82.

Benetos, A., Thomas, F., Bean, K., Pannier, B. and Guize, L. (2003) Estimation of cardiovascular risk in French men according to age: the IPC cohort. *Am J Hypertens*. 16 (5): 206A–206A.

Bertoldi, A. D., Hallal, P. C. and Barros, A. J. D. (2006) Physical activity and medicine use: evidence from a population-based study. *BMC Public Health,* 6:224.

Bijnen, F. C., Feskens, E. J., Caspersen, C. J., Giampaoli, S., Nissinen, A. M., Menotti, A., Mosterd, W. L. and Kromhout, D. (1996) Physical activity and cardiovascular risk factors among elderly men in Finland, Italy, and the Netherlands. *Am J Epidemiol,* 15;143(6):553-561.

Bijnen, F. C., Caspersen, C. J., Feskens, E. J. M., Saris, W. H. M., Mosterd, W. L. and Kromhout, D. (1998) Physical activity and 10-year mortality from cardiovascular diseases and all causes: the Zutphen Elderly Study. *Arch Intern Med,* 158: 1499–1505.

Bjorntorp, P. (2001) Do stress reactions cause abdominal obesity and comorbidities? *Obes Rev,* 2: 73–86.

Blair, S. N. (1984) How to assess exercise habits and physical fitness. In: Matarazzo JD et al. Eds. Behavioural Health: *A Handbook of Health Enhancement and Disease Prevention*. Wiley & Sons (New York).

Blair, S. N., Haskell, W. L., Ho, P., Paffenbarger, R. S., Vranizan, K. M., Farquhar, J. W. and Wood, P. D. (1985) Assessment of habitual physical activity by a seven-day recall in a community survey and controlled experiments. Am J Epidemiol, 122(5):794-804.

Blair, S. N., Kohl, H. W., Paffenbarger, R. S., Clark, D. G., Cooper, K. H. and Gibbons, L. W. (1989) Physical fitness and all-cause mortality. A prospective study of healthy men and women. *JAMA,* 3;262(17):2395-401.

Blair, S. N., Kohl, H. W. and Barlow, C. E. (1993) Physical activity, physical fitness, and all-cause mortality in women: do women need to be active? *J Am Coll Nutr,* 12:368-371.

Blair, S. N., Kohl, H. W., Barlow, C. E., Paffenbarger, R. S., Gibbons, L. W. and Macera, C. A. (1995) Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA,* 12;273(14):1093-8.

Blair, S. N. and Connelly, J. C. (1996) How much physical activity should we do? The case for moderate amounts and intensities of physical activity. *Res Q Exerc Sport,* 67(2):193-205.

Blair, S. N. and Brodney, S. (1999) Effects of physical inactivity and obesity on morbidity and mortality: current evidence and research issues. Med Sci Sports Exerc, 31(11 Suppl): S646- 2.

Blair, S. N., Cheng, Y. and Holder, J. S. (2001) Is physical activity or physical fitness more important in defining health benefits? *Med Sci Sports Exerc,* 33: S379–S399.

Bland, J. M. and Altman, D. G. (1986) Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1(8476):307-10.

Blumenthal, J. A., Siegel, W. C. and Appelbaum, M. (1991) Failure of exercise to reduce blood pressure in patients with mild hypertension. Results of a randomized controlled trial. *JAMA*, 16;266(15):2098-104.

Boer, J. M., Feskens, E. J., Verschuren, W. M., Seidell, J. C. and Kromhout, D. (1999) The joint impact of family history of myocardial infarction and other risk factors on 12-year coronary heart disease mortality. *Epidemiology*, 10: 767–770.

Booth, F. W. and Thomason, D. B. (1991) Molecular and cellular adaptation of muscle in response to exercise: perspectives of various models. *Physiol Rev,* 71: 541 –585.

Borg, P., Kukkonen-Harjula, K., Fogelholm, M. and Pasanen, M. (2002) Effects of walking or resistance training on weight loss maintenance in obese, middle-aged men: a randomized trial. *Int J Obes Relat Metab Disord*, 26(5):676-83.

Bornstein, S. R. (1997) Is leptin a stress related peptide? *Nature Med*, 3: 937.

Bouchard, C., Leon, A. S., Rao, P. C., Skinner, J. S. and Wilmore, J. H. (1990) Fitness and risk factors for coronary disease. *J Clin Epidemiol*, 43(9):1005-12.

Bouchard, C. and Pérusse, L. (1994) Heredity, activity level, fitness, and health. In: Bouchard C, Shephard RJ, Stephens T, editors. *Physical Activity, Fitness, and Health*. Champaign, IL: *Human Kinetics*, 106.

Bouchard, C. and Blair, S. N. (1999) Introductory comments for the consensus on physical activity and obesity. *Med Sci Sports Exerc*, 31(11):S498-501.

Bouchard, C. (2001) Physical activity and health: introduction to the dose–response symposium. *Med Sci Sports Exerc*, 33:347–350.

Boule, N. G., Weisnagel, S. J., Lakka, T. A., Tremblay, A., Bergman, R. N., Rankinen, T., Leon, A. S., Skinner, J. S., Wilmore, J. H., Rao, D. C, Bouchard, C. and HERITAGE Family Study. (2005) Effects of exercise training on glucose homeostasis: the HERITAGE Family Study. *Diabetes Care*, 28(1):108-14.

Bouten, C. V., Westerterp, K. R., Verduin, M. and Janssen, J. D. (1994) Assessment of energy expenditure for physical activity using a triaxial accelerometer *Med Sci Sports Exerc,* 26,1516-1523.

Brage, S., Wedderkopp, N., Ekelund, U., Franks, P. W., Wareham, N. J., Andersen, L. B., Froberg, K. and European Youth Heart Study (EYHS). (2004) Features of the metabolic syndrome are associated with objectively measured physical activity and fitness in Danish children: the European Youth Heart Study (EYHS). *Diabetes Care*, 27(9):2141-8.

British Diabetic Association. (1998) Joint British recommendations on prevention of coronary heart disease in clinical practice. *Heart*, 80: 1–29.

British Hypertension Society programme (BHS). Available at: http://www.bhsoc.org/default.stm

Brown, W. J. and Bauman, A. E. (2000) Comparison of estimates of population levels of physical activity using two measures. *Aust N Z J Public Health*, 24(5):520-5.

Brown, W. J., Bauman A., Chey T., Trost S. and Mummery K (2004a). Comparison of surveys used to measure physical activity. A*ust N Z J Public Health*, 28(2):128-34.

Brown, W. J., Trost S. G., Bauman A., Mummery K. and Owen N (2004b). Test-retest reliability of four physical activity measures used in population surveys. *J Sci Med Sport,* 7(2):205-15.

Bruce, C. R., Anderson, M. J. and Carey, A. L. (2003) Muscle oxidative capacity is a better predictor of insulin sensitivity than lipid status. *J Clin Endocrinol Metab*, 88: 5444–5451.

Bryner, R. W., Toffle, R. C., Ullrich, I. H. and Yeater, R. A. (1997) The effects of exercise intensity on body composition, weight loss, and dietary composition in women. *J Am Coll Nutr*, 16(1):68-73.

Buchholz, A., Rafii, M. and Pencharz, P. (2001) Is resting metabolic rate different between men and women? *Br J Nutr*, 86:641–6.

Bucksch, J. (2005) Physical activity of moderate intensity in leisure time and the risk of all cause mortality. *Br J Sports Med*, 39: 632–638.

Burt, V. L., Cutler, J. A., Higgins, M., Horan, M. J., Labarthe, D., Whelton, P., Brown, C. and Roccella, E. J. (1995) Trends in the prevalence, awareness, treatment and control of hypertension in the adult US population. *Hypertension*, 26:60–9.

Cabrera, C., Wilhelmson, K., Allebeck, P., Wedel, H., Steen, B. and Lissner, L. (2003) Cohort differences in obesity-related health indicators among 70-year olds with special reference to gender and education. *Eur J Epidemiol*, 18(9):883-90.

Carnethon, M. R., Gidding, S. S., Nehgme, R., Sidney, S., Jacobs, D. R., and Liu, K. (2003) Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. JAMA, 290(23): 3092-100.

Carr, M. C., Hokanson, J. E. and Deeb, S. S. (1999) A hepatic lipase gene promoter polymorphism attenuates the increase in hepatic lipase activity with increasing intra-abdominal fat in women. *Arterioscler Thromb Vasc Biol*, 19:2701–7.

Carson, P., Phillips, R., Lloyd, M., Tucker, H., Neophytou, M., Buch, N. J., Gelson, A., Lawton, A. and Simpson, T. (1982) Exercise after myocardial infarction: a controlled trial. *J R Coll Physicians Lond*, 16(3):147-51.

Cavelaars, M., Tulen, J. H., van Bemmel, J. H., ter Borg, M. J., Mulder, P. G. and van den Meiracker, A. H. (2002) Determinants of ambulatory blood pressure response to physical activity. *J Hypertens*, 20(10):2009-15.

Celermajer, D. S., Sorensen, K. E., Gooch, V. M., Spiegelhalter, D. J., Miller, O. I., Sullivan, I. D., Lloyd, J. K. and Deanfield, J. E. (1992) Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis, *Lancet*, 340: 1111–1115.

Centers for Disease Control (CDC) and Prevention. (2000) Prevalence of leisure-time and occupational physical activity among employed adults, United States. 1990 *MMWR Morb Mortal Wkly Rep*, 49: 420–424.

Chambers, J. C., Eda, S. and Bassett, P. (1999) C-reactive protein, insulin resistance, central obesity, and coronary heart disease risk in Indian Asians from the United Kingdom compared with European whites. *Circulation*, 104:145–150.

Chan, C. B., Spangler, E., Valcour, J. and Tudor-Locke, C. (2003) Cross-sectional relationship of pedometer-determined ambulatory activity to indicators of health. *Obes Res*, 11(12):1563-70.

Chasan-Taber, L., Erickson, J. B. and McBride, J. W. (2002) Reproducibility of a self-administered lifetime physical activity questionnaire among female college alumnae. *Am J Epidemiol*, 155: 282– 289.

Chasan-Taber, S., Rimm, E. B., Stampfer, M. J., Spiegelman, D., Colditz, G. A., Giovannucci, E., Ascherio, A. and Willett, W. C. (1996) Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. *Epidemiology*, 7(1):81-6.

Chen, H. C., Bandyopadhyay, G., Sajan, M. P., Kanoh, Y., Standaert, M., Farese, R. V. and Farese, R. V. (2002) Activation of the ERK pathway and atypical protein kinase C isoforms in exercise- and aminoimidazole-4-carboxamide-1-beta-D-riboside (AICAR)-stimulated glucose transport. *J Biol Chem*, 277, 23554–23562.

Chew, G. T., Gan, S. K. and Watts, G. F. (2006) Revisiting the metabolic syndrome. *MJA*, 185 (8): 445-449.

Church, T. S., Barlow, C. E., Earnest, C. P., Kampert, J. B., Priest, E. L. and Blair, S. N. (2002) Associations between cardiorespiratory fitness and C-reactive protein in men, *Arterioscler Thromb Vasc Biol*, 22: 1869–1876.

Church, T. S., Cheng, Y. J., Earnest, C. P., Barlow, C. E., Gibbons, L. W., Priest, E. L. and Blair, S. N. (2004) Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care*, 27(1):83-8.

Church, T. S., Earnest, C. P., Skinner, J. S. and Blair, S. N. (2007) Effects of Different Doses of Physical Activity on Cardiorespiratory Fitness Among Sedentary, Overweight or Obese Postmenopausal Women With Elevated Blood Pressure: A Randomized Controlled Trial. *JAMA,* 297:2081-2091.

Churilla, J. R. and Zoeller, R. F. (2008) Physical Activity: Physical Activity and the Metabolic Syndrome: A Review of the Evidence. *Am J Lifestyle Medicine*. 2(2): 118 - 125.

Christ-Roberts, C. Y. and Mandarino, L. J. (2004) Glycogen synthase: key effect of exercise on insulin action. *Exercise Sport Sci Rev*, 32: 90–94.

Ciampricotti, R., El Gamal, M., Relik, T., Taverne, R., Panis, J., de Swart, J., van Gelder, B., and Relik-van Wely, L. J. (1990) Clinical characteristics and coronary angiographic findings of patients with unstable angina, acute myocardial infraction, and survivors of sudden ischemic death occurring during and after sport. *Am Heart J*, 120: 1267-1277.

Cohen, J.A. (1960) coefficient of agreement for nominal scales. *Educational and Psychological Measurement*, 20:37–46.

Cohen, J.A. Statistical power analysis for the behavioral sciences (2nd edition). Laurence Erlbaum Associates, Publishers, New Jersey, London 1988.

Compher, C., Frankenfield, D., Keim, N. and Roth-Yousey, L. (2006) Evidence Analysis Working Group. Best practice methods to apply to measurement of resting metabolic rate in adults: a systematic review. *J Am Diet Assoc*, 106(6):881-903.

Considine, R. V. (1997) Invited editorial on "Acute and chronic effects of exercise on leptin levels in humans". J Appl Physiol 83, 3–4.

Cook, D. G., Mendall, M. A. and Whincup, P. H. (2000) C-reactive protein concentration in children: Relationship to adiposity and other cardiovascular risk factors. *Atherosclerosis,* 149:139–150.

Cooper, K. H., Pollock, M. and Martin, R. P. (1976) Physical fitness levels vs. selected coronary risk factors. *JAMA*, 236,166-169.

Cortright, R. N., Azevedo, J. L., Zhou, Q., Sinha, M., Pories, W. J., Itani, S. I. and Dohm, G. L. (2000) Protein kinase C modulates insulin action in human skeletal muscle. *Am J Physiol Endocrinol Metab*, 278, E553–E562.

Couillard, C., Despres, J. P. and Lamarche, B. (2001) Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arterioscler Thromb Vasc Biol*. 2001; 21:1226–32.

Cox, K. L., Burke, V., Beilin, L. J., Grove, J. R., Blanksby, B. A. and Puddey, I. B. (2006) Blood pressure rise with swimming versus walking in older women: the Sedentary Women Exercise Adherence Trial. *J Hypertens*, 24(2):307-14.

Craig, C. L., Marshall, A. L. and Sjostrom, M. (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*, 35:1381-95.

Crespo, C. J., Palmieri, M. R. and Perdomo, R. P. (2002) The relationship of physical activity and body weight with all-cause mortality: results from the Puerto Rico Heart Health Program. *Ann Epidemiol*, 12:543-552.

Cushman, M., Legault, C. and Barrett-Connor, E. (1999) Effect of postmenopausal hormones on inflammation-sensitive proteins: the Postmenopausal Estrogen/Progestin Interventions (PEPI) Study. *Circulation,* 100: 717–722.

Danesh, J., Whincup, P. and Lennon, L. (2000) Low grade inflammation and coronary heart disease: Prospective study and updated meta-analyses. *Br Med J*, 321:199–204.

Davidsen, E. S., Liseth, K., Omvik, P., Hervig, T. and Gerdts, E. (2007) Reduced exercise capacity in genetic haemochromatosis. *Eur J Cardiovasc Prev Rehabil*, 14(3):470-5.

Danielson, M. E., Cauley, J. A. and Rohay, J. M. (1993) Physical activity and its association with plasma lipids and lipoproteins in elderly women. *Ann Epidemiol*, 3(4):351-7.

DeBusk, R. F., Stenestrand, U., Sheehan, M. and Haskell, W. L. (1990) Training effects of long versus short bouts of exercise in healthy subjects. *Am J Cardiol*, 65:1010-1013.

Delanghe, J., Langlois, M. and De Bacquer, D. (2002) Discriminative value of serum amyloid A and other acute-phase proteins for coronary heart disease. *Atherosclerosis*, 160: 471–476.

de Luis, D. A., Aller, R., Izaola, O., Gonzalez Sagrado, M. and Conde, R. (2005) Resting energy expenditure, cardiovascular risk factors and insulin resistance in obese patients. *Ann Nutr Metab*, 49(6):381-5.

Delvaux, K., Philippaerts, R., Lysens, R., Vanhees, L., Thomis, M., Claessens, A. L., Vanreusel, B., Eynde, B. V., Beunen, G. and Lefevre, J. (2000) Evaluation of the influence of cardiorespiratory fitness on diverse health risk factors, independent of waist circumference, in 40-year-old Flemish males. *Obes Res*, 8(8):553-8.

Dempsey, E. C., Newton, A. C., Mochly-Rosen, D, Fields, A. P., Reyland, M. E., Insel, P. A. and Messing, R. O. (2000) Protein kinase C isozymes and the regulation of diverse cell responses. *Am J Physiol Lung Cell Mol Physiol*, 279: L429–L438.

Department of Health. (1996) Strategy statement on physical activity. London. Department of Health.

Department of Health. (2004) At least five a week: evidence on the impact of physical activity and its relationship to health. Retrieved July 2005. http://www.dh.gov.uk/assetRoot/04/08/09/81/04080981.pdf

Department of Health and Human Services-US (DHHS-US). (1996) Physical Activity and Health: A Report of the Surgeon General. US Dept of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Atlanta, Ga.

Department for Transport. NTS Personal Travel factsheet 4 January 2001. London Department of Transport.

Desmeules, S., Arcand-Bosse, J. F., Bergeron, J., Douville, P. and Agharazii, M. (2005) Nonfasting non-high-density lipoprotein cholesterol is adequate for lipid management in hemodialysis patients. *Am J Kidney Dis*, 45(6):1067-72.

DeSouza, C., Shapiro, L., Clevenger, C., Dinenno, F., Monahan, K., Tanaka, H. and Seals, D. (2000) Regular Aerobic Exercise Prevents and Restores Age-Related Declines in Endothelium-Dependent Vasodilation in Healthy Men. *Circulation,*102:1351.

Després, J. P., Pouliot, M. C. and Moorjani, S. (1991) Loss of abdominal fat and metabolic response to exercise training in obese women. *Am J Physiol*, 261:E159–E167.

Dey, S. K., Ghosh, C., Debray, P. and Chatterjee, M. (2002) Coronary artery disease risk factors & their association with physical activity in older athletes. *J Cardiovasc Risk*, 9(6):383-92.

Dishman, R., Washburn, R. and Heat, G. (2004) Physical activity epidemiology. Champaign, IL, USA, Human Kinetics.

Donahue, R. P., Orchard, T. J., Becker, D. J., Kuller, L. H. and Drash, A. L. (1988) Physical activity, insulin sensitivity, and the lipoprotein profile in young adults: the Beaver County Study. *Am J Epidemiol*, 127(1):95-103.

Donahue, R. P., Zimmet, P., Bean, J. A., Decourten, M., DeCarlo, M., Donahue, R. A., Colier, G., Goldberg, R. B., Prineas, R. J., Skyler, J. and Schneiderman, N. (1999) Cigarette smoking, alcohol use, and physical activity in relation to serum leptin levels in a multiethnic population: The Miami Community Health Study. *Ann Epidemiol*, 9: 108–113.

Dorn, J. P., Cerny, F. J. and Epstein, L. H. (1999) Work and leisure time physical activity and mortality in men and women from a general population sample. *Ann Epidemiol,* 9: 366–373.

Dunn, A. L., Marcus, B. H., Kampert, J. B., Garcia, M. E., Kohl, H. W. And Blair, N. (1999) Comparison of lifestyle and structured interventions to increase physical activity and cardiorespiratory fitness: a randomized trial. *JAMA*, 27;281(4):327-34.

Dunstan, D. W., Puddey, I. B., Beilin, L. J., Burke, V., Morton, A. R. and Stanton, K. G. (1998) Effects of a short-term circuit weight training program on glycaemic control in NIDDM. *Diabetes Res Clin Pract*, 40(1):53-61.

Durstine, J. L., Grandjean, P. W., Davis, P. G., Ferguson, M. A., Alderson, N. L. and DuBose, K. D. (2001) Blood lipid and lipoprotein adaptations to exercise: a quantitative analysis. *Sports Med*, 31(15):1033-62.

Dvorak, R. V., Tchernof, A., Starling, R. D., Ades, P. A., DiPietro, L. and Poehlman, E. T. (2000) Respiratory fitness, free living physical activity, and cardiovascular disease risk in older individuals: a doubly labeled water study. *J Clin Endocrinol Metab*, 85(3):957-63.

Dzimiri, N., Muiya, P., Andres, E. and Al-Halees, Z. (2004) Differential functional expression of human myocardial G protein receptor kinases in left ventricular cardiac diseases. *European Journal of Pharmacology*, 489:3: 167-177.

Ebisu, T. (1985) Splitting the distance of endurance running: on cardiovascular endurance and blood lipids. *Jpn J Phys Educ*, 30:37-43.

Eckel, R. H., Grundy, S. M. and Zimmet, P. Z. (2005) The metabolic syndrome. *Lancet*, 365: 1415-1428.

Einhorn, D., Reaven, G.M. and Cobin, R.H. (2003) American College of Endocrinology position statement on the insulin resistance syndrome. *Endocr Pract.* 9: 237–252.

Ekelund, U., Brage, S., Franks, P. W., Hennings, S., Emms, S. and Wareham, N. J. (2005) Physical activity energy expenditure predicts progression toward the metabolic syndrome independently of aerobic fitness in middle-aged healthy Caucasians: the Medical Research Council Ely Study. *Diabetes Care*, 28(5):1195-200.

Ekelund, U., Sepp, H., Brage, S., Becker, W., Jakes, R., Hennings, M. and Wareham, N. (2006) Criterion-related validity of the last 7-day, short form of the International Physical Activity Questionnaire in Swedish adults. *Public Health Nutrition*, 9:258-265.

Ekelund, U., Griffin, S. J. and Wareham, N. J. (2007) ProActive Research Group. Physical Activity and Metabolic Risk in Individuals with a Family History of Type 2 Diabetes. *Diabetes Care*, 30:337-342.

Erens, B., Primatesta, P. and Prior, G. (2001) Health Survey for England The Health of Minority Ethnic Groups 1999: Volume 2: *Methodology and Documentation*. TSO (London, 2001).

ERICA Research Group. (1991) Prediction of coronary heart disease in Europe. The 2nd report of the WHO-ERICA Project. *Eur Heart J,* 12: 291– 7.

Eriksson, J., Taimela, S. and Koivisto, V. A. (1997) Exercise and the metabolic syndrome. *Diabetologia*, 40:125–35.

Eskurza, I., Monahan, K. D. and Robinson, J. A. (2004) Seals DR Effect of acute and chronic ascorbic acid on flow-mediated dilatation with sedentary and physically active human ageing, *J Physiol*, 556: 315–324.

European Group for the Study of Insulin Resistance (EGIR). (1999) The 'EGIR definition' of the metabolic syndrome. Available at: http://www.egir.org/load.php?menu=public&page=http://www.egir.org/activity.html

Fagard, R. H., Staessen, J. and Amery, A. (1991) Exercise blood pressure and target organ damage in essential hypertension. *J Hum Hypertens*, 5(2):69-75.

Fagard, R. H. (1999) Physical activity in the prevention and treatment of hypertension in the obese. *Med Sci Sports Exerc*, 31(11): S624-30.

Fagard RH. (2001). Exercise characteristics and the blood pressure response to dynamic physical training. Med Sci Sports Exerc, 33(6 Suppl): S484-92.

Fan, Y., Laaksonen, R. and Janatuinen, T. (2001) Hepatic lipase gene variation is related to coronary reactivity in healthy young men. *Eur J Clin Invest*, 31:574–80.

Farese, R. V. (2001) Insulin-sensitive phospholipid signaling systems and glucose transport: update II. *Exp Biol Med,* 226 :283 –295.

Farrell, S. W., Cheng, Y. J. and Blair, S. N. (2004) Prevalence of the metabolic syndrome across cardiorespiratory fitness levels in women. *Obes Res*, 12(5):824-30.

Fenicchia, L. M., Kanaley, J. A., Azevedo, J. L., Miller, C. S., Weinstock, R. S., Carhart, R. L. and Ploutz-Snyder, L. L. (2004) Influence of resistance exercise training on glucose control in women with type 2 diabetes. *Metabolism*, 53(3):284-9.

Festa, A., D'Agostino, R., Howard, G., Mykkanen, L., Tracy, R. P. and Haffner, S. M. (2000) Chronic subclinical inflammation as part of the insulin resistance syndrome the insulin resistance atherosclerosis study (IRAS). *Circulation*, 102: 42–47.

Fitzgerald, S. J., Barlow, C. E., Kampert, J. B., Morrow, J. R., Jackson, A. W. and Blair, S. N. (2004) Muscular fitness and all cause mortality: prospective observations. *J Phys Activity Health*, 1:7–18.

Fletcher, G. F., Balady, G. J. and Amsterdam, E. A. (2001) Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation,* 104: 1694–1740.

Folsom, A. R., Prineas, R. J., Kaye, S. A. and Munger, R. G. (1990) Incidence of hypertension and stroke in relation to body fat distribution and other risk factors in older women. *Stroke,* 21: 701–706.

Folsom, A. R., S. A. Kaye, T. A. Sellers, C. P. Hong, J. R. Cerhan, J. D. Potter and R. J. Prineas (1993). Body fat distribution and 5-year risk of death in older women. JAMA 269(4): 483-7.

Food Standards Agency. (2004) National Diet & Nutrition Survey. Adults aged 19 to 64, Volume 4. http://www.food.gov.uk/multimedia/pdfs/ndnsfour.pdf

Ford, E. S., Merritt, R. K. and Heath, G. S. (1991) Physical activity behaviors in lower and higher socioeconomic status populations. *Am J Epidemiol*, 133: 1246–1256.

Ford, E.S. (2005a) Risks for all-cause mortality, cardiovascular disease and diabetes associated with the metabolic syndrome. A summary of the evidence. *Diabetes Care*. 28:1769-78.

Ford, E.S., Kohl, H.W., Mokdad, A.H. and Ajani, U.A. (2005b) Sedentary behavior, physical activity, and the metabolic syndrome among US adults. *Obes Res* 13: 608–614.

Ford, E.S. and Li, C. (2006) Physical activity or fitness and the metabolic syndrome. *Expert Rev Cardiovasc Ther* 4: 897–915.

Franks, P. W., Farooqi, S., Luan, J., Wong, M. Y., Halsall, I., O'Rahilly, S. and Warham, N. J. (2003) Does physical activity energy expenditure explain the between-individual variation in plasma concentrations after adjusting for differences in body composition? *J Clin Endocrinol Metab*, 88, 3258–3263.

Franks, P. W., Ekelund, U., Brage, S., Wong, M. Y. and Wareham, N. J. (2004) Does the association of habitual physical activity with the metabolic syndrome differ by level of cardiorespiratory fitness? *Diabetes Care*, 27(5):1187-93.

Fransson, E. I., L. S. Alfredsson, U. H. de Faire, A. Knutsson and P. J. Westerholm (2003). Leisure time, occupational and household physical activity, and risk factors for cardiovascular disease in working men and women: the WOLF study. Scand J Public Health 31(5): 324-33.

Franzoni, F., Ghiadoni, L., Galetta, F., Plantinga, Y., Lubrano, V., Huang, Y., Salvetti, G., Regoli, F., Taddei, S., Santoro, G. and Salvetti, A. (2005) Physical activity, plasma antioxidant capacity, and endothelium-dependent vasodilation in young and older men. *Am J Hypertens*, 18(4 Pt 1):510-6.

Freedson, P. S., Melanson, E. and Sirard, J. (1998) Calibration of the Computer Science and Applications, Inc. accelerometer *Med Sci Sports Exerc,* 30,777-81.

Friedlander, Y. (1994) Familial clustering of coronary heart disease: a review of its significance and role as a risk factor for the disease. In: U. Goldbourt, U. de Faire and K. Berg Editors, *Genetic Factors in Coronary Heart Disease* Kluwer Academic Dordrecht, Boston.

Friedlander, Y., Siscovick, D. S., Weinmann, S., Austin, M. A., Psaty, B. M., Lemaitre, R. N., Arbogast, P., Raghunathan, T. E. and Cobb, L. A. (1998) Family history as a risk factor for primary cardiac arrest. *Circulation*, 97(2):155-60.

Frohlich, M., Imhof, A. and Berg, G. (2000) Association between C-reactive protein and features of the metabolic syndrome. A population-based study. *Diabetes Care,* 23:1835–1839.

Fung, T. T., Hu, F. B., Yu, J., Chu, N. F., Spiegelman, D. and Tofler, G. H. (2000) Leisure-time physical activity, television watching, and plasma biomarkers of obesity and cardiovascular disease risk. *Am J Epidemiol,* 152: 1171–78.

Gaeta, G., De Michele, M. and Cuomo, S. (2000) Arterial abnormalities in the offspring of patients with premature myocardial infarction. *N Engl J Med,* 343: 840–846.

Gale, C. R., Martyn, C. N. and Kellingray, S. (2001) Intrauterine programming of adult body composition. *J Clin Endocrinol Metab*, 86:267–72.

Gannage-Yared, M. H., Khalife, S., Semaan, M., Fares, F., Jambart, S. and Halaby, G. (2006) Serum adiponectin and leptin levels in relation to the metabolic syndrome, androgenic profile and somatotropic axis in healthy non-diabetic elderly men. *Eur J Endocrinol*, 155(1):167-76.

Geffken, D., Cushman, M. and Burke, G. (2001) Association between physical activity and markers of inflammation in a healthy elderly population. *Am J Epidemiol,* 153 (3): 242–250.

Ghiadoni, L., Huang, Y., Magagna, A., Buralli, S., Taddei, S. and Salvetti, A. (2001) Effect of acute blood pressure reduction on endothelial function in the brachial artery of patients with essential hypertension. *J Hypertens*, 19: 547–551.

Giada, F., Baldo-Enzi, G. and Baiocchi, M. R. (1991) Specialized physical training programs: effects on serum lipoprotein cholesterol, apoproteins A-I and B and lipolytic enzyme activities. *J Sports Med Phys Fitness*, 31:196–203.

Gill, J. M. R. and Hardman, A. E. (2003) Exercise and postprandial lipid metabolism: an update on potential mechanisms and interactions with high-carbohydrate diets. *J Nutr Biochem*, 14, 122–132.

Gill, J. and Malkova, D. (2006) Physical activity, fitness and cardiovascular disease risk in adults: interactions with insulin resistance and obesity. *Clinical Science*, 110: 409–425.

Gilson, N., McKenna, J., Cooke, C. and Brown, W. (2007) Walking towards health in a university community: a feasibility study. *Prev Med*, 44(2):167-9.

Giovannucci, E. L., Liu, Y., Leitzmann, M. F., Stampfer, M. J. and Willett, W. C. (2005) A prospective study of physical activity and incident and fatal prostate cancer. *Arch Intern Med*. 2005; 165, 1005–1010.

Glasser, S. P., Selwyn, A. P. and Ganz, P. (1996) Atherosclerosis: risk factors and the vascular endothelium. *Am Heart J,* 131:379–384.

Goodfellow, J., Ramsey, M. W., Luddington, L. A., Jones, C. J., Coates, P. A., Dunstan, F., Lewis, M. J., Owens, D. R. and Henderson, A. H. (1996) Endothelium and inelastic arteries an early marker of vascular dysfunction in non-insulin dependent diabetes. *Br Med J*, 312: 744–745.

Goodyear, L. J., and Kahn, B. B. (1998) Exercise, glucose transport, and insulin sensitivity. *Annu Rev Med,* 49: 235-261.

Gordon, P. M., Goss, F. L., Visich, P. S., Warty, V., Denys, B. J., Metz, K. F. and Robertson, R. J. (1994) The acute effects of exercise intensity on HDL-C metabolism. *Med Sci Sports Exerc,* 26: 671–677.

Gordon, P. M., Fowler, S., Warty, V., Danduran, M., Visich, P. and Keteyian, S. (1998) Effects of acute exercise on high density lipoprotein cholesterol and high density lipoprotein subfractions in moderately trained females. *Br J Sports Med*, 32(1):63-7.

Gregory, J. R., Lowe, S., Bates, C. J., Prentice, A., Jackson, L. V., Smithers, G., Wenlock, R. and Farron, M. (2000) *National Diet and Nutrition Survey: young people aged 4 to 18 years*. Volume 1: Report of the diet and nutrition survey. TSO (London, 2000).

Grundy, S. M., Pasternak, R., Greenland, P., Smith, S. and Fuster, V. (1999) Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation,* 100: 1481– 92.

Grundy, S.M., Cleeman, J.I., Daniels, S.R., Donato, K.A., Eckel, R.H., Franklin, B.A., Gordon, D.J., Krauss, R.M., Svagae, P.J., Smith, S.C., Spertus, J.A., Costa, F., American Heart Association; National Heart, Lung and Blood Institute. (2005) Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung and Blood Institute scientific statement. *Circulation*. 112 (17): 2735-52.

Guagnano, M. T., Manigrasso, M. R and Ballone, E. (2003) Association between serum leptin levels and 24-hour blood pressure in obese women. *Obes Res*, 11,549-555.

Guedes, D. P. and Guedes, J. (2001) Physical activity, cardiorespiratory fitness, dietary content and risk factors that cause a predisposition towards cardiovascular disease. *Arq Bras Cardiol,* 77: 251–257.

Guize, L., Pannier, B., Thomas, F., Bean, K., Jego, B. and Benetos, A. (2008) Recent advances in metabolic syndrome and cardiovascular disease. Archive of Cardiovascular Disease. 101: 577-583.

Gulati, M., Pandey, D. K. and Arnsdorf, M. F. (2003) Exercise capacity and the risk of death in women: the St James Women Take Heart Project. *Circulation,* 108: 1554–1559.

Gutin, B., Barbeau, P., Owens, S., Lemmon, C. R., Bauman, M., Allison, J., Kang, H. S. and Litaker, M. S. (2002) Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *Am J Clin Nutr*, 75(5): 818-826.

Gwinup, G. (1975) Effect of exercise alone on the weight of obese women. *Arch Int Med*, 135: 676-680.

Gyllenborg, J., Rasmussen, S. L., Borch-Johnsen, K., Heitmann, B. L., Skakkebaek, N. E. and Juul, A. (2001) Cardiovascular risk factors in men: The role of gonadal steroids and sex hormone-binding globulin. *Metabolism*, 50(8):882-8.

Haapanen-Niemi, N., Miilunpalo, S., Pasanen, M., Vuori, I., Oja, P. and Malmberg, J. (2000) Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality--16 y follow-up of middle-aged and elderly men and women. *Int J Obes Relat Metab Disord*, 24(11):1465-74.

Haennel, R. G. and Lemire, F. (2002) Physical activity to prevent cardiovascular disease. How much is enough? *Can Fam Physician*, 48:65-71.

Haffner, S. M., Ferrannini, E., Hazuda, H. P. and Stern, M. P. (1992) Clustering of cardiovascular risk factors in confirmed prehypertensive individuals. *Hypertension*, 20:38–45.

Hakim, A. A., Petrovitch, H. and Burchfiel, C. M. (1998) Effects of walking on mortality among nonsmoking retired men. *N Engl J Med,* 338:94–99.

Hakim, A. A., Curb, J. D. and Petrovitch, H. (1999) Effects of walking on coronary heart disease in elderly men: the Honolulu Heart Program, *Circulation*, 100: 9–13.

Halaas, J. L., Gajiwala, K. S., Maffei, M., Cohen, S. L., Chait, B. T., Rabinowitz, D., Lallone, R. L., Burley, S. K. and Friedman, J. N. (1995) Weight-reducing effects of the plasma protein encoded by the obese gene. *Science*, 269: 543–546.

Hales, C. N., Barker, D. J. P., Clark, P. M. S., Cox, L. J., Fall, C. , Osmond, C. and Winter, P. D. (1991) Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ,* 303:1019-1022.

Hales, C. N. and Barker, D. J. (2001) The thrifty phenotype hypothesis. *Br Med Bull*, 60: 5–20.

Hardcastl,e S., Taylor, A., Bailey, M. and Castle, R. (2008) A randomised controlled trial on the effectiveness of a primary health care based counselling intervention on physical activity, diet and CHD risk factors. *Patient Educ Couns*, 70(1):31-9.

Harrap, S. B. (1994) Hypertension: genes versus environment. *Lancet,* 344: 169–171.

Haskell, W. L., Min Lee, I., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., Macera, C. A, Heath, G. W., Thompson, B. D. and Bauman, A. (2007) The American College of Sports Medicine and the American Heart Association Physical Activity and Public Health: Updated Recommendation for Adults From. *Circulation,* 116;1081-1093.

Hassinen, M., Lakka, T.A., Savonen, K., Litmanen, H., Kiviaho, L., Laaksonen, D.E., Komulainen, P. and Rauramaa, R. (2008) Cardiorespiratory Fitness as a Feature of Metabolic Syndrome in Older Men and Women: The Dose-Responses to Exercise Training Study (DR's EXTRA). *Diabetes Care*. 31(6): 1242 - 1247.

Haugen, H. A., Melanson, E. L., Tran, Z. V., Kearney, J. T. and Hill, J. O. (2003) Variability of measured resting metabolic rate. *Am J Clin Nutr*, 78: 1141–1144.

Hawe, E., Talmud, P. J., Miller, G. J. and Humphries, S. E. (2003) Family History is a Coronary Heart Disease Risk Factor in the Second Northwick Park Heart Study. *Annals of Human Genetics*, 67 (2):97–106.

Health Education Authority (1994). *Moving on: International perspectives in promoting physical activity*. London: Health Education Authority.

Health Survey for England. Joint Health Surveys Unit (2000). London: TSO.

Heath, G. W., Gavin, J. R., Hinderliter, J. M., Hagberg, J. M., Bloomfield, S. A. and Holloszy, J. O. (1983) Effects of exercise and lack of exercise on glucose tolerance and insulin sensitivity. *J Appl Physiol*, 55(2):512-7.

Heilbronn, L, and Clifton, P. M. (2002) C-reactive protein and coronary artery disease: influence of obesity. *J. Nutritional Biochem,* 13: 316–321.

He, J. and Whelton, P. K. (1999) Elevated systolic blood pressure and risk of cardiovascular and renal disease: overview of evidence from observational epidemiologic studies and randomized controlled trials. *Am Heart J*, 138:211-9.

Hendelman, D., Miller, K., Baggett, C., Debold, E. and Freedson, P. (2000) Validity of accelerometry for the assessment of moderate intensity physical activity in the field. *Med Sci Sports Exerc*, 32: S442-S4S9.

Heuvellen, M., Kempen, G. And Ormel, J. (1998) Physical fitness related to age and physical activity in older persons, *Med Sci Sports Exerc,* 30: 434–441.

Hicks, A. L., MacDougall, J. D. and Muckle, T. J. (1987) Acute changes in high-density lipoprotein cholesterol with exercise of different intensities. *J Appl Physiol*, 63(5):1956-60.

Higashi, Y., Sasaki, S., Kurisu, S., Yoshimizu, A., Sasaki, N., Matsuura, H., Kajiyama, G. and Oshima, T. (1999) Regular aerobic exercise augments endothelium-dependent vascular relaxation in normotensive as well as hypertensive subjects role of endothelium-derived nitric oxide, *Circulation*, 100: 1194–1202.

Hinkleman, L. L. and Nieman, D. C. (1993) The effects of a walking program on body composition and serum lipids and lipoproteins in overweight women. *J Sports Med Phys Fitness*, 33(1):49-58.

Hokanson, J. E., Hamman, R. F. and Eckel, R. H. (2001) Gene-environment interaction in the regulation of HDL: the hepatic lipase promoter polymorphism modulates the physical activity associated increase in HDL. *Circulation*, 103:P08.

Hokanson, J. E., Cheng, S. and Snell-Bergeon, J. K. (2002) A common polymorphism in the hepatic lipase gene (*LIPC*-480 *C>T*) is associated with an increase in coronary artery calcification in type 1 diabetes. *Diabetes*, 51:1208–13.

Holloszy, J. O. (2005) Exercise-induced increase in muscle insulin sensitivity. *J Appl Physiol*, 99: 338–343.

Holme, I., Tonstad, S., Sogaard, A. J., Larsen, P. G. and Haheim, L. (2007) Leisure time physical activity in middle age predicts the metabolic syndrome in old age: results of a 28-year follow-up of men in the Oslo study. *BMC Public Health*, 7: 154.

Howell, W., Earthman, C., Reid, P., Delaney, J. and Houtkooper, L. (1999) Doubly Labeled water validation of the compendium of physical activities in lean and obese college women. *Med Sci Sports Exerc*, 31: S142.

Howley, E. T. (2001) Type of activity: resistance, aerobic and leisure versus occupational physical activity. *Med Sci Sports Exerc*, 33(6): S364-S369.

Hubert, H. B., Feinleib M., McNamara P. M. and Castelli W. P. (1983) Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation, 67(5): 968-77.

Hu, F. B., Sigal, R. J. and Rich-Edwards, J. W. (1999) Walking compared with vigorous physical activity and risk of type 2 diabetes in women: a prospective study. *JAMA*, 282, 1433–1439.

Hu, F. B., Stampfer, M. J., Colditz, G. A., Ascherio, A., Rexrode, K. M., Willett, W. C. and Manson, J. E. (2000) Physical activity and risk of stroke in women. *JAMA*, 14;283(22):2961-7.

Hu, G., Pekkarinen, H., Hanninen, O., Tian, H. and Guo, Z. (2001) Relation between commuting, leisure time physical activity and serum lipids in a Chinese urban population, *Ann Hum Biol*, 28: 412–421.

Hu, G., Pekkarinen H. and Hanninen, O. (2002) Commuting, leisure-time physical activity, and cardiovascular risk factors in China, *Med Sci Sports Exerc*, 34: 234–238.

Hu, G., Qiao, Q. and Silventoinen, K. (2003) Occupational, commuting, and leisure-time physical activity in relation to risk for type 2 diabetes in middle-aged Finnish men and women, *Diabetologia*, 46: 322–329.

Hu, G., Tuomilehto, J., Silventoinen, K., Barengo, N. C., Peltonen, M. and Jousilahti, P. (2005) The effects of physical activity and body mass index on cardiovascular, cancer and all-cause mortality among 47 212 middle-aged Finnish men and women. *Int J Obes,* 29(8):894-902.

Hu, G., Tuomilehto J., Borodulin K, and Jousilahti P. (2007a) The joint associations of occupational, commuting, and leisure-time physical activity, and the Framingham risk score on the 10-year risk of coronary heart disease. *Eur Heart J*, 28(4):492-8.

Hu, G., Jousilahti P., Borodulin K., Barengo N. C., Lakka T.A., Nissinen A. and Tuomilehto J. (2007b) Occupational, commuting and leisure-time physical activity in relation to coronary heart disease among middle-aged Finnish men and women. *Atherosclerosis*, 194(2): 490-497.

Hu, G., Jousilahti P., Antikainen R. and Tuomilehto J. (2007c) Occupational, Commuting, and Leisure-Time Physical Activity in Relation to Cardiovascular Mortality Among Finnish Subjects With Hypertension. *Am J Hyperten*, 20 (12):1242-1250.

Humphries, S. E., Peacock, R. E and Talmud, P. J. (1995) The genetic determinants of plasma cholesterol and response to diet. *Bailiére's Clin. Endocrinol. Metab,* 9: 797–823.

Hunter, G. R., Kekes-Szabo, T., Snyder, S. W., Nicholson, C., Nyikos, I. and Berland, L. (1997) Fat distribution, physical activity, and cardiovascular risk factors. *Med Sci Sports Exercise*, 29:362–369.

International Diabetes Federation (IDF). (2005) The IDF consensus worldwide definition of the metabolic syndrome. Brussels: IDF, 2005. Available at: http://www.idf.org/webdata/docs/IDF_Metasyndrome_definition.pdf.

International Obesity Task Force. (1998) Obesity: preventing and managing the global epidemic. Report of WHO consultation on obesity, Geneva, 3-5 June 1998. *WHO.* (Geneva).

Irwin, M. L., Ainsworth, B. E., Mayer-Davis, E. J., Addy, C. L., Pate, R. P. and Durstine, J. L. (2002) Physical Activity and the Metabolic Syndrome in a Tri-ethnic Sample of Women. *Obesity Research*, 10:1030-1037.

Itani, S. I., Ruderman, N. B., Schmieder, F. and Boden, G. (2002) Lipid-induced insulin resistance in human muscle is associated with changes in diacylglycerol, protein kinase C, and IκB-α. *Diabetes*, 51: 2005–2011.

Ivy, J. L., Zderic, T. W., and Fogt, D. L. (1999) Prevention and treatment of non-insulin-dependent diabetes mellitus. *Exerc Sport Sci Rev*, 27: 1–35.

Jacobs, D. R., Ainsworth, B. E., Hartman, T. J. and Leon, A. S. (1993) A simultaneous evaluation of 10 commonly used physical activity questionnaires. *Med Sci Sports Exerc*, 25: 81̃91.

Jakes, R. W., Day N. E., Khaw K. T., Luben R., Oakes S., Welch A., Bingham S. and Wareham N. J. (2003) Television viewing and low participation in vigorous recreation are independently associated with obesity and markers of cardiovascular disease risk: EPICNorfolk population-based study. Eur J Clin Nutr, 57(9): 1089-96.

Jakicic, J. M. (2001) American College of Sports Medicine position stand. Appropriate intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc*, 33: 2145–2156.

James, W. P. T. (1995) A public health approach to the problem of obesity. *Int J Obes Relat Metab Disord*, 19:S37-S45.

Jia, W. P., Yang, M., Shao, X. Y., Bao, Y. Q., Lu, J. X. and Xiang, KS. (2005) Resting energy expenditure and its relationship with patterns of obesity and visceral fat area in Chinese adults. *Biomed Environ Sci*, 18(2):103-7.

Johansson, S. E. and Sundquist, J. (1999) Change in lifestyle factors and their influence on health status and all-cause mortality. *Int J Epidemiol*, 28:1073-1080.

Kahn, H. S., Narayan, K. M. and Williamson, D. F. (2000) Relation of birth weight to lean and fat thigh tissue in young men. *Int J Obes Relat Metab Disord*, 24:667–72.

Kajiura, J. S., MacDougall, J. D., Ernst, P. B. and Younglai, E. V. (1995) Immune response to changes in training intensity and volume in runners. *Med Sci Sports Exerc*, 27:1111–7.

Kang, J., Robertson, R. J., Hagberg, J. M., Kelley, D. E., Goss, F. L., DaSilva, S. G., Suminski, R. R. and Utter, A. C. (1996) Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. *Diabetes Care*, 19(4):341-9.

Katzel, L. I., Bleecker, E. R., Colman, E. G., Rogus, E. M., Sorkin, J. D. and Goldberg, A. P. (1995) Effects of weight loss vs aerobic exercise training on risk factors for coronary disease in healthy, obese, middle-aged and older men. A randomized controlled trial. *JAMA*, 274:1915–1921.

Katzmarzyk, P. T. and Craig, C. L. (2002) Musculoskeletal fitness and risk of mortality. *Med. Sci. Sport Exerc*, 34:740–744.

Katzmarzyk, P. T., Leon A. S. and Wilmore J. H. (2003a) Targeting the metabolic syndrome with exercise: evidence from the HERITAGE family study. *Med Sci Sports Exerc*, 35,1703-1709.

Katzmarzyk, P. T., Janssen I. and Ardern C. I. (2003b) Physical inactivity, excess adiposity and premature Mortality. *Obesity reviews*, 4: 257–290.

Kelley, G. A., Kelley, K. A. and Tran, Z. V. (2001) Aerobic exercise and resting blood pressure: a meta-analytic review of randomized, controlled trials. *Prev Cardiol,* 4: 73–80.

Kelley, G. A., Kelley, K. A. and Tran, Z. V. (2004) Aerobic exercise and lipids and lipoproteins in women: a meta-analysis of randomized controlled trials. *J Womens Healt,* 13(10): 1148-64.

Kelly, J. P., Rosenberg, L., Kaufman, D. W. and Shapiro, S. (1990) Reliability of personal interview data in a hospital-based case-control study. *Am J Epidemiol,* 131: 79-90.

Kelliny, C., William, J., Riesen, W., Paccaud, F., and Bovet, P. (2008) Metabolic syndrome according to different definitions in a rapidly developing country of the African region. *Cardiovascular Diabetology*. 7:27.

Kensara, O. A., Wooton, S. A., Phillips, D. I., Patel, M., Jackson, A. A. and Elia, M. (2005) Fetal programming of body composition: relation between birth weight and body composition measured with dual-energy X-ray absorptiometry and anthropometric methods in older Englishmen. *Am J Clin Nutr*, 82:980–7.

Kensara, O., Wootton, S., Phillips, D., Patel, M., Hoffman, D., Jackson, A. and Elia, M. (2006) Substrate-energy metabolism and metabolic risk factors for cardiovascular disease in relation to fetal growth and adult body composition. *Am J Physiol Endocrinol Metab*, 291(2):E365-71.

Keppel, G., & Wickens, T.D. (2004). Design and analysis: A researchers handbook (4th ed.). Upper Saddle river. New Jersey, Pearson, Prentice Hall.

Kesaniemi, Y. A., Danforth, E. J., Jensen, M. D., Kopelman, P. G., Lefebvre, P. and Reeder, B. A. (2001) Dose–response issues concerning physical activity and health: an evidence-based symposium. *Med Sci Sports Exerc*, 33:S351–358.

Khaw, K. T., Jakes, R., Bingham, S., Welch, A., Luben, R., Day. N. and Wareham, N. (2006) Work and leisure time physical activity assessed using a simple, pragmatic, validated questionnaire and incident cardiovascular disease and all-cause mortality in men and women: The European Prospective Investigation into Cancer in Norfolk prospective population study *Inter J Epidem*, 35(4):1034-1043.

Kingwell, B. A. and Jennings, G. (1993) Effects of walking and other exercise programs upon blood pressure in normal subjects. *Med J Austr*, 158: 234-238.

Kirk, A., Mutrie, N., MacIntyre, P. and Fisher, M. (2003) Increasing physical activity in people with type 2 diabetes. *Diabetes Care*, 26(4):1186-92.

Kjelsberg, M. O., Cutler, J. A. and Dolecek, T. A. (1997) Brief description of the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr*, 65(1):191S-195S.

Kohl, H. W. (2001) Physical activity and cardiovascular disease: evidence for a dose response. *Med Sci Sports Exerc*, 33(6):S472-83.

Kosaki, A., Yamada, K. and Kuzuya, H. (1996) Reduced expression of the leptin gene (ob) by catecholamine through a G(S) protein pathway in 3T3-L1 adipocytes. *Diabetes*, 45: 1744–1749.

Krauss, W. E., Houmard, J. A., Duscha, B. D., Knetzger, K. J., Wharton, M. B., McCartney, J. S., Bales, C. W., Hened, R. D., Samsa, G. P., Otvos, J. D., Kulkarni, K. R. and Slentz, C. A. (2002) Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*, 347 (19): 1483–1524.

Kriska, A. M. and Bennett, P. H. (1992) An epidemiological perspective of the relationship between physical activity NIDDM: from activity assessment to intervention. *Diabetes Metab. Rev,* 8:355372.

Kriska, A. M., Pereira, M. A., Hanson, R. L., de Courten, M. P., Zimmet, P. Z., Alberti, K. G., Chitson, P., Bennett, P. H., Narayan, K. M. and Knowler, W. C. (2001a) Association of physical activity and serum insulin concentrations in two populations at high risk for type 2 diabetes but differing by BMI. *Diabetes Care*, 24 (7):1175-80.

Kriska, A. M., Hanley, A. J., Harris, S. B. and Zinman, B. (2001b) Physical activity, physical fitness, and insulin and glucose concentrations in an isolated Native Canadian population experiencing rapid lifestyle change. *Diabetes Care*, 24 (10):1787-92.

Kronenberg, F., Pereira, M. A., Schmitz, M. K., Arnett, D. K., Evenson, K. R. and Crapo, R.O. (2000) Influence of leisure time physical activity and television watching on atherosclerosis risk factors in the NHLBI Family Heart Study. *Atherosclerosis*, 153: 433–43.

Krousel-Wood, M. A., Berger, L., Jiang, X., Blonde, L., Myers, L. and Webber, L. (2008) Does home-based exercise improve body mass index in patients with type 2 diabetes? Results of a feasibility trial. *Diabetes Res Clin Pract*, 79(2):230-6.

Kujala, U. M. and Kaprio, J. (1998) Relationship of leisure-time physical activity and mortality: the Finnish twin cohort. *JAMA*, 279:440-444.

Laaksonen, D. E., Lakka, H. M., Salonen, J. T., Niskanen, L. K., Rauramaa, R. and Lakka, T. A. (2002) Low levels of leisure-time physical activity and cardiorespiratory fitness predict development of the metabolic syndrome. *Diabetes Care*, 25: 1612–1618.

LaCroix, A. Z., Leveille, S. G., Hecht, J. A., Grothaus, L. C. and Wagner, E. H. (1996) Does walking decrease the risk of cardiovascular disease hospitalizations and death in older adults? *J Am Geriatr Soc,* 44:113–20.

Lagrand, W., Visser, C. and Hermens, W. (1999) C-reactive protein as a cardiovascular risk factor: more than a epiphenomenon? *Circulation*, 100: 96–102.

Lahti-Koski, M., Pietinen, P., Heliövaara, M. and Vartiainen, E. (2002) Associations of body mass index and obesity with physical activity, food choices, alcohol intake, and smoking in the 1982–1997 FINRISK Studies. *Am J Clin Nutr*, 75: 809 - 817.

Lakka, H.M., Laaksonen, D.E., Lakka, T.A., Niskanen, L.K., Kumpusalo, E., Tuomilehto, J. and Salonen, J.T. (2002) The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA*. 288: 2709–2716.

Lakka, T. A. and Salonen, J. T. (1992) Physical activity and serum lipids: a cross-sectional population study in eastern Finnish men. *Am J Epidemiol*, 136(7):806-18.

Lakka, T. A., Venalainen, J. M., Rauramaa, R., Salonen, R., Tuomilehto, J. and Salonen, J. T. (1994) Relation of leisure time physical activity and cardiorespiratory fitness to the risk of acute myocardial infraction in men. *N Engl J Med*, 330: 1549-1554.

Lakka, T. A., Laaksonen, D. E., Lakka, H. M., Mannikko, N., Niskanen, L. K.and Rauramaa, R. (2003) Sedentary lifestyle, poor cardiorespiratory fitness, and the metabolic syndrome, *Med Sci Sports Exerc*, 35: 1279–1286.

Lakka, T. A., Rankinen, T., Weisnagel, G., Chagnon, Y., Lakka, H., Ukkola, O., Boulé, N., Rice, T., Leon, A., Skinner, J., Wilmore, J., Rao, D., Bergman, R., and Bouchard, C. (2004) Leptin and Leptin Receptor Gene Polymorphisms and Changes in Glucose Homeostasis in Response to Regular Exercise in Nondiabetic Individuals. *Diabetes*, 53:1603-1608.

LaMonte, M. J., Durstine, J. L. and Yanowitz, F.G. (2002) Cardiorespiratory fitness and C-reactive protein among a tri-ethnic sample of women, *Circulation*, 106: 403–406.

Lampman, R. M., Schteingart, D. E., Santinga, J. T., Savage, P. J., Hydrick, C. R., Bassett, D. R. and Block, W. D. (1987) The influence of physical training on glucose tolerance, insulin sensitivity, and lipid and lipoprotein concentrations in middle-aged hypertriglyceridaemic, carbohydrate intolerant men. *Diabetologia*, 30(6):380-5.

Lapidus, L., Lindstedt, G. and Lundberg, P. A. (1986) Concentrations of sex-hormone binding globulin and corticosteroid binding globulin in serum in relation to cardiovascular risk factors and to 12-year incidence of cardiovascular disease and overall mortality in postmenopausal women. *Clin Chem.* 1986; 32: 146–152.

LaRosa, J. C., Cleary, P., Muesing, R. A., Gorman, P., Hellerstein, H. K. and Naughton, J. (1982) Effect of long-term moderate physical exercise on plasma lipoproteins. The National Exercise and Heart Disease Project. *Arch Intern Med*, 142(13):2269-74.

Law, C. M., de Swiet, M., Osmond, C., Fayers, P. M., Barker, D. J. P., Cruddas, A. M. and Fall, C. H. D. (1993) Initiation of hypertension in utero and its amplification throughout life. *BMJ,* 306:24-27.

Lee, C. D. and Blair, S. N. (2002) Cardiorespiratory fitness and stroke mortality in men. *Med Sci Sports Exerc,* 34:592–595.

Lee, I. M. and Paffenbarger, R. S. (1998) Physical activity and stroke incidence: the Harvard Alumni Health Study. *Stroke,* 29: 2049–2054.

Lee, I. M., Sesso, H. D. and Paffenbarger, R. S. (2000a) Physical activity and coronary heart disease risk in men: does the duration of exercise episodes predict risk? *Circulation*, 102: 981–986.

Lee, I. M. and Paffenbarger R. S. (2000b) Associations of light, moderate, and vigorous intensity physical activity with longevity. The Harvard Alumni Health Study. *Am J Epidemiol*, 151 (3), 293–299.

Lee, I. M., Rexrode K. M., Cook N. R., Manson J. E., Buring J. E. (2001a) Physical activity and coronary heart disease in women: is 'no pain, no gain' passe? *JAMA,* 285:1447–54.

Lee, I. M and Skerrett P. J. (2001b) Physical activity and all-cause mortality: what is the dose–response relation? *Med Sci Sports Exerc,* 33: S459–S471.

Lee, K. W. and Lip, G. Y. (2003) Effects of lifestyle on hemostasis, fibrinolysis, and platelet reactivity: a systematic review. *Arch Intern Med*, 163: 2368–2392.

Lehmann, R., Engler, H., Honegger, R., Riesen, W. and Spinas, G. A. (2001) Alterations of lipolytic enzymes and high-density lipoprotein subfractions induced by physical activity in type 2 diabetes mellitus. *Eur J Clin Invest*, 31(1):37-44.

Lemieux, S., Prud'homme D., Bouchard C., Tremblay A. and Despres J. P. (1993) Sex differences in the relation of visceral adipose tissue accumulation to total body fatness. Am J Clin Nutr, 58(4): 463-7.

Leon, A. S., Connett, J., Jacobs, D. R. and Rauramaa, R. (1987) Leisure-time physical activity levels, and risk of coronary heart disease and death. The Multiple Risk Factor Intervention Trial. *JAMA*, 258:2388–2395.

Leon, A. S., Connett, J. and MRFIT research group. (1991) Physical Activity and 10.5 Year Mortality in the Multiple Risk Factor Intervention Trial (MRFIT). *International Journal of Epidemiology*, 20: 690-697.

Leon, A. S., Casal, D. and Jacobs, D. (1996) Effects of 2,000 kcal per week of walking and stair climbing on physical fitness and risk factors for coronary heart disease. *J Cardiopulm Rehabil*, 16(3):183-92.

Leon, A. S., Myers, M. J. and Connett, J. (1997) Leisure time physical activity and the 16-year risks of mortality from coronary heart disease and all-causes in the Multiple Risk Factor Intervention Trial (MRFIT). *Int J Sports Med*, 18(3):S208-15.

Leon, A. S. and Sanchez, O. A. (2001) Response of blood lipids to exercise training alone or combined with dietary intervention. *Med Sci Sports Exerc*, 33(6): S502-15.

Liao, D., Myers, R. and Hunt, S. (1997) Family history of stroke and stroke risk: the Family Heart Study. *Stroke,* 28: 1908–1912.

Ligtenberg, P. C., Hoekstra, J. B., Bol, E., Zonderland, M. L. and Erkelens, D. W. (1997) Effects of physical training on metabolic control in elderly type 2 diabetes mellitus patients. *Clin Sci (Lond)*, 93(2):127-35.

Lindstrom, J., Eriksson, J. G., Valle, T. T., Aunola, S., Cepaitis, Z. and Hakumaki, M. (2003) Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish diabetes prevention study: results from a randomized clinical trial, *J Am Soc Nephrol*, 14: S108–S113.

Li G, Zhang P, Wang J, Gregg EW, Yang W, Gong Q, Li H, Li H, Jiang Y, An Y, Shuai Y, Zhang B, Zhang J, Thompson TJ, Gerzoff RB, Roglic G, Hu Y, Bennett PH. (2008) The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. *Lancet*. 24;371(9626):1783-9.

Li, R., Bensen, J. T., Hutchinson, R. G., Province, M. A., Hertz-Picciotto, I., Sprafka, J. M. and Tyroler, H. A. (2000) Family risk score of coronary heart disease (CHD) as a predictor of CHD: the Atherosclerosis Risk in Communities (ARIC) study and the NHLBI family heart study. *Genet Epidemiol*, 18: 236–250.

Livingstone, M. B. E. (1997) Heart-rate monitoring: the answer for assessing energy expenditure and physical activity in population studies? *Br J Nutr,* 78,869-871.

Lucia, A., Gómez-Gallego, F., Barroso, I., Rabadán, M., Bandrés, F., San Juan, A. F., Chicharro, J. L., Ekelund, U. L. F., Brage, S., Earnest, S. P., Wareham, N. J., and Franks, P. W. (2005) *Role of Exercise in Reducing the Risk of Diabetes and Obesity*: *PPARGC1A* genotype (Gly482Ser) predicts exceptional endurance capacity in European men. *J Appl Physiol,* 99: 344-348.

Luscher, T. F. and Vanhoutte, P. M. (1990) The Endothelium Modulator of Cardiovascular Function. Boca Raton, FL, CRC Press.

Lynch, J., Helmrich, S. P., Lakka, T. A., Kaplan, G. A., Cohen, R. D., Salonen, R. and Salonen, J. T. (1996) Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. *Arch Intern Med,* 156:1307–1314.

Mäder, U., Martin, B. W., Schutz, Y. and Marti, B. (2006) Validity of four short physical activity questionnaires in middle-aged persons. *Med Sci Sports Exerc*, 38(7):1255-66.

Macera, C. A. and Powell, K. E. (2001) Population attributable risk: implications of physical activity dose. *Med Sci Sports Exerc*, 33: S635–639.

Magnus, K., Matroos, A. and Strachee, J. (1979) Walking, cycling, or gardening, with or without seasonal interruption , in relation to coronary events. *Am J Epidemiol*, 110: 724-33.

Mahar, M. T. and Ainsworth, B. E. (2000) Measurement of physical activity: the Cooper Institute conference series. *Res Qu Exerc Sport,* 71(2),S1-S158.

Maiorana, A., O'Driscoll, G., Goodman, C., Taylor, R. and Green, D. (2002) Combined aerobic and resistance exercise improves glycemic control and fitness in type 2 diabetes. *Diabetes Res Clin Pract*, 56(2):115-23.

Malik, S., Wong, N. D. and Franklin, S. S. (2004) Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. *Circulation*, 110: 1245-1250.

Manson, J. E., Hu, F. B., Rich-Edwards, J. W., Colditz, G. A., Stampfer, M. J., Willett, W. C., Speizer, F. E. and Hennekens, C. H. (1999) A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *N Engl J Med*, 26;341(9):650-8.

Manson, J. E., Greenland, P., LaCroix, A. Z., Stefanick, M. L., Mounton, C. P. and Oberman A. (2002) Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *N Engl J Med*, 347:716-725.

Margaglione, M., Cappucci, G., Colaizzo, D., Vecchione, G., Grandone, E. and Di Minno, G. (2000) C-reactive protein in offspring is associated with the occurrence of myocardial infarction in first-degree relatives. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 20: 198–203.

Marquez, D. X., Bustamante, E. E., McCauley, E. and Roberts D. E. (2008) Active or sedentary? Objectively measured physical activity of latinos and implications for intervention. J Phys Act Health, 5(4):559-70.

Masuzaki, H., Ogawa, Y., Sagawa, N., Hosoda, K., Matsumoto, T., Mise, H., Nishimura, H., Yoshimasa, Y., Tanaka, I., Mori, T. and Nakao, K. (1997) Nonadipose tissue production of leptin: leptin as a novel placenta-derived hormone in humans. *Nature Med*, 3: 1029–1033.

Matthews, C. E., Ainsworth, B. E., Hanby, C., Pate, R. R., Addy, C., Freedson, P. S., Jones, D. A. and Macera, C. A. (2005) Development and testing of a short physical activity recall questionnaire. *Med Sci Sports Exerc*, 37(6):986-94.

Mayer, C. J., Steinman, L., Williams, B., Topolski, T. D. and LoGerfo, J. (2008) Developing a Telephone Assessment of Physical Activity (TAPA) questionnaire for older adults. *Prev Chronic Dis*, 5(1):A24.

Mayer-Davis, E. J., D'Agostino, R. and Karter, A. J. (1998) Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study, *J Am Med Assoc,* 279(9): 669–674.

Mbalilaki JA, Hellènius ML, Masesa Z, Høstmark AT, Sundquist J, Strømme SB. Physical activity and blood lipids in rural and urban Tanzanians. *Nutrition, Metabolism and cardiovascular diseases*. 2007; 17(5):344-348.

McNeill, G. (2000) *Human Nutrition and Dietetics 10th edition*. Energy intake and expenditure, 25-36.

McPherson, K., Britton, A. and Causer, L. (2002) Coronary heart disease. Estimating the impact of changes in risk factors. London: The Stationery Office.

Mendelsohn, M. E. and Karas, R. H. (1999) The protective effects of estrogen on the cardiovascular system. *N Engl J Med*, 340:1801-1811.

Mendoza, S. G., Carrasco, H. and Zerpa, A. (1991) Effect of physical training on lipids, lipoproteins, apolipoproteins, lipases, and endogenous sex hormones in men with premature myocardial infarction. *Metabolism*, 40:368–77.

Menotti, A., Lanti, M., Puddu, P. E. and Kromhout, D. (2000) Coronary heart disease incidence in northern and southern European populations: a reanalysis of the seven countries study for a European coronary risk chart. *Heart,* 84: 238– 44.

Mensink, G. B., Ziese, T. and Kok, F. J. (1999) Benefits of leisure-time physical activity on the cardiovascular risk profile at older age. *Int J Epidemiol*, 28(4):659-66.

Meriwether, R. A., McMahon, P. M., MBBS, N. I. and Steinmann, W. C. (2006) Physical Activity Assessment Validation of a Clinical Assessment Tool. *Am J Prevention Med*, 31(6): 484-491.

Meyer, H. E., Sogaard, A. J. and Tverdal, A. (2002) Body mass index and mortality: the influence of physical activity and smoking. *Med Sci Sports Exerc*, 34:1065-1070.

Milesis, C. A., Pollock, M. L., Bah, M. D., Ayres, J. J., Ward, A. and Linnerud, A. C. (1976) Effects of different durations of training on cardiorespiratory function, body composition and serum lipids. *Research Quarterly*, 47: 716- 725.

Monninkhof, E. M., Elias, S. G. and Vlems, F. A. (2007) Physical activity and breast cancer: a systematic review. *Epidemiology*, 18, 137–157.

Montague, C. T., Farooqi, I. S., Whitehead, J. P., Soos, M. A., Rau, H., Wareham, N. J., Sewter, C. P., Digby, J. E., Mohammed, S. N., Hurst, J. A., Cheetham, C. H., Earley, A. R., Barnett, A. H., Prins, J. B. and O'Rahilly, S. (1997) Congenital leptin deficiency is associated with severe early-onset obesity in humans. *Nature*, 387:903 – 908.

Montoye, H. J. and Taylor, H. (1984) Measurement of physical activity in population studies: a review. *Hum Bioi,* 56:195-216.

Moreau, K. L., Degarmo, R., Langley, J., McMahon, C., Howley, E. T., Bassett, D. R. and Thompson, D. L. (2001) Increasing daily walking lowers blood pressure in postmenopausal women. *Med Sci Sports Exerc*, 33(11):1825-31.

Morris, J. N., Heady, J. A., Raffle, P. A. B., Roberts, C. G. and Parks, J. W. (1953) Coronary heart disease and physical activity of work. *Lancet*, 2:1053-7, 111-20.

Morris, J. N., Heady, J. A. and Raffle, P. A. B. (1956) Physique of London busmen: epidemiology of uniforms. *Lancet*, 2: 569-70.

Morris, J. N. and Crawford, M. D. (1958) Coronary heart disease and physical acticity of work: evidence of a national necropsy survey. *Br. Med. Journal*, 2:1485-96.

Murphy, M. H., Murtagh, E. M., Boreham, C. A., Hare, L. G. and Nevill, A. M. (2006) The effect of a worksite based walking programme on cardiovascular risk in previously sedentary civil servants. *BMC Public Health*, 22;6:136.

Murray, C. J., Lauer, J. A. and Hutubessy, R. C. (2003) Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. *Lancet,* 361: 717– 25.

Myers, J., Prakash, M. and Froelicher, V. (2002) Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med,* 346: 793–801.

Myers, R. H., Kiely, D. K., Cupples, L. A. and Kannel, W. B. (1990) Parental history is an independent risk factor for coronary artery disease: the Framingham Study. *Am Heart J*, 120: 963–969.

Nakayama, T., Date, C., Yokoyama, T., Yoshiike, N., Yamaguchi, M. and Tanaka, H. (1997) A 15.5-year follow-up of stroke in Japanese provincial city: the Shibata Study. *Stroke,* 28: 45–52.

National Cholesterol Education Program III (NCEP III). (2002) Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Final report. *Circulation*. 106: 3143–3421.

National Diet and Nutrition Survey (NDNS). (2004) Adults aged 19-64 years (volume 4). Food Standards Agency. Available online at: http://www.food.gov.uk/multimedia/pdfs/ndnsfour.pdf

National Health and Examination Survey-III (*NHANES-III*). Available at: http://www.cdc.gov/nchs/nhanes.htm

National Institutes of Health (NIH) Consensus Development Panel on Physical Activity and Cardiovascular Health. (1996) Physical activity and cardiovascular health. NIH Consensus Development Panel on Physical Activity and Cardiovascular Health. *JAMA*, 276:241–6.

National Statistics (UK). 2004 Available at: http://www.statistics.gov.uk/cci/nugget.asp?id=919

Nora, J. J., Lortscher, R. H., Spangler, R. D., Nora, A. H. and Kimberling, W. J. (1980) Genetic–epidemiologic study of early-onset ischemic heart disease. *Circulation,* 61: 503–508.

Norman, A., Bellocco, R., Bergstrom, A. and Wolk, A. (2001) Validity and reproducibility of self-reported total physical activity–differences by relative weight. *Int J Obes Relat Metab Disord*, 25: 682–88.

O'Donovan, G., Owen, A., Kearney, E. M., Jones, D. W., Nevill, A. M. and Woolf-May, K. (2005) Cardiovascular disease risk factors in habitual exercisers, lean sedentary men and abdominally obese sedentary men. *Int J Obes Relat Metab Disord*, 29 (9): 1063-1069.

O'Donovan, G. and Shave, R. (2007) British adults' views on the health benefits of moderate and vigorous activity. *Prev Med*, Available online at: www.sciencedirect.com

Oida, Y., Kitabatake, Y., Nishijima, Y., Nagamatsu, T., Kohno, H., Egawa, K. and Arao, T. (2003) Effects of a 5-year exercise-centered health-promoting programme on mortality and ADL impairment in the elderly. *Age Ageing*, 32(6):585-92.

Oja, P. (2001) Dose response between total volume of physical activity and health and fitness, *Med Sci Sports Exerc*, 33: S428–S437.

Onat, A., Özhan, H., Metin-Esen, A., Albayrak, S., Karabulut, A., Can, G. and Hergenc, G. (2007) Prospective epidemiologic evidence of a "protective" effect of smoking on metabolic syndrome and diabetes among Turkish women—Without associated overall health benefit. *Atherosclerosis*. 193: 380-388.

Oshida, Y., Yamanouchi, K., Hayamizu, S. and Sato, Y. (1989) Long-term mild jogging increases insulin action despite no influence on body mass index or VO2 max. *J Appl Physiol*, 66(5):2206-10.

Paffenbarger, R. S., Wing A. L., Hyde R. T. and Jung D. L. (1983) Physical activity and incidence of hypertension in college alumni. Am J Epidemiol 117(3): 245-57.

Paffenbarger, R. S., Hyde, R. T., Wing, A. L. and Hsieh, C. C. (1986) Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med*, 314:605–613.

Paffenbarger, R. S., Blair, S. N., Lee, I. M. and Hyde, R. T. (1993a) Measurement of physical activity to assess health effects in free-living populations. *Med Sci Sports Exerc*, 25: 60–70.

Paffenbarger, R. S., Hyde R. T., Wing A. L., Lee I. M., Jung D. L. and Kampert J. B. (1993b) The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med,* 328: 538–545.

Panagiotakos, D. B., Pitsavos, C., Chrysohoou, C., Skoumas, J., Zeimbekis, A. and Papaioannou, I. (2003) Effect of leisure time physical activity on blood lipid levels: the ATTICA study. *Coron Artery Dis*, 14: 533–39.

Pankow, J. S., Folsom, A. R., Province, M. A., Rao, D. C., Eckfeldt, J. and Heiss, G. (1997) Family history of coronary heart disease and hemostatic variables in middle-aged adults. *Thromb Haemost*, 77: 87–93.

Pan, X.R., Li, G.W., Hu, Y.H., Wang, J.X., Yang, W.Y., An, Z.X., Hu, Z.X., Lin, J., Xiao, J.Z., Cao, H.B., Liu, P.A., Jiang, X.G., Jiang, Y.Y., Wang, J.P., Zheng, H., Zhang, H., Bennett, P.H. and Howard, B.V. (1997) Effects of diet and exercise in preventing

NIDDM in people with impaired glucose tolerance: The Da Qing IGT and Diabetes Study. *Diabetes Care.* 20:537–544.

Parker, E. D., Schmitz, K. H., Jacobs, D. R., Dengel, D. R. and Schreiner, P. J. (2007) Physical activity in young adults and incident hypertension over 15 years of follow-up: the CARDIA study. *Am J Public Health*, 97(4):703-9.

Park, S., Park, H., Togo, F., Watanabe, E., Yasunaga, A., Yoshiuchi, K., Shephard, R.J. and Aoyagi, Y. (2008) Year-Long Physical Activity and Metabolic Syndrome in Older Japanese Adults: Cross-Sectional Data From the Nakanojo Study. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 63:1119-1123.

Parkkari, J., Natri, A. and Kannus, P. (2000) A controlled trial of the health benefits of regular walking on a golf course. *Am J Med,* 109:102–08.

Pate, R. R., Pratt, M., Blair, S. N., Haskell, W. L., Macera, C. A. and Bouchard, C. (1995) Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA*, 273 (5), 402–407.

Paul DR, Novotny JA, Rumpler WV. Effects of the interaction of sex and food intake on the relation between energy expenditure and body composition. *Am J Clin Nutr*. 2004; 79(3):385-9.

Pearson, T. and Mensah, G. (2003) Markers of inflammation and cardiovascular disease. Application to clinical and public health practice: a statement for healthcare professionals from the centers for disease control and prevention and the American Heart Association. *Circulation*, 107: 499.

Peate, W. F., Lundergan, L. and Johnson, J. J. (2002) Fitness self-perception and Vo2max in firefighters. *J Occup Environ Med*, 44(6):546-50.

Peltonen, P., Marniemi, J., Hietanen, E., Vuori, I. and Ehnholm, C. (1981) Changes in serum lipids, lipoproteins, and heparin releasable lipolytic enzymes during moderate physical training in man: a longitudinal study. *Metabolism*, 30(5):518-26.

Petersen, A. M. and Pedersen, B. K. (2005) The anti-inflammatory effect of exercise. *J Appl Physiol*, 98: 1154–1162.

Phillips, D. I. W, Taylor, D. J. and Kemp, G. J. (1994) Programming of muscle metabolism in adults who experienced growth retardation in utero. *Diabetologia*, 37:A57.

Phillips, D. I. W. (1995) Relation of fetal growth to adult muscle mass and glucose tolerance. *Diabet Med*, 12:686–90.

Phillips, G. B., Jing, T. Y. and Laragh, J. H. (1997) Serum sex hormone levels in postmenopausal women with hypertension. *J Hum Hypertens,* 11: 523–526.

Phipps, K., Barker, D. J. P., Hales, C. N., Fall, C. H. D., Osmond, C. and Clark, P. M. S. (1993) Fetal growth and impaired glucose tolerance in men and women. *Diabetologia,* 36:225-228.

Pilegaard, H., Saltin, B. and Neufer, P. D. (2003) Exercise induces transient transcriptional activation of the PGC-1alpha gene in human skeletal muscle. *J Physiol*, 546: 851–858.

Plaisance, E. P. and Grandjean, P. W. (2006) Physical activity and high-sensitivity C-reactive protein. Sports Med, 36(5):443-58.

Poehlman, E. T., Melby, C. L. and Badylak, S. F. (1988(Resting metabolic rate and postprandial thermogenesis in highly trained and untrained males. *Am J Clin Nutr*, 47(5):793-8.

Pohjola-Sintonen, S., Rissanen, A., Liskola, P. and Luomanmaki, K. (1998) Family history as a risk factor of coronary heart disease in patients under 60 years of age. *European Heart Journal*, 19: 235–239.

Pollock, M. L., Miller, H. S., Linnerud, A. C. and Cooper, K. H. (1975) Frequency of training as a determinant for improving in cardiovascular function and body composition of middle-age men. *Arch Phys Med Rehab*, 56: 141- 145.

Pollock, M. L. and Jackson, A. (1977) Body composition: measurement and changes resulting from physical training. Proceedings National College Physical Education Association for men and women, 125-137.

Powell, K. E., Thompson, P. D., Caspersen, C. J. and Kendrick, J. S. (1987) Physical activity and the incidence of coronary heart disease. *Annu Rev Public Health*, 8: 253-287.

Powell, K. E. and Blair, S. N. (1994) The public health burdens of sedentary living habits: theoretical but realistic estimates. *Med Sci Sports Exerc*, 26:851-856.

Pratley, R. E., Hagberg, J. M., Dengel, D. R., Rogus, E. M., Muller, D. C. and Goldberg, A. P. (2000) Aerobic exercise training-induced reductions in abdominal fat and glucose-stimulated insulin responses in middle-aged and older men. *J Am Geriatr Soc*, 48(9):1055-61.

Prokopec, M. and Bellesle, F. (1993) Adiposity in Czech children followed from 1 month of age to adulthood: analysis of individual BMI patterns. *Ann Hum Biol,* 20:517-525.

Prud'homme, D., Bouchard, C., Leblance, C., Landry, F. and Fontaine, E. (1984) Sensitivity of maximal aerobic power to training is genotype-dependent. *Med Sci Sports Exerc,* 16: 489–493.

Rankinen, T., Perusse, L., Rauramaa, R., Rivera, M. A., Wolfarth, B. and Bouchard, C. (2004) The human gene map for performance and health-related fitness phenotypes: the 2003 update. *Med Sci Sports Exerc*, 36: 1451–1469.

Raven, P. B., Perrel, A. W, Robertson, D. M, Kohl, H. W, Kibbe, D. L, Trost, S. (2000) Measurement of moderate physical activity: advances in assessment techniques. *Med Sci Sports Exerc,* 33(9),S439-S516.

Raz, I., Rosenblit H. and Kark J. D. (1988a) Effect of moderate exercise on serum lipids in young men with low high density lipoprotein cholesterol. *Arteriosclerosis*, 8(3):245-51.

Raz, I., Israeli A., Rosenblit H. and Bar-On H. (1988b) Influence of moderate exercise on glucose homeostasis and serum testosterone in young men with low HDL-cholesterol level. *Diabetes Res*.; 9(1):31-5.

Ready, A. E., Drinkwater, D. T., Ducas, J., Fitzpatrick, D. W., Brereton, D. G. and Oades, S. C. (1995) Walking program reduces elevated cholesterol in women postmenopause. *Can J Cardiol*, 11(10):905-12.

Reaven, G. M. (1994) Syndrome X: is one enough? *Am Heart J*, 127:1439–42.

Rennie, K. L., McCarthy, N., Yazdgerdi, S., Marmot, M. and Brunner, E. (2003) Association of the metabolic syndrome with both vigorous and moderate physical activity. *Int J Epidemiol*, 32: 600–606.

Reuben, D., JuddHamilton, L. and Harris, T. (2003) The associations between physical activity and inflammatory markers in high-functioning older persons: MacArthur studies of succesfull aging. *J Am Geriatrics Soc,* 51: 1125–1130.

Ricardo, M. F, Markus, P., Aulikki, N. and Jaakko, T. (2002) ACE gene and physical activity, blood pressure, and hypertension: a population study in Finland. *J Appl Physiol*, 92: 2508 - 2512.

Rifai, N. and Ridker, P. (2002) High-sensitivity C-reactive protein: a novel and promising marker of coronary artery disease. *Clin Chem*, 47: 403–411.

Rinder, M. R., Spina, R. J. and Ehsani, A. A. (2000) Enhanced endothelium-dependent vasodilation in older endurance-trained men, *J Appl Physiol*, 88: 761–766.

Rising, R., Harper, I. T., Fontvielle, A. M., Ferraro, R. T., Spraul, M. and Ravussin, E. (1994) Determinants of total daily energy expenditure: variability in physical activity. *Am J Clin Nutr,* 59:800-4.

Rogers, M. W., Probst, M. M., Gruber, J. J., Berger, R. and Boone, J. B. (1996) Differential effects of exercise training intensity on blood pressure and cardiovascular response to stress in borderline hypertensive humans. *J hypertens*, 14: 1369-1375.

Roncaglioni, M. C., Santoro, L. and D'Avanzo, B. (1992) Role of family history in patients with myocardial infarction: an Italian case-control study. *Circulation,* 85: 2065–2072.

Rosengren, A. and Wilhelmsen, L. (1997) Physical activity protects against coronary death and deaths from all causes in middle-aged men. Evidence from a 20-year follow-up of the primary prevention study in Goteborg. *Ann Epidemiol,* 7: 69–75.

Ross, R. (1999) Atherosclerosis—an inflammatory disease. *N Engl J Med*, 340: 115–126.

Rose, S. B., Elley, C. R., Lawton, B. A. and Dowell, A. C. (2008) A single question reliably identifies physically inactive women in primary care. *N Z Med J*, 121(1268):U2897.

Rowell LB. (1993) Human cardiovascular control. New York: Oxford University Press.

Rubanyi, G. M. (1993) The role of endothelium in cardiovascular homeostasis and diseases. *J Cardiovasc Pharmacol*, 22(4):S1–S14.

Ruige, J. B., Dekker, J. M., Blum, W. F., Stehouwer, C. D., Nijpels, G., Mooy, J., Kostense, P. J., Bouter, L. M. and Heine, R. J. (1999) Leptin and variables of body adiposity, energy balance, and insulin resistance in a population-based study. The Hoorn Study. *Diabetes Care*, 22: 1097–1104.

Russell, A. P., Feilchenfeldt, J., Schreiber, S., Praz, M., Crettenand, A., Gobelet, C., Meier, C. A., Bell, D. R., Kralli, A., Giacobino, J. P. and Deriaz, O. (2003) Endurance training in humans leads to fiber type-specific increases in levels of peroxisome proliferator-activated receptor-gamma coactivator-1 and peroxisome proliferator-activated receptor-alpha in skeletal muscle. *Diabetes*, 52: 2874–2881.

Rutten, A., Ziemainz, H., Schena, F., Stahl, T., Stiggelbout, M., Auweele, Y. V., Vuillemin, A. and Welshman, J. (2003) Using different physical activity measurements in eight European countries. Results of the European Physical Activity Surveillance System (EUPASS) time series survey. *Public Health Nutr*, 6(4):371-6

Sakuta, H. and Suzuki, T. (2006) Physical activity and selected cardiovascular risk factors in middle-aged male personnel of self-defense forces. *Industrial Health*, 44: 184-189.

Sallis, J. F. and Saelens, B. E. (2000) Assessment of physical activity by self-report: status, limitations, and future directions. *Res Qu Exerc Sport,* 71(2):S1-S14.

Saltin, B. and Gollnick, P. D. (1983) Skeletal muscle adaptability, significance for metabolism and performance. In: Peachey LD, editor. Handbook of Physiology. Section 10: Skeletal muscle. Baltimore: *Williams and Wilkins*, 555.

Sandvik, L., Erikssen, J., Thaulow, E., Erikssen, G., Mundal, R. and Rodahl, K. (1993) Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *N Engl J Med*, 328:533–537.

Saris, W. H., Blair, S. N. and van Baak, M. A. (2003) How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st Stock Conference and consensus statement. *Obes Rev*, 4 (2), 101–114.

Savage, M. and Petratis, M. (1986) Thomson W, Berg K, Smith J, Sady S. Exercise training effects on serum lipids of prepubescent boys and adult men. *Med Sci Sports Exerc*, 18:197–204.

Schoeller, D. A., Shay, K. and Kushner, R. F. (1997) How much physical activity is needed to minimize weight gain in previously obese women? *Am J Clin Nutr*, 66(3):551-6.

Schaller, N., Seiler, H., Himmerich, S., Karg, G., Gedrich, K. and Wolfram, G. (2005) Estimated physical activity in Bavaria, Germany, and its implications for obesity risk: results from the BVS-II Study. *Int J Behav Nutr Phys Act*, 2:6.

Schmidt, M. E. and Steindorf, K. (2006) Statistical methods for the validation of questionnaires discrepancy between theory and practice. *Methods Inf Med*, 45(4):409-13.

Scriba, D., Aprath-Husmann, I., Blum, W. F. and Hauner, H. (2000) Catecholamines suppresses leptin release from in vitro differentiated subcutaneous human adipocytes in primary culture via β1- and β2-adrenergic receptors. *Eur J Endocrinol*, 143: 439–445.

Seals, D. R., Hagberg, J. M., Allen, W. K., Hurley, B. F., Dalsky, G. P., Ehsani, A. A. and Holloszy, J. O. (1984) Glucose tolerance in young and older athletes and sedentary men. *J Appl Physiol*, 56(6):1521-5.

Sesso, H. D., Paffenbarger, R. S. and Lee, I. M. (2000) Physical activity and coronary heart disease in men: The Harvard Alumni Health Study. *Circulation*, 29;102(9):975-80.

Shaper, A. G. and Wanamathee, G. (1991) Physical activity and ischaemic heart disease in middle-aged British men, British Heart Journal, 66:384-394.

Shephard, R. J. (2001) Absolute versus relative intensity of physical activity in a dose-response context. *Med Sci Sport Exer*, 33 (6): S400-S418.

Shephard, R. J. (2003) Limits to the measurement of habitual physical activity by questionnaires. *Br J Sports Med*, 37:197–206.

Short, K. R., Vittone, J. L., Bigelow, M. L., Proctor, D. N., Rizza, R. A., Coenen-Schimke, J. M. and Nair, K. S. (2003) Impact of aerobic exercise training on age-related changes in insulin sensitivity and muscle oxidative capacity. *Diabetes*, 52: 1888–1896.

Sigal, R. J., Kenny, G. P., Wasserman, D. H. and Castaneda-Sceppa, C. (2004) Physical activity/exercise and type 2 diabetes. *Diabetes Care,* 27:2518–2539.

Simoneau, J. A. and Bouchard, C. (1995) Genetic determinism of fiber type proportion in human skeletal muscle. *FASEB J*, 9: 1091–1095.

Simmons, R. (2005) Developmental origins of adult metabolic disease: concepts and controversies. *Trends Endocrinol Metab*, 16: 390–394.

Siscovick, D. C., Ekelund, L. G. and Hyde, J. S. (1998) Physical activity and coronary heart disease among asymptomatic hypercholesterolaemic men: The Lipid Research Clinics Coronary Primary Prevention Trial. *Am J Publ Health*, 78: 1428-31.

Skinner, C. J. and Holmes, D. (2001) The 2000–2001 National Diet and Nutrition Survey of Adults Aged 19–64 years: The Impact of Non-response. *University of Southampton*.

Slattery, M. L. (2004) Physical activity and colorectal cancer. *Sports Med*, 34, 239–252.

Slentz, C. A., Duscha, B. D., Johnson, J. L., Ketchum, K., Aiken, L. B., Samsa, G. P., Houmard, J. A., Bales, C. W. and Kraus, W. E. (2004) Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE--a randomized controlled study. *Arch Intern Med*, 12;164(1):31-9.

Smith, D. T., Hoetzer, G. L., Greiner, J. J., Stauffer, B. L. and DeSouza, C. A. (2003) Effects of ageing and regular aerobic exercise on endothelial fibrinolytic capacity in humans. *J Physiol*, 546: 289–298.

Smith, J. E. (2003) Effects of strenuous exercise on haemostasis. *Br J Sports Med*, 37(5):433-5.

Smith, S. C. and Blair, S. N. (1995) Preventing heart attack and death in patients with coronary disease. *Circulation*, 92:2–4.

Smith, S. C., Blair, S. N. and Bonow, R. O. (2001) AHA/ACC Scientific Statement: AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation*, 104: 1577– 9.

Soderberg, S., Ahren, B. and Jansson, J. H. (1999) Leptin is associated with increased risk of myocardial infarction. *J Intern Med*, 246: 409-418.

Stamakis, E., Hillsdon, M. and Primatesta. (2007) Domestic Physical Activity in Relationship to Multiple CVD Risk Factors. *Am J Prev Med*, 32(4):320-327.

Sternfeld, B., Bhat, A. K., Wang, H., Sharp, T. and Quesenberry, C. P. (2005) Menopause, physical activity, and body composition/fat distribution in midlife women. *Med Sci Sports Exerc*, 37: 1195–202.

Stern, M. P., Williams, K. and Gonzalez-Villalpando, C. (2004) Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care*, 27: 2676-2681.

Stewart, K. J., Bacher, A. C., Turner, K. L., Fleg, J. L., Hees, P. S., Shapiro, E. P., Tayback, M. and Ouyang, P. (2005) Effect of exercise on blood pressure in older persons: a randomized controlled trial. *Arch Intern Med*, 11;165(7):756-62.

Storlien, L. H., Pan, D. A., Kriketos, A. D., O'Connor, J., Caterson, I. D., Cooney, G. J., Jenkins, A. B. and Baur, L. A. (1996) Skeletal muscle membrane lipids and insulin resistance. *Lipids*, 31: S261–265.

Strath, S. J., Swartz, A. M., Bassett, D. R., O'Brien, W. L., King, G. A. and Ainsworth, B. E. (2000) Evaluation of heart rate as a method for assessing moderate intensity physical activity *Med Sci Sports Exerc*, 32:S465-SS70.

Sugiura, H., Sugiura, H., Kajima, K., Mirbod, S. M., Iwata, H. and Matsuoka, T. (2002) Effects of long-term moderate exercise and increase in number of daily steps on serum lipids in women: randomised controlled trial. *BMC Womens Health*, 2(1):3.

Sullivan, P. W., Morrato, E. H., Ghushchyan, V., Wyatt, H. R. and Hill, JO. (2005) Obesity, inactivity, and the prevalence of diabetes and diabetes-related cardiovascular comorbidities in the U.S., 2000-2002. *Diabetes Care*, 28(7):1599-603.

Sumner, A. E., Farmer, N. M., Tulloch-Reid, M. K., Sebring, N. G., Yanovski, J. A., Reynolds, J. C., Boston, R. C. and Premkumar, A. (2002) Sex differences in visceral adipose tissue volume among African Americans. *Am J Clin Nutr*, 76(5):975-9.

Sundquist, K., Qvist, J., Johansson, S. E. and Sundquist, J. (2005) The long-term effect of physical activity on incidence of coronary heart disease: a 12-year follow-up study. *Prev Med*, 41(1):219-25.

Sundstrom, J., Vallhagen, E. and Riserus, U. (2006) Risk associated with the metabolic syndrome versus the sum of its individual components. *Diabetes Care*, 29: 1673-1674.

Suzuki, I., Yamada, H., Sugiura, T., Kawakami, N. and Shimizu, H. (1998) Cardiovascular fitness, physical activity and selected coronary heart disease risk factors in adults. *J Sports Med Phys Fitness*, 38(2):149-57.

Swain, D. P. and Franklin, B. A. (2006) Comparison of cardioprotective benefits of vigorous versus moderate intensity aerobic exercise. *Am J Cardiol*, 97:141–147,

Swartz, A. M., Strath, S. J., Bassett, D. R., Moore, J. B., Redwine, B. A., Groer, M. and Thompson, D. L. (2003) Increasing daily walking improves glucose tolerance in overweight women. *Prev Med*, 37(4):356-62.

Taddei, S., Galetta, F., Virdis, A., Ghiadoni, L., Salvetti, G., Franzoni, F., Giusti, C. and Salvetti, A. (2000) Physical activity prevents age-related impairment in nitric oxide availability in elderly athletes, *Circulation*, 101: 2896–2901.

Taddei, S., Virdis, A., Ghiadoni, L., Salvetti, G., Bernini, G., Magagna, A. and Salvetti, A. (2001) Age-related reduction of NO availability and oxidative stress in humans, *Hypertension*, 38:274–279.

Tanaka, H., Clevenger, C. M., Jones, P. P., Seals, D. R. and DeSouza, C. A. (1998) Influence of body fatness on the coronary risk profile of physically active postmenopausal women. *Metabolism*, 47(9):1112-20.

Tanaka, H., Dinenno, F. A., Monahan, K. D., Clevenger, C. M., DeSouza, C. A. and Seals, D. R. (2000) Aging, habitual exercise, and dynamic arterial compliance. *Circulation,* 102: 1270–1275.

Tanaka, S., Togashi K., Rankinen T., Perusse L., Leon A. S., Rao D. C., Skinner J. S., Wilmore J. H. and Bouchard C. (2002) Is adiposity at normal body weight relevant for cardiovascular disease risk? Int J Obes Relat Metab Disord, 26(2): 176-83.

Tanasescu, M., Leitzmann, M. F., Rimm, E. B., Willett, W. C., Stampfer, M. J. and Hu, F. B. (2002) Exercise Type and Intensity in Relation to Coronary Heart Disease in Men. *JAMA,* 288: 1994-2000.

Tataranni, P. and Ravussin, E. (1995) Variability in metabolic rate: biological sites of regulation. *Int J Obesity*, 19: S102–S106.

Taylor, H., Jacobs, D. R., Shucker, B., Knudsen, J., Leon, A. S. and DeBacker, G. (1978) A questionnaire for the assessment of leisure time physical activities. *J Chronic Dis*, 31: 741-755.

Tchernof, A., Nolan, A. and Sites, C. (2002) Weight loss reduces C-reactive protein levels in obese postmenopausal women. *Circulation*, 105:564.

The Chief Medical Officer. (2004) At least five a week: evidence on the impact of physical activity and its relationship to health. Department of Health. London.

The Diabetes Prevention Program Research Group (DPP). (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 346:393–403.

The Expert Panel. (2001) Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA,* 285,2486-2497.

The Health of the Nation. (1995) A strategy for health in England, HMSO, London, 1992; More people more active more often. Physical activity in England: A consultation paper. Department of Health, London.

The Joint National Committee (JNC) on Detection, Evaluation, and Treatment of High Blood Pressure. (1993) The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNCV). *Arch Intern Med*, 153:154–83.

Thompson, P. D., Crouse, S. F., Goodpaster, B., Kelley, D., Moyna, N. and Pescatello, L. (2001) The acute versus the chronic response to exercise. *Med Sci Sports Exerc*, 33(6): S438-45.

Thong, F. S., Derave, W., Urso, B., Kiens, B. and Richter, E. A. (2003) Prior exercise increases basal and insulin-induced p38 mitogen-activated protein kinase phosphorylation in human skeletal muscle. *J Appl Physiol,* 94 :2337 –2341.

Thune, I., Njolstad I., Lochen M. L. and Forde O. H. (1998) Physical activity improves the metabolic risk profiles in men and women: the Tromso Study. Arch Intern Med, 158(15): 1633- 40.

Tikkanen, H. O., Härkönen, M., Näveri, H., Hämäläinen, E., Elovainio, R., Sarna, S. and Frick, M. H. (1991) Relationship of skeletal muscle fiber type to serum high density lipoprotein cholesterol and apolipoprotein A-I levels. *Atherosclerosis*, 90: 49–57.

Tikkanen, H. O., Hämäläinen, E., Sarna, S., Adlercreutz, H. and Härkönen, M. (1998) Associations between skeletal muscle properties, physical fitness, physical activity and coronary heart disease risk factors in men. *Atherosclerosis*, 137(2):377-89.

Tonino, R. P. (1989) Effect of physical training on the insulin resistance of aging. *Am J Physiol*, 256(3 Pt 1):E352-6.

Torjesen, P. A., Birkeland, K. I., Anderssen, S. A., Hjermann, I., Holme, I. and Urdal, P. (1997) Lifestyle changes may reverse development of the insulin resistance syndrome. The Oslo Diet and Exercise Study: a randomized trial. *Diabetes Care*, 20:26–31.

Trayhurn, P., Duncan, J. S., Hoggard, N. and Rayner, D. V. (1998) Regulation of leptin production: a dominant role for the sympathetic nervous system? *Proc Nutr Soc*, 57: 413–419.

Tremblay, A., Despres, J. P. and Leblanc, C. (1990) Effect of intensity of physical activity on body fatness and fat distribution. *Am J Clin Nutr*, 51:153–7.

Tremblay, A., Simoneau, J. and Bouchard, C. (1994) Impact of exercise intensity on body fatness and skeletal muscle metabolism. *Metab Clin Exp*, 43:814–8.

Troiano, R. P., Macera, C.A. and Ballard-Barbash R. (2001) Be physically active each day How can we know? *J Nutr*, 131: 451S–460S.

Tudor-Locke, C. and Bassett D. R. (2004) How many steps/day are enough? Preliminary pedometer indices for public health. Sports Med, 34(1):1-8.

Tully, M. A., Cupples, M. E., Chan, W. S., McGlade, K. and Young, I. S. (2005) Brisk walking, fitness, and cardiovascular risk: a randomized controlled trial in primary care. *Prev Med*, 41(2):622-8.

Tunstall-Pedoe, H. (1991) The Dundee coronary risk-disk for management of change in risk factors. *BMJ,* 303: 744– 7.

Tunstall, R. J., Mehan, K. A., Wadley, G. D., Collier, G. R., Bonen, A., Hargreaves, M. and Cameron-Smith, D. (2002) Exercise training increases lipid metabolism gene expression in human skeletal muscle. *Am J Physiol Endocrinol Metab*, 283: E66–E72.

Tuomilehto, J., Lindström, J., Eriksson, J.G., Valle, T.T., Hamalainen, H., Ilanne-Parikka, P., Keinanen-Kiukaanniemi, S., Laakso, M., Louheranta, A., Rastas, M., Salminen, V. and Uusitupa, M. (2001) Finnish Diabetes Prevention Study Group: Prevention of type

2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med.* 344:1343–1350.

Unwin, N. (2003) Definitions of the Metabolic Syndrome. *JAMA.* 289(10):1240.

Utter, A. C., Nieman, D. C., Shannonhouse, E. M., Butterworth, D. E. and Nieman, C. N. (1998) Influence of diet and/or exercise on body composition and cardiorespiratory fitness in obese women. *Int J Sport Nutr*, 8(3):213-22.

Vaitkevicius, P. V., Fleg, J. L., Engel, J. H., O'Connor, F. C., Wright, J. G., Lakatta, L. E., Yin, F. C. P. and Lakatta, E. G. (1993) Effect of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation,* 88 (1): 1456–1462.

van den Burg, P. J. M., Hospers J. E. H., Mosterd W. L., Bouma B. N. and Huisveld I. A. (2000) Aging, physical conditioning, and exercise-induced changes in hemostatic factors and reaction products. *J Appl Physiol*, 88(5): 1558 - 1564.

Wade, A. J., Marbut, M. M. and Round, J. M. (1990) Muscle fibre type and aetiology of obesity. *Lancet*, 335: 805–808.

Waden, J., Tikkanen, H., Forsblom, C., Fagerudd, J., Pettersson-Fernholm, K., Lakka, T., Riska, M., Groop, P. H., and FinnDiane Study Group. (2005) Leisure time physical activity is associated with poor glycemic control in type 1 diabetic women: the FinnDiane study. *Diabetes Care*, 28(4):777-82

Waldrop, T. G., Eldridge, F. L., Iwamoto, G. A. and Mitchell, J. H. (1996) Central neural control of respiration and circulation during exercise. In: *Rowell LB, Shepherd JT*, eds. Handbook of physiology, section 12: exercise: regulation and integration of multiple systems. New York: Oxford University Press, 333–80.

Wallace, A. M., McMahon, A. D. and Packard, C. J. (2001) Plasma leptin and the risk of cardiovascular disease in the west of Scotland coronary prevention study (WOSCOPS) *Circulation,* 104,3052-3056.

Wannamethee, S. G., Shaper, A. G. and Walker, M. (1998) Changes in physical activity, mortality, and incidence of coronary heart disease in older men. *Lancet,* 351:1603–08.

Wannamethee, S. G., Lowe, G. D., Whincup, P. H., Rumley, A., Walker, M. and Lennon, L. (2002) Physical activity and hemostatic and inflammatory variables in elderly men. *Circulation,* 105: 1785–1790.

Warburton, D. E., Katzmarzyk, P. T., Rhodes, R. E. and Shephard, R. J. (2007) Evidence-informed physical activity guidelines for Canadian adults. Can J Public Health, 98 Suppl 2:S16-68.

Wareham, N. J. and Rennie, K. (1998) The assessment of physical activity in individuals and populations: why try to be more precise about how physical activity is assessed? *Int J Obes Relat Metab Disord*, 22: S30–8.

Wareham, N. J., Jakes, R. W., Rennie, K. L., Mitchell, J., Hennings, S. and Day, N. E. (2002) Validity and repeatability of the EPIC-Norfolk Physical Activity Questionnaire. *Int J Epidemiol*, 31:168–74.

Wasserman, D. H. and Zinman, B. (1995) Fuel homeostasis. In: Ruderman N, Devlin JT, eds. The Health Professional's Guide to Diabetes and Exercise. Alexandria, VA: *American Diabetes Association*, 29–47.

Westerterp, K. R. and Plasqui, G. (2004) Physical activity and human energy expenditure. *Curr Opin Clin Nutr Metab Care*, 7:607–13.

Weihang, B. and Others, N. (1994) Persistence of multiple cardiovascular risk clustering related to syndrome X from childhood to young adulthood. *Arch Intern Med,* 154:1842-1847.

Wei, M., Macera C. A., Hornung C. A. and Blair S. N. (1997) Changes in lipids associated with change in regular exercise in free-living men. J Clin Epidemiol, 50(10): 1137-42.

Wei, M., Kampert, J. B., Barlow, C. E., Nichaman, M. Z., Gibbons, L. W., Paffenbarger, R. S. And Blair, S. N. (1999) Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *JAMA*, 27;282(16):1547-53.

Weinsier, R. L., Hunter, G. R., Zuckerman, P. A., Redden, D. T., Darnell, B. E., Larson, D. E., Newcomer, B. R. and Goran, M. I. (2000) Energy expenditure and free-living physical activity in black and white women: comparison before and after weight loss. *Am J Clin Nutr*, 71(5): 1138-1146.

Wennlof, A. H., Yngve, A., Nilsson, T. K. and Sjostrom, M. (2005) Serum lipids, glucose and insulin levels in healthy schoolchildren aged 9 and 15 years from Central Sweden: reference values in relation to biological, social and lifestyle factors. *Scand J Clin Lab Invest*, 65(1):65-76.

Westerterp, K. R., Brouns, F., Saris, W. H. and ten Hoor, F. (1988) Comparison of doubly labeled water with respirometry at low-and high-activity levels. *J Appl Physiol,* 65:53–6.

Westerterp, K. R. and Goran, M. I. (1997) Relationship between physical activity related energy expenditure and body composition: a gender difference. *Int J Obes Relat Metab Disord,* 21:184-8.

Westerterp, K. R. (1999) Assessment of physical activity in relation to obesity: current evidence and research issues. *Med Sci Sports Exerc*, 31: S522-S5S5.

Whaley, M. H. and Kaminsky, L. A. (2001) Epidemiology of physical activity, physical fitness, and selected chronic diseases, In: Roitman, J.L. (Ed.), ACSM's Resource Manual for Guidelines for Exercise Testing and Prescription, 4th ed. Lippincott Williams & Wilkins, Philadelphia, pp. 17–33.

Wheeler, G. D., Wall, S. R., Belcastro, A. N. and Cumming, D. C. (1984) Reduced serum testosterone and prolactin levels in male distance runners. *J Am Med Assoc,* 252: 514–516.

Whelton, S. P., Chin, A., Xin, X. and He, J. (2002) Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann Intern Med,* 136: 493–503.

Whitt, M. C., Dubose, K. D., Ainsworth, B. E. and Tudor-Locke, C. (2004) Walking patterns in a sample African American, Native American, and Caucasian women the Cross-Cultural Activity Participation Study. *Health Educ Behav*, 31: 45S–56S.

Wilder, L. B., Bachorik, P. S., Finney, C. A., Moy, T. F. and Becker, D. M. (1995) The effect of fasting status on the determination of low-density and high-density lipoprotein cholesterol. *Am J Med*, 99(4):374-7.

Williams, P. T. (2001) Health effects resulting from exercise versus those from body fat loss. Med Sci Sports Exerc, 33(6 Suppl): S611-21; discussion S640-1.

Williams, P. T. (2008) Vigorous exercise, fitness and incident hypertension, high cholesterol, and diabetes. Med Sci Sports Exerc, 40(6):998-1006.

Wilmore, J. H. (1989) Design issues and alternatives in assessing physical fitness among apparently healthy adults in a health examination survey of the general population. In: Assessing physical fitness and physical activity in population-based surveys. Washington, DC: *National Center for Health Statistics*. (DHHS-US publication 89-1253.).

Wilmore, J. H., Stanforth, P. R., Gagnon, J., Rice, T., Mandel, S., Leon, A. S., Rao, D. C., Skinner, J. S. and Bouchard, C. (2001) Heart rate and blood pressure changes with endurance training: the HERITAGE Family Study. *Med Sci Sports Exerc*, 33(1): 107-16.

Wilson, P. W., D'Agostino, R. B. and Levy, D. (1998) Prediction of coronary heart disease using risk factor categories. *Circulation,* 97: 1837–1847.

Wilson, P. W. F., D'Agostino, R. B., Parise H., Sullivan L. and Meigs, J. B. (2005) Metabolic Syndrome as a Precursor of Cardiovascular Disease and Type 2 Diabetes Mellitus. *Circulation.*112:3066-3072.

Wojtaszewski, J. F., Jorgensen, S. B., Frosig, C., MacDonald, C., Birk, J. B. and Richter, E. A. (2003) Insulin signalling: effects of prior exercise. *Acta Physiol Scand*, 178: 321–328.

World Health Organization (WHO). (1999) International Society of Hypertension Guidelines for the management of hypertension. *Journal of Hypertension*, 17: 151–183.

World Health Organization (WHO). (1999) Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO Consultation. Part 1:

diagnosis and classification of diabetes mellitus. Geneva, Switzerland: World Health Organization; 1999. Available at: http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf.

Yancey, A. K., Wold C. M. and McCarthy W. J. (2004a) Physical inactivity and overweight among Los Angeles County adults *Am J Prev Med,* 27,146-152.

Yancey, A. K., McCarthy W. J. and Taylor W. C. (2004b) The Los Angeles Lift Off: a sociocultural environmental change intervention to integrate physical activity into the workplace *Prev Med,* 38,848-856.

Yeh, E. and Willerson, J. (2003) Coming of age of c-reactive protein: using inflammation parameters in cardiology. *Circulation*, 107: 370.

Yeo, W. W. and Yeo, K. R. (2001) Predicting CHD risk in patients with diabetes mellitus. *Diabet Med,* 18: 341– 4.

Young, D. R., Haskell, W. L., Jatulis, D. E. and Fortmann, S. P. (1993) Associations between changes in physical activity and risk factors for coronary heart disease in a community-based sample of men and women: the Stanford Five-City Project. *Am J Epidemiol*, 15;138(4):205-16.

Young, J. C., Enslin, J. and Kuca, B. (1989) Exercise intensity and glucose tolerance in trained and nontrained subjects. *J Appl Physiol*, 67(1):39-43.

Yudkin, J. S., Stehouwer, C. D., Emeis, J. J. and Coppack, S. W. (1999) C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol*, 19: 972–978.

Yu, S., Yarnell, J. W. G., Sweetnam, P. M. and Murray, L. (2003) What level of physical activity protects against premature cardiovascular death? The Caerphilly study. *Heart*, 89:502-506.

Zambon, A., Deeb, S. S. and Bensadoun, A. (2000) In vivo evidence of a role for hepatic lipase in human apoB-containing lipoprotein metabolism, independent of its lipolytic activity. *J Lipid Res*, 41:2094–9.

Zhang, K., Werner, P., Sun, M., Pi-Sunyer, F. X. and Boozer, C. N. (2003) Measurement of human daily physical activity. *Obes Res,* 11:33–40.

Zhang, Y., Proenca, R., Maffei, M., Barone, M., Leopold, L. and Friedman, J. M. (1994) Positional cloning of the mouse obese gene and its human homologue. *Nature*, 372: 425–432.

Zierath, J. R. (2002) Invited review: Exercise training-induced changes in insulin signaling in skeletal muscle. *J Appl Physiol*, 93: 773–781.

Zmuda, J. M., Yurgalevitch, S. M., Flynn, M. M., Bausserman, L. L., Saratelli, A., Spannaus-Martin, D. J., Herbert, P. N. and Thompson, P. D. (1998) Exercise training has little effect on HDL levels and metabolism in men with initially low HDL cholesterol. *Atherosclerosis*, 137(1):215-21.

Zurlo, F., Lillioja, S., Esposito-Del Puente, A., Nyomba, B. L., Raz, I., Saad, M. F., Swinburn, B. A., Knowler, W. C., Bogardus, C. and Ravussin, E. (1990) Low ratio of fat to carbohydrate oxidation as predictor of weight gain: study of 24-h RQ. *Am J Physiol Endocrinol Metab,* 259: E650-657.