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# **PHYSICAL ACTIVITY AND MYOCARDIAL INFARCTION**

**–Epidemiological studies on the  
association between various types of  
physical activity and the risk of  
myocardial infarction, including certain  
aspects of methodology**

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## ABSTRACT

The aim of this thesis was to study the associations between physical activity during leisure time, occupational and household work, and established risk factors for cardiovascular disease, as well as the risk of acute myocardial infarction. Methodological aspects concerning the presence of recall bias in epidemiological case-control studies on physical activity and myocardial infarction were also considered.

The associations between physical activity and hypertension, cholesterol levels, and plasma fibrinogen were studied through a large cross-sectional study including 10,413 persons. In this study we observed that regular leisure-time physical activity was associated with markedly lower prevalence of the cardiovascular risk factors studied. Several aspects of occupational physical activity were related to favourable HDL-cholesterol levels, especially among men. However, overweight women who perceived their occupational workload as strenuous had an increased prevalence of hypercholesterolemia. Physical activity related to household work was not as strongly associated with the risk factors that were studied. However, perception of household work as physically strenuous was associated with higher plasma fibrinogen and unfavourably low HDL-cholesterol levels in women. A combination of regular exercise, a job involving a lot of standing or walking, and physically demanding household work was associated with markedly decreased prevalence of the cardiovascular risk factors studied, in both men and women.

The relationship between physical activity and risk of acute myocardial infarction was investigated in a large case-control study comprising 1,754 persons with myocardial infarction and 2,315 control subjects. We found that leisure-time physical activity was inversely related to the risk of myocardial infarction. In analyses stratified by body mass index, we observed this inverse relationship between leisure-time physical activity and myocardial infarction among lean, normal-weight and overweight persons, but not in the group of obese persons. A job that involved a lot of standing or walking was also associated with decreased risk of myocardial infarction, especially among women; whereas repetitive or heavy lifting at work, or perceiving occupational physical workload as strenuous, seemed to be associated with an increased risk. However, leisure-time physical activity was found to confer protection against myocardial infarction, irrespective of occupational physical activity level. The combination of regular exercise, standing or walking a lot at work, and having demanding household tasks was strongly related to a decreased risk of myocardial infarction.

In a methodological study including 78 persons who had suffered from a myocardial infarction and 243 control subjects, we found some differences in how individuals in these two groups remembered and reported previous physical activity levels. This kind of recall bias had the largest effect on the estimated associations between myocardial infarction, and repetitive or heavy lifting at work and perception of occupational physical workload. These findings should be taken into account when interpreting the results of retrospective case-control studies on physical activity and myocardial infarction.

## LIST OF PUBLICATIONS

This thesis is based on the following original articles/manuscripts, which will be referred to in the text by their Roman numerals.

- I. Fransson E, Alfredsson L, de Faire U, Knutsson A, Westerholm P. Leisure time, occupational and household physical activity, and risk factors for cardiovascular disease in working men and women: the WOLF study. *Scand J Publ Health* 2003; 31: 324-333.
- II. Fransson E, de Faire U, Ahlbom A, Reuterwall C, Hallqvist J, Alfredsson L. The risk of acute myocardial infarction: Interactions of types of physical activity. *Epidemiology* 2004;15:573-5 82.
- III. Fransson E, de Faire U, Ahlbom A, Reuterwall C, Hallqvist J, Alfredsson L. The effect of leisure-time physical activity on the risk of acute myocardial infarction depending on body mass index. Submitted.
- IV. Fransson E, Knutsson A, Westerholm P, Alfredsson L. Recall bias regarding physical activity in retrospective studies of myocardial infarction. Submitted.

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## LIST OF ABBREVIATIONS

CVD	Cardiovascular Disease
CHD	Coronary Heart Disease
BMI	Body Mass Index
PR	Prevalence Ratio
OR	Odds Ratio
CI	Confidence Interval
TEE	Total Energy Expenditure
BMR	Basal Metabolic Rate
MET	Metabolic Equivalents



# 1 INTRODUCTION

## 1.1 CARDIOVASCULAR DISEASE AND MYOCARDIAL INFARCTION

*Cardiovascular disease* (CVD) is a common term for diseases that affect the heart or other parts of the vascular system in the body. Examples of cardiovascular diseases are stroke, myocardial infarction, heart failure and peripheral artery disease. CVD is one of the leading causes of death globally, and the World Health Organisation estimates that 17.5 million people around the world died due to cardiovascular diseases in 2005, which corresponds to 30 percent of the total number of deaths<sup>1</sup>

The cardiovascular diseases which affect the coronary arteries of the heart are often called *coronary heart diseases* (CHD). *Myocardial infarction* is the most common diagnosis within CHD;<sup>2</sup> this is when the blood flow to a part of the heart muscle is suddenly disrupted, and the decrease in blood supply results in a damage to the heart muscle.

Both the incidence and mortality of cardiovascular diseases, including myocardial infarction, have steadily declined\* over the last 30 years in Sweden.<sup>2,3</sup> Despite this decline, cardiovascular diseases still constitute one of the largest public health issues in Sweden today.<sup>2</sup> Almost 39,000 people suffered from an acute myocardial infarction in Sweden during 2002, and almost 14,000 died within 28 days of their myocardial infarction.<sup>3</sup> Myocardial infarction is one of the leading causes of death among both men and women, but women are affected on average 10 years later than men. Compared with many other countries, Sweden has a high incidence of CHD.<sup>2</sup>

The major underlying cause of cardiovascular diseases and myocardial infarction is atherosclerosis.<sup>4</sup> In the atherosclerotic process, fibrous plaques build up within the inner layer of the artery walls and narrow the artery lumen, which reduces the blood flow. High levels of blood cholesterol, especially in the form of LDL cholesterol, play an important role in the formation of atherosclerotic plaques, but inflammatory mechanisms are also key issues in the development of atherosclerosis.<sup>5</sup> If an atherosclerotic plaque in a coronary artery ruptures, thrombocytes and plasma coagulation factors are activated and form a thrombus, which may occlude the coronary artery completely or in part. If an occlusion persists for more than 20 minutes, heart muscle cells start to die, and a permanent damage to the heart muscle will eventually develop.<sup>4</sup>

Several risk factors for CVD and myocardial infarction have been identified, and some of the major established risk factors are increasing age, male gender, smoking, hypertension, and dyslipidemia. Diabetes, obesity, unfavourable dietary habits and physical inactivity have also been shown to be important risk factors.<sup>2,6,7,8,9</sup>

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\* A small increase in the incidence of acute myocardial infarction has been registered after 2001, most likely due to the changes of diagnostic criteria for acute myocardial infarction implemented during 2001.<sup>3</sup>

## 1.2 PHYSICAL ACTIVITY, EXERCISE AND FITNESS

The following definitions have been suggested regarding physical activity, exercise and physical fitness.<sup>10</sup> However, the definitions are not always consistently used, and the terminology regarding physical activity, exercise and fitness may vary from one study to another.

*Physical activity* is defined as any bodily movement produced by skeletal muscles that substantially increase energy expenditure. *Leisure-time physical activity* is a broad descriptor of activities performed during free time, based on personal interests and needs. *Exercise* is a type of leisure-time physical activity that is planned, structured, and repetitive, and done to improve or maintain physical fitness. *Occupational physical activity* is associated with the performance of a job, usually within the time frame of an 8-hour working day.

*Physical fitness* is a set of attributes (i.e. cardiorespiratory endurance, skeletal muscle strength, or flexibility) that people have or achieve, which relate to the ability to perform physical activity. *Cardiorespiratory fitness* reflects the ability of the cardiovascular and respiratory systems to supply oxygen to the working muscles during heavy dynamic exercise.

Physical, as well as cardiorespiratory fitness is influenced by genetic factors and individual characteristics (age, sex, body size, trainability etc), as well as environment and lifestyle factors (e.g. amount and type of exercise).<sup>11</sup> The individual response in change of maximum oxygen uptake ( $\dot{V}O_{2\max}$ ) after a standardised exercise programme may be very heterogeneous.<sup>12</sup> It has been proposed that about 35 percent of the variability in cardiorespiratory fitness level ( $\dot{V}O_{2\max}$ ) may be attributed to physical activity level.<sup>13</sup>

## 1.3 PHYSICAL ACTIVITY AND FITNESS IN RELATION TO CVD MORTALITY AND MORBIDITY

A large number of observational studies have found that regular leisure-time physical activity and exercise are associated with decreased risks of CVD and CHD morbidity and mortality.<sup>13,14,15,16,17,18</sup> Most studies have found a clear dose-response pattern, showing continuously lower risk with higher levels of physical activity.<sup>13</sup> Several cross-sectional studies have also found that leisure-time physical activity is associated with decreased prevalence of established risk factors for CVD, such as hypertension, dyslipidemia, plasma fibrinogen, inflammatory markers and obesity.<sup>19,20,21,22,23</sup>

In recent years, it has been pointed out that it does not seem necessary to be engaged in vigorous exercise to obtain health benefits.<sup>15</sup> Compared with being sedentary, even rather moderate intense physical activity will probably lower the risk of disease. The suggested recommendation regarding physical activity to the healthy general population is that they should be physically active for at least 30 minutes on most days of the week, preferably everyday, and that the activities should be of moderate intensity, which is equivalent to a brisk walk (9-13 minutes per kilometer).<sup>24</sup>

Directly after vigorous physical exertion, a transient increased risk of sudden cardiac death and myocardial infarction has been observed.<sup>25,26,27,28</sup> In most of these studies, the acutely increased risk was more pronounced among those who were not usually physically active and who suddenly participated in vigorous exercise, while the lowest risk was observed among those who usually exercised on a regular basis.<sup>25,26,28</sup> One study found that the effect-modification by habitual physical activity level was U-shaped.<sup>27</sup> It should be pointed out that acute coronary events in connection with physical activity and exercise are very rare, and the transient increased risk is far outweighed by the long-term beneficial effect of being physical active.<sup>26,28</sup>

Like physical activity, cardiorespiratory fitness has also been shown to be related to decreased risk of mortality and morbidity.<sup>13,29</sup> However, it seems as if the dose-response patterns differ between physical activity and cardiorespiratory fitness in relation to CVD. In general, the association between fitness and CVD seems to be stronger than for physical activity. Furthermore, a steep drop in the CVD risk has been observed around the 25<sup>th</sup> percentile of the fitness distribution, while the association between physical activity and CVD seems to be more linear.<sup>13</sup>

Earlier studies of physical activity in relation to mortality and morbidity were predominantly conducted in male study populations. Today several large studies focusing on women, such as the Nurses' Health Study and Women's Health Initiative Observational Study, have shown that the inverse relationship between leisure-time physical activity and CVD are valid also in women.<sup>30,31,32</sup>

Nevertheless, there is a need to evaluate the associations between physical activity and CVD risk in different subgroups, and in various populations. Lately there has been a great deal of interest in the question of whether physical inactivity or obesity is the most important predictor of CVD. It has been suggested that physical activity or a high level of cardiorespiratory fitness attenuates much of the increased risk seen in connection with overweight and obesity.<sup>33</sup> However, the results have not always been consistent, and more studies are needed, especially in women.

Although one of the first studies in the field of physical activity, conducted by Morris and colleagues in the 1950s, evaluated the effect of occupational physical activity in relation to coronary heart disease,<sup>34</sup> more recent studies of physical activity in relation to CVD and CHD have mostly focused on leisure-time physical activity and exercise.<sup>14</sup> In some studies, a measure of total activity or total energy expenditure has been used, including all types of physical activities during leisure, work and domestic work. Household activities have sometimes been included in the measure of leisure-time physical activity and other times in occupational physical activity. When studied separately, the results from later studies regarding occupational physical activity have not been as consistent as for leisure-time physical activity,<sup>35,36,37,38,39,40</sup> and physical activity by household work has rarely been studied as a separate factor.

In leisure time, people are free to choose type and intensity of physical activity. They are also able to adjust their activity level if they are not feeling perfectly healthy one day. This is not always the case with occupational activity, and maybe not for

household activity either. Furthermore, leisure-time activities are mostly conducted during a limited time frame (e.g. 30 minutes – 1 hour), while occupational activity often continues for eight hours during a normal working day. The long duration of physical activity in occupational work puts quite different demands on the physical capacity of the individual. In order to be able to carry on with a physical work for a long time (i.e. a working day) the workload should not exceed 40% of an individual's maximal aerobic power.<sup>11</sup>

#### **1.4 BIOLOGICAL MECHANISMS**

Several biological mechanisms by which physical activity is supposed to affect the risk of cardiovascular disease have been proposed, as described below.

Hypertension is one of the major risk factors for CVD and CHD. A synthesis of 44 randomised controlled trials on the effect that aerobic exercise programmes lasting for at least 4 weeks have on blood pressure, showed an average reduction of systolic and diastolic blood pressure of 3.4 / 2.4 mmHg in the exercise groups. A more pronounced reduction in blood pressure was observed among hypertensive persons, compared with normotensive persons.<sup>41</sup> The mechanism behind the lowering effect of exercise on blood pressure is not clear. Decreased total peripheral resistance by reduced sympathetic nerve activity and improved endothelial function has been proposed as one likely explanation.<sup>42</sup> Immediately after an aerobic exercise session, resting blood pressure is reduced, a phenomenon which is called “post-exercise hypotension”.<sup>42,43</sup> Post-exercise hypotension may persist up to 16-22 hours after ending the exercise session, and has been noted already at an exercise intensity of 40% of maximum oxygen uptake. Post-exercise hypotension may be part of the long-term effect of regular exercise on blood pressure, but is unlikely to provide a full explanation of this effect.

Dyslipidemia is another major risk factor for CVD, and it seems as if aerobic exercise of moderate to hard intensity can improve blood lipid profiles. Most consistent results have been found regarding increased HDL-cholesterol levels after at least 12 weeks of exercise intervention.<sup>44</sup> The results regarding total cholesterol, LDL cholesterol and triglycerides have been less consistent. Physical activity probably increases the synthesis of HDL cholesterol by increasing lipoprotein lipase activity, an important enzyme in triglyceride hydrolysis. Reduced hepatic lipase activity and decreased removal of apo A1 is also likely to play a part in this process.<sup>45,46</sup> Even if increased physical activity does not always result in lower LDL-cholesterol levels, physical activity appears to increase the average size of the LDL particle, and reduce the number of small, dense LDL particles, which are considered to be more atherogenic.<sup>45</sup>

Furthermore, physical activity and exercise have been found to improve glucose metabolism and insulin sensitivity, and decrease the risk of diabetes type II.<sup>47,48,49</sup> Improved glucose transportation in the skeletal muscle by increased expression and/or translocation of glucose transporter isoform 4 (GLUT4) protein, as well as other adaptations in the skeletal muscle such as increased capillarization, appears to contribute to this effect.<sup>48</sup>

The hypothesis that regular physical activity lowers C-reactive protein (CRP) levels and reduces inflammation is supported by cross-sectional and also a few intervention studies.<sup>50</sup> The mechanism of long-term effects of regular exercise on inflammation and CRP is not fully understood, but exercise training probably reduces the production of certain cytokines (mainly IL-6), which plays a part in the synthesis of CRP. Some of the inflammatory lowering effect may also be mediated by the lower body weight associated with regular exercise, as obesity and adipose tissue increase the inflammatory processes in the body.<sup>50,51</sup>

Regarding the effect of regular physical activity on the coagulation and fibrinolytic system, the data are rather sparse. It appears that regular physical activity decreases platelet adhesion and aggregation.<sup>52</sup> Regarding plasma fibrinogen, the data are conflicting; cross-sectional studies and some small intervention studies indicate reduced fibrinogen levels in association with exercise training, while other studies have not observed any effect on fibrinogen levels after exercise intervention.<sup>52,53</sup>

Exercise training has also been shown to increase myocardial perfusion in patients with CHD. Earlier it was thought that formation of collaterals and regression of coronary artery stenosis was the explanation for this, but later studies have found that the most likely explanation for the increased myocardial perfusion after exercise training is improved endothelial function in the coronary arteries.<sup>54</sup>

It should be noted that the described effects of physical activity and exercise on mediating risk factors, such as blood pressure and blood lipids, are based on group averages and may vary considerably between individuals.<sup>12</sup>

## **1.5 MEASURING PHYSICAL ACTIVITY IN EPIDEMIOLOGICAL STUDIES**

There are several ways of measuring physical activity, using both objective and subjective methods.<sup>55</sup> Objective assessments of physical activity can be made using certain instruments which register bodily movements, e.g. pedometers and accelerometers, or indirectly by measuring heart rate. Subjective methods rely on self-reports of physical activity. Subjective methods include more or less detailed questionnaires, physical activity diaries, and interviews. Sometimes a measure of energy expenditure is used instead of physical activity.

Even though physical activity and energy expenditure are closely related, these two terms describe different things. Physical activity is a behaviour, while increased energy expenditure is the result of that behaviour.<sup>56</sup> Total energy expenditure (TEE) can be divided into three major components: basal metabolic rate (BMR), diet-induced energy expenditure, and energy expenditure associated with physical activity.<sup>55,57</sup> BMR is the energy required at rest to maintain basal body functions (temperature, circulation and respiration), and accounts for 60-70 % of TEE. Diet-induced energy expenditure is the energy expenditure associated with digestion and absorption of food, and accounts for approximately 10 % of TEE. Physical activity-related energy expenditure encompasses energy expenditure from all types of activities in daily life: occupational, leisure-time,

and household activities, transportation, personal care, keeping an upright posture, fidgeting, etc., and accounts for the remaining part of the TEE.

One of the methods that are used to assess energy expenditure is the doubly-labelled water method.<sup>55,57</sup> This method is expensive and rather complicated to carry out. As a result, the doubly-labelled water method is usually not suitable for large-scale epidemiological studies. However, it is often used in validation studies of other instruments which are aimed at assessing physical activity or energy expenditure.

In most large-scale epidemiological studies, various questionnaires are used to measure physical activity or energy expenditure. By using questionnaires it is possible to approach a large number of people in a short period of time; this is a relatively inexpensive method, and it does not interfere with people's everyday life (except for the time and effort required to fill in the questionnaire). However, there are several limitations when measuring physical activity by questionnaires. Questionnaires rely on self-reports, and the participants may under- or overestimate their activity level. In general, people tend to over-report their habitual physical activity level, most likely due to social desirability.<sup>58</sup> Several personal characteristics may influence the recall of physical activity, e.g. age, educational level, fitness level, body mass index, and the cultural context in which the subject is living.<sup>58,59,60</sup> How the questionnaire is worded, the number of items included, and the length of the time period covered by the questionnaire (e.g. the past week, month, year, or life-time) are also of importance.

Attempts have been made to construct standardised and validated questionnaires regarding physical activity, which could be used in different populations and in various settings.<sup>61,62</sup> This would clearly improve the comparability of results between studies. However, it has been pointed out that these questionnaires need further development,<sup>60,63</sup> and they are not yet widely used. To date most studies have used their own uniquely developed questionnaire regarding physical activity. Questionnaires regarding physical activity in epidemiological studies can be classified into three groups according to how detailed they are: the global questionnaire, the recall questionnaire, and the quantitative history instruments.<sup>56</sup> Global questionnaires most often cover one to four items regarding physical activity, and physical activity can only be divided into a few categories. Recall questionnaires usually comprise 10-20 items, and are more detailed regarding types, frequency and duration of physical activity. From this type of questionnaire it is possible to derive physical activity scores with several levels, which enables further dose-response analysis in relation to different health outcomes. Quantitative history questionnaires are usually very detailed, and include more than 20 items. From this type of questionnaire it is possible to derive physical activity scores on a continuous scale.

If detailed information of type, duration and intensity of various physical activities are collected, the information on physical activity can be used to estimate activity-related energy expenditure. A coding scheme has been developed, which links approximately 600 different physical activity modalities with their metabolic equivalent (MET) levels.<sup>64</sup> A MET for a specified activity is defined as the ratio of the work metabolic rate for that activity to a standard resting metabolic rate (i.e. the multiple of the resting MET level). One MET is defined as the energy expenditure for sitting quietly, which

approximately corresponds to 3.5 ml O<sub>2</sub> per kg body weight and minute, or 1 kcal per kg body weight and hour for an average adult person.<sup>65</sup>

## **1.6 MISCLASSIFICATION OF PHYSICAL ACTIVITY IN EPIDEMIOLOGICAL STUDIES**

As has been pointed out above, large-scale epidemiological studies most often have to rely on information about physical activity collected by self-reports in questionnaires. It is therefore likely that misclassification of physical activity will occur to some extent, i.e. some sedentary people will report that they are physically active, and some active persons will incorrectly classify themselves as inactive. If the aim of the study is to relate physical activity to a certain health outcome, this misclassification of physical activity level may produce a bias in the estimated relationship between physical activity and outcome.

The misclassification of an exposure, in this case physical activity, can be of two types: non-differential or differential with regard to the outcome.<sup>66</sup> In the former case, the misclassification is not related to the outcome; i.e., the likelihood of being placed in an incorrect physical activity category is the same among those who have the disease, as among those without the disease. This type of misclassification tends to dilute the estimated relationship between exposure and outcome towards the null-value, at least when the two most extreme groups are compared with each other. In the case of differential misclassification, the misclassification is dependent on the outcome; i.e., the probability or direction of the misclassification differs between those who have the disease and those who do not. Differential misclassification of exposure with regard to the outcome will most likely result in either an under- or overestimation of the association between exposure and outcome.

When physical activity is based on self-report, non-differential misclassification of physical activity may exist in epidemiological studies. If the follow-up time is long in cohort studies, increasing non-differential misclassification is also likely to occur over time, since people may change physical activity patterns during the years, and the baseline physical activity level may be less and less valid. This may result in seriously diluted estimates between physical activity and outcome.<sup>67</sup> However, this problem could, at least in part, be overcome if exposure information is gathered repeatedly during the follow-up period.

Differential misclassification is seldom a problem in cohort studies, as the exposure information is usually collected before the cases have been diagnosed with the disease. However, in case-control studies (and to some extent also in cross-sectional studies), where information on previous physical activity level is collected retrospectively, i.e. after the cases have been diagnosed as cases, the problem of differential misclassification may be present. The hypothesis is that individuals who have been diagnosed with a disease remember and report previous exposure differently compared with those who have not been given a diagnosis. This is probably more likely to occur when there is common knowledge, or concern, among people in general about the association between the studied exposure and outcome. This kind of differential

misclassification of exposure is often called *recall bias*.<sup>66</sup> It has been suggested that the likelihood of recall bias is larger if recall of the exposure in general is poor.<sup>68</sup>

Several studies have evaluated the ability to recall physical activity in the past.<sup>69,70,71,72,73</sup> However, there is still limited knowledge on how different personal characteristics influence the process of recalling physical activity, and further studies have been called for, focusing on potential sources of bias in the recall of physical activity when using questionnaires.<sup>56</sup> The potential role of recall bias in retrospective studies of physical activity and coronary heart diseases has, for example, not yet been evaluated. However, the presence of recall bias has been found in other studies of various exposures and outcomes, e.g. in studies of family history and breast cancer, family history and lymphoma, tanning ability and melanoma, and lifestyle factors and hypertension.<sup>74,75,76,77</sup>

## **2 AIMS OF THE THESIS**

The general objective of the thesis was to evaluate the association between various types of physical activity and the risk of cardiovascular disease, with special focus on myocardial infarction.

The specific aims of the thesis were:

-To study the associations between leisure-time, occupational and household physical activity, and selected risk factors for cardiovascular disease.

-To study the association between leisure-time, occupational and household physical activity, and the risk of first-time acute myocardial infarction, as well as the interaction between these different types of physical activities with regard to the risk of myocardial infarction.

-To study the joint effect of leisure-time physical activity and body mass index with regard to the risk of first-time acute myocardial infarction.

-To evaluate the potential influence of recall bias in retrospective case-control studies of physical activity and myocardial infarction.

## **3 MATERIAL AND METHODS**

### **3.1 STUDY DESIGN AND SUBJECTS**

#### **3.1.1 The WOLF study (paper I)**

The Work, Lipids, and Fibrinogen (WOLF) study was conducted in 1992-1998, with the first part in Stockholm County (1992-1995), and the second part in the Jämtland and Västernorrland area (1996-1998). The initial aim of the WOLF study was to examine the associations between occupational characteristics and cardiovascular risk factors. The study participants were recruited through the occupational health service units at approximately 60 companies in the two study areas. Not all employees of these companies were included in the study, but all employees at certain workplaces were asked to participate. Individuals who were living abroad or chronically ill were not included in the study population. The participants were asked to fill in an extensive questionnaire, covering a large range of occupational, lifestyle and health-related topics. They also participated in a small clinical examination, including measurements of weight, height and blood pressure. Blood samples were also collected.

In total, 10,413 persons (7,168 men and 3,245 women) both answered the questionnaire and took part in the clinical examination. This corresponds to 82% of the invited subjects. The mean age was 42 years (range 19-70 years).

#### **3.1.2 The SHEEP study (papers II and III)**

The Stockholm Heart Epidemiology Program (SHEEP) study is a population-based case-control study of first-time acute myocardial infarction. Case identification was carried out during 1992-1993 (men), and 1992-1994 (women). The study base was defined as all Swedish citizens, aged 45-70 years (up to 31 October 1992, the upper age limit was 65 years), living in Stockholm County, and free from clinically diagnosed myocardial infarction. The cases were identified from the coronary and intensive-care units at the internal medicine departments at all the emergency hospitals within the Stockholm County area, the hospital discharge register for the Stockholm County area, and through death certificates from the National Cause of Death Register.

In total, 1,754 cases (1,204 men and 550 women) of first-time acute myocardial infarction were included in the study. For each case, at least one control subject was sampled from the study base, stratified for age (5-year intervals), sex and hospital catchment area. In total, 2,315 controls (1,538 men and 777 women) were included in the study. As in the WOLF study, the SHEEP participants were asked to fill in an extensive questionnaire on occupational, lifestyle and health-related topics. In the case of a fatal myocardial infarction, or if the case had died before he or she had been contacted, the questionnaire was sent to a close relative. This was done at the earliest 6 months after the date of death of the case subject.

The participation rate was 78 % for cases (84 % for non-fatal cases and 62 % for fatal cases), and 72 % for controls. There was a slightly higher response rate for men than for women.

The surviving cases and their controls were invited to a clinical examination, including measurements of weight, height and blood pressure. Blood samples were also collected.

### **3.1.3 The recall bias study (paper IV)**

In 2005, we matched the WOLF study with the Swedish Myocardial Infarction Register and the Hospital Discharge Register, to find out who had suffered from a non-fatal myocardial infarction from the time of inclusion in the WOLF study up to 31 December 2003. During the follow-up, 104 persons (95 men and 9 women) in the WOLF population had a first-time non-fatal myocardial infarction event registered. Of these, 15 had died due to other reasons during follow-up, or had declined further participation in the WOLF study, which left 89 subjects to be included in the recall bias study. Two more cases were later found to have died between the end of follow-up and the start of the study, and one case did not have a matching address in the Swedish Population and Address Register. Three control subjects for each case (267 subjects) were selected from the WOLF study population, matched for sex, age (5 year-intervals) and study area.

In total, 78 cases (6 women and 72 men), and 243 control subjects (22 women and 221 men) responded to the questionnaire in the recall bias study, which corresponds to 91% of the invited participants. The mean age among the respondents was 61 years (range 39-76 years).

## **3.2 EXPOSURES**

### **3.2.1 Physical activity (papers I-IV)**

Exposure information about the different aspects of physical activity was collected by questionnaires in all studies included in this thesis. The questions regarding physical activity were constructed in similar ways in the WOLF, SHEEP and recall bias studies, with some small differences, as described below.

For all questions regarding physical activity, the WOLF questionnaire concerned activity level at the time of inclusion in the study. In the SHEEP study the participants were asked to report activity level during different age intervals (15-24, 25-34, 35-44, 45-54, 55-64, 65-69 years of age). The questions in the recall bias study were constructed in the same way as in the WOLF study, but the respondents were asked to report past activity level in 5-year intervals from 1990 to 2004 (1990-1994, 1995-1999, 2000-2004), as well as present activity level in 2005.

#### *3.2.1.1 Leisure-time physical activity / exercise (papers I-IV)*

In papers I and IV leisure-time physical activity / exercise corresponds to the question: How often do you exercise? Four predefined answers were given: 1) never, 2) very little, occasional walks, 3) now and then, and 4) regularly.

The participants were asked to include walking or biking to and from work.

In papers II and III (the SHEEP study) the following definition was added to the above question on how often the study participants had exercised during different age intervals:

“Exercise is defined as sports, fitness training, or other physically demanding leisure-time activities, which last for at least 30 minutes, and make you out of breath.”

Four predefined answers were given: 1) very little, 2) occasional walks, 3) now and then, and 4) regularly (at least once per week).

In the SHEEP study we also used information given in a further question, for those who reported regular exercise. In that question the respondents were asked about how often (1 time/week, 2-3 times/week, more than 3 times/week) and which type of exercise they usually participated in, such as weight training (barbells, rowing machine, or the like), moderate exercise (jogging, table tennis, folk dancing, golf, gymnastics, horse riding, or the like), or vigorous exercise (football, handball, cross-country skiing, running, squash, tennis, or the like).

### *3.2.1.2 Occupational physical activity*

The following aspects of occupational physical activity were included in the thesis:

#### *Sitting / not sitting at work (papers I, II, IV)*

In the WOLF study and recall bias study (paper I and paper IV), two levels were predefined: Sitting more than half of the working day: yes or no.

In the SHEEP study (paper II), three levels were predefined: Sitting almost all of the working day, sitting approximately half of the day, or sitting less than half of the working day.

#### *Lifting or carrying burdens at work (papers I, II, IV)*

Lifting or carrying burdens of more than 5 kg during at least 2 hours per working day: yes or no. (Papers I, II, IV)

Lifting or carrying burdens of more than 20 kg (women) or 30 kg (men) at least five times per working day: yes or no. (Papers I, II, IV)

#### *Perceived physical load at work (papers I, II, IV)*

The study participants in the WOLF, SHEEP and recall bias studies (papers I, II, IV) were asked to report how physically demanding they thought their work was. They were asked to estimate this on a 15-graded scale (0-14: very, very light to very, very demanding).

### *3.2.1.3 Household physical activity*

#### *Demanding household tasks (papers I, II, IV)*

The respondents were asked to report if their part of the household work included physically demanding tasks, such as shovelling snow, mowing grass and the like: yes or no (papers I, II, IV).

#### *Perceived physical load in household work (papers I, IV)*

In the WOLF and recall bias studies (papers I, IV) the study subjects reported how physically demanding they thought their household work was. As with the corresponding question for perceived physical occupational load, this was estimated on a 15-graded scale (0-14: very, very light to very, very demanding).

#### *Total physical activity (papers I, II)*

In the WOLF and SHEEP study, a measure of a combination of leisure-time physical activity, sitting at work and demanding household activities was constructed and was labelled “total activity”. Participants were considered to be physically passive if they reported leisure-time physical activity seldom or sometimes, had jobs where they were seated during the major part of their working hours, and did not have demanding household activities. Those who reported regular leisure-time physical activity, were seated less than 50% of the working day, and had physically demanding household tasks were considered as active. Subjects who reported that they were active in at least one of these aspects, but not in all, were considered as “somewhat active”.

### **3.2.2 Body Mass Index (paper III)**

In paper III, the joint effect of leisure-time physical activity and body mass index (BMI) was evaluated. BMI was defined as weight (kg) / height (m)<sup>2</sup>. Data from the clinical examination were used as the primary source of information, which were available for 88 % of the non-fatal cases and 68 % of the controls. For the fatal cases, and the non-fatal cases and controls for whom we did not have data from the clinical examination, information on weight and height from the questionnaire was used. Four BMI categories were constructed: lean (BMI<20), normal weight (20≤BMI<25), overweight (25≤BMI<30), and obesity (BMI≥30).

## **3.3 OUTCOMES**

### **3.3.1 Cardiovascular risk factors / risk indicators (paper I)**

The clinical examination in the WOLF study was carried out at the different occupational health service units by specially trained nurses. All participants were asked not to eat or drink anything (except water) for nine hours before the clinical examination. Blood pressure was measured on the right arm in supine position after five minutes' rest. Two measurements were taken, separated by one minute. The mean of the two measurements was used as the recorded blood pressure. Total cholesterol and HDL (high density lipoprotein) cholesterol were measured enzymatically. HDL cholesterol was measured after precipitation with phosphotungstic acid and magnesium chloride. Plasma fibrinogen was determined by a spectrophotometric test. All analyses of blood lipids and plasma fibrinogen were carried out at the same laboratory (CALAB Medical Laboratories AB, Stockholm, Sweden).

#### *3.3.1.1 Hypertension*

Hypertension was defined as having a systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg, or current medical treatment for hypertension.

### 3.3.1.2 *Hypercholesterolemia*

Hypercholesterolemia was defined as total cholesterol level >6.4 mmol/l.

### 3.3.1.3 *Low HDL cholesterol*

Low HDL-cholesterol level was defined as a HDL-cholesterol level <1.0 mmol/l for men, and <1.2 mmol/l for women.

### 3.3.1.4 *High plasma fibrinogen*

Plasma fibrinogen was considered to be elevated if it was  $\geq 3.66$  g/l for men, and  $\geq 3.83$  for women, corresponding to the 90<sup>th</sup> percentile for each gender in the Stockholm part of the study population.

## 3.3.2 **Acute myocardial infarction (paper II and III)**

Acute myocardial infarction was defined using criteria set up by the Swedish Association of Cardiologists in 1991. These criteria included: 1) certain symptoms, 2) specified changes in blood levels of the enzymes serum creatine kinase and serum lactate dehydrogenase, 3) and specified changes in ECG, or 4) autopsy findings of myocardial necrosis compatible with the time of disease onset. Two of the first three criteria, or autopsy findings, were required to be met in order to result in the diagnosis of an acute myocardial infarction. A myocardial infarction was considered as fatal if the patient died within 28 days of diagnosis. The SHEEP study included both non-fatal and fatal cases.

## 3.4 **STATISTICAL ANALYSES**

### 3.4.1 **Paper I**

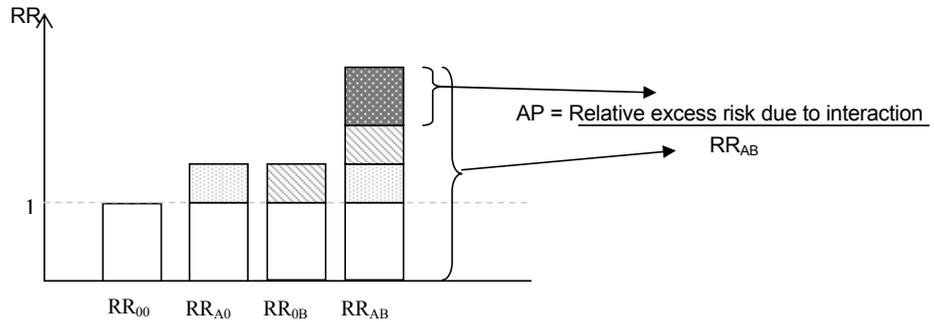
To evaluate the associations between different aspects of physical activity and the selected risk factors, adjusted prevalence ratios were calculated by the Mantel-Haenszel's method. Test-based 95% confidence intervals were calculated to assess the random variability in the estimated prevalence ratios.<sup>78</sup>

### 3.4.2 **Papers II and III**

In paper II and paper III unconditional logistic regression was used to calculate odds ratios (OR) together with 95% confidence intervals, to estimate the associations between physical activity and the risk of acute myocardial infarction.<sup>79</sup> In epidemiological case-control studies, the odds ratio can be viewed as an estimate of the incidence rate ratio, given that certain study design and sampling criteria have been fulfilled. In paper II we also used conditional logistic regression to calculate the odds ratios. The results of the conditional and the unconditional analyses were very similar, and we therefore only presented the results of the unconditional analyses.

In paper II, we evaluated the interaction between two different types of physical activity as departure from additivity of effects.<sup>80</sup> We calculated the attributable proportion due to interaction (AP), together with 95% confidence intervals.<sup>81</sup> The attributable proportion due to interaction is the proportion of the relative risk for those

who are simultaneously exposed to both of the investigated exposures (A and B) that can be attributed to the effect beyond the sum of the effects of exposure A and exposure B.



$$AP = \frac{RR_{AB} - RR_{A0} - RR_{0B} + 1}{RR_{AB}}$$

In the calculations of the attributable proportions due to interaction, each exposure was turned into a risk factor (not a preventive factor), and the category with the presumably lowest risk was used as the reference category (i.e. those unexposed to both of the risk factors).

In paper III, we evaluated the presence of effect measure modification (i.e. statistical interaction) between leisure-time physical activity and BMI by including product terms of physical activity and BMI categories in the logistic regression models. The p-values for statistical interaction were derived through likelihood ratio tests.<sup>79</sup>

### 3.4.3 Paper IV

In paper IV, the proportions of coherent answers between recalled and originally reported physical activity level, as well as the proportions that recalled a lower or higher level of physical activity compared with their original report, were calculated for the group of myocardial infarction cases, as well as for the group of control subjects. For each proportion a 95% continuity-adjusted confidence interval was calculated. To compare the proportions between cases and controls, continuity-adjusted chi-square statistics were used. Exact confidence intervals and p-values from Fisher's exact test were used in the case of small numbers. To estimate the agreement beyond chance between the answers in the original and recall questionnaires, kappa values with 95% confidence intervals were derived, for cases as well as for controls.<sup>82</sup>

To evaluate the potential effect of recall bias on the association between physical activity and myocardial infarction, crude odds ratios with 95% confidence intervals were calculated, using the data from the original questionnaire and the data from the recall questionnaire.

## 4 RESULTS

### 4.1 PHYSICAL ACTIVITY AND CARDIOVASCULAR RISK FACTORS (PAPER I)

In paper I, we found that various types of physical activity were clearly associated with the selected cardiovascular risk factors. The analyses were adjusted for age (5-year intervals), smoking, and socio-economic status. Leisure-time physical activity was adjusted for sitting / not sitting at work and demanding household activities; occupational physical activity was adjusted for leisure-time physical activity and demanding household activity; and household physical activity was adjusted for leisure-time physical activity and sitting / not sitting at work.

Leisure-time physical activity and the measure of total activity were inversely associated with several of the selected cardiovascular risk factors, in both men and women. Regarding leisure-time physical activity, the adjusted prevalence ratio of e.g. low HDL cholesterol was 0.54 (95% CI 0.46-0.65) for men and 0.55 (95% CI 0.41-0.73) for women, for the most active group compared with the most passive group. The corresponding numbers for the measure of total activity were 0.36 (95% CI 0.26-0.50) for men and 0.18 (95% CI 0.08-0.44) for women, when comparing the most active group with the most passive group.

Regarding occupational activity the results were not as consistent, with several of the estimated prevalence ratios close to unity for active compared with passive groups. However, in men and women, sitting less than half of the working day was associated with a decreased prevalence of low HDL cholesterol (PR 0.71, 95% CI 0.62-0.82 and PR 0.68, 95% CI 0.53-0.88 for men and women, respectively). In men, a workload perceived as strenuous was associated with lower prevalence of both hypertension and low HDL cholesterol, while in women strenuous workload was associated with an increased prevalence of hypercholesterolemia. Both repetitive lifting (lifting/carrying more than 5 kg at least 2 hours/day) and heavy lifting (lifting/carrying more than 20 kg (women) or 30 kg (men) at least 5 times/day) were associated with decreased prevalence of low HDL cholesterol in men, but not in women.

A household physical workload perceived as moderate/strenuous, as well as demanding household activities (such as snow shovelling and mowing grass), were associated with a decreased prevalence of elevated plasma fibrinogen in men (PR 0.84, 95% CI 0.71-1.00 and PR 0.80, 95% CI 0.68-0.95, respectively), while in women a perceived moderate or strenuous physical household workload was associated with an increased prevalence of low HDL cholesterol (PR 1.33, 95% CI 1.05-1.68) as well as increased prevalence of elevated plasma fibrinogen levels (PR 1.25, 95% CI 1.00-1.57).

In stratified analyses by body mass index and smoking, we found indications of a stronger inverse relationship between leisure-time activity and the measure of total activity, and the studied cardiovascular risk factors for overweight persons (BMI>25), compared with the group of normal-weight persons (BMI≤25). Smokers seemed to

have a weaker association between leisure-time physical activity and e.g. plasma fibrinogen, compared with non-smokers. The increased prevalence of hypercholesterolemia with a self-perceived strenuous occupational workload as noted in the total group of women, was only seen among the overweight women, and not in the normal-weight women, and was also enhanced among the women who smoked.

## **4.2 PHYSICAL ACTIVITY AND THE RISK OF ACUTE MYOCARDIAL INFARCTION (PAPERS II, III)**

### **4.2.1 Physical activity and myocardial infarction**

In paper II, we found a strong inverse association between leisure-time physical activity, the measure of total activity, as well as demanding household activities, and the risk of acute myocardial infarction. The odds ratios were 0.53 (95% CI 0.38-0.73) and 0.31 (95% CI 0.15-0.66) for men and women respectively, when comparing the most active group with the most passive group, regarding leisure-time physical activity when all cases (fatal and non-fatal) and controls were included in the analyses. In women, a decreased risk was also noted for those who were sitting less than half of their working day (OR 0.47, 95% CI 0.31-0.69). Regarding the other aspects of occupational physical activity, we noted that a higher level of self-perceived physical workload, as well as repetitive lifting or carrying at work, was associated with an increased risk among men (OR 1.57, 95% CI 1.15-2.15, non-fatal cases only; and OR 1.23, 95% CI 1.00-1.51, respectively). Heavy lifting at work was associated with an increased risk when only non-fatal cases were included in the analyses (OR 1.27, 95% CI 1.00-1.60). The same tendencies were noted among women; however, the results were not statistically significant. The analyses were adjusted for age (5-year intervals), hospital catchment area, smoking, socio-economic status, fiber intake, and alcohol consumption.

### **4.2.2 Interaction between various forms of physical activity**

In paper II, we evaluated the combined effect of different aspects of physical activity and the risk of acute myocardial infarction. We observed that regular leisure-time physical activity was associated with a decreased risk of myocardial infarction, irrespective of occupational physical activity level. We also found that simultaneous lack of leisure-time physical activity and having a sedentary job, where the persons were sitting most of their working day, was associated with substantial increased risk of myocardial infarction, particularly in women, with an attributable proportion due to interaction of 0.20 (95% CI -0.08-0.48) for men, and 0.60 (95% CI 0.36-0.84) for women (figure 4.1). Sitting a lot at work, in combination with lack of demanding household activities, was also associated with an increased risk of myocardial infarction in women (attributable proportion due to interaction 0.46, 95% CI 0.15-0.76).

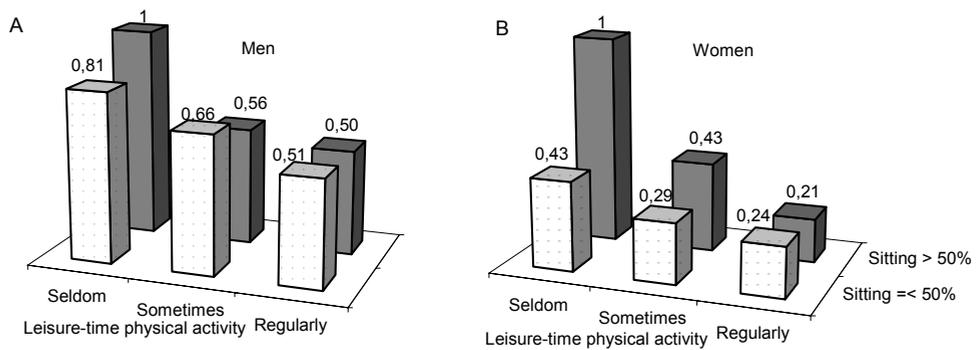


Figure 4.1 The combined effect of leisure-time physical activity and sitting / not sitting at work on the risk of acute myocardial infarction. Men (A) and women (B) in the SHEEP study. The numbers in the figures represent the estimated odds ratios.

#### 4.2.3 Interaction between leisure-time physical activity and body mass index

In paper III, we studied the joint effect of leisure-time physical activity and body mass index (BMI) on the risk of acute myocardial infarction. We found an inverse relationship between leisure-time physical activity and the risk of myocardial infarction in the groups of lean ( $BMI < 20$ ), normal-weight ( $20 \leq BMI < 25$ ), and overweight persons ( $25 \leq BMI < 30$ ). However, we did not observe any beneficial effect of participating in leisure-time physical activities twice a week or more, within the group of obese persons ( $BMI > 30$ ) (figure 4.2). The p-value for statistical interaction between leisure-time physical activity and BMI was 0.05 when all cases and all controls were included in the analyses, and 0.06 in the analyses based on the non-fatal cases. When compared with the normal-weight but sedentary group, the overweight and active group seemed to have a lower risk of myocardial infarction (OR 0.79, 95% CI 0.59-1.06), while the obese but active group had an increased risk (OR 1.85, 95% CI 1.07-3.18), in the analyses based on both fatal and non-fatal cases. When only non-fatal cases were included in the analyses, the overweight but active group had an equal risk of myocardial infarction compared with the normal-weight but sedentary group (OR 0.97, 95% CI 0.72-1.32), while the obese but active group had an estimated odds ratio of 2.27 (95% CI 1.30-3.95). Similar findings were made for both men and women. The analyses were adjusted for age, sex, hospital catchment area, socio-economic status and smoking.

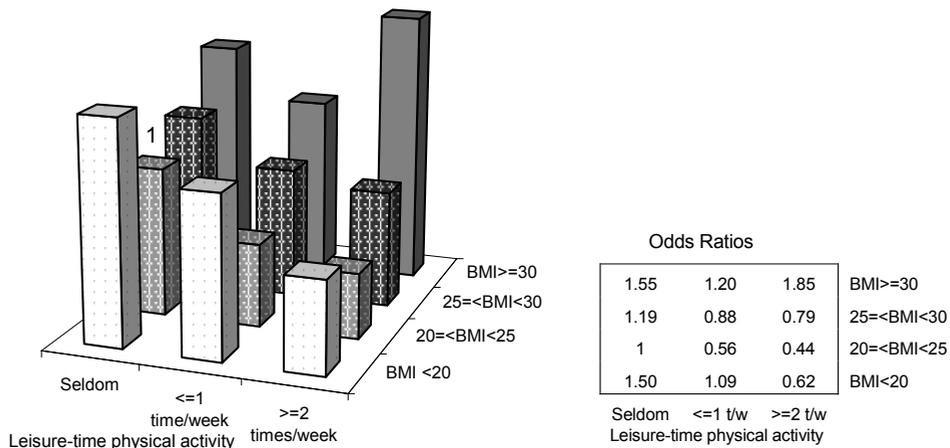


Figure 4.2 The combined effect of leisure-time physical activity and body mass index (BMI) on the risk of acute myocardial infarction. Men and women in the SHEEP study. Analyses based on all cases (fatal and non-fatal). The estimated odds ratios are presented in the table on the right-hand side of the figure.

### 4.3 RECALL BIAS REGARDING PHYSICAL ACTIVITY (PAPER IV)

#### 4.3.1 Differences in recall between cases and controls

In the study on recall bias, the myocardial infarction cases and the control subjects were equally likely to “correctly” recall whether they used to be engaged in leisure-time physical activity / exercise on a regular basis or not in the past (77 % of the cases, vs. 75 % of the control subjects) (table 4.1). The cases were much more likely to recall whether they used to be sitting most of their working hours or not (96 % of the cases, vs. 80 % of the controls), and the kappa value was markedly higher for the cases, as compared with the controls. However, the cases were not as good as the controls at remembering whether their work used to imply lifting or carrying more than 5 kg at least 2 hours per working day. The cases tended to over-report this type of exposure more often than the controls (25 % vs. 14 %) (table 4.1).

No large differences between cases and controls were found in the ability to recall whether they used to lift or carry heavy things (20 kg for women, 30 kg for men) at least 5 times per working day; whether they used to perceive their occupational workload as strenuous; whether their household work used to involve physically demanding tasks (such as shovelling snow or mowing grass); or in the recall of past self-perceived physical household workload. The ability to recall whether household work used to be perceived as strenuous or not was, however, very low in both cases and controls (kappa values 0.07 and 0.21 for cases and controls, respectively).

Table 4.1 Recall of past physical activity among 78 myocardial infarction cases and 240 control subjects in Sweden (selected aspects of physical activity).

	Cases*		Controls*		p-value
<i>Leisure-time physical activity / exercise</i>					
Recalled same level <sup>†</sup> (95% C.I.)	77%	(67-87%)	75%	(69-80%)	p=0.80
Recalled lower level <sup>‡</sup> (95% C.I.)	8%	(1-15%)	9%	(5-13%)	p=1.00
Recalled higher level <sup>§</sup> (95% C.I.)	15%	(6-24%)	16%	(11-21%)	p=0.91
Sensitivity (95% C.I.)	0.73	(0.52-0.94)	0.73	(0.62-0.83)	p=1.00
Specificity(95% C.I.)	0.79	(0.67-0.91)	0.76	(0.69-0.83)	p=0.78
Kappacoefficient (95% C.I.)	0.48	(0.28-0.69)	0.46	(0.34-0.57)	p=0.83
<i>Sitting at work or not</i>					
Recalled same level <sup>†</sup> (95% C.I.)	96%	(91-100%)	80%	(74-85%)	p=0.002
Recalled lower level <sup>‡</sup> (95% C.I.)	1%	(0-7%) <sup>#</sup>	8%	(5-12%) <sup>#</sup>	p=0.05 <sup>#</sup>
Recalled higher level <sup>§</sup> (95% C.I.)	3%	(0-7%)	13%	(8-17%)	p=0.03
Sensitivity (95% C.I.)	0.96	(0.80-1.00) <sup>#</sup>	0.82	(0.74-0.89) <sup>#</sup>	p=0.12 <sup>#</sup>
Specificity (95% C.I.)	0.96	(0.89-1.00)	0.78	(0.70-0.85)	p=0.01
Kappacoefficient (95% C.I.)	0.91	(0.81-1.00)	0.59	(0.49-0.70)	p<0.0001
<i>Lifting 5 kg 2 hours /day</i>					
Recalled same level <sup>†</sup> (95% C.I.)	69%	(58-80%)	83%	(78-89%)	0.01
Recalled lower level <sup>‡</sup> (95% C.I.)	5%	(1-13%) <sup>#</sup>	3%	(1-6%) <sup>#</sup>	0.27 <sup>#</sup>
Recalled higher level <sup>§</sup> (95% C.I.)	25%	(15-36%)	14%	(9-19%)	0.03
Sensitivity (95% C.I.)	0.73	(0.45-0.92) <sup>#</sup>	0.87	(0.74-0.95) <sup>#</sup>	0.24 <sup>#</sup>
Specificity(95% C.I.)	0.68	(0.56-0.81)	0.83	(0.77-0.88)	0.03
Kappacoefficient (95% C.I.)	0.30	(0.10-0.51)	0.57	(0.46-0.69)	0.02

\*Control and case status by the Swedish Myocardial Infarction Register. Three control subjects who had a self-reported myocardial infarction with reported incidence date after 2003 were excluded.

95% C.I., 95% confidence interval.

<sup>†</sup> "Recalled same level" refers to when the participants recalled the same level of past physical activity as reported in the original questionnaire. <sup>‡</sup> "Recalled lower level" refers to when the participants recalled a lower level of past physical activity as compared with the original report. <sup>§</sup> "Recalled higher level" refers to when the participants recalled a higher level of past physical activity as compared with the original report.

<sup>#</sup> Exact 95% confidence intervals; p-values derived from Fischer's Exact test.

### 4.3.2 Influence of recall bias on the estimated odds ratios

To evaluate the influence of recall bias on the association between physical activity and myocardial infarction, we calculated the crude odds ratios using the data from the original WOLF questionnaires for the study subjects in the recall bias study, as well as the data from the recall questionnaire. The results are shown in table 4.2.

The estimated odds ratios for leisure-time physical activity / exercise did not differ no matter whether the original or the recalled data were used, and only small differences were observed for sitting at work, demanding household activities and perceived physical load in household work.

However, a clear tendency was observed regarding the other aspects of occupational activity: repetitive or heavy lifting / carrying at work, and perceived occupational physical workload. For these exposures the odds ratios were pointed towards an increased risk when data from the recall questionnaire were used, but were close to or below one, when the original data were used.

Table 4.2 The recall bias study. Estimated odds ratios (OR) and 95% confidence intervals (95% C.I.), using data from the original WOLF questionnaire and the recall questionnaire. 78 cases and 240 control subjects.

	OR <sub>original quest</sub>	95% C.I.	OR <sub>recall quest</sub>	95% C.I.
<i>Leisure-time physical activity / exercise</i>				
Passive (non-regularly)	1		1	
Active (regularly)	0.86	(0.49-1.51)	0.85	(0.50-1.46)
<i>Sitting at work</i>				
Passive (yes)	1		1	
Active (no)	0.69	(0.40-1.19)	0.60	(0.35-1.04)
<i>Lifting 5 kg 2 hours /day</i>				
Passive (no)	1		1	
Active (yes)	1.00	(0.52-1.92)	1.46	(0.85-2.51)
<i>Lifting 20/30 kg 5 times /day</i>				
Passive (no)	1		1	
Active (yes)	0.72	(0.29-1.84)	1.11	(0.56-2.23)
<i>Perceived physical workload at work</i>				
Passive (light, 0-6)	1		1	
Active (strenous, 7-14)	1.06	(0.61-1.84)	1.43	(0.84-2.44)
<i>Demanding household activities</i>				
Passive (no)	1		1	
Active (yes)	1.11	(0.62-1.99)	0.96	(0.51-1.81)
<i>Perceived physical workload in household work</i>				
Passive (light, 0-6)	1		1	
Active (strenous, 7-14)	1.33	(0.75-2.38)	1.22	(0.71-2.11)

## 5 DISCUSSION

### 5.1 MAIN RESULTS

In the studies on which this thesis is based, we found strong inverse associations between leisure-time physical activity, and established risk factors for cardiovascular disease as well as the risk of acute myocardial infarction. However, leisure-time physical activity did not seem to confer protection against acute myocardial infarction among those who were obese. The results regarding different aspects of occupational and household physical activity were heterogeneous. In the methodological study on recall bias, we found indications that recall bias might influence the estimated odds ratios in retrospective case-control studies on physical activity and myocardial infarction, especially regarding occupational physical activity.

#### 5.1.1 Leisure-time physical activity

Regarding leisure-time physical activity and exercise, the overall results from the WOLF and SHEEP studies are in agreement with other observational studies.<sup>17,18,19,20,21,23,30,37,83</sup> In a meta-analysis using data from 10 studies it was found that the pooled relative risk of CHD was 0.70 for being physically active compared with inactive.<sup>84</sup> Similar estimates were found in another meta-analysis on physical activity with regard to CVD and CHD risk.<sup>13</sup> Several studies on physical activity in relation to CVD or CHD, have found relative risks close to 0.5 or lower, for the most active group compared with the sedentary group.<sup>18,29,32,38</sup> Case-control studies have been found to show slightly stronger associations than cohort studies.<sup>84</sup> This may indicate influence of recall bias in the case-control studies, but could also be explained by the dilution effect in cohort studies due to long follow-up periods.

We observed a stronger association between leisure-time physical activity and myocardial infarction when all cases (or only the fatal cases) were included in the analyses, compared with when only non-fatal cases were included. This effect may in part be explained by the use of proxy information about physical activity for the fatal cases, but it could also be an effect of a higher survival rate among the physically active cases. Higher survival rates after an acute myocardial infarction in relation to habitual physical activity have been observed in a study by Wannamethee and co-workers.<sup>85</sup>

We found that leisure-time physical activity was inversely related to myocardial infarction risk among lean, normal-weight and overweight persons, but not among those who were classified as obese (BMI>30). On the other hand, when we carried out analyses that were stratified according to BMI in the WOLF study, we found that people with high BMI had a relatively stronger inverse association between leisure-time physical activity and several of the studied CVD risk factors. However, in the WOLF study BMI was only categorised into two groups, with the cut-off point at BMI = 25.

There are several studies that have found that physical activity is inversely related to CVD, CHD, or all-cause mortality also within the higher BMI groups, which is in contrast to our results regarding myocardial infarction.<sup>30,31,86,87</sup> However, the results have not always been consistent, and there are studies where lack of an inverse relationship between physical activity and CVD or CHD in the higher BMI strata has been noted.<sup>16,88,89</sup> It has also been found that irrespective of an inverse association between physical activity and morbidity and mortality, the physically active obese persons still had an increased risk of CVD, CHD, or all-cause mortality, compared with sedentary normal-weight persons.<sup>90,91,92</sup> Few of these previous studies have been limited to the diagnosis of CHD, and even less to myocardial infarction. Instead broader diagnosis groups, such as CVD or even all-cause mortality have been used, which may explain some of the differences between studies. Obesity is associated with several adverse cardiovascular conditions, and it may be hypothesised that intense physical activity puts a very high strain on the cardiovascular system in obese subjects, which could result in an increased risk of acute myocardial infarction. It has e.g. been observed that vigorous physical activity increased the risk of CHD compared with being moderately physically active among hypertensive men, but not in normotensive men.<sup>15</sup>

### **5.1.2 Occupational physical activity**

Regarding occupational physical activity, the results were not as consistent as for leisure-time physical activity. In the WOLF study most of the other studied associations between occupational physical activity and hypertension, total cholesterol and plasma fibrinogen were close to the null value, while associations to favourable levels of HDL cholesterol were found, particularly among men. In the SHEEP study, we found signs of a protective effect from having a job implying standing or walking most of the working day, regarding the risk of acute myocardial infarction. This effect was more pronounced in women than in men. On the other hand, having a job which was perceived as strenuous, or a job that included a lot of lifting or carrying, seemed to be associated with an increased risk of myocardial infarction. It was, however, notable that leisure-time physical activity seemed to confer protection against myocardial infarction irrespective of occupational physical activity. Our results from the WOLF and SHEEP study indicate a preventive effect of having a job where you walk or stand during the major part of the working day, but the results are inconclusive regarding the other aspects of occupational activity, especially with taking the indications of recall bias from our methodological study into account.

Other studies on occupational physical activity have shown beneficial,<sup>35,36,93,94</sup> null,<sup>37,38</sup> or indications of adverse<sup>20,39,40,95,96</sup> associations to CVD risk factors and CVD or CHD risk. Elwood et al., as well as Barengo et al., found beneficial associations between occupational physical activity and HDL cholesterol, but null or adverse associations to blood pressure, total cholesterol and/or plasma fibrinogen,<sup>19,83</sup> which corresponds to our results in the WOLF study to a high extent. Stender and co-workers found beneficial associations between occupational physical activity and CVD risk factors (blood pressure, total cholesterol and HDL cholesterol), but signs of an increased risk of myocardial infarction incidence as well as total mortality, with higher level of occupational physical activity.<sup>97</sup> Most often a global measure of occupational physical

activity has been used. In general, those studies which have measured subjective ratings of physical workload have shown indications of increased risks, while other studies which have based the measure of occupational physical activity on walking/standing or walking in combination with heavy lifting have shown decreased or null effects.

In a study by Karlqvist et al. it was found that a large proportion of those who have a physically demanding job in Sweden today, are working at a level beyond their own physical capacity.<sup>98</sup> The prevalence of e.g. low cardiorespiratory fitness was more common among those with heavy jobs, compared with subjects with lighter physical demands. Based on these results, it does not seem as if having a demanding job is enough to guarantee the physical benefits that many people experience by being physically active and doing exercise during their leisure time.

### **5.1.3 Household physical activity**

We found that having physically demanding household tasks, such as mowing grass and shovelling snow, was associated with a decreased risk of myocardial infarction in both men and women in the SHEEP study. It was also associated with a lower prevalence of plasma fibrinogen in men in the WOLF study. However, no clear association was found to the rest of the studied risk factors in the WOLF study. Among the women who rated their household work as physically strenuous an increased prevalence of high plasma fibrinogen and low HDL cholesterol was noted, while this type of exposure was associated with a decreased prevalence of high plasma fibrinogen in men. Few previous studies have evaluated the association between household physical activity as a separate factor and CVD risk. Pols and colleagues found that housework activity was associated with higher level of blood pressure among women.<sup>20</sup> It has been proposed that household physical activity should be considered in studies of physical activity in addition to exercise and sports activities, and that this aspect of physical activity may be more important for women than for men.<sup>99</sup> Based on our results we cannot say that these aspects of physical activity seem more important for women than for men. However, in Sweden women participate in working life to a very great extent, and the household part of overall physical activity levels may be more important in contexts where women are employed outside the home to a lesser degree. It is however notable that the subjective rating of household workload as strenuous was associated with lower prevalence of elevated plasma fibrinogen in men, but higher prevalence of elevated plasma fibrinogen and low HDL cholesterol in women, indicating an effect measure modification by gender.

### **5.1.4 Total activity**

In both the WOLF and the SHEEP study, the combined measure of leisure-time physical activity, sitting / not sitting at work, and demanding household work (such as shovelling snow and mowing grass), called “total activity”, showed very strong inverse associations to both myocardial infarction and the studied CVD risk factors. This strengthens the idea that it is better to be at least somewhat active, compared with being completely sedentary.

In the measure of “total activity” we used information of physical activity that, at least to some extent, may be considered as frequency based and of aerobic type. Subjective

ratings of occupational and household workload, and lifting or carrying things at work were not included in this measure, which could have yielded different results. However, we think that these factors, in particular the subjective ratings of physical workload, cover quite different aspects of physical demands and workload, and that it is not evident to combine these factors with the before mentioned types of physical activity.

### **5.1.5 Recall bias**

Since the information about physical activity is based on self-report and was collected after the cases had been diagnosed as cases, one of the major methodological considerations in the SHEEP study has been whether recall bias has influenced the results or not. This is particularly important regarding the association between occupational physical activity and myocardial infarction, since previous findings have been less consistent and based on fewer studies, compared with leisure-time physical activity. Indeed, in our study on recall bias, we found indications of the presence of recall bias, especially regarding the exposures of occupational physical activity. This has to be considered when interpreting the results from the SHEEP study.

The largest differences in recall between cases and controls were found in the occupational physical activity factors *mainly sitting / not sitting at work*, and *lifting or carrying burdens of more than 5 kg at least 2 hours per working day*. However, the largest influence on the estimated odds ratios was found regarding *lifting or carrying burdens of more than 5 kg at least 2 hours per working day*, *lifting or carrying burdens of more than 20 or 30 kg at least 5 times per working day*, and *perceived physical load at work*. Thus, even if the largest differences in accuracy in recall were noted regarding sitting / not sitting at work, these differences did not have any major impact on the estimated odds ratios.

To our knowledge, this is the first study assessing the influence of recall-bias in retrospective case-control studies on physical activity and myocardial infarction.

## **5.2 METHODOLOGICAL CONSIDERATIONS**

In both the WOLF and the SHEEP study a large number of men and women were included, which made it possible to carry out separate analyses for men and women. Few studies have included such large number of women, especially regarding the number of female myocardial infarction cases as in the SHEEP study.

The cross-sectional study design in the WOLF study prevents us from drawing any firm conclusions about cause-and-effect relationships. We cannot preclude that some degree of reverse causation has been present, i.e. that individuals with low health status have changed their physical activity pattern and become more sedentary due to their health problems. If so, this selection process of previously ill persons into the sedentary groups could have inflated the observed associations between e.g. leisure-time physical activity and the cardiovascular risk factors. However, all study subjects in the WOLF study were currently employed when they were included in the study, and the vast majority worked full-time (40 hours/week). Furthermore, persons on long-term sick leave were not included in the study. This leads us to believe that the selection of

people with bad health to sedentary groups is not a major problem in the WOLF study. Furthermore, we also performed analyses where we excluded individuals with self-reported cardiovascular-related diseases (stroke, angina pectoris, heart failure, earlier myocardial infarction, and claudication intermittens). However, excluding them did not change the results in any major way.

The SHEEP study is a population-based case-control study, comprising a large number of incident myocardial infarction cases, both male and female. An advantage of the SHEEP study is that both non-fatal and fatal cases were included in the study, which is important if the studied exposure is thought to influence the probability of surviving after a myocardial infarction. However, care must be taken when interpreting the results from analyses including the fatal cases, due to the fact that the exposure information was provided by close relatives. The potential role of reverse causation should also be considered in the SHEEP study. In the main analyses we used information on physical activity in the same age interval as the subjects belonged to at inclusion in the study. However, activity level might have changed as a result of previous illness, which could lead to lower activity levels among cases. To account for this, we also performed analyses where we used the information on physical activity in the age period prior to inclusion. However, that did not change the results in any substantial way. In paper III, we also performed analyses where we excluded those who had reported prior cardiovascular diseases in the questionnaire, but this did not change the major results either.

### **5.2.1 Selection bias**

Selection bias arises if (non-)participation in the study is related to both exposure and outcome. This is probably not a major problem in the WOLF study, since the participation rate was high (82 %), and it is not likely that the non-participation was related simultaneously to both physical activity level and the studied CVD risk factors. However, the potential effect of selection bias should be considered in the SHEEP study. Selection bias in a case-control study could arise if cases are more willing to participate in the study than control subjects, and if non-response is associated with socio-economic and other lifestyle-related factors. In the SHEEP study the overall participation rate was quite similar for cases and controls (78 % for cases, 72 % for controls), which probably makes the potential role of selection bias less severe. However, the response rate was higher for non-fatal than for fatal cases (84 % and 62 %, respectively). Under the assumption that non-response was related to physical activity level (i.e. that low physical activity level was more common among non-respondents, and the proportion of non-respondents was higher among controls than non-fatal cases), we would expect the analyses based on the non-fatal cases to be biased away from the null value. However, we noted weaker associations when only non-fatal cases were included, compared with analyses including all cases.

### **5.2.2 Exposure information**

In all studies included in this thesis, information on physical activity was collected by questionnaires. These questionnaires covered different aspects of physical activity, but were rather limited in details regarding frequency and duration of the different activities. Despite these limitations, we found strong associations in both the WOLF

and the SHEEP study between various aspects of physical activity and CVD risk factors and myocardial infarction risk, respectively. An imprecise measure which potentially increases the misclassification of exposure, tends to dilute the estimated associations towards the null value. This would mean that the observed associations in our studies underestimate the true relationships. However, it has been found that simple global questions regarding physical activity are sometimes more strongly related to e.g. cardiorespiratory fitness compared with more detailed and complex batteries of questions.<sup>58,60</sup>

For the fatal cases in the SHEEP study, we had to rely on proxy information regarding physical activity. It is not unlikely that the information given by relatives differs in quality from the information given by cases themselves. Indeed, a small methodological study carried out in connection with the SHEEP study indicated that relatives tended to report lower activity level than the cases themselves. As pointed out earlier, this might be part of the explanation for the differences found in the estimated odds ratios when all-cases vs. only non-fatal cases were included in the analyses. However, it is not likely that this explains all of the observed differences.

A major concern in the SHEEP study has been the potential role of differential misclassification of physical activity. This was the main reason for conducting the methodological study on recall bias, as presented and discussed in paper IV. Based on the results from that study, recall bias could have influenced the estimated odds ratios away from the null value in the SHEEP study, especially regarding occupational physical activity. Recall bias could also have been present in the WOLF study, if awareness of the studied outcomes influenced the reporting of physical activity level. However, we found the strongest associations between physical activity and HDL cholesterol and plasma fibrinogen. These factors have usually not been considered for medical treatment by general practitioners, and we believe that it is unlikely that awareness of HDL cholesterol and plasma fibrinogen levels has influenced the reporting of physical activity to such an extent that it would explain the observed results.

In paper III we used BMI as an exposure together with leisure-time physical activity. BMI was primarily based on data on weight and height from the clinical examination; secondarily, self-reported data from the questionnaire were used. In the study subjects for whom we had information on weight and height from both the clinical examination and the questionnaire, BMI based on self-report was highly correlated with BMI based on data from the clinical examination ( $r=0.92$ ). We also had information on weight and height for a limited number of non-fatal cases which was reported by close relatives. The correlation between BMI calculated from reports on height and weight by relatives, and the reports by the cases themselves, also showed relatively high correlation ( $r = 0.88$ ).

### **5.2.3 Classification of outcome**

Misclassification may occur not only with regard to the exposures under study, but also regarding the outcomes.

In the WOLF study hypertension, total and HDL cholesterol, and plasma fibrinogen were used as outcomes. Blood pressure was measured on one occasion. It is well known that blood pressure may fluctuate over the day, and one single measurement may be less representative of the actual blood pressure of an individual. This potential misclassification of blood pressure, if present, is probably not related to physical activity level and would then result in a bias of the estimated associations towards the null value. Blood lipids and plasma fibrinogen were analysed at the same laboratory, and any misclassification due to errors in the analyses of these factors is not likely to be associated with physical activity either, and would, if present, also result in dilution of the estimated associations.

In the SHEEP study, the case ascertainment was high. Crosschecks based on various registers in combination with SHEEP data have shown that at least 97% of the cases who met the inclusion criteria were identified in the SHEEP study. This leads us to believe that misclassification of disease (non-differential as well as differential) is a minor problem in the SHEEP study.

#### **5.2.4 Residual confounding**

In both the WOLF and the SHEEP study we tried to take several potential confounding factors into account in the analyses. Although it seems as if age, sex, socio-economic status and smoking are the main confounding factors when analysing the association between physical activity and CVD risk factors and acute myocardial infarction, we cannot rule out that residual confounding may have influenced the results to some extent. As an example, we only had crude measures on dietary habits in both the WOLF and the SHEEP study.

#### **5.2.5 The recall bias study**

The study on recall bias included in this thesis addressed the question of whether recall bias should be regarded as a major problem in retrospective cases-control studies. As described earlier, we found indications that recall bias might very well be present and should be taken into account when interpreting the results from such studies. However, several methodological aspects also have to be considered with regard to the recall bias study.

It should be noted that the estimated odds ratios between the originally reported physical activity level and myocardial infarction risk should not be viewed as estimates of the true associations between physical activity and myocardial infarction. This is due to the fact that the participants who had suffered from a myocardial infarction in the recall bias study only constitute a sub-fraction of the cases that would have been included in a cohort- or case-control study with incident cases. The recall bias study was not only restricted to non-fatal cases, but also to cases that had survived for a long time after their myocardial infarction. Furthermore, we only calculated and presented crude odds ratios, as the main purpose of the study was to compare originally reported physical activity levels with later recalled levels, and not to draw any conclusions about actual associations per se. Another limitation in the recall bias study was the small numbers of myocardial infarction cases.

The period of time since the cases in the recall bias study had experienced their first-time myocardial infarction varied between two and 11 years. It has been observed that present physical activity level may influence how past activity is recalled.<sup>100</sup> As it is not unlikely that subjects change their level of activity after a myocardial infarction event, we also conducted analyses restricted to the individuals who reported the same activity level during 2005 as at their inclusion in the WOLF study. In these analyses, there was an increase in the proportion who recalled the same activity level as they originally reported. However, the difference remained in the estimated odds ratio regarding repetitive lifting or carrying, when original data compared with recalled data were used.

In our main analysis regarding recall bias we analysed the various types of physical activities using only two levels, i.e. physically inactive vs. physically active, even if some of the physical activity variables were originally measured with several levels. However, analyses were also performed where we used the different numbers of levels regarding leisure-time physical activity, perceived occupational and perceived household physical workload as originally measured. Although the numbers in each cross-tabulation cell became small, we found further indications of recall bias regarding leisure-time physical activity in these analyses.

### **5.3 GENERAL DISCUSSION AND FUTURE RESEARCH**

Based on the studies included in this thesis and several other studies, leisure-time physical activity and exercise should be regarded as a very strong preventive factor against cardiovascular diseases such as myocardial infarction.

In the WOLF study 37 % answered that they exercised on a regular basis. It was found that almost the same proportion (35 %) answered that they exercise at least once per week in the control group in the SHEEP study. In a somewhat differently worded question, about 54 % of men and 61 % of women aged 45-64 years reported that they exercised at least once per week in a national survey in Sweden 2002/2003.<sup>2</sup> Although participation in leisure-time physical activities and exercise has increased since the 1980s in Sweden, a large proportion of the adult population is still mainly sedentary during leisure time. Given the high incidence of CVD and the large number of persons who are physically sedentary, the potential to lower the public health burden of CVD by increased physical activity in the population should be considerable. Physical activity has also been found to decrease the risk of diabetes type II, certain types of cancer, and osteoporosis,<sup>101</sup> which further enhances the beneficial effect of physical activity in a public health perspective.

In the SHEEP study we found indications of higher survival rate after myocardial infarction in persons who exercised on a regular basis. Due to methodological considerations, no firm conclusion about this relationship can be drawn based on our results. However, similar findings have been made by others.<sup>85</sup> In future studies, more attention should be paid to the issue that leisure-time physical activity and exercise not only seems to prevent the incidence of myocardial infarction, but may also decrease the likelihood of dying if a myocardial infarction event occurs.

The case-control study design is extensively used in epidemiological research. It is especially useful in studies of rare diseases, since it is a very efficient study design compared with the corresponding cohort study. However, the potential role of recall bias should be considered if exposure information relies on retrospective self-reports. We approached the issue of recall bias regarding physical activity in relation to myocardial infarction. However, our findings should be confirmed in larger studies with more incident cases. It is also necessary to evaluate how different questionnaires regarding physical activity influence the probability of recall bias, and the potential role of recall bias in studies of physical activity in relation to other diseases.

## 6 CONCLUSION

- Overall beneficial associations between regular leisure-time physical activity, and CVD risk factors as well as myocardial infarction were found in both men and women. Stronger associations between leisure-time physical activity and myocardial infarction were found in analyses including both fatal and non-fatal cases, compared with analyses that only included non-fatal cases. This indicates that regular leisure-time physical activity might increase the probability of surviving after an acute myocardial infarction.
- Beneficial effects of leisure-time physical activity were found in the strata of lean, normal-weight and overweight people, but not in the group of obese individuals. Compared with normal-weight and sedentary people, those who were overweight and physically active had an equal or lower risk of acute myocardial infarction, while those who were obese and active had an almost twofold risk of acute myocardial infarction compared with normal-weight but sedentary persons.
- Various aspects of occupational physical activity seemed to be beneficially related to HDL cholesterol in men. Regarding hypertension, hypercholesterolemia and plasma fibrinogen, most associations were close to the null value.
- Walking or standing at work lowered the risk of myocardial infarction among women. Lifting or carrying burdens at work or perceiving a strenuous workload increased the risk in both men and women. However, recall bias might have influenced these results.
- Leisure-time physical activity was associated with a lower myocardial infarction risk, irrespective of occupational physical activity level.
- Lack of regular leisure-time physical activity in combination with a job where the subjects were mainly sitting, or a sedentary job in combination with lack of demanding household work, were in particular associated with an increased risk of myocardial infarction, especially in women.
- We found that recall bias might affect the estimated associations between physical activity and myocardial infarction in epidemiological case-control studies with retrospectively collected information on physical activity, particularly regarding some aspects of occupational physical activity.

## 7 SAMMANFATTNING (SUMMARY IN SWEDISH)

Syftet med avhandlingen var att studera sambanden mellan fysisk aktivitet på fritiden, i arbetet samt i hushållsarbetet, och kända riskfaktorer för hjärt-kärlsjukdomar (högt blodtryck, ogynnsamma blodfettsnivåer och förhöjt plasma fibrinogen), samt risken att drabbas av akut hjärtinfarkt. Även förekomsten av s.k. recall-bias i retrospektiva fall-kontroll studier av fysisk aktivitet och hjärtinfarkt har studerats.

Sambanden mellan fysisk aktivitet och högt blodtryck, blodfetter och plasma fibrinogen studerades med hjälp av en tvärsnittsstudie som omfattade 10 413 personer. Personer som motionerade regelbundet på fritiden hade betydligt lägre förekomst av de studerade riskfaktorerna för hjärt-kärlsjukdom. Flera aspekter på yrkesrelaterad fysisk aktivitet var kopplat till gynnsamma HDL-kolesterolvärden, framför allt bland männen. Överviktiga kvinnor som själva uppfattade sitt arbete som ansträngande hade dock en ökad förekomst av höga totalkolesterolvärden. Fysisk aktivitet genom hushållsarbete var inte så tydligt relaterat till de studerade riskfaktorerna, men att uppfatta sitt hushållsarbete som ansträngande var kopplat till höga plasma fibrinogen nivåer och ogynnsamt låga HDL-kolesterolvärden bland kvinnor. En kombination av regelbunden motion, ett arbete där man står eller går mycket, samt fysiskt krävande moment i hushållsarbetet var mycket starkt relaterat till lägre förekomst av de studerade riskfaktorerna för hjärt-kärlsjukdom.

Sambanden mellan fysisk aktivitet och risk för akut hjärtinfarkt studerades i en stor fall-kontrollstudie, vilken inkluderade 1 754 personer som drabbats av akut hjärtinfarkt och 2 315 kontrollpersoner. I den studien fann vi generellt en starkt skyddande effekt av regelbundna motionsvanor med avseende på risken att drabbas av akut hjärtinfarkt. Vid analyser stratifierat efter body mass index sågs den skyddande effekten av regelbunden motion i grupperna med smala, normalviktiga och överviktiga personer, dock ej i gruppen med kraftigt överviktiga (feta) personer. Att ha ett jobb där man står eller går mycket verkade ha en skyddande effekt mot hjärtinfarkt, särskilt hos kvinnor. Upprepade eller tunga lyft på arbetet, eller att uppfatta sitt arbete som ansträngande verkade vara kopplat till en ökad risk för hjärtinfarkt. Dock noterades att alla hade gynnsam effekt av regelbundna motionsvanor, oavsett fysisk ansträngning på arbetet. Att ha fysiskt krävande moment i hushållsarbetet var relaterat till en lägre risk för hjärtinfarkt hos både män och kvinnor. Kombinationen av regelbunden motion, att stå eller gå på arbetet samt att ha fysiskt krävande hushållsarbete var kopplat till en betydligt lägre risk för hjärtinfarkt jämfört med om man var fysiskt inaktiv.

I en metodologisk studie som inkluderade 78 personer som tidigare haft hjärtinfarkt och 243 kontrollpersoner, fann vi vissa skillnader i hur man kom ihåg och rapporterade tidigare fysisk aktivitetsnivå mellan dessa två grupper. Störst effekt på de skattade sambanden mellan fysisk aktivitet och hjärtinfarkt hade denna recall-bias för upprepade eller tunga lyft på arbetet, samt om man uppfattade sitt arbete som ansträngande. Dessa fynd bör beaktas när man tolkar resultaten om fysisk aktivitet i relation till hjärtinfarkt i retrospektiva fall-kontrollstudier.

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