

# **Movement and Circulation**

**Population Studies on Physical Activity  
and Cardiovascular Disease Risk**

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## **Population Studies on Physical Activity and Cardiovascular Disease Risk**

### **Proefschrift**

ter verkrijging van de graad van doctor  
op gezag van de rector magnificus,  
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WAGENINGEN

## Stellingen

1. Mensen van middelbare leeftijd die meer dan twee uur per week sporten, hebben vergeleken met inactieven een drie- tot viervoudig verlaagde kans vroegtijdig te sterven, met name aan hart- en vaatziekten. *(Dit proefschrift)*
2. Onafhankelijk van intensiteit en duur, kan een hogere frequentie van sportbeoefening bijdragen aan een gunstiger risicoprofiel voor hart- en vaatziekten. *(Dit proefschrift)*
3. Lichamelijke inactiviteit in de vrije tijd komt vooral voor bij mensen met een lage sociaal-economische status. *(Dit proefschrift)*
4. Het in de laatste jaren aangetoonde gezondheidsvoordeel van matige lichamelijke activiteit wordt mogelijk beïnvloed door de vergelijking met een steeds inactiever geworden referentiegroep.
5. De toegenomen bewegingsvrijheid als gevolg van het verdwijnen van de Berlijnse Muur heeft tot een hogere levensverwachting geleid.
6. De uitspraak „het is puur toeval“ is statistisch gezien veel informatiever dan „het is zeer waarschijnlijk“.
7. Zowel inspanning als ontspanning door sport kan mogelijk overspanning voorkomen.
8. Bisher ist es fraglich, ob Epidemiologen sich eher mit Mortalitätsraten oder mit Mortalität-Raten beschäftigen.
9. De dichtregel van Horatio: „Het zou wenselijk zijn dat een gezonde geest huist in een gezond lichaam (Orandum est ut sit mens sana in corpore sano)“ suggereert in de veel geciteerde verkorte vorm („een gezonde geest in een gezond lichaam“) een samenhang die juist door de dichter werd betwijfeld en er waarschijnlijk ook niet is.
10. Netsurfen brengt ons in feite nergens heen en leidt mogelijk tot een explosieve toename van veel zittend thuiswerk. Daarom zou de slogan van een bekende softwaregigant eigenlijk moeten luiden: „Where do you not want to go today?“.
11. A'w eier ha'n, ko'w ei met ham et'n, a'w ham ha'n.  
*(Twents voor: Als we eieren hadden, konden we ei met ham eten, als we ham hadden)*
12. Twijfel is een onaangename toestand, zekerheid een absurde. *(Voltaire)*
13. Haastige spoed is zelden goed behalve als je er veel bij bewegen moet.
14. Ren voor je leven!

*Stellingen behorende bij het proefschrift "Movement and circulation: population studies on physical activity and cardiovascular disease risk" van Gert Mensink, Wageningen, 22 september 1997*

# Abstract

## Movement and Circulation: Population Studies on Physical Activity and Cardiovascular Disease Risk

*PhD thesis by Gert B.M. Mensink, Robert Koch-Institute, Berlin, Germany, and Agricultural University Wageningen, The Netherlands, September 22, 1997*

The relationship of leisure-time physical activity with cardiovascular risk factors and mortality was determined using data from the German Cardiovascular Prevention Study, conducted from 1984-1991. Three nationally representative cross-sectional samples, with a total of 7 689 men and 7 747 women, ages 25-69, were part of this study, originally designed to estimate the impact of community intervention on cardiovascular health. Additionally we analyzed regional cross-sectional and follow-up samples.

Physically active individuals were more often urbanized, more likely to have high socioeconomic status, less often smokers and had healthier eating patterns and lower body mass index. Compared with sedentary individuals, the most active quartile of men (> 18 kcal/kg/week spent on conditioning activities) had significantly favorable levels of serum total cholesterol (-2.5%), HDL/total cholesterol ratio (+4.2%) and resting heart rate (-4.3%). The most active women (> 12 kcal/kg/week) had significantly better HDL cholesterol (+3.7%), HDL/total cholesterol ratio (+3.9%), triglycerides (-5.1%), diastolic (-1.3%) and systolic (-1.6%) blood pressure, body mass index (-2.8%) and resting heart rate (-2.5%). With duration and intensity constant, significantly better risk factor levels were observed with increased frequency of physical activity. For active men, we observed a relative risk of 0.33 (95% CI 0.11-0.94) for cardiovascular disease mortality and of 0.67 (95% CI 0.36-1.25) for all-cause mortality (5-8 year follow-up) compared with the least actives, independent of baseline risk factor levels. The elderly (ages 50-69) showed substantial benefits from participation in light to moderate activities, such as walking and cycling, most apparent when conducted frequently ( $\geq 5$  times/week). Using data from the Spandau Health Test (1 827 men and 2 929 women, ages 40-80, followed from 1982-1994) we estimated an all-cause mortality relative risk of 1.7 (95% CI 1.4-2.2) for men and 1.4 (95% CI 1.1-1.8) for women for each 20 beats/min higher resting heart rate.

More than 40% of German adults are sedentary. We recommend them regularly, preferably daily, to conduct moderately intense activities, such as brisk walking, running, swimming or cycling, for at least 30 minutes. Elderly may prefer light activities, such as walking or gardening. An active lifestyle may substantially improve the cardiovascular risk profile of the German population. For example, if only 50% of sedentary German men, ages 40-69, would become modestly active more than 6 500 cardiovascular deaths could be prevented each year.

## Kurzfassung

Die Beziehung zwischen körperlicher Freizeitaktivität und kardiovaskulären Risikofaktoren sowie Mortalität wurde anhand von Daten der Deutschen Herz-Kreislauf-Präventionsstudie (1984-1991) untersucht. Diese Studie – ursprünglich durchgeführt, um die Auswirkung von kommunaler Intervention auf das Herz-Kreislauf-Risiko zu bestimmen – enthielt drei national repräsentative Querschnitt-Stichproben mit einer Gesamtzahl von 7 689 Männern und 7 740 Frauen im Alter von 25-69 Jahren. Zusätzlich wurden regionale Querschnitt- und Longitudinalstudien ausgewertet.

Es zeigte sich, daß (in der Freizeit) körperlich aktive Personen eher Stadtbewohner sind, häufiger einen hohen sozioökonomischen Status haben und nicht rauchen, sich gesünder ernähren und einen geringeren Body Mass Index haben. Im Vergleich zu inaktiven hatten die körperlich aktivsten Männer (viertes Quartil; > 18 kcal/kg/Woche an konditionsfördernden Aktivitäten) signifikant günstigere Werte von Serum-Gesamtcholesterin (-2.5%), Quotient HDL-/Gesamtcholesterin (+4.2%) und Ruhepuls (-4.3%). Bei den körperlich aktivsten Frauen (> 12 kcal/kg/Woche) gab es signifikant bessere Werte von HDL-Cholesterin (+3.7%), Quotient HDL-/Gesamtcholesterin (+3.9%), Triglyceriden (-5.1%), diastolischem (-1.3%) und systolischem (-1.6%) Blutdruck, Body Mass Index (-2.8%) und Ruhepuls (-2.5%). Bei konstanter wöchentlicher Sportintensität und -dauer zeigten sich mit zunehmender Häufigkeit der Aktivität signifikant positive Auswirkungen auf die Höhe der Risikofaktoren. Die körperlich aktiven Männer wiesen ein geringeres Herz-Kreislauf-Mortalitätsrisiko (relatives Risiko (RR) 0.33; 95% KI: 0.11-0.94) und ein geringeres Gesamtmortalitätsrisiko (RR 0.67; 95% KI: 0.36-1.25) über einen 5-8-jährigen Zeitraum im Vergleich zur Gruppe der körperlich am wenigsten Aktiven auf, unabhängig von der Höhe der anderen kardiovaskulären Risikofaktoren. Ältere Personen (Alter 50-69) profitierten gesundheitlich erheblich durch häufig durchgeführte ( $\geq 5$  mal/Woche), aber wenig intensive körperliche Aktivitäten wie z.B. Spaziergehen und Fahrradfahren. In einer Teilgruppe des Spandauer Gesundheitstests (1 827 Männer und 2 929 Frauen im Alter von 40-80 Jahren, beobachtet von 1982-1994) wurde ein relatives Risiko für Herz-Kreislaufmortalität bei Männern von 1.7 (95% KI: 1.4-2.2) und bei Frauen von 1.4 (95% KI: 1.1-1.8) bei einer mittleren Zunahme der Ruhepulsfrequenz von jeweils 20 pro Minute festgestellt.

Über 40% der erwachsenen Deutschen sind körperlich inaktiv. Als Empfehlung für diesen Personenkreis gilt, regelmäßig, am besten täglich, mindestens 30 Minuten lang gemäßigt körperliche Aktivitäten durchzuführen (wie z.B. Laufen, Schwimmen, Fahrradfahren). Für ältere Personen wären Spaziergehen und Gartenarbeit angemessen. Es wurde geschätzt, daß mehr als 6 500 Herz-Kreislauf-Todesfälle pro Jahr vermieden würden, wenn lediglich die Hälfte der körperlich inaktiven Männer im Alter von 40-69 Jahren gemäßigten körperlichen Aktivitäten nachginge. Eine Förderung der körperlichen Aktivität würde einen wichtigen Beitrag zur Gesundheit der Bevölkerung leisten.

Ook voor mijn ouders  
en Zωή

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chapter

1

## General Introduction

*„Der tägliche Grundumsatz ist erstmals seit Menschengedenken  
unter das biologisch notwendige Mindestmaß gesunken.“*

Wildor Hollmann

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## Introduction

In ancient times, physical activity was essential for survival and to satisfy daily needs. Technological advancements resulted in affluent societies characterized by a highly sedentary lifestyle and high tobacco, alcohol and fat consumption, most noticeably during the last decades. During the last century, hygiene, medical knowledge and vaccination use improved, resulting in lower infant mortality rates and a longer life expectancy. These changes are probably responsible for the increased occurrence of chronic diseases, like cardiovascular disease and cancer, which generally develop at an advanced age. Cardiovascular disease also affects a large part of morbidity in middle age and is responsible for many premature deaths.

In Germany, cardiovascular disease is the major cause of death<sup>1</sup>. In recent years, a modest decline was observed in former West Germany and a strong decline in former East Germany. Still about 50% of mortality cases in 1993 were due to cardiovascular diseases (521 per 100 000 in West, 625 per 100 000 in East Germany). Cardiovascular disease is not attributable to a single cause, it has a multi-factorial etiology and several risk factors have been established e.g. obesity, diabetes, high levels of low density lipoprotein (LDL) cholesterol, low levels of high density lipoprotein (HDL) cholesterol and hypertension. Apart from heredity, lifestyle aspects such as smoking, diet and lack of physical activity seem to have an important influence on cardiovascular disease risk factors and occurrence.

### *Terminology of physical activity*

Physical activity comprises any bodily movement produced by the contraction of skeletal muscles that substantially increases energy expenditure<sup>2</sup>. Training or exercise can be regarded as a subset of physical activity which is planned, structured, repetitive, and has the improvement or maintenance of physical fitness as an objective. Physical fitness is defined as a set of attributes that people have or achieve that relates to the ability to perform physical activity<sup>3</sup>. Activities which have an exercise potential are often referred to as conditioning physical activities. Exercise may be classified as endurance (predominantly aerobic; isotonic and dynamic, prolonged action, involving large skeletal muscle groups) or resistance (power, strength, predominantly static and isometric) training. Physical activity occurs throughout the day, even while sleeping, but major contributions to energy expenditure come from occupational and leisure-time physical activity.

Leisure-time physical activity (which will be referred to as leisure activity) is an activity undertaken in the individual's discretionary time that leads to any substantial increase in the total energy expenditure. The element of personal choice is inherent to the definition<sup>4</sup>. Leisure activity may be subdivided into sports (containing some competitive element), conditioning exercises, recreational and other activities. Household tasks and being in transit can be regarded as leisure activity or as distinct categories<sup>2,3</sup>.

### Physical activity in Germany

The German population is largely sedentary. Whereas 24% of young males and 31% of young females (ages 25-29) report no participation in sports, for men and women ages 50-59, the reported figures are more than 50% and almost 60% respectively (see Figure 1.1).

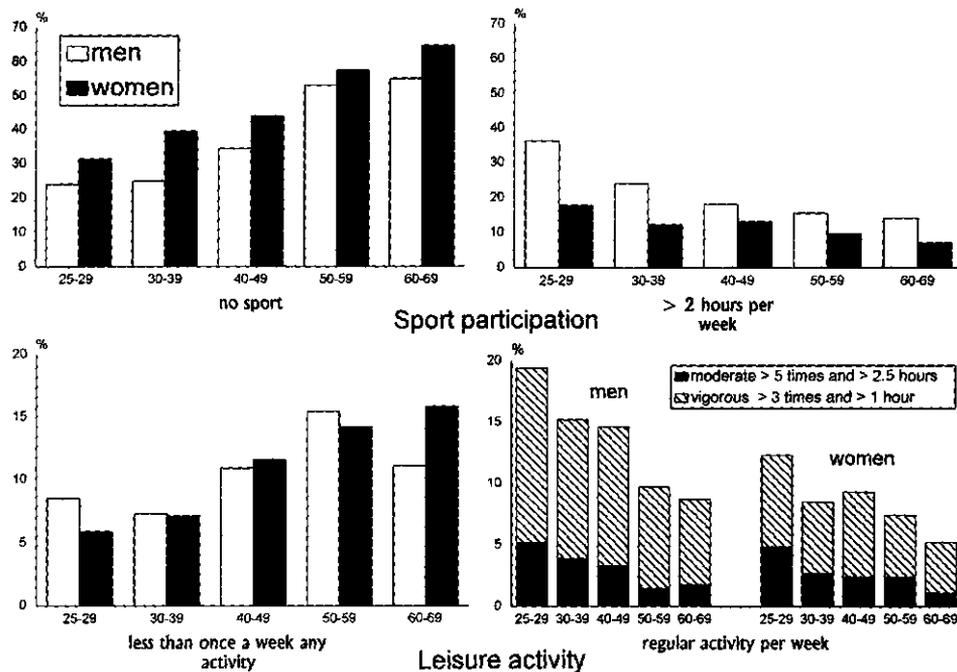


Figure 1.1 Physical activity patterns in former West Germany, 1991

About half of the population reports regular participation in leisure activities like walking, cycling and gardening. 10% of men and 5% of women perform regular vigorous activity (one hour duration, 3 or more times per week), but 8.5% of young men and 6% of young women participate less than

## Chapter 1

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Chapter **2**

**Reduction of Coronary Heart Disease Risk Factors  
in the German Cardiovascular Prevention Study**

H. Hoffmeister, G.B.M. Mensink, H. Stolzenberg, J. Hoeltz, H. Kreuter,  
U. Laaser, E. Nüssel, K.-D. Hüllemann, H. v. Troschke.  
*Preventive Medicine* 1996; 25: 135-145

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This chapter gives an overview of the objectives, design and results of the German Cardiovascular Prevention Study, which provided the data for most analyses presented in the subsequent chapters. The intervention results, however, are beyond the scope of this thesis.

## Abstract

*In six regions of former West Germany, a community-oriented prevention program for coronary heart disease (CHD) was conducted over a 7-year period. In the intervention regions, CHD prevention activities were performed with special emphasis on healthy nutrition, increased physical activity, and reduction of smoking, hypertension and hypercholesterolemia. The impact of these activities on CHD risk factor trends was observed in three independent samples of the intervention regions. Three independent representative samples of the total West German population were used as a reference. Linear regression models with interaction terms to represent the intervention effects were used to test for differences in risk factor trends. In the pooled intervention regions, a net reduction in mean values of systolic (-2.0%) and diastolic (-2.0%) blood pressure, total serum cholesterol (-1.8%), as well as the percentage of smokers (-6.7%) was observed compared with the nationwide trend. From the major CHD risk factors, only body mass index was not influenced in the intervention population. The community-oriented German Cardiovascular Prevention program can effectively be used to reduce CHD risk factors in a broad population.*

## Introduction

In the German Cardiovascular Prevention Study (GCP), a community-oriented, multi center disease prevention program was conducted over a 7-year period. The design of the study differs from the traditional design of cardiovascular intervention trials, in that the six intervention regions, with a total population of more than a million, are scattered throughout former West Germany, while the reference population is a representative sample of the West German population<sup>1-3</sup>. This design has the advantage that the reference population (which is not a neighboring control population) will not easily be influenced by intervention carried out in the study population. Secular trends and spillover effects can thus be better accounted for.

The main goal of the study is to reduce, by primary prevention, the four cardiovascular risk factors: hypertension, hypercholesterolemia, smoking and obesity. The desirable reduction of risk factors to be achieved after 7 years of intervention were pinpointed at the beginning of the study<sup>1</sup>. As a consequence of reaching these pinpointed risk factor reductions, an 8% reduction of ischemic heart disease (ICD 410-414) and cerebrovascular disease (ICD 430-438) should occur in the pooled intervention regions.

Three city districts (of Berlin, Bremen, and Stuttgart), an entire medium-sized city (Karlsruhe) with two small neighboring communities (Bruchsal, Mosbach), and finally a rural district (Traunstein) were chosen as intervention regions. When pooled these regions had a similar demographic and socioeconomic structure as the total West German population. This chapter presents the effects of broad-scale measures which were realized during nearly 7 years of intervention in this large population.

## Methods

### *Intervention efforts*

In order to achieve a reduction of cardiovascular risk factors in the intervention communities, the GCP study group tried to improve health knowledge, awareness, attitude and behavior in the population by implementing a multifaceted prevention program. To reach these goals, existing facilities were used and access to health care providers within the community was extended and improved. This was achieved by close collaboration with well-established institutions: public health services, voluntary welfare federations, institutions for adult education, and sports and consumer associations, with the participation of physicians, medical assistants, pharmacists, and teachers.

Special emphasis was put on healthy nutrition, more physical activity, quitting smoking, and the screening of a larger part of the population for hypertension and hypercholesterolemia. To improve nutritional habits, campaigns at community festivals, at public events, in restaurants, in supermarkets, in canteens, and in schools were conducted. Weight reduction courses and seminars on nutritional topics and menus and information about ingredients and preparation of foods beneficial to cardiovascular health were offered. A diet low in meat, fat, salt, and calories was promoted and higher consumption of vegetables and cereal products was encouraged. Availability of low-salt and low-fat products was enhanced through the involvement of

local food suppliers. Information spots and advertisements in the local media were published or broadcast. To enhance physical activity, recreational sporting events with varying intensity levels and educational sport circuits were initiated and organized. To discourage smoking, nonsmoking areas in public places were established. Also conducted were courses to help smokers quit, anti-smoking campaigns in the local media and an intensive anti-smoking poster campaign.

To reduce hypertension and hypercholesterolemia, blood screenings were organized at social events, in factories, and at other occasions in close cooperation with physicians, pharmacists, and health insurance companies. A large part of the inhabitants of the intervention region was screened. The aim of these screenings was to enhance awareness about hypercholesterolemia and hypertension as risk factors. Personal consultations to lower these risk factors by prevention measures and, if needed, medical treatment were offered. After the midsurvey, which showed unfavorable trends for cholesterol levels in several regions, an intensified cholesterol-lowering program that focused on dietary changes was initiated. Reports of health activities were regularly published in the local media. During the entire intervention period, individual consultations, health management programs, regular health festivals, and health weeks were provided. Comprehensive health information materials (like brochures, leaflets, and posters) were widely distributed. There were several hundred health expositions and activities during the intervention time in each intervention region, which are described in detail<sup>4-7</sup> and in summary<sup>1</sup> elsewhere. Improvements in health knowledge, attitudes, and behavior will be evaluated in a future publication.

### *Evaluation and Sampling Design*

The impact of intervention efforts is measured by the changes in mean levels and prevalences of important cardiovascular risk factors. The intended net reductions are presented in Table 2.1. Representative, independent samples of the national population of West Germany and of the intervention populations were examined. For evaluation of risk factor trends, a net sample of about 1 900 men and women ages 25-69 for each intervention region was examined before intervention (May 1984 until March 1986). At midstudy (February 1988 until April 1989) and at the end of the intervention period (April 1991 until April 1992) subsequent surveys with about 1 400 persons per region were conducted. Nationally representative reference samples of about 5 000 persons each were examined in almost the same periods (June 1984 until April 1986, September 1987 until October 1988, and April 1990 until May 1991).

For the intervention samples the response rates were 74.5, 73.0 and 71.6% and for the national samples 66.7, 71.4 and 69.0%, respectively.

In 1989, the former East and West Germany were unified. Both the final intervention samples and the reference sample, however, included only former West Germans. Therefore, bias in risk factors in the samples related to these population structure changes were avoided. In addition, a national survey was conducted in the same period for the former East German population (8) which will, however, not be discussed in this chapter.

Table 2.1 Intended and achieved reductions of risk factors at midstudy and end of study period (relative change in means and prevalences) <sup>a</sup>

Risk factor	Midstudy (1985-1988)				Study end (1985-1991)			
	Means		Prevalences		Means		Prevalences	
	Target	Achieved	Target	Achieved	Target	Achieved	Target	Achieved
Systolic BP (mmHg)	-0.7%	-1.6%			-1.5%	-2.0%		
Diastolic BP (mmHg)	-0.7%	-1.0%			-1.5%	-2.0%		
Total cholesterol (mg/dl)	-1.5%	+0.9%	-2.0% <sup>b</sup>	-0.5%	-3.5%	-1.8%	-5.0% <sup>b</sup>	-6.5%
			-4.0% <sup>c</sup>	+4.6%			-9.0% <sup>c</sup>	-11.0%
Smoking			-3.5%	-7.8%			-7.5%	-6.7%
BMI (kg/m <sup>2</sup> ) <sup>d</sup>	-0.4%	+0.7%	-2.0%	+5.3%	-1.0%	±0.0%	-5.0%	+1.9%
Hypertension <sup>e</sup>		-6.0%	-6.8%		-13.0%	-21.1%		

<sup>a</sup> Net change (%)=[(value last/value first year)<sub>pooled regions</sub> - (value last/value first year)<sub>reference</sub>] × 100;

<sup>b</sup> Borderline value: ≥ 220 mg/dl

<sup>c</sup> Borderline value: ≥ 250 mg/dl

<sup>d</sup> Borderline value: ≥ 25 kg/m<sup>2</sup>

<sup>e</sup> According to WHO-criteria

Participants of the intervention samples as well as from the national samples were invited for a physical examination. The examination included assessment of height, weight, and systolic and diastolic blood pressure. Blood pressure was measured twice, while subjects were sitting (second measurement after 3 min using a Hawksley Random-Zero-Sphygmomanometer); only the second ones were used in the presented analyses. Blood samples were taken from lying subjects in a nonfasting state. A trained medical team performed all measurements, whereas an independent team checked them frequently during the entire survey periods. This team performed cross-checks to ascertain the quality of the field work. Serum was analyzed at the laboratory of the former Institute for Social Medicine and Epidemiology of the German Federal Health Office (now Robert Koch-Institute). This laboratory participates in the Lipid Standardization Program of the WHO's Lipid Reference Centre in Prague, Czechoslovakia. Total serum

cholesterol levels and HDL cholesterol levels were analyzed enzymatically using the CHOD-PAP method<sup>9</sup> on a Technicon SMAC analyzer (Technicon Instruments Corporation, Tarrytown, NY). The HDL cholesterol fraction was isolated after precipitation of chylomicrons, VLDL and LDL fractions with magnesium phosphotungstate<sup>10</sup>.

In addition, the participants received a self-administered questionnaire pertaining to their medical history and health behavior. The questionnaire was checked for proper completion at the medical examination. The nonrespondents were asked to fill in a short questionnaire. The evaluation of these questionnaires for the first survey showed no significant differences in smoking habits and body mass index (BMI) between respondents and nonrespondents. Also, subsamples of early and late respondents were analyzed for differences in the main cardiovascular risk factors. Selection bias due to differences in response rates could not be detected<sup>11</sup>. Details about study design, sampling, methods, and the scope of questionnaire information are published elsewhere<sup>1,3</sup>.

### *Statistical Analyses*

The presented results were calculated using a weighting factor to adjust for slight deviations in the samples of the intended age (5-year age group), sex, community size, and federal state distribution caused by nonparticipation and nonrandom information losses. This adjustment makes the intervention and national samples comparable. The national sample is representative of the German population 25-69 years of age in 1987<sup>3</sup>. In a previous publication<sup>12</sup> of preliminary results, a different weighting factor, based on the German population of 1984 was applied. For the presented final results the more recent population census data of 1987 were used to construct the weighting factor. This, however, resulted only in small differences in the presented risk factor levels.

Net change in risk factor levels was calculated as quotient of value (mean or prevalence) last survey/first survey in intervention population minus quotient of value last survey/first survey in reference population.

The differences in trends between the national and the intervention samples were tested against the null hypothesis: change in risk factor level in the intervention population does not differ from the national change. To test this hypothesis, we used a linear regression model with interaction terms for intervention population and survey period (PROC REG of SAS; *F* test for contribution of interaction terms to the model). In these models age, sample (intervention or national reference) and survey time (1985, 1988, 1991) were

added as additional independent variables ( $Y = \text{age} + \text{sample} + \text{time}_1 + \text{time}_2 + \text{sample} \times \text{time}_1 + \text{sample} \times \text{time}_2$ ). The significant contributions of the interaction terms („sample  $\times$  time<sub>1</sub>“ and „sample  $\times$  time<sub>2</sub>“) represent the intervention impacts at midstudy (1988) and end of intervention (1991), respectively. This model uses the individual as unit of analysis but simultaneously adjusts for differences in initial levels and variances in the intervention and reference population samples (units of observation). The dependent variables (Y) were systolic blood pressure, diastolic blood pressure, total serum cholesterol, HDL cholesterol, HDL/total cholesterol ratio, and BMI. For dichotomous outcome variables like smoking, prevalence of untreated hypertension (according to WHO criteria), or hypercholesteremia, a logistic regression model was used. The same hypotheses as for the continuous variables were tested using the covariance matrices of the logistic model (Wald-statistic; PROC LOGIST and PROC IML of SAS;) <sup>13,14</sup>.

It is assumed, that a reduction in the mean levels of cardiovascular risk factors will reduce coronary heart disease (CHD) mortality. This reduction will be most effective if the percentage of people with high risk factor levels can be successfully lowered. So, changes in prevalences of those with high risk factors are especially interesting. To test whether these high-risk groups were reached by intervention, the trends in prevalences of people with cholesterol levels equal to or above, respectively 220 and 250 mg/dl as well as those with HDL cholesterol levels below 35 mg/dl were additionally analyzed. For BMI levels, those at higher risk were defined as being  $\geq 25 \text{ kg/m}^2$  and  $\geq 30 \text{ kg/m}^2$ . Change in percentage of hypertensive persons according to WHO criteria (diastole  $\geq 95$  and/or systole  $\geq 160 \text{ mmHg}$ ) was also verified.

## Results

Mean values of the CHD risk factors of interest are presented in Table 2.2. In the reference population, there were no pronounced changes in risk factors during the study period except an unfavorable rise in serum cholesterol. In the pooled intervention population, however, changes in risk factors were observed, almost all in a favorable direction.

For both systolic and diastolic blood pressure, a statistically significant decrease in the intervention population in relation to the national population was seen. The decline in systolic and diastolic blood pressure was not as strong among males as among females (Tables 2.2 and 2.3 and Figures 2.1 and 2.2). The prevalence of untreated hypertension shows an even more favorable reduction compared with the reference (Tables 2.4 and 2.5 and Figure 2.3).

Table 2.2. Development in mean levels (standard deviation) of risk factors for cardiovascular disease in the German population ages 25-69 and in the pooled intervention regions

Risk factor	National reference				Intervention				Net changes (%) <sup>a,b</sup>			
	1985 n = 4 790	1988 n = 5 335	1991 n = 5 311	1985 n = 11 548	1988 n = 8 743	1991 n = 8 636	1985- 1988	1988- 1991	1985- 1988	1988- 1991	1985- 1991	1985- 1991
Systolic BP (mmHg)	131.7 (20.1)	133.4 (19.5)	133.2 (19.5)	132.2 (20.0)	131.7 (20.0)	131.0 (19.4)	-1.6***	-0.4 ns	-1.6***	-0.4 ns	-2.0***	-2.0***
Diastolic BP (mmHg)	81.8 (12.4)	81.4 (11.9)	81.8 (11.6)	81.9 (12.2)	80.7 (12.1)	80.3 (11.7)	-1.0***	-1.0 ns	-1.0***	-1.0 ns	-2.0***	-2.0***
Cholesterol (mg/dl)	233.5 (49.6)	235.5 (48.5)	236.9 (47.1)	232.7 (48.6)	236.7 (47.8)	231.8 (45.1)	0.9 ns	-2.6***	0.9 ns	-2.6***	-1.8***	-1.8***
HDL chol. (mg/dl)	57.6 (17.5)	56.6 (16.7)	60.2 (18.3)	57.2 (17.1)	57.7 (17.9)	59.0 (17.5)	2.7***	-4.0***	2.7***	-4.0***	-1.3 ns	-1.3 ns
HDL/total chol. (%)	25.7 (9.2)	25.0 (8.7)	26.3 (9.0)	25.6 (9.0)	25.3 (9.0)	26.3 (9.0)	1.6*	-1.4 ns	1.6*	-1.4 ns	0.2 ns	0.2 ns
BMI (kg/m <sup>2</sup> )	26.1 (4.3)	26.2 (4.4)	26.5 (4.5)	25.8 (4.1)	26.0 (4.3)	26.2 (4.3)	0.7 ns	-0.7 ns	0.7 ns	-0.7 ns	0.0 ns	0.0 ns

<sup>a</sup> Net change (%) = [(value last/value first year) pooled regions - (value last/value first year) reference] × 100;

<sup>b</sup> F values for the contribution of the corresponding interaction terms to the regression model are statistically significant with prob > F of \* < 0.05; \*\* < 0.01; \*\*\* < 0.001; ns = not significant.

Table 2.3 Development in mean levels (standard deviation) of risk factors for cardiovascular disease in the German population ages 25-69 and in the pooled intervention regions, men and women separately

Risk factor	National reference				Intervention				Net changes (%) <sup>a,b</sup>	
	1985	1988	1991	1985	1988	1991	1988	1991	1985-1988	1988-1991
	n	n	n	n	n	n	n	n		
<b>Men</b>										
Systolic BP (mmHg)	134.7 (18.8)	135.6 (18.0)	135.3 (18.3)	134.6 (18.5)	134.1 (18.7)	133.1 (18.1)	134.1 (18.7)	133.1 (18.1)	-1.1**	-0.5 ns
Diastolic BP (mmHg)	84.0 (12.3)	83.1 (11.9)	83.4 (11.7)	83.9 (12.1)	82.3 (12.3)	82.0 (11.7)	82.3 (12.3)	82.0 (11.7)	-1.0**	-0.6 ns
Cholesterol (mg/dl)	232.0 (48.5)	234.4 (46.9)	235.6 (46.8)	232.0 (47.1)	236.1 (46.9)	231.3 (44.8)	236.1 (46.9)	231.3 (44.8)	0.7 ns	-2.6***
HDL chol. (mg/dl)	50.7 (14.8)	49.7 (13.5)	52.4 (15.1)	50.6 (14.8)	50.7 (15.4)	51.4 (14.3)	50.7 (15.4)	51.4 (14.3)	2.2*	-4.1***
HDL/total chol. (%)	22.8 (8.2)	22.1 (7.7)	23.1 (7.9)	22.7 (7.9)	22.3 (8.0)	23.1 (7.7)	22.3 (8.0)	23.1 (7.7)	2.2 ns	-1.5 ns
BMI (kg/m <sup>2</sup> )	26.5 (3.5)	26.5 (3.5)	26.8 (3.8)	26.2 (3.5)	26.4 (3.7)	26.6 (3.8)	26.4 (3.7)	26.6 (3.8)	1.0 ns	-0.6 ns
<b>Women</b>										
Systolic BP (mmHg)	128.8 (20.9)	131.3 (20.7)	131.1 (20.5)	129.8 (21.2)	129.5 (20.9)	129.0 (20.4)	129.5 (20.9)	129.0 (20.4)	-2.2***	-0.2 ns
Diastolic BP (mmHg)	79.8 (12.1)	79.8 (11.8)	80.4 (11.3)	80.0 (12.1)	79.2 (11.7)	78.7 (11.5)	79.2 (11.7)	78.7 (11.5)	-1.0**	-1.3*
Cholesterol (mg/dl)	235.0 (50.7)	236.6 (50.1)	238.0 (47.3)	233.3 (50.0)	237.2 (48.8)	232.2 (45.5)	237.2 (48.8)	232.2 (45.5)	1.0 ns	-2.7***
HDL chol. (mg/dl)	64.4 (17.3)	63.2 (16.7)	67.4 (18.1)	63.3 (16.8)	64.3 (17.6)	66.3 (17.3)	64.3 (17.6)	66.3 (17.3)	3.4***	-3.5***
HDL/total chol. (%)	28.5 (9.2)	27.8 (8.8)	29.3 (9.1)	28.3 (9.0)	28.1 (9.0)	29.5 (9.0)	28.1 (9.0)	29.5 (9.0)	1.5 ns	-1.0 ns
BMI (kg/m <sup>2</sup> )	25.8 (4.82)	26.0 (5.1)	26.2 (5.1)	25.5 (4.6)	25.7 (4.8)	25.8 (4.8)	25.7 (4.8)	25.8 (4.8)	0.4 ns	-0.8 ns

<sup>a</sup> Net change (%) = [(value last/value first year)<sup>pooled regions</sup> - (value last/value first year)<sup>reference</sup>] × 100;

<sup>b</sup> F values for contribution of the corresponding interaction terms to the regression model are statistically significant with prob > F of \* < 0.05; \*\* < 0.01; \*\*\* < 0.001; ns = not significant.

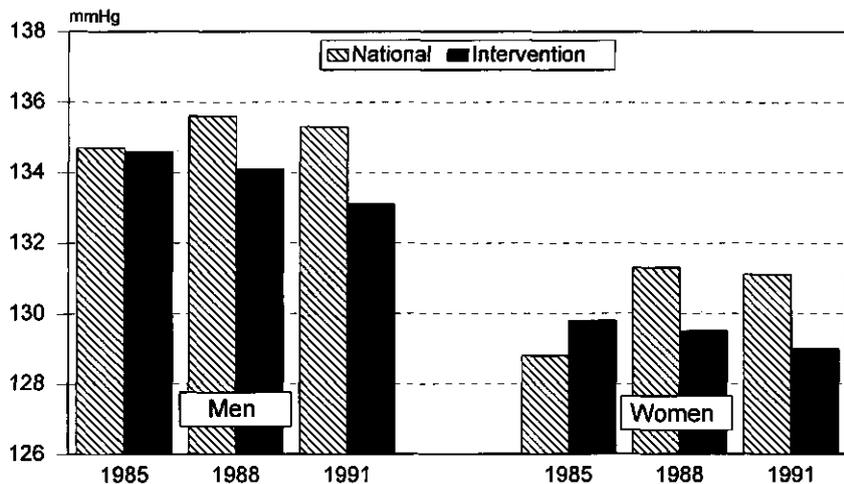


Figure 2.1 Weighted mean values of systolic blood pressure of the national and intervention population

The percentage of hypertensive persons was reduced by approximately 21%. The decrease was much stronger (and statistically significant) among women than among men. In summary, the blood pressure distribution in the intervention population has become narrower.

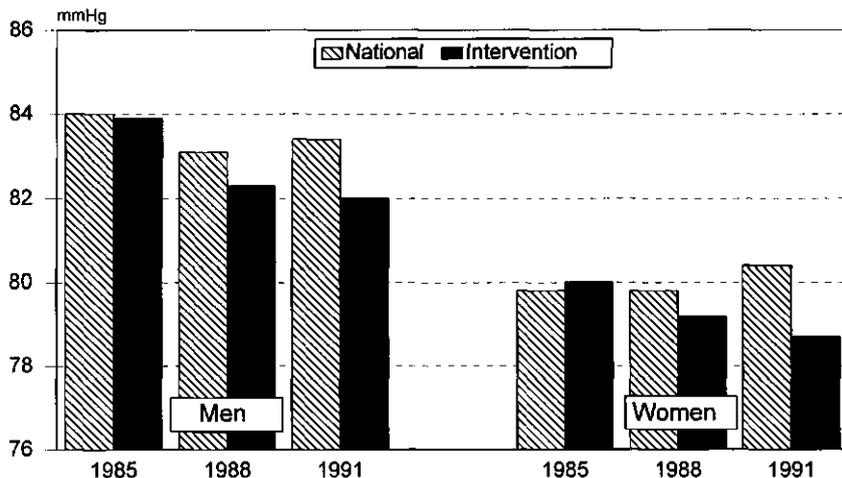


Figure 2.2 Weighted mean values of diastolic blood pressure of the national and intervention population

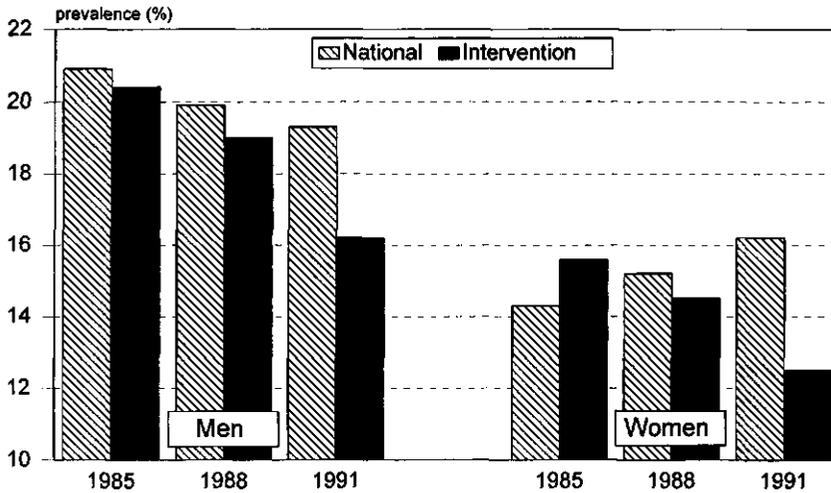


Figure 2.3 Weighted prevalences of hypertension of the national and intervention population

The net decrease in serum cholesterol levels was also statistically significant for both genders, although more obvious in the male intervention population (see Tables 2.2 and 2.3 and Figure 2.4). This reduction was accompanied by an unfavorable decline in HDL cholesterol, although not statistically significant. For men the HDL cholesterol levels decreased; for women there was no change. However, this does not lead to a significant change in HDL/total serum cholesterol ratio.

In the intervention population, statistically significant reductions in the prevalences of persons with hypercholesteremia were achieved (Tables 2.4 and 2.5 and Figure 2.5). Relative to the national trend, a 6% reduction in the levels of those with cholesterol  $\geq 220$  mg/dl and an 11% reduction in the levels of those with cholesterol  $\geq 250$  mg/dl was attained after 7 years of intervention. The male population shows a reduction in prevalence of both hypercholesterolemic groups. For women the reduction was within the confidence bounds. The larger net effects on prevalence of hypercholesterolemia compared with changes in mean values is partly due to the reduction of people having low and very low cholesterol levels at the end of the intervention period. The percentage of those with low HDL levels ( $< 35$  mg/dl) was slightly increased, but not statistically significant. Among women there was a strong drop in instances of low HDL.

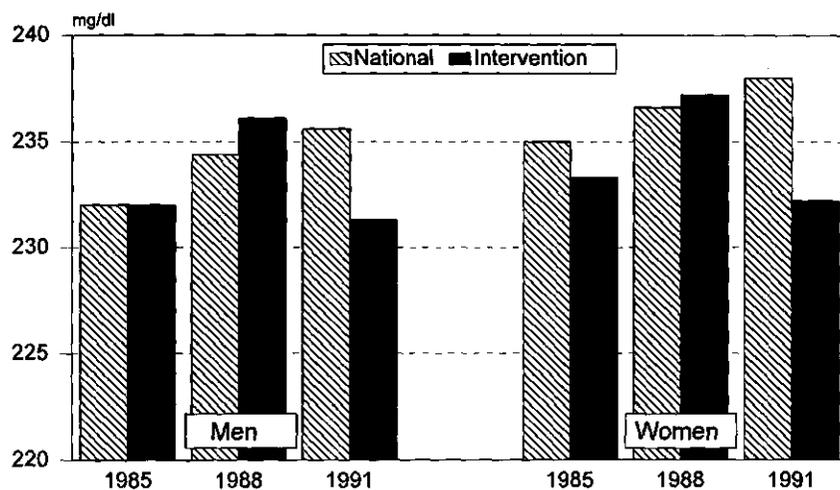


Figure 2.4 Weighted mean values of total serum cholesterol of the national and intervention population

A significant decrease in percentage of smokers in the intervention regions compared with the national trend was also observed. The reduction was significant only for the male population (see Table 2.5 and Figure 2.6). Among the group of younger women, no change in smoking habits against the nationwide trend could be achieved.

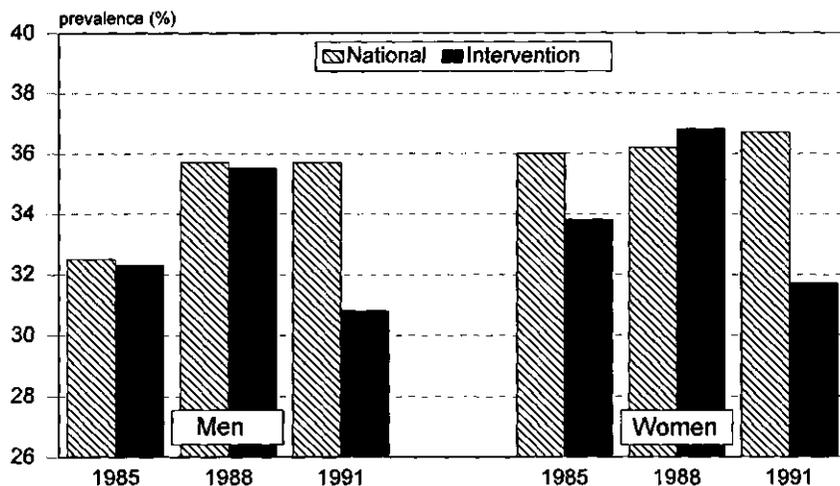


Figure 2.5 Weighted prevalences of cholesterol ( $\geq 250$  mg/dl) of the national and intervention population

No obvious change in mean values of the BMI was observed relative to the national trend. Mean values increased in both intervention and reference groups among men and women. Men showed an unfavorable net change in obesity, though not significant (see Tables 2.3 and 2.5 and Figure 2.7).

## Discussion

It is generally assumed, that CHD can be prevented by reducing cardiovascular risk factors in a population<sup>15-17</sup>. In the past, attempts to lower risk factors in unselected populations or persons at high risk were made in many countries. Risk factors were influenced by blood pressure and cholesterol-lowering drugs as well as by means of primary prevention with varying degrees of success. In a few studies, the successful reduction of some risk factors was accompanied by a rise in other risk factors. Several of the important randomized clinical trials and controlled intervention studies did not achieve a meaningful reduction of CHD<sup>18-20</sup> or failed to show a decrease, especially in total mortality<sup>21-25</sup>. In some of the intervention studies, the study design did not allow the separation of the observed effects on risk factors and/or on coronary heart disease mortality from secular trends<sup>26,27</sup>. Often there were not enough morbidity or mortality events to confirm the risk factor effects.

At present, only a few controlled intervention trials were conducted in a broader population<sup>28-33</sup>. In the North Karelia Project, cardiovascular risk factors were lowered in the intervention region and also in the reference population. In the intervention population the decline was only slightly higher than that in the reference population for serum cholesterol (12.1% intervention versus 11.5% reference) and blood pressure (6.6% versus 5.9%). Only tobacco consumption was lowered significantly in comparison with the reference<sup>27</sup>. Additional preventive activities in Finland were carried out after the original trial. After 20 years a substantial decline in risk factor levels and an associated decline in coronary heart disease mortality were observed, but also in the rest of Finland<sup>26,28</sup>. In the Stanford Five-City Project, the reduction of most risk factors could be confirmed only in a cohort sample with its much stronger intervention exposure but not in independent cross-sectional samples<sup>30</sup>. Nevertheless, the risk factor reductions resulted in a 15% decline in total mortality risk score. More recent U.S. studies showed only limited success in reduction of risk factor levels, possibly due to already existing favorable secular trends<sup>31,32</sup>.

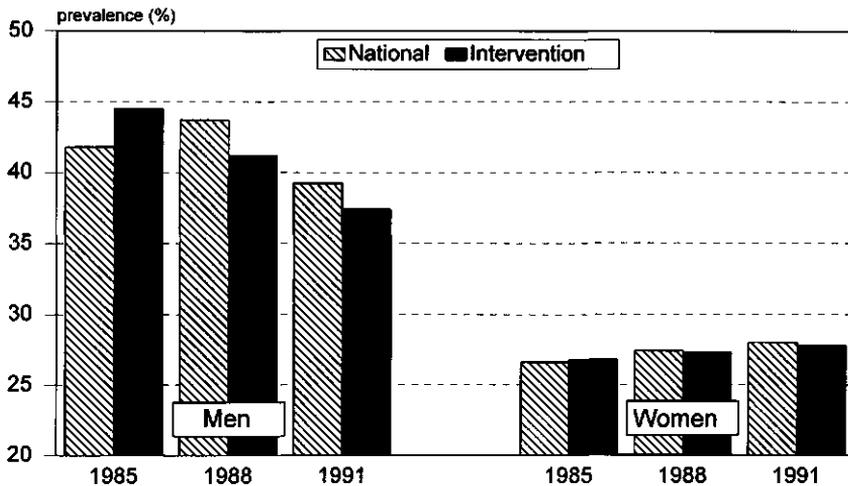


Figure 2.6 Weighted prevalences of smokers of the national and intervention population

Compared with previously conducted community-based intervention studies, the GCP could ascertain more significant net reductions in cardiovascular risk factors. The study design was planned for a pooled analysis of the intervention regions, because together they are comparable with the national reference. Nevertheless, in a future publication, the intervention effect in single regions will be reported. Although the starting levels in both the pooled intervention regions and the reference region were very similar, differences in these starting levels have been accounted for in the formulas used to calculate the net changes and in the multiple linear regression models used to test the statistical significance of the net changes. Differences in health behavior between urbanized and more rural areas have been previously observed<sup>34-36</sup>. It is unlikely, however, that secular risk factor trends in the GCP urban regions can account for the effects seen in the intervention population, since the structure of this population vis-à-vis rural and urban regions, landscape, and cultural differences, etc. was similar to the reference.

In general, the results show that community-oriented intervention can be effective in reducing cardiovascular disease risk factors. The levels of the main CHD risk factors in Germany are high in comparison with present U.S. levels and some of them are still rising<sup>2</sup>. For several risk factors, the GCP intervention program could successfully alter these trends.

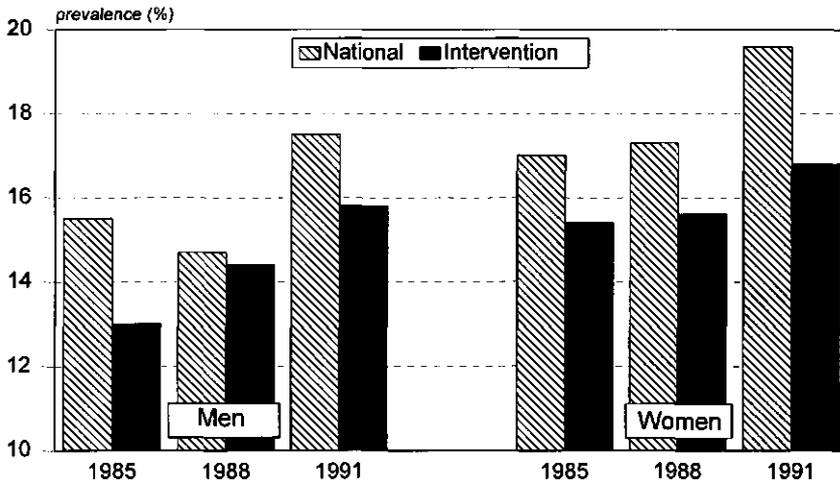


Figure 2.7 Weighted prevalences of body mass index ( $\geq 30$  kg/m<sup>2</sup>) of the national and intervention population

It might be that the effects of community intervention are easier to achieve or to detect against rising risk factor levels, as opposed to realizing an additional reduction against already declining risk factor levels, as was the case in the U.S. intervention trials<sup>31</sup>. Nevertheless, our results demonstrate that community intervention can be successful in countries where risk factor levels and trends are unfavorable.

A reduction in blood pressure and total cholesterol level against the increasing nationwide trend could be achieved during the 7 years of intervention. At the end of the intervention period, the mean levels of these risk factors are lower than the national levels, although the contrary was the case at the beginning of the study. It could be argued that the net reduction was partly achieved by the unfavorable trends in the reference. In the GCP, however, the reference represents the total of (former West) Germany. This means that those trends would very likely be the same for the intervention regions if there was no intervention impact. For these risk factors, the intervention measures have halted the undesirable national trend. The same could be observed for the prevalence rates of persons with untreated hypertension or hypercholesterolemia. The favorable change in cholesterol levels was not related to a net change in consumption of blood lipid-lowering medications. We assume this effect was mainly caused by the intensive cholesterol program after midstudy focused on healthy diet. A reduction of mean cholesterol levels is often accompanied by an unfavorable decrease in

HDL cholesterol levels. Although not statistically significant, this was also the case in the GCP. With adapted intervention strategies this side effect should be avoided in future. However, a certain reduction of HDL cholesterol is hardly avoidable. The HDL/total cholesterol ratio did not change substantially, so, in summary, the result of the achieved blood lipid reduction is favorable from a health perspective.

The failure to reduce BMI in spite of the other reduced risk factors was also observed in other intervention studies. In the GCP there were no intensified intervention strategies focused on obesity. Although special emphasis was put on improvement of nutrition and physical activity, those intervention measures were not conceived mainly to reduce weight. On the contrary, the other presented risk factors were all explicit topics of intervention activities. Among women, a prevalence reduction in the  $\geq 30$  kg/m<sup>2</sup> BMI group was observed (although not statistically significant). This could reflect the differences in motivation and reasons to change nutritional habits between men and women. For women, the intention to lose weight is stronger than it is for men, as we know from their answers in the questionnaire.

The failure to reduce BMI in the intervention regions could be partly influenced by the successful reduction of smoking. A rise of BMI after quitting smoking has been observed before<sup>37</sup>. Therefore additional analyses of BMI trends for the groups of smokers, nonsmokers and ex-smokers were carried out. There was a significantly lower BMI level among the female smokers compared with the nonsmokers and a significantly higher BMI level among the male ex-smokers compared with smokers. These results indicate an interaction of smoking habits and BMI. The failure to decrease BMI will not disturb the net positive health effect of the changes in other risk factors. In reviewing the results of this and other intervention studies, it can be concluded that BMI is the most difficult risk factor to reduce on a community level.

Changes of mean levels in the intervention population compared with the reference population in this study appear small. These, however, have been measured in independent samples, thus reflecting changes in a total population of more than 1 200 000 persons. In the population at risk we could achieve a substantial decrease of prevalences for the main risk factors. We are therefore optimistic to find a substantial reduction in CHD mortality in the intervention population.

## Acknowledgements

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Chapter **3**

**Physical Activity and its Association with other  
Lifestyle Factors**

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*European Journal of Epidemiology, 1997, in press*

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## Abstract

*The association of several lifestyle factors with leisure-time physical activity was examined from 1990 to 1991 in a representative sample of 2 623 men and 2 688 women, ages 25-69, in Germany. Individuals who were active during leisure time were less likely to live in small villages, to smoke and generally had a lower body mass index as compared to sedentary. Men and women with high socioeconomic status were, respectively, four and three times more likely to have an active leisure time than those with low socioeconomic status. After adjustment for age, body mass index, urbanization, socioeconomic status, smoking and average monthly temperature, they less often felt the need to sleep early, consumed fruit more often, salad, whole grain bread and vitamin supplements, less often white bread and meat and a higher amount of fluids as compared to sedentary individuals. They were more likely to be single and to eat breakfast regularly. Higher levels of leisure-time physical activity were associated with a generally healthier lifestyle.*

## Introduction

Enhanced leisure-time physical activity is assumed to be protective against cardiovascular diseases, independent of other risk factors<sup>1-9</sup>. Regular physical activity may improve cardiovascular functioning. Benefits include optimization of blood pressure, the electrical stabilization of the heart muscle, and changes in metabolic functions<sup>10</sup>. High levels of leisure-time physical activity were associated with more favorable cardiovascular risk profiles including lower blood pressures and total cholesterol level<sup>11,12</sup>.

An overall healthier lifestyle, associated with physical activity, might partly explain the observed association with cardiovascular disease. Nutritional habits, medicine consumption and socioeconomic status may differ between the sedentary and the physically active. Associations of leisure-time activity with smoking, following a special diet, alcohol consumption, obesity, marital status, medication use, education and employment were observed<sup>13-17</sup>. An insight in such interrelationships on a population level is important both to unravel the etiology and for cardiovascular prevention policy. We studied the relationship of physical activity with lifestyle factors in a representative sample of the former West German population<sup>18</sup>.

## **Materials and methods**

The main purpose of the German Cardiovascular Prevention Study was to determine changes in cardiovascular risk factors as an effect of community intervention. The aims and methods are described in detail elsewhere<sup>19,20</sup>. Independent nationally representative samples, contacted by mail, were examined from June 1984 to May 1986, September 1987 to August 1989, and April 1990 to April 1991 in five regions in former West Germany. The sampling procedure was stratified by five year age groups, sex, community size and state. In the first survey, residents were invited to undergo a physical examination at 200 different sample locations (40 per area) in former West Germany. For the midpoint and final surveys, residents were invited to 100 sample locations (80 per area). For the intervention samples the response rates were 74.5, 73.0, and 71.6 % and for the national samples 66.7, 71.4, and 69.0 %, respectively. The evaluation of short questionnaires filled in by nonrespondents of the first survey showed no significant differences in smoking habits and body mass index between respondents and nonrespondents. Subsamples of early and late respondents were analyzed for differences in the main cardiovascular risk factors. Selection bias due to nonresponse was not observed. In the presented analyses we used data from the final national survey (1990-1991), comprising 2 623 men and 2 688 women, ages 25-69.

### ***Data collection***

Physical activity, sociodemographic characteristics and other lifestyle factors, such as smoking and medical history were assessed by a self-administered questionnaire. The physical activity section was a short adaptation from the Minnesota leisure-time activity questionnaire<sup>21</sup> and was previously significantly associated with cardiovascular risk factors and mortality<sup>9,12</sup>. The questionnaire included a short food frequency list. Completion of the questionnaire was supervised by a trained interviewer. Trained physicians performed medical and anthropometric examinations. Body weight (kg) and height (m) were measured in light clothes without shoes<sup>18</sup>. The body mass index is the weight divided by the squared height.

### ***Variable definitions***

The questionnaire contained detailed questions about frequency and time spent during the last three months on 18 leisure-time physical activity categories, most of which were sport categories. For frequencies of once a week or more, the hours and minutes spent per week on these activities were

reported. In addition, the average hours spent sleeping, weekly hours at work and the predominate occupational posture during the day (mainly sitting, standing, moving, or an almost equal mixture of sitting, standing and moving) were reported. The questionnaire included a question about profession with answers classified as laborers, employees, civil servants and self-employed and subclassified by occupational situation (such as full-time profession, part-time profession, unemployed or retired).

Physical activity was estimated using a conditioning leisure-time physical activity index in which activities were weighted with metabolic cost units (MET) obtained from literature<sup>22</sup>. One MET is the energy cost of an activity in comparison to the resting metabolic rate resembling 1 kcal/kg/hour. The conditioning activity index was constructed using the 15 leisure-time physical activity categories with MET values above 4.5 as described previously<sup>9</sup>. For each of these categories, the energy expenditure per kilogram body weight was calculated by multiplying the time spent on this category with the corresponding MET value.

According to MET spent per week and per kilogram body weight on conditioning physical activity, participants were categorized as sedentary (no conditioning physical activity during leisure time; ca. 50% of the population), moderate (0-18 MET for men and 0-12 MET for women) or active (upper quartile; > 18 MET for men and > 12 MET for women). For cross-tabulation and logistic regression analyses, conditioning activity was dichotomized with a cut point of 0 MET (sedentary vs. active).

A socioeconomic status index was constructed, based on education level, occupation and household income and was classified in three groups; low, middle and high socioeconomic status<sup>23</sup>. In the logistic regression model this variable was entered as two dichotomous variables with low socioeconomic status as the reference. Being employed was defined as actually having a job, unemployed as having no job (but not student, housewife, or pensioner). Residence size was defined as small (rural, small village, below 5 000 inhabitants), middle (between 5 000 and 100 000 inhabitants), and big (large cities, above 100 000 inhabitants). Living in a small village was the reference in logistic regression analyses.

Marital status was dichotomized as being single (living alone, separated, or widowed) or living with a partner. Answers to questions assessing stressful situations at the workplace, such as working overtime, heavy physical work and high work pressure were dichotomized as „stresses strongly“ versus „stresses little or not at all“. Answers to the questions „How often do you worry about your work during the evening?“ and „In the evening, how often do you feel the need to go to bed early and to sleep?“ with possible answers

„often“, „sometimes“, „rare“ or „never“ were dichotomized as „often“ versus other possibilities.

For 30 food items, the intake frequencies were assessed (possible answers: never, once a month, 2-3 times a month, once a week, several times a week, almost daily) and recalculated as times per week. The amount of beverages consumed daily and frequency of vitamin supplement use were also reported. Dietary practices were assessed by the questions „Do you follow a special diet?“ and „Is this diet prescribed?“ with possible answers „yes“ and „no“, and „Do you eat breakfast daily?“ and „How often do you eat in a canteen?“ with four possible answers, dichotomized as „never or rare“ versus „sometimes or frequent“.

The total fluid index summarizes the amounts of alcoholic and non-alcoholic beverages (in litres) consumed daily. The alcohol index cumulates the amount of wine, beer and liquors multiplied with their alcoholic content (grams alcohol per day). The total fat index cumulates the fat content of all food items per day, with frequency information weighted by estimated food quantities for men and women separately. The survey period was about one year and seasonal differences in both leisure-time physical activity and other lifestyles were expected. Therefore, all associations were additionally corrected for the average temperature of the month of investigation as a measure of seasonal variation.

Participants who reported more than 35 hours of leisure-time physical activity per week were excluded from all analyses (n=22). They reported high activity because of unusually high amounts of leisure time due to holiday, retirement, unemployment etc., and their responses may not correspond to their long-term physical activity habits<sup>9</sup>, so they could be misclassified as very active.

### ***Statistical analysis***

All analyses were performed for men and women separately. Mean frequencies per week of food intake, daily amounts of beverages and frequencies of medication were calculated with 95 percent confidence intervals (CI), adjusted for age, body mass index, socioeconomic status, smoking and seasonal temperature for the three physical activity groups. The dichotomous lifestyle factors were cross-tabulated with the physical activity groups and tested for differences with Pearson's chi square, in the total sample and in age groups (24-29, 30-39, 40-49, 50-59 and 60-69 years). Age-stratified Mantel-Haenzel tests were performed. The associations of sociodemographic and lifestyle factors with physical activity were studied, independent of each other,

with multivariate logistic regression analyses. The dichotomous physical activity variable was used as the dependent variable. Prevalence odds ratios with 95 percent CIs for the determinants of physical activity were calculated. For all analyses the SAS version 6.10 package was used<sup>24</sup>.

## RESULTS

Table 3.1 presents the differences in 17 lifestyle factors between active and sedentary people. Physically active men and women were less likely to smoke or to perform heavy physical work, and less often felt the need to go to bed and sleep early as compared to sedentary individuals. We did not observe a significant difference in average sleeping hours. Individuals with low socioeconomic status had a very low tendency to be active. Urbanized individuals and those with high socioeconomic status were more often active than others.

The physically active were more often employed, routine breakfast consumers, and more often voluntarily followed a special diet. Among men, the active ate in canteens more often, and were less likely to work overtime than the sedentary. Active women were less often housewives as compared to sedentary women.

The association of marital and socioeconomic status with physical activity slightly differed among age groups. Among young people (ages 25-29) singles were more likely to be active whereas among older (ages 60-69) singles were more likely to be sedentary. Age did not affect the relationship of physical activity with other lifestyle variables (data not presented). Generally, the association of physical activity with other lifestyle variables was similar after age-adjustment. However, the association with „being employed“ and „regularly working overtime“ among men and „being a housewife“ among women was no longer significant after age adjustment. On the other hand, following a diet was significantly associated with physical activity after age adjustment. Further adjustment for season did not essentially change the results either.

Table 3.2 presents the average food frequencies per week, adjusted for age, body mass index, socioeconomic status, smoking, and season among activity groups. Fruit, salad and whole grain bread were consumed significantly less often and white bread, meat and sausages more often by sedentary men and women as compared to others. The active used vitamin supplements more often. Among men, poultry was consumed less and coffee more frequently by the sedentary. Among women, fresh vegetables, fish and

wine were more frequently consumed by the active as compared with the sedentary. Both active men and women drank significantly more total fluid per day than sedentary (Table 3.3).

Table 3.1 Prevalence rate (percent) of lifestyle factors among sedentary and active men and women <sup>a</sup>

Lifestyle factor	Men			Women		
	Sedentary	Active <sup>b</sup>	Age-strat. <sup>c</sup>	Sedentary	Active	Age-strat.
Smokers	43.9	34.0***	***	30.4	25.7**	***
Regular breakfast	85.3	88.8*	***	87.7	91.0**	***
Eating in canteen	16.8	22.4***	*	5.9	7.1	-
Special diet	10.9	12.4	*	13.5	16.0	**
Prescribed diet	7.1	6.5	-	6.7	5.4	-
Chosen diet	3.9	5.8*	*	6.7	10.6**	***
Socioeconomic status:						
Low	21.7	7.5***	***	33.1	13.8**	***
Middle	57.5	53.6	*	52.2	56.7*	-
High	20.8	38.9***	***	14.7	29.5**	***
Small town	20.8	14.9***	***	18.8	14.7**	**
City	50.0	55.3**	*	52.0	53.8	-
Large city	29.2	29.8	-	29.2	31.5	-
Employed	75.7	83.0***	-	51.9	60.8**	-
Unemployed	3.8	2.0**	**	2.4	2.3	-
Housewife/husband	0.1	0.4	-	31.4	27.1*	-
Single	15.6	17.8	-	21.4	22.0	-
Work overtime	16.0	12.9*	-	10.3	10.3	-
Heavy physical work	15.8	9.3***	***	11.3	6.9**	***
High work pressure	25.7	22.7	-	19.5	17.8	-
Feel need to sleep	18.9	11.0***	***	27.3	19.7**	***
Worry about work	23.9	25.0	-	19.8	19.5	-

<sup>a</sup> Statistically significant differences in prevalences at \*  $p < 0.05$ ; \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  (for chi-square and age-stratified Mantel-Haenzel test)

<sup>b</sup> Physical activity is dichotomized with active defined as activity above 0 MET per week

<sup>c</sup> Mantel-Haenzel test stratified by age groups: 24-29, 30-39, 40-49, 50-59 and 60-69 years

The odds ratios (with 95 % CI) of relevant determinants of physical activity derived from a multivariate logistic regression are shown in Table 3.4. For both genders, age, body mass index, smoking, being single, white bread consumption, meat consumption and feeling the need to sleep early were negatively associated with a higher physical activity level. Average temperature, moderate and high socioeconomic status, living in urban

Table 3.4 Odds ratios for the associations between physical activity and other lifestyle factors <sup>a</sup>

Lifestyle factor	Men (N = 2 358)		Women (N = 2 530)	
	OR <sup>b</sup>	95% CI	OR	95% CI
Age (years)	0.97	0.96-0.98	0.97	0.96-0.98
Body mass index (kg/m <sup>2</sup> )	0.97	0.95-1.00	0.97	0.95-0.99
Seasonal temperature (°C)	1.02	1.00-1.03	1.02	1.00-1.04
Smoking (yes)	0.57	0.57-0.82	0.65	0.53-0.80
Middle socioeconomic status (yes) <sup>c</sup>	2.43	1.83-3.22	2.01	1.60-2.52
High socioeconomic status (yes) <sup>c</sup>	4.05	2.97-5.53	3.08	2.33-4.09
Middle size city <sup>c</sup>	1.56	1.22-1.98	1.25	0.98-1.60
Large city <sup>c</sup>	1.33	1.01-1.74	1.18	0.90-1.54
Being single (yes)	0.83	0.65-1.07	0.71	0.57-0.88
Regular breakfast (yes)	1.35	1.03-1.76	1.42	1.07-1.88
Fruit (per week)	1.11	1.06-1.15	1.09	1.04-1.14
Salad (per week)	1.09	1.03-1.14	1.04	1.00-1.09
Whole grain bread (per week)	1.05	1.01-1.09	1.05	1.01-1.10
White bread (per week)	0.94	0.90-0.97	0.94	0.90-0.98
Meat (per week)	0.93	0.88-0.97	0.96	0.92-1.01
Vitamin (per week)	1.08	1.00-1.17	1.08	1.02-1.14
Feel need to sleep (yes)	0.58	0.45-0.75	0.62	0.51-0.77
Total fluid intake (l/day)	1.12	1.00-1.24	1.24	1.11-1.40

<sup>a</sup> From logistic regression analyses with physical activity as dependent, and all others simultaneously as independent variables

<sup>b</sup> OR, odds ratio for reported physical activity level above 0 MET per week; CI, confidence interval.

<sup>c</sup> Compared to, respectively, low socioeconomic status and living in a small town

The highly educated in Australia, Canada and the United States are 1.5-3 times more likely to be active during leisure time<sup>33</sup>. Their occupational activity level might be low and they could compensate for this during leisure time. A higher level of education may also have an impact on health consciousness. Stronger correlations between physical activity and other health behavior were seen in recent years, which might relate to increased health consciousness<sup>34</sup>. Financial aspects of sport may also explain socioeconomic differences.

Active individuals were less likely to smoke than sedentary, as previously shown<sup>13-16,26,27,29,34</sup>. Active people may be more health conscious and may notice negative effects of smoking on physical performance<sup>27</sup>.

Age, body mass index, socioeconomic status, urbanization, smoking and average monthly outdoor temperature may be determinants of lifestyle. The multivariate logistic regression results show associations between other lifestyle factors and physical activity, independent of these possible confounders and of each other. For men, a significant association between

physical activity and urbanization level was observed. Such a relationship was not previously shown although urban surroundings may be an important determinant of lifestyle. Nevertheless, it did not substantially affect the relationship between physical activity and other lifestyle variables.

For the total sample, active people were more likely to be single than sedentary, as seen before<sup>15,17</sup>. But not previously observed was that the active young (25-29 years) were more likely to be single and the active elderly (60-69 years) less likely. For young married individuals, circumstances such as lack of leisure time because of young children, home improvements, family visits and less need for additional social contacts (provided by sport participation), could explain their lower leisure activity. Having a partner may stimulate leisure activities among the elderly.

Active participants less often reported feeling the need to sleep early in the evening than the sedentary. The underlying question is supposed to measure well-being and vitality. This may be influenced by personality, coping capabilities, depression and sleep disorders. We observed no association with tiredness or sleeping hours. This substantial association with such a particular feeling was not previously shown although associations of leisure-time physical activity with well-being and sleep disorders have been observed<sup>25,33,35,36</sup>. A causal direction is not clear since people who feel tired or depressed in the evening, may not want to be active in leisure time.

We observed generally healthier dietary habits among active people, as previous studies did<sup>14-16,29,30</sup>. However, they did not always analyze separate food items or make multivariate adjustments. Like others, we observed more vegetable and fruit<sup>16,29,37</sup> and less meat consumption<sup>37</sup> among active individuals. The independent associations with white and whole grain bread, total liquid, vitamin supplement and routine breakfast consumption were not shown previously, although more fiber<sup>38,39</sup> was generally consumed by active individuals. The associations with canteen visits and special diets, which may also indicate healthy eating patterns, were no longer significant after multivariate adjustments.

The use of self-administered questionnaires may cause misclassification, for example, because not all activities have been covered. We measured activity through reported conditioning physical activities during leisure time. These activity levels do not reflect total physical activity nor physical activity at work. We constructed an index for total physical activity based on sleeping time, employment and predominate posture during the day (standing, sitting, moving, or a mixture of these). This index showed only weak associations with the presented lifestyle variables. This may partly reflect the crudeness of this estimate compared with the conditioning activity index. Occupational activity

may highly correlate with socioeconomic status<sup>35</sup>. We observed a fairly strong association between leisure activity and socioeconomic status and urbanization which could partly reflect differences in occupational activity level, since a sedentary job may be compensated by a physically active leisure time. So high leisure activity may indicate low occupation activity and vice versa. Nevertheless, a stronger association of other lifestyle habits with leisure activity than occupational activity has been suggested because leisure activity more strongly reflects personal choices<sup>30,40</sup>. Leisure-time activity may also be more relevant for public health. A person can change his or her leisure activities more easily than occupational or other routine activities, therefore leisure time behavior should be the focus in cardiovascular disease prevention.

Physical inactivity can partly be the consequence of a weak physical constitution or underlying illnesses. We observed similar relationships when excluding those who reported a previous heart attack, diabetes mellitus, a generally bad health or being limited in the performance of daily chores. Therefore it is rather unlikely that our findings are mainly a result of underlying disabilities. Physical disability may restrict physical activities, but this restriction is not necessarily related to unhealthy behavior in a different way as it is for nondisabled individuals.

Clustering of health habits in populations has been observed before and gains attention in health research. The pathways of development of health behavior are largely unknown and cannot be derived from these cross-sectional observations. Factors like genetic predisposition, constitution, education and peer-groups could have an important influence on healthier behavior pattern. This overall healthier behavior pattern should be considered when population based research on the impact of physical activity on health outcomes is performed. It seems likely that leisure-time physical activity could act as an initiator for preferable changes in other lifestyle factors. Health promotion and prevention could profit from further insight in these processes.

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Chapter **4**

**Physical Activity and its Association with  
Cardiovascular Risk Factors and Mortality**

*„Unheil droht dagegen dem Verweigern schweißtreibender Körperertüchtigung.“  
Der Spiegel, 22.5.1995*

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*Epidemiology, 1996; 7: 391-397*

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## Abstract

*We compared various indices for physical activity and their association with cardiovascular risk factors as well as total and cardiovascular disease mortality. We used data from three independent national representative samples in Germany, with a total of 7 689 men and 7 747 women, age 25-69 years. Persons with high conditioning physical activity had more favorable risk factor levels compared with sedentary persons, after adjustment for age, body mass index, smoking, survey period, and socioeconomic status. We observed a clear association with mortality only for intense physical activity. The rate ratio (RR) for total mortality was 0.36 [95% confidence interval (CI) 0.16-0.79] and 0.26 (95% CI 0.08-0.83) for cardiovascular disease mortality for men spending more than 2 hours per week on sports, compared with sedentary men. Among women, the corresponding RR for total mortality was 0.28 (95% CI 0.07-1.17). The effect of physical activity on cardiovascular disease mortality among women was not clear owing to few fatal cardiovascular events.*

## Introduction

Evidence grows that regular exercise has health-promoting effects. In particular, several studies reported an inverse association between increased physical activity and cardiovascular risk<sup>1-12</sup>. The observed effect of physical activity on cardiovascular disease risk factors<sup>13-19</sup> is partly responsible for this association, but recent studies show an association independent of these risk factors<sup>2-5,7-9,11,12</sup>.

In industrialized societies, intense physical activity during daily occupations has almost vanished. Therefore, leisure-time physical activity is now an important factor in cardiovascular disease prevention. In a large cross-sectional sample of the German Cardiovascular Prevention Study, we analyzed the relation of different indices of physical activity (total physical activity, leisure-time physical activity, and conditioning physical activity) with cardiovascular risk factors. The data included quantitative items on physical activity, from which we constructed the indices. In an additional regional sample of this study, which included mortality follow-up data, we analyzed the association of these physical activity indices and reported sports time with total and cardiovascular disease mortality (International Classification of Diseases, 9th revision, codes 390-460).

## Subjects and methods

The main purpose of the German Cardiovascular Prevention Study was to determine changes in cardiovascular risk factors as an effect of community-based intervention. In independent samples of the intervention population and representative samples of the former West German population as a reference, the study team measured risk factors and other variables during three periods (May 1984 to March 1986, September 1987 to October 1988 and April 1990 to May 1991). Previous publications describe the aims and methods of the German Cardiovascular Prevention Study in detail<sup>20,21</sup>.

A total of 7 689 men and 7 747 women took part in the national survey samples. The investigation of the regional samples of Berlin-Spandau (1 061 men and 1 212 women) included a mortality follow-up, conducted in May-June 1993. We obtained mortality data from the Federal Registry (Statistisches Bundesamt) and causes of death from hospital records (44%) and from spouses (56%). The reliability of these sources in Germany is comparable for broad mortality categories (cancer, cardiovascular diseases etc.). We analyzed mortality data of the 40 to 69-year-old participants of the first and second survey [first measured from June 1984 to September 1986 (8-year follow-up) and from March 1988 until October 1988 (5-year follow-up)].

Trained physicians performed examinations including measurements of body weight and height, blood pressure, resting heart rate, and peak expiratory flow on all participants. The participants wore light clothes and no shoes while body weight and height were measured. They sat during systolic and diastolic blood pressure measurements, obtained twice. We used the second measurements, obtained with a Hawksley random-zero sphygmomanometer, in the analyses. Resting heart rate was measured by 30-second pulse rate counting. We analyzed the higher of two measurements of peak expiratory flow (with a Roland Pulmo-test). The laboratory of the Institute for Social Medicine and Epidemiology of the German Federal Health Office, which participates in the Lipid Standardization Program of the World Health Organization Lipid Reference Center in Prague, Czechoslovakia, analyzed serum lipid levels in the blood samples that were obtained from participants lying down in a nonfasting state. The participants informed us about their sociodemographic characteristics, smoking status, nutrition and health behavior through a self-administered questionnaire. A trained interviewer supervised the completion of this questionnaire. Questions about education level, occupation and income were the basis for defining socioeconomic status categories, a process that is described elsewhere<sup>22</sup>.

A separate question block examined the frequency and time spent on 18 leisure-time activity categories during the previous 3 months. If the participants reported a frequency of leisure-time activity of once a week or higher, they had to write down the corresponding time in hours and minutes spent per week. Other questions covered the hours spent sleeping and the main occupational posture during the day, with possible answers: mainly sitting, mainly standing, mainly moving, and an almost equal mixture of sitting, standing and moving.

We used these questions to construct indices for total physical activity, leisure-time physical activity, and conditioning physical activity. For each leisure-time physical activity category, we calculated the energy expenditure per kilogram body weight by multiplying the time spent on this category with the corresponding MET value. One MET unit is the energy cost of an activity resembling 1 kcal per kg per hour. We derived the MET values for the 18 activity categories from the literature<sup>13,23-27</sup> (see Appendix of this chapter).

The leisure-time physical activity index is the sum of energy spent on all 18 categories. The conditioning activity index is the sum of the energy spent on conditioning leisure-time activities (all leisure-time activities except walking, cycling and gardening). We estimated total physical activity through the sum of energy expended during leisure time, sleeping time (MET = 0.6 kcal per kg per hour), sitting time (minimal time = 21 hours per week for eating etc.) and main occupational activity (MET for sitting 1, for standing 2, for moving 3, and for equal mixture of sitting, standing, and moving 2 kcal per kg per hour).

We compared these indices with a question about weekly time spent at sports with the possible answers: > 2 hours per week, 1 to 2 hours per week, < 1 hour per week, and no participation in sports. We tested the consistency between reported conditioning activity time and sports time with Kendall's tau-b (in 4 categories: 0, 0-1, 1-2, and > 2 hours weekly), which was 0.54 for men and 0.57 for women.

We excluded participants who reported no time but who were not clearly inactive (672 subjects in crosssectional, 72 in cohort sample). Few reported frequencies were below 3 times per month (about 5%) and we could not detect any systematic differences in these frequencies among activity groups. We also excluded participants who reported > 35 hours of conditioning physical activity per week (54 subjects in crosssectional sample, 17 in cohort sample). These subjects reported high activity levels because of unusually high amounts of leisure time owing to holiday, retirement, unemployment etc., and their responses may not have corresponded to their long-term practices. In a validation study, the leisure-time physical activity index showed only a weak association with resting heart rate (Pearson correlation coefficient -0.06 for

7 689 men and -0.03 for 7 747 women), peak expiratory flow (0.05 for men and women), high density lipoprotein/total cholesterol ratio (0.05 for men and 0.03 for women) and some other cardiovascular risk factors<sup>28</sup>. The correlations improved (0.10-0.20) for the conditioning activity index and were of similar direction and magnitude as those observed by others<sup>15-17</sup>.

We categorized the activity indices into three groups: low (no reported activities), moderate, and high activity. In these groups, we compared the mean levels of risk factors, adjusted for age (years), smoking (yes/no), social economic status (three categories), survey period (three categories), and, except for body mass index (BMI) itself, BMI (kg/m<sup>2</sup>). We also compared crude and age-adjusted mortality rates among activity groups in the cohort sample. We used direct standardization with the former West German population of 1987 as the standard; weights were, for ages 40-49 years: 1 265; for 50-59 years: 1 176; and for 60-69 years: 923.

Using proportional hazard models, we analyzed the relation of all activity indices and sports time with total and cardiovascular disease mortality, calculating rate ratio (RRs) with 95% confidence intervals (CIs) adjusted for age, systolic blood pressure, serum total cholesterol, smoking and BMI. We included sports time as three dummy variables (< 1, 1-2, and > 2 hours per week), with no time spent on sports as the referent. We conducted all statistical analyses for men and women separately. For these analyses, we used the SAS version 6.10 package<sup>29</sup>.

## Results

Table 4.1 displays the distributions of indices for total, leisure-time and conditioning physical activity among age and socioeconomic status groups. In all age groups, men and women show almost equal levels of total physical activity per kg body weight. Women have, however, lower levels of leisure-time and conditioning activity than men. The mean levels of total physical activity are higher in the older age groups, for both genders. Older men (> 60 years) also report a higher leisure-time activity level than younger men. Conditioning activity is highest in the younger age groups. Participants of higher socioeconomic status have, on average, a lower total physical activity level but a higher level of conditioning activities.

The leisure-time physical activity levels are similar to levels in the Minnesota Heart Survey<sup>16</sup> and slightly higher than those reported in the Framingham study<sup>4</sup>. The conditioning physical activity levels correspond very well with previously reported levels<sup>5,6,30</sup>. Our observed energy expenditure

values of 2 800-3 000 kcal for a 70-kg man and 2 400-2 600 kcal for a 60-kg woman were in good accordance with daily energy requirements<sup>31</sup>.

Table 4.1 Mean (and 95% CI) levels of activity indices by age, socioeconomic status, and gender, in kcal per kg per week

	Number	Physical activity indices		
		Total	Leisure-time	Conditioning leisure-time
<b>Men</b>				
Age (years)				
25-29	1 043	285 (280-290)	42 (39-44)	23 (21-25)
30-39	1 780	284 (280-287)	41 (39-44)	20 (18-21)
40-49	1 949	286 (282-289)	42 (40-44)	17 (16-19)
50-59	1 773	292 (288-296)	41 (39-43)	12 (11-14)
60-69	1 108	301 (297-305)	52 (49-55)	11 ( 9-12)
Socioeconomic status				
Low	1 285	309 (305-313)	38 (36-41)	8 (7-9)
Middle	4 396	298 (295-300)	44 (43-45)	15 (14-15)
High	1 939	258 (255-261)	44 (42-46)	20 (19-22)
<b>Women</b>				
Age (years)				
25-29	994	281 (277-286)	39 (37-42)	15 (13-16)
30-39	1 808	291 (288-295)	38 (36-40)	13 (11-14)
40-49	1 841	293 (289-296)	38 (36-39)	13 (12-14)
50-59	1 667	302 (299-306)	36 (34-37)	8 (7-9)
60-69	1 419	303 (300-306)	38 (36-40)	7 (6-7)
Socioeconomic status				
Low	2 121	307 (304-310)	34 (32-35)	5 (4-6)
Middle	4 162	290 (288-292)	38 (36-39)	10 (10-11)
High	1 406	290 (286-294)	44 (42-47)	17 (16-19)

Important contributors to total time spent on leisure-time physical activity in this population are walking (35% in men and 42% in women), gardening (25% in men and 22% in women), cycling (14% in men and 16% in women) and cross-country walking (6% in men and 5% in women). Relative time spent on walking and gardening increased with age, whereas other activities, such as jogging, soccer, tennis, and gymnastics were more popular among young persons (data not presented).

Table 4.2 presents the mean levels of risk factors by conditioning activity groups and gender adjusted for age, smoking, socioeconomic status, and BMI. Highly active men and women have more favorable risk factor levels than

inactive men and women. Similar analyses for total and leisure-time physical activity showed only weak associations (data not presented). Age is a strong confounder for the observed associations. Therefore, we conducted separate analyses for persons younger and older than 50 years. The associations with risk factors were similar in these subgroups and are not presented separately.

*Table 4.2 Adjusted mean (and 95% CI) cardiovascular risk factor levels by conditioning activity groups<sup>a</sup>*

	Conditioning activity groups		
	Low	Moderate	High
<b>Men</b>			
Weekly MET-ranges <sup>b</sup>	0 (n=3 272)	0.1-18 (n=1 593)	18-932 (n=1 974)
Total cholesterol (mmol/l)	6.12 (6.08-6.16)	6.11 (6.05-6.17)	5.97 (5.91-6.03)
HDL cholesterol (mmol/l)	1.32 (1.30-1.33)	1.30 (1.28-1.32)	1.34 (1.32-1.36)
HDL/total cholesterol (%)	22.47 (22.19-22.74)	22.17 (21.78-22.55)	23.41 (23.05-23.77)
Triglycerides (mmol/l)	2.35 (2.30-2.39)	2.34 (2.28-2.40)	2.26 (2.21-2.32)
Diastolic BP (mmHg)	84.01 (83.59-84.43)	82.84 (82.25-83.43)	83.07 (82.52-83.62)
Systolic BP (mmHg)	136.14 (135.51-136.77)	134.51 (133.63-135.39)	135.19 (134.36-136.01)
Body mass index (kg/m <sup>2</sup> )	26.64 (26.51-26.76)	26.55 (26.37-26.73)	26.36 (26.20-26.53)
Heart rate (beats/min)	74.91 (74.50-75.33)	73.50 (72.92-74.08)	71.68 (71.13-72.22)
Peak expiratory flow (l/min)	509.15 (505.03-513.28)	521.98 (516.12-527.84)	530.33 (524.68-535.98)
<b>Women</b>			
Weekly MET-ranges	0 (n=3 717)	0.1-12 (n=1 635)	12-682 (n=1 869)
Total cholesterol (mmol/l)	6.09 (6.05-6.13)	6.13 (6.07-6.19)	6.07 (6.02-6.13)
HDL cholesterol (mmol/l)	1.64 (1.62-1.66)	1.67 (1.64-1.69)	1.70 (1.67-1.72)
HDL/total cholesterol (%)	27.96 (27.66-28.27)	28.39 (27.96-28.82)	29.04 (28.64-29.45)
Triglycerides (mmol/l)	1.77 (1.74-1.80)	1.73 (1.69-1.78)	1.68 (1.64-1.72)
Diastolic BP (mmHg)	80.07 (79.67-80.47)	79.49 (78.92-80.06)	79.02 (78.48-79.55)
Systolic BP (mmHg)	130.38 (129.75-131.01)	129.30 (128.41-130.20)	128.25 (127.41-129.08)
Body mass index (kg/m <sup>2</sup> )	25.83 (25.66-26.00)	25.12 (24.88-25.36)	25.10 (24.88-25.33)
Heart rate (beats/min)	75.82 (75.43-76.21)	74.80 (74.25-75.35)	73.92 (73.41-74.44)
Peak expiratory flow (l/min)	374.08 (371.05-377.12)	381.36 (377.06-385.65)	392.85 (388.60-397.10)

HDL = high density lipoprotein, BP = blood pressure

<sup>a</sup> Adjusted for age, smoking, survey period, socioeconomic status, and BMI

<sup>b</sup> Ranges of MET spent on conditioning activities in kcal per kg per week

We found an inverse relation of conditioning activity and sports time with total and cardiovascular disease mortality. The crude and age-adjusted mortality rates (Table 4.3) are substantially lower for higher activity groups. The proportional hazard models show similar results after adjustment for age, systolic blood pressure, total serum cholesterol, smoking, and BMI (Table 4.4).

Men with higher conditioning activity levels have a lower cardiovascular mortality risk than inactive men (RR 0.33; 95% CI 0.11-0.94).

Table 4.3 Crude and age-adjusted mortality rates by activity groups, ages 40-69 years

	Observed person- years	All-cause mortality			Cardiovascular disease mortality		
		Events	Crude rates <sup>a</sup>	Age- adjusted rates <sup>a</sup>	Events	Crude rates <sup>a</sup>	Age- Adjusted Rates <sup>a</sup>
<b>Men</b>							
Total activity							
Sedentary	1 701	21	123	248	11	65	160
Moderate	2 371	23	97	120	10	42	56
High	2 021	23	114	140	13	64	82
Leisure-time activity							
Sedentary	2 135	36	169	231	20	94	135
Moderate	2 267	22	97	126	11	49	71
High	2 256	28	124	151	14	62	77
Conditioning activity							
Sedentary	3 471	60	173	211	39	112	140
Moderate	1 576	17	108	138	6	38	53
High	1 820	13	71	99	4	22	32
Sports time							
no sport	2 866	59	206	236	36	126	149
< 1 hour	1 485	11	74	117	3	20	31
1-2 hours	1 279	11	86	96	5	39	45
> 2 hours	1 349	8	59	87	4	30	40
<b>Women</b>							
Total activity							
Sedentary	2 081	12	58	65	2	10	9
Moderate	2 994	21	70	73	9	30	30
High	2 212	15	68	75	6	27	31
Leisure-time activity							
Sedentary	2 769	27	98	104	9	33	36
Moderate	2 368	18	76	83	7	30	30
High	2 856	20	70	73	7	25	24
Conditioning activity							
Sedentary	4 652	49	105	106	15	32	32
Moderate	1 401	4	29	28	2	14	12
High	2 150	13	60	75	6	28	36
Sports time							
no sport	4 307	49	114	111	17	39	38
< 1 hour	1 128	3	27	45	0	0	0
1-2 hours	1 731	7	40	54	3	17	25
> 2 hours	936	3	32	29	2	21	22

<sup>a</sup> Per 10 000 person-years

Table 4.4 Adjusted<sup>a</sup> risk ratios (and 95% CI) of total and cardiovascular mortality by activity groups, ages 40-69 years

	Men			Women		
	n	Total mortality	CVD mortality	n	Total mortality	CVD mortality
<b>Total activity</b>						
Low	255	1.00 (Referent)	1.00 (Referent)	294	1.00 (Referent)	1.00 (Referent)
Moderate	340	0.56 (0.30-1.04)	0.38 (0.15-0.97)	424	1.24 (0.60-2.58)	3.20 (0.68-15.07)
High	293	0.78 (0.42-1.44)	0.80 (0.34-1.85)	316	1.29 (0.58-2.85)	2.83 (0.54-14.80)
N events/n at risk		64/871	32/839		46/999	16/969
<b>Leisure-time activity</b>						
Low	326	1.00 (Referent)	1.00 (Referent)	408	1.00 (Referent)	1.00 (Referent)
Moderate	319	0.61 (0.35-1.05)	0.54 (0.25-1.15)	337	0.94 (0.51-1.75)	1.24 (0.43-3.57)
High	328	0.79 (0.48-1.31)	0.66 (0.33-1.34)	397	0.81 (0.44-1.49)	0.86 (0.28-2.62)
N events/n at risk		83/954	43/914		60/1098	20/1058
<b>Conditioning activity</b>						
Low	524	1.00 (Referent)	1.00 (Referent)	685	1.00 (Referent)	1.00 (Referent)
Moderate	227	0.76 (0.44-1.34)	0.47 (0.20-1.12)	193	0.38 (0.13-1.06)	0.92 (0.20-4.28)
High	264	0.67 (0.36-1.25)	0.33 (0.11-0.94)	308	0.80 (0.42-1.54)	1.63 (0.54-4.93)
N events/n at risk		86/986	46/946		61/1129	20/1088
<b>Sports activity</b>						
No sports	444	1.00 (Referent)	1.00 (Referent)	639	1.00 (Referent)	
<1 hour	203	0.49 (0.26-0.95)	0.23 (0.07-0.75)	153	0.38 (0.12-1.23)	
1-2 hours	185	0.57 (0.30-1.09)	0.43 (0.17-1.11)	237	0.52 (0.23-1.17)	<sup>b</sup>
>2 hours	191	0.36 (0.16-0.79)	0.26 (0.08-0.83)	129	0.28 (0.07-1.17)	
N events/n at risk		85/1001	44/960		57/1111	

<sup>a</sup> Adjusted for age, systolic blood pressure, total serum cholesterol, BMI and smoking

<sup>b</sup> Not enough events to calculate a stable model

Among male sports time groups of <1, 1-2, and >2 hours per week, respectively, the RRs are 0.49 (95% CI 0.26-0.95), 0.57 (95% CI 0.30-1.09), and 0.36 (95% CI 0.16-0.79) for total mortality and 0.23 (95% CI 0.07-0.75), 0.43 (95% CI 0.17-1.11) and 0.26 (95% CI 0.08-0.83) for cardiovascular disease mortality with the sedentary group as the referent. For women, the corresponding total mortality RRs are, respectively, 0.38 (95% CI 0.12-1.23), 0.52 (95% CI 0.23-1.17), and 0.28 (95% CI 0.07-1.17). There are not enough events among women to calculate stable RRs for cardiovascular disease mortality. Among men, associations of mortality with total and leisure-time physical activity are in a similar direction as for conditioning activity and sports time, but very weak.

## Discussion

The questionnaire has a considerable potential for misclassification, because it combines some activities with different MET values and does not cover others. Other methods, however, are less practical for large population studies<sup>32</sup>. MET values are measured on relatively few persons<sup>33</sup>. We use them as weighting factors but do not account for between-person variation due to heredity, age, race, sex, body weight, body composition, seasonal variation, disease, and environmental temperature<sup>24,33,34</sup>.

Persons with high levels of conditioning physical activity show more beneficial cardiovascular risk factor levels, as was observed previously<sup>14-17,35</sup>. This association persists after adjustment for age, smoking, BMI, survey period, and socioeconomic status. In addition, high physical activity is associated with lower total and cardiovascular mortality risk independent of main cardiovascular risk factors.

Many previous studies report a beneficial effect of physical activity on total, cardiovascular disease or coronary heart disease (CHD) mortality<sup>1-12,36-38</sup>. In an extensive review<sup>10</sup>, only three cohort studies show no such association. The other studies find RRs ranging from 1.5 to 2.4 with a median RR of 1.9 for CHD mortality among inactive men, compared with more active men. Recent studies report RRs between 1.7 and 2.2 for total mortality<sup>1-3,38,39</sup> or RRs for active vs sedentary men between 0.4 and 0.9 for total or CHD mortality<sup>6-9,11,36</sup>. Only few studies give results for women, with total mortality RRs between 1.3 and 2.1 for inactive vs active<sup>2,38</sup>, no association<sup>39</sup> or a reduced risk for total mortality (RR 0.7 for active vs sedentary), but not for cardiovascular disease mortality<sup>37</sup>.

We also observe a much weaker association among women. The mortality rate among German women in this age range is relatively low, especially for cardiovascular mortality, so an association with physical activity is hard to detect. Furthermore, the questionnaire focuses on typical male leisure-time activities and is therefore less accurate for women<sup>39</sup>.

Our results, in accordance with previous reports, show that the RR varies depending on how physical activity is defined. We observed the strongest association for persons with high levels of conditioning exercises or sports. Possible biological mechanisms such as retardation of atherosclerosis, modification of coronary artery structure, reduction of vasospasms, enhancement of myocardial electrical stability, and increase of fibrinolysis through physical activity have been proposed<sup>10</sup>. Inactivity at baseline could be an indicator of an underlying disease that affects survival time. Nevertheless, when we repeated our analyses with the first 2 years of follow-up excluded, we obtained similar

results. Furthermore, risk factor adjustment partly corrects for subclinical illness.

Recent reports<sup>40-42</sup> indicate a reduced mortality for persons who have increased their activity. Better health, however, could be an underlying reason for change in physical activity. Some reports<sup>40,41</sup> imply that a certain intensity of activity is needed to achieve cardiovascular disease protection. Although we see gradients in mortality risk for higher and more intense physical activity, we cannot detect a threshold. We cannot separate intensity levels of activity clearly, because persons with high conditioning activity also had high total activity. Our indices also do not distinguish between intensity levels and duration of activities. Furthermore, the sources of nondifferential misclassification may have especially weakened the observed associations of total physical activity with (risk factors and) mortality. Since seasonal differences, holidays etc. do not affect answers to the sports time question as strongly as to other questions, it is probably less affected by misclassification.

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**Appendix**

**Metabolic values of leisure-time physical activities**

We derived the MET values of the 18 categories from published studies<sup>13,23-27</sup>. For some activity categories, for which different intensity MET values existed, we averaged MET values. If different values for one category were published, we took the value of Ainsworth et al.<sup>24</sup> plus the average value of other studies divided by 2. We gave values from Ainsworth et al. a higher weight, because their study provides a very recent and complete list of MET values. Table 4A.1 shows the MET values that we used.

*Table 4A.1 MET values of leisure-time activities*

Leisure-time activity category	MET value (kcal/kg/hour)
Walking (also shopping) <sup>a</sup>	3.5
Hiking, mountain climbing	7.0
Cycling <sup>a</sup>	4.5
Gardening <sup>a</sup>	4.0
Dancing, ballet, jazz dancing	5.0
Gymnastics	4.5
Fitness gymnastics	6.0
Skating, roller-skating	7.0
Swimming	7.5
Jogging, running, athletics	9.0
Baseball, volleyball, handball, soccer, etc.	7.0
Rowing	6.0
Cross-country skiing	7.5
Alpine skiing	7.0
Boxing, fighting, judo, karate	9.0
Table tennis, badminton	5.0
Tennis, squash	8.0
Home exercise (weight lifting etc.)	6.5

<sup>a</sup> We excluded these activities in the conditioning activity index.

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Chapter **5**

**The Relationship between Resting Heart Rate and  
All-Cause, Cardiovascular and Cancer Mortality**

*„Herz, mein Herz, warum so traurig?  
Und was soll das Ach und Weh?“  
Johann Rudolf Wyss d.J.*

Gert B.M. Mensink, Hans Hoffmeister  
*European Heart Journal, 1997, in press*

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## Abstract

*The association between resting heart rate and changes in heart rate with all-cause, cardiovascular and cancer mortality was studied among 1 827 men and 2 929 women, aged 40-80 years, followed for 12 years. After adjustment for initial age, serum cholesterol, body mass index, systolic blood pressure, smoking and diabetes, the all-cause mortality hazard ratio was 1.7 (95% confidence interval (CI) 1.4-2.2) for heart rate increments of 20 beats/min for men and 1.4 (95% CI 1.1-1.8) for women. For cardiovascular mortality, the risk estimates were 1.7 (95% CI 1.2-2.6) for men and 1.3 (95% CI 0.9-2.0) for women. We observed no significant association between heart rate and cancer mortality. For women, stronger predictive information for all-cause mortality was provided if changes in heart rate were evident at the 2-year review. The resting heart rate is a predictor of mortality, independent of major cardiovascular risk factors.*

## Introduction

Feeling the pulse has a long tradition in medicine as a non-invasive, easily obtained indicator of illness. The heart rate changes dramatically during fever, physical exercise and in stressful situations. However, its use as a predictor of survival was emphasised only recently. An elevated resting heart rate has been associated with cardiovascular<sup>1-3</sup> and all-cause mortality<sup>5,6</sup> independent of major cardiovascular risk factors, and with cancer mortality<sup>7</sup>. It partly reflects physical inactivity, which has been shown to increase the cardiovascular disease risk<sup>8,9</sup>. It is suspected that the resting heart rate has an effect on atherosclerosis because it has been positively related to the occurrence of atherosclerotic plaques in primates<sup>10</sup>.

Few reports exist on the association between heart rate and mortality among women<sup>2,4,5</sup>. We present the relationship between resting heart rate for both men and women with all-cause, cardiovascular and cancer mortality, adjusted for other risk factors. We analyzed longitudinal data from 1 827 men and 2 929 women, ages 40-80, at initial survey. These were followed for 12 years, during which time there were health examinations at 2-year intervals. In addition, effects of changes in heart rate on survival time were studied.

## Materials and Methods

The first survey of the Spandau Health Test was conducted on a voluntary basis in 1982/83 among citizens of Berlin-Spandau aged 16 and older. Participants were recruited by local newspaper advertisements. Every 2 years (1984/85; 1986/87; 1988/89; 1990/91) the participants were re-invited for follow-up surveys. Additionally, a small number of new participants was allowed to enter the study after the first survey (see Table 5.1). For all 6 410 subjects (2 502 men and 3 908 women) at least one primary medical record and a follow-up were assessed. From these subjects we selected the 40-80 year-olds (at initial survey) for the present analyses.

Medical assistants, using computerized questionnaires, interviewed the participants regarding their education, profession, drinking and smoking habits, and medical history. The medical examination included assessment of height and weight, blood pressure and resting heart rate. Blood pressure and resting heart rate were measured twice, after 5 min rest, at the start of the medical examination and about 1 h later at the end of the examination. Korotkoff sounds were recorded at a paper speed of 25 mm/sec during blood pressure readings. The heart rate was calculated from five consecutive cardiac cycles. The average of both heart rate measurements during one visit was used in the present analyses. Additionally, blood and urine samples were obtained. In the blood samples total serum cholesterol, HDL cholesterol (since second survey), serum triglycerides, and several other parameters were analysed. Subjects were coded as diabetic if they were receiving medical treatment or if their blood glucose level exceeded 180 mg/dl.

In March 1994, all participants were followed-up for mortality. Sixty-seven subjects had moved and eight were lost to follow-up for other reasons. Their data were removed from the study. A total of 430 (214 men and 216 women) deaths were reported. Causes of death were obtained from death certificates from the regional health office (27 %), or from hospital records (26 %). If these sources were not available, the cause of death was obtained by a physician from interviews with relatives or neighbours of the deceased (47 %). Information was gained about the primary cause of death, the underlying illness and up to three accompanying diseases, the death location and the information source. For the presented analyses, mortality causes were coded as cardiovascular disease (International Classification of Diseases, 9th revision, codes 390-459.9), cancer (codes 140-208.9) or others, using the information of the underlying illness.

Analyses were conducted for men and women separately. We calculated the age-standardized mortality rates for four heart rate groups (< 60, 60-70,

70-80, > 80 beats/min) using the German population of 1987 as the standard. With use of proportional hazard models<sup>11</sup>, the risk ratios for initial heart rate expressed in units of 20 beats/min (two standard deviations), adjusted for age (in years), serum cholesterol (mmol/l), body mass index (kg/m<sup>2</sup>), systolic blood pressure (mmHg), smoking (yes/no) and diabetes (yes/no) were estimated. We inspected smoothed Schoenfeld's residuals plots<sup>12,13</sup> of all covariates to check for violations of the proportional hazard assumption. Similar analyses were performed excluding deaths occurring during the first 2 years of follow-up. We tested for effect modification by other risk factors using log likelihood ratio tests<sup>14</sup> and calculated the risk ratios for relevant subgroups. Furthermore, we estimated the impact of the 2-year change in resting heart rate on all-cause mortality stratified by initial level.

## Results

The presented analyses are based on a total of 15 250 person years of follow-up for men and 25 106 person years for women. On average, the participants were examined three times in this period (see Table 5.1). The mean heart rate level was 70 beats/min for men and 73 beats/min for women. Initial resting heart rate levels above 90 beats/min were observed for 99 men and 212 women. Among them, 29 men and 54 women had heart rates above 100 beats/min. For 41 men and 18 women we observed heart rates below 50 beats/min. The age structure differed from the German population due to a slight over-representation of the 40-49 year age groups.

An almost linear increase in all-cause mortality with initial heart rate level is seen among men (Figure 5.1). The age-standardized all-cause and cardiovascular mortality rates according to initial resting heart rate are presented in Table 5.2. An increase in all-cause and cardiovascular mortality with higher heart rate is observed for men in both age groups. For women a similar trend is observed only in the 60-80 year age group. Among younger women with heart rates below 70 beats/min no cardiovascular mortality was observed.

With proportional hazard models, the effect of heart rate on survival time was modelled with adjustment for initial age, serum cholesterol, body mass index, systolic blood pressure, smoking and diabetes. The proportional hazard assumption was appropriate for all covariates. For persons with a 20 beats/min higher heart rate level (about two standard deviations), an all-cause mortality hazard ratio of 1.7 (95% CI 1.4-2.2) for men and of 1.4 (95% CI 1.1-1.8) for women was calculated.

Table 5.1 Sample characteristics for persons aged 40-80 years at initial survey

	Men	Women
Participants <sup>a</sup>	1 827	2 929
40 - 60 years	1 281	1 853
60 - 80 years	546	1 076
Initial survey 82-83	1 102	1 763
Initial survey 84-85	200	334
Initial survey 85-86	380	589
Initial survey 87-88	145	243
Total person years follow-up	15 250	25 106
Average person years	8.4	8.6
Average survey participation	3.0	2.9
Initial risk factor levels:		
Heart rate (beats/min)	70.0 (11.6) <sup>b</sup>	73.3 (10.6)
Cholesterol (mmol/l)	6.2 (1.1)	6.4 (1.2)
HDL cholesterol (mmol/l)	1.3 (0.4)	1.6 (0.4)
Systolic blood pressure (mmHg)	146.1 (19.6)	139.5 (21.0)
Diastolic blood pressure (mmHg)	84.2 (11.4)	83.1 (10.9)
Body mass index (kg/m <sup>2</sup> )	26.0 (2.9)	25.2 (10.6)
Smoker (%)	26.9	16.6
Exsmoker (%)	41.0	16.3

HDL, high density lipoprotein

<sup>a</sup> Valid heart rates were obtained for 1 798 men and 2 908 women<sup>b</sup> Mean (standard deviation)

For cardiovascular mortality the hazard ratios were of the same magnitude although not significant for women (see Table 5.3). We repeated the analyses with the first 2 years of observation excluded. Among men and women, the cardiovascular mortality hazard ratios were slightly smaller, for all-cause mortality the risk remained the same.

For cancer mortality, we observed no significant higher risk for elevated resting heart rate levels. We repeated the analyses, excluding those who had been taking medical treatment for cardiovascular diseases (427 men and 1 018 women) or hypertension (364 men and 646 women) within 6 months prior to the initial survey. For all-cause mortality the hazard ratio was 1.4 (95% CI 1.0-2.0) for men and 1.3 (95% CI 0.9-1.9) for women, when persons under treatment for cardiovascular diseases were excluded. A similar reduction was observed for cardiovascular disease, cancer and other mortality causes. When persons under treatment for hypertension were excluded, the all-cause

mortality hazard ratio was 1.9 (95% CI 1.5-2.5) for men and 1.7 (95% CI 1.2-2.3) for women. We observed similar increases for cardiovascular disease, cancer and other mortality causes.

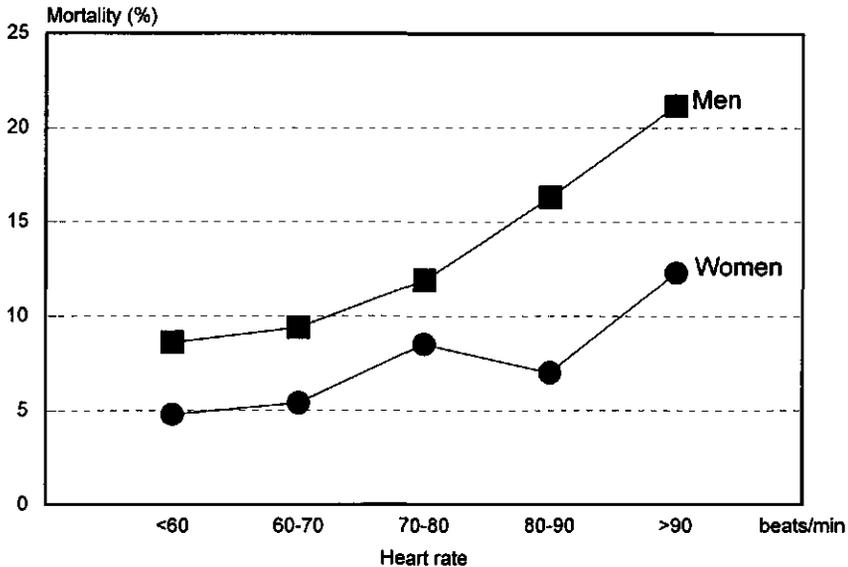


Figure 5.1 All-cause mortality during 12 years against resting heart rate levels, men and women, aged 40-80 years

Serum cholesterol level for men and body mass index for women affected the relationship between heart rate and mortality. In Table 5.4, we present the risk ratios for all-cause and cardiovascular mortality for heart rate levels above and below 80 beats/min and divided in tertiles of cholesterol level for men and of body mass index for women. Persons with heart rate levels below 80 beats/min in the lowest risk factor tertiles were used as reference.

For men, the increased risk associated with elevated heart rate is highest for persons with cholesterol levels below 5.7 mmol/l (hazard ratio 2.6, 95% CI 1.6-4.3). The association of heart rate and survival disappears when cholesterol levels are above or equal to 6.7 mmol/l. For cardiovascular mortality, the hazard ratio for both elevated cholesterol and heart rate is less than one would expect from the separate risks for one risk factor. For all-cause mortality, a less than additive effect of smoking and elevated heart rate was observed. This was not observed for cardiovascular mortality but for mortality from cancer and other causes among male smokers with an elevated pulse rate at baseline (non-significant). Effect modification was observed for body mass index among

women. Only among women with a body mass index below 24 kg/m<sup>2</sup>, was the hazard ratio for heart rate levels above or equal to 80 beats/min significantly higher as the reference (hazard ratio 1.8, 95% CI 1.1-2.8).

In Table 5.5, we present the estimated all-cause mortality hazard ratios of heart rate changes between first and second visit of more than 10 beats/min, between 0 and 10 beats/min, and negative changes (<0 beats/min) for persons with initial levels above and below the population mean (72 beats/min). A total of 119 men and 208 women showed an increase above 10 beats/min between first and second measurement, of which 18 men and 25 women showed increases above 20 beats/min. For both men and women the risk estimates are highest for those with a positive change and initial levels above the population mean. A similar trend was seen for those with initial levels below 72, but this could partly reflect reaching their true level (regression to the mean).

Table 5.2 Age standardized mortality rates and mean risk factor levels (95% CI) according to initial heart rate <sup>a</sup>

	Heart rate (beats/min)			
	< 60	60-70	70-80	> 80
<b>Mortality Men</b>				
Ages 40-60: persons at risk	234	452	344	239
Events (total/cardiovascular disease)	7/3	19/11	21/8	18/9
All-cause	34.0	48.0	65.2	80.0
Cardiovascular disease mortality	10.8	18.4	22.7	32.3
Ages 60-80: persons at risk	94	176	159	100
Events (total/cardiovascular disease)	21/12	40/26	39/19	42/23
All-cause	220.8	246.6	277.5	462.8
Cardiovascular disease mortality	107.1	146.1	102.3	216.0
<b>Mortality Women</b>				
Ages 40-60: persons at risk	127	631	640	449
Events (total/cardiovascular disease)	0/0	5/1	20/7	6/1
All-cause	0	9.1	35.2	18.2
Cardiovascular disease mortality	0	0	6.1	0
Ages 60-80: Persons at risk	84	340	386	251
Events (total/cardiovascular disease)	10/4	47/31	67/33	54/28
All-cause	120.6	159.2	186.1	222.4
Cardiovascular disease mortality	24.7	75.4	63.9	70.0

<sup>a</sup> All-cause and cardiovascular mortality rates per 1 000 persons from 1982 till 1994

Table 5.3 All-cause, cardiovascular and cancer mortality hazard ratios<sup>a</sup> for initial heart rate (per 20 beats/min) and with exclusion of first 2 years of follow-up

	Events	Hazard ratio (95% CI)	Excluding first 2 years	
			Events (95% CI)	Hazard ratio
All-cause				
Men	205	1.7 (1.4-2.2)	175	1.7 (1.3-2.3)
Women	207	1.4 (1.1-1.8)	183	1.4 (1.1-1.8)
Cardiovascular disease				
Men	85	1.7 (1.2-2.6)	69	1.6 (1.0-2.5)
Women	68	1.3 (0.9-2.0)	61	1.3 (0.8-2.0)
Cancer				
Men	60	1.5 (1.0-2.5)	48	1.3 (0.8-2.2)
Women	66	1.1 (0.7-1.7)	56	1.1 (0.7-1.8)
Other				
Men	60	2.5 (1.7-3.9)	58	2.6 (1.7-4.0)
Women	73	2.1 (1.5-3.2)	66	2.1 (1.4-3.2)

<sup>a</sup> Adjusted for initial age, serum cholesterol, body mass index, systolic blood pressure, smoking and diabetes. Number of events are lower as stated earlier due to missing values for these covariates

## Discussion

The study population has a higher proportion of 40 to 50 year-olds than the German population as a whole. This, however, has no influence on the presented risk estimates. Several cardiovascular risk factors are related to resting heart rate level, as observed by others<sup>15</sup>. Smoking was observed to elevate catecholamine levels and heart rate<sup>16</sup>. In our study, age shows almost no association with resting heart rate. A similar lack of association with age was observed in a representative sample of the German population<sup>9</sup>, so it is unlikely that this indicates a selection bias. Small sex differences in heart rate were observed, but women had much lower mortality rates than men. We observed almost no cardiovascular mortality among the 40-60 year-old women, and only a few events among women with initial heart rates above 70 beats/min. These low mortality rates are probably responsible for the absence of a significant association between heart rate and cardiovascular mortality among women.

Table 5.4 All-cause and cardiovascular mortality hazard ratios<sup>a</sup> for heart rates above and below 80 beats/min for different levels of other risk factors

	Men			
	All-cause mortality		Cardiovascular mortality	
	< 80 beats/min <sup>b</sup>	≥ 80 beats/min	< 80 beats/min	≥ 80 beats/min
<b>Cholesterol</b>				
<5.7 mmol/l	1	2.6 (1.6-4.3)	1	2.4 (0.9-6.6)
5.7-6.7 mmol/l	0.9 (0.6-1.4)	2.1 (1.3-3.5)	0.8 (0.4-1.7)	3.7 (1.7-7.9)
≥6.7 mmol/l	1.2 (0.8-1.8)	1.2 (0.7-2.2)	1.9 (1.0-3.4)	2.3 (1.0-5.2)
	p <sup>a</sup> = 0.034		p = 0.073	
<b>Nonsmokers</b>	1	2.5 (1.7-3.7)	1	2.3 (1.3-4.2)
<b>Smokers</b>	2.8 (2.0-4.0)	3.1 (1.9-5.2)	2.2 (1.3-3.9)	4.5 (2.2-9.1)
	p = 0.010		p = 0.790	
	Women			
	All-cause mortality		Cardiovascular mortality	
	< 80 beats/min	≥ 80 beats/min	< 80 beats/min	≥ 80 beats/min
<b>Body mass index</b>				
<24 kg/m <sup>2</sup>	1	1.8 (1.1-2.8)	1	1.9 (0.8-4.6)
24-26.5 kg/m <sup>2</sup>	0.8 (0.5-1.1)	0.9 (0.5-1.7)	0.5 (0.2-1.1)	0.9 (0.3-2.5)
≥26.5 kg/m <sup>2</sup>	0.9 (0.6-1.4)	0.6 (0.4-1.1)	1.0 (0.5-1.9)	0.6 (0.2-1.4)
	p = 0.024		p = 0.096	

<sup>a</sup> Adjusted for initial age, serum cholesterol, body mass index, systolic blood pressure, smoking and diabetes

<sup>b</sup> P-value of the likelihood ratio test for significant contribution of the interaction term

Our analyses show a positive association between heart rate and total and cardiovascular mortality, even after adjustment for major cardiovascular risk factors. Several studies reported a similar association<sup>1,2,5</sup>. To the extent that heart rate is positively associated with unspecific mortality causes, it could be argued that it is an indicator of general poor health. Persons with known cardiovascular diseases were excluded in additional analyses, but there was still a positive association between heart rate and mortality. When the first 2 years of follow-up are excluded (excluding early mortality cases) the risk estimates remain almost the same. This indicates that the association between heart rate and mortality cannot be subscribed to the role of heart rate as an indicator of pre-existing illnesses. Although there is a tendency for a positive association between cancer mortality and heart rate, this does not reach statistical significance. A positive association between cancer and heart rate was observed by Persky et al.<sup>7</sup>. They assumed that excessive alcohol intake

could be an important confounder. Correction for alcohol intake in our study does not, however, change the magnitude of association.

Table 5.5 All-cause mortality hazard ratios<sup>a</sup> for 2-year changes in resting heart rate stratified by initial levels above and below the population mean

Change	Men Initial level		Women Initial level	
	< 72 beats/min	≥ 72 beats/min	< 72 beats/min	≥ 72 beats/min
≥ 10 beats/min	1.5 (0.7-3.3) n = 99	2.3 (0.9-6.4) n = 20	2.2 (1.1-4.7) n = 154	2.9 (1.2-7.2) n = 54
0-10 beats/min	1.3 (0.7-2.3) n = 363	1.9 (0.9-3.6) n = 124	1.1 (0.6-2.3) n = 451	1.9 (1.0-3.7) n = 272
< 0 beats/min	1 n = 361	1.3 (0.7-2.3) n = 367	1 n = 431	1.6 (0.9-2.9) n = 772
(n events/at risk)	(110/1334)		(120/2134)	

<sup>a</sup> Adjusted for initial age, serum cholesterol, body mass index, systolic blood pressure, smoking and diabetes

The effect of heart rate on mortality is somewhat modified by other risk factors. We observed the largest hazard ratio for elevated heart rates among men with a low cholesterol level and among women with low body mass index. In both cases, the estimated hazard ratio for the combined presence of risk factors was lower than expected from the isolated risks. This could possibly indicate that elevated levels of these risk factors, as well as elevated heart rate result from the same atherogenic process which increases the mortality risk. For men, we observed a stronger association between heart rate and all-cause mortality among nonsmokers. This was not observed for cardiovascular mortality and appeared to be due to a less than additive effect for cancer and other mortality causes.

The resting heart rate level is sensitive to such things as infections, recent physical activity, anxiety, and stress<sup>17-19</sup>. Intra-individual fluctuations will partly be a result of measurement error and of daily variations. Therefore changes in resting heart rate, as an independent predictor of mortality should be treated with caution<sup>20</sup>. It may not be possible to separate an observed effect of measured changes from effects due to regression to the mean, or effects of true changes. We tried to avoid such misinterpretations by stratification for initial level. For persons with an initial level above the population average there was an additional predictive value of a 2-year change on survival. Without stratification by initial level, the higher risk for a change above

10 beats/min will be diluted due to regression to the mean, and the positive risk for negative changes could be misinterpreted.

Several mechanisms on the relationship between heart rate and cardiovascular mortality have been proposed. The beneficial effects of beta-blockers on survival were partly associated with their heart rate lowering capabilities<sup>21</sup>. We did not have sufficient information on the use of beta-blockers at baseline, but conducted analyses excluding persons who reported they were in medical treatment prior to initial survey for cardiovascular disease as well as for hypertension. The initial heart rate distributions in these groups are not significantly different. Nevertheless, because of differences in mortality risks in these groups, differences in magnitude of the association between heart rate and mortality are observed. The hazard ratios for all-cause, cardiovascular disease, cancer and other mortality causes are lower when excluding persons under treatment for cardiovascular disease. This is expected because high risk persons are excluded. The hazard ratios, when excluding persons under treatment for hypertension, however, were higher than the ratios in Table 5.3. In the 1980s, hypertension was often treated with beta-blockers. Such persons will have a higher mortality risk but lower heart rates compared to non-hypertensives, which will dilute the observed relationship.

Heart rate is an indicator of physical fitness and can be modified by physical exercise<sup>8,22</sup>. Both physical fitness and physical activity are associated with cardiovascular mortality, which could explain a part of the association between heart rate and mortality. However, the association between heart rate and mortality among hypertensives remained after correction for physical activity levels<sup>5</sup>.

The resting heart rate is also a marker of haemodynamic and autonomic nervous system states that could promote cardiovascular mortality by inducing atherosclerosis and by producing rhythm disturbances<sup>23</sup>. A chronic predominance of sympathetic over parasympathetic activity could promote atherosclerosis. An elevated heart rate level was associated with atherogenic serum lipid fractions<sup>24</sup> and a faster progression of atherosclerosis in clinical experiments with primates<sup>10,25</sup>. Higher heart rates were associated with progression of diffuse atherosclerosis and of distinct coronary stenosis<sup>26</sup>. It was suggested that local haemodynamic effects of heart rate contribute to faster plaque formation in the coronary arteries. Other mechanisms could also be involved. A low heart rate will result in longer diastolic filling time; this will to a certain degree, increase stroke volume<sup>27</sup> and improve the oxygen supply of the heart muscle. Haemodynamic disturbances could predispose persons to sudden death<sup>23</sup> or to lower survival chance after myocardial infarction<sup>6</sup>. The inability to reduce heart rate during sleep could also be a damaging factor<sup>28</sup>.

An inverse relationship of heart rate with heart rate variability was observed and lower variability, indicating lower adaptability (sympathetic predominance), was associated with increased mortality after myocardial infarction<sup>29</sup>.

An elevated heart rate could also be a result of increased insulin resistance induced by high carbohydrate and/or fat intake, physical inactivity and obesity. As a consequence, chronic high insulin levels will increase sympathetic activity<sup>30,31</sup>. The observed lower impact of elevated heart rate among men with high cholesterol levels and women with high body mass index would fit in this hypothesis, because these elevated risk factors and elevated heart rate could be indicators of the insulin resistance syndrome. The strong effect of heart rate among men with low levels of cholesterol and women with low body mass index, however, suggests that other mechanisms could also be important. Overall, the resting heart rate (favorably based on repeated measurements) seems to be an important predictor of survival and can be used to select persons at higher risk. Recently, we observed a difference of about 3-5 beats/min between former East and West Germany. This may partly explain the discrepancy in life expectancy between the two parts of Germany<sup>32</sup>.

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# Chapter 6

## **Intensity, Duration and Frequency of Physical Activity and Coronary Risk Factors**

*„Zwischen den verschiedenen Sportdisziplinen zu vergleichen, das ist praktisch allerdings nicht in objektiver Weise möglich: Wie will man die Leistung eines Marathonläufers mit der eines Eiskunstläufers oder Gewichthebers >objektiv< vergleichen? In Prozentanteilen vom jeweiligen Weltrekord... ? Dies unterstellte ein lineares Modell der Leistungshöhe oder ihres Anstiegs, das höchst unrealistisch ist. Außerdem würde sich die Bewertung mit jedem neuen Weltrekord verändern. Und wie wollte man Weltrekorde selbst untereinander vergleichen?“*

Hans Lenk, 1972

Gert B.M. Mensink, Désirée W. Heerstrass, Sabine E. Neppelenbroek,  
Albertine J. Schuit, Bärbel-Maria Bellach  
*Medicine and Science in Sports and Exercise, 1997, in press*

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## Abstract

*Relationships between coronary risk factors and intensity, duration, and frequency of leisure activity were studied in 5 943 men and 6 039 women, ages 25-69. Age, smoking, socioeconomics, season, body mass index (BMI), urbanization, occupational activity, and liquid, alcohol and saturated/total fat intake were adjusted using multivariate regressions. Among men each 100 kcal/kg/week spent on vigorous activities (7.5-9.0 MET) was associated with significant ( $p < 0.01$ ) average differences of -0.36 mmol/l total cholesterol, +0.17 mmol/l HDL cholesterol ( $p < 0.001$ ), +0.05 HDL/total cholesterol ( $p < 0.001$ ), -0.33 mmol/l triglycerides, -3 mmHg diastolic blood pressure, -10 beats/min heart rate ( $p < 0.001$ ), +30 l/min peak flow, and -1.1 kg/m<sup>2</sup> BMI. Among women it was associated with: -7 mmHg systolic blood pressure, -6 beats/min heart rate ( $p < 0.001$ ), +50 l/min peak flow ( $p < 0.001$ ) and -1.4 kg/m<sup>2</sup> BMI ( $p < 0.05$ ). Moderate activity (either 3.0-4.5 MET or 5.0-7.0 MET) was significantly ( $p < 0.05$ ) associated with HDL cholesterol, BMI, and, for men, heart rate; for women it was associated with HDL/total cholesterol, triglycerides, diastolic blood pressure and peak flow. With duration and intensity constant, increasing frequency by one time per week was significantly ( $p < 0.05$ ) associated with -0.014 mmol/l total cholesterol, +0.001 HDL/total cholesterol, -0.36 beats/min heart rate, -0.093 kg/m<sup>2</sup> BMI among men, and +0.009 mmol/l HDL cholesterol, +0.001 HDL/total cholesterol, -0.014 mmol/l triglycerides, -0.31 beats/min heart rate and -0.098 kg/m<sup>2</sup> BMI among women. Serum lipids and BMI showed stronger associations with frequency than with intensity or duration.*

## Introduction

Several studies report a lower occurrence of coronary heart disease (CHD) among individuals with greater engagement in leisure-time physical activity (LTPA)<sup>2,9,10,11,17,19,22</sup>. Available results remain inconclusive about the preventive effect of low intensity activities<sup>2,4,20,21</sup>.

The amount, intensity and frequency of exercise required for beneficial cardiovascular health changes are outlined in recent recommendations<sup>24</sup>. These assign health benefits to moderate levels of physical activity. However, lower levels may have beneficial effects on single CHD risk factors<sup>6,14</sup>. These exercise recommendations focus on a generally better cardiorespiratory health or fitness rather than on single CHD risk factors<sup>7</sup>. They are based on both population studies and intervention trials but only a few of these studies have addressed the issue of different intensity levels, especially of low levels. In

addition, little information exists about the impact of activity for women. We investigated different components of LTPA and their relationship with several major CHD risk factors in a cross-sectional population based sample of 5 943 men and 6 039 women, ages 25-69, free of CHD.

## **Materials and Methods**

### ***Subjects***

As part of the German Cardiovascular Prevention Study (GCP), three independent representative samples of the former West German population were examined in 1984-1986, 1987-1989 and 1990-1991. Detailed information about the aims and methods of the GCP study is described elsewhere<sup>6</sup>. Response rates after excluding people who moved prior to the start of the study, who could not be located owing to an incorrect address, or who had died, were 66.0% in the first, 71.4% in the second, and 69.0% in the final period. The analyses are based on this population, consisting of 7689 men and 7747 women, ages 25-69.

### ***Biochemical and anthropometric measurements***

All participants underwent a medical examination by trained physicians. The medical examination included measurements of body weight and height, blood pressure, resting heart rate, peak expiratory flow and blood sampling for serum cholesterol and triglyceride assessment. Measurements, except for peak expiratory flow, were performed in all three periods of the GCP. During weight and height measurement the participants wore light clothes and no shoes. Blood pressure was measured twice, 3 minutes apart, in sitting position, with a Hawksley random-zero device. We used the second measurement for our analyses. Resting heart rate was assessed by 30-second heart rate counting in sitting position. Blood samples were drawn from the nonfasting subjects who were in lying position. All laboratory assessments were performed at the Laboratory Division of the former Institute for Social Medicine and Epidemiology of the Federal Health Office (now Robert Koch-Institute) in Berlin, which participates in the Lipid Standardization Program of the WHO Lipid Reference Center in Prague. Peak expiratory flow was measured twice with a Roland Pulmo-test. We used the highest of these two measurements for the analyses.

### Physical activity assessment

For further data collection a self-administered questionnaire was used including structured questions concerning sociodemographic variables, diet (food frequency questionnaire including daily amounts of beverages), smoking history, LTPA and a medical history. The completion of the questionnaire was supervised by a trained interviewer. Physical activity was assessed with a questionnaire that examined the frequency and time spent on 18 LTPA categories during the previous three months. The physical activity questionnaire was a short, adapted version of the Minnesota leisure-time physical activity questionnaire<sup>29</sup>. The reliability was tested in a sample of 598 German men and women, ages 20-75<sup>13</sup>. Most activity categories showed a test-retest correlation between 0.5-0.8 (Pearson). Some categories, like gardening (0.39), showed lower correlations probably because of seasonal changes (test-retest from the end of January to the end of March 1982). If the participants reported a frequency of once a week or higher, they had to fill in the time in hours and minutes per week. We used these questions to construct indices for LTPA. Total LTPA energy expenditure was calculated as the sum of time spent on these activity categories multiplied by corresponding MET values (minus 1). MET values are multiples of resting metabolic rate with an energy cost of about 1 kcal per kg per hour. We obtained MET values for the 18 activity categories from literature as described previously<sup>19</sup>. The values were predominantly based on a recent comprehensive table<sup>1</sup>. Individuals reporting no LTPA will still spend an amount of energy with a MET value of approximately 1. Therefore, we subtracted the value 1 from each given MET value to calculate excess energy expenditure indices. Energy spent on physical activities was calculated for three levels based on their MET values: low (3-4.5 MET), moderate (5-7 MET), and high (7.5-9 MET) intensity activities (see Table 6.1).

Table 6.1 Energy indices for activity intensity levels

Intensity	Activity categories (MET)
Low (3.5-4.5 MET)	Walking/shopping (3.5), cycling (4.5), gardening (4.0), gymnastics (4.5)
Moderate (5.0-7.0 MET)	Hiking/mountain climbing (7.0), dancing/ballet/jazz dancing (5.0), fitness-gymnastics/aerobics (6.0), skating/roller-skating (7.0), soccer/basketball/handball/volleyball (7.0), rowing (6.0), alpine skiing (7.0), table tennis/badminton (5.0), home exercises (6.5)
High (7.5-9.0 MET)	Swimming (7.5), long distance running (9.0), cross-country skiing (7.5), boxing/wrestling/fighting/judo/karate (9.0), tennis/squash (8.0)

For every person, the amount of energy spent on each of these levels was calculated. For the analyses of activity components, we constructed an additional mean intensity index which was the sum of energy (MET  $\times$  time) spent on each sport activity categorie divided by summarized activity time. Duration is the sum of all time spent on sports categories, in hours per week. Frequency is the sum of sport occasions per week.

We constructed an index for other, mainly occupational activities based on questions about the hours spent sleeping (0.6 MET) and the predominant occupational posture during the day, with categories sitting (1 MET), standing (2 MET), moving (3 MET) or a mixture of sitting, standing and moving (2 MET).

### *Construction of other indices*

A socioeconomic status index was constructed with information about education, income, and occupation as described elsewhere<sup>15</sup>. Indices for total beverage and alcohol intake were calculated from reported consumption of beverages (such as milk, soft drinks, mineral water, and alcoholic drinks, in liters per day) respectively alcohol intake from beer, wine, and liquor (in grams per day). Total fat and saturated fat consumption indices were constructed by multiplying the reported frequencies of intake of different food items by estimated average portion sizes, for men and women separately, and by total fat respectively saturated fat content of these items, derived from the German Federal Food Table<sup>12</sup>. A fat ratio was calculated by dividing the summarized saturated fat intake by the summarized total fat intake.

### *Exclusions*

We excluded individuals who reported a LTPA of more than 35 hours per week from the analyses (n=306). These participants could be misclassified as very active because they reported high activity levels not corresponding to their long-term practices predominantly as a consequence of recent holiday, unemployment or retirement. For similar reasons, and because illness or disabilities may have influenced their actual physical activity pattern, we excluded participants who spent more than 5 days in bed in the last 4 weeks prior to the interview (n=301). Participants with pre-existing heart disease (n=1 972), stroke, brain hemorrhage (n=498), or diabetes (n=377) were excluded as well. In these cases the physical activity pattern could have changed as a result of their disease. After these exclusions, 5 943 men and 6 039 women remained for the analyses.

## Statistical analysis

The distribution of energy spent on LTPA and LTPA intensity levels was calculated. We analyzed the relationship of the three activity intensity levels, independent of each other, with several coronary risk factors using multivariate regression models, adjusting for age, smoking, socioeconomic status, monthly outdoor temperature, body mass index, place of residence (country, small or large city), survey period, liquid consumption, alcohol consumption, ratio of saturated/total fat consumption and occupational activity. In additional models, we analyzed the simultaneous association of intensity, duration and frequency of sport activity with the risk factors. All analyses were conducted with the SAS version 6.11 package<sup>28</sup>.

## Results

Relevant population characteristics are presented in Table 6.2. The distribution of LTPA is skewed to the left as shown in Table 6.3. Most energy was spent on low intensity activities like walking, cycling and gardening. More women than men spent energy on these low intensity activities. The mean energy expenditure for low intensity activity was also higher among women.

The results of multivariate regression analysis for coronary risk factors with activity intensity levels are presented in Table 6.4. Energy spent on low intensity activities at a constant level of energy spent on other activities was significantly associated in health beneficial directions with HDL cholesterol ( $p < 0.01$ ) and body mass index ( $p < 0.05$ ) in men and with triglycerides ( $p < 0.05$ ), diastolic blood pressure ( $p < 0.05$ ) and body mass index ( $p < 0.05$ ) in women. Energy spent on moderate intensity activities was significantly associated with heart rate ( $p < 0.001$ ) in men and with HDL cholesterol ( $p < 0.05$ ), HDL/total cholesterol ratio ( $p < 0.01$ ), triglycerides ( $p < 0.05$ ), peak expiratory flow ( $p < 0.01$ ), and body mass index ( $p < 0.01$ ) in women.

The strongest relationship with coronary risk factors was observed for high intensity activities, which show significant associations for all observed risk factors, except for systolic blood pressure, among men. Significant associations were observed with systolic blood pressure ( $p < 0.01$ ), heart rate ( $p < 0.001$ ), peak expiratory flow ( $p < 0.001$ ) and body mass index ( $p < 0.05$ ) in women, all in health preferable directions. As an example of interpretation of these coefficients, a hypothetical man spending 100 kcal/kg/week (this is 1 000 kcal/day for a 70 kg man) on a high intensity activity would have, on average, a 0.36 mmol/l lower total cholesterol level compared with a man who

does not participate in high intensity activity but with the same levels of low and moderate activity.

Table 6.2 Population characteristics<sup>a</sup>

	Men (n=5 943)		Women (n=6 039)	
Age (years)	42.3	(11.5)	43.2	(12.1)
Total serum cholesterol (mmol/l)	6.00	(1.21)	5.96	(1.24)
HDL cholesterol (mmol/l)	1.33	(0.37)	1.71	(0.45)
HDL/total cholesterol ratio	0.23	(0.08)	0.30	(0.09)
Total serum triglycerides (mmol/l)	2.24	(1.25)	1.60	(0.88)
Systolic blood pressure (mmHg)	133.8	(0.37)	127.9	(19.3)
Diastolic blood pressure (mmHg)	83.2	(11.9)	79.3	(11.5)
Heart rate (beats/min)	73.2	(11.5)	74.9	(10.5)
Peak expiratory flow (l/min) <sup>b</sup>	538.9	(101.7)	390.4	(74.0)
BMI (kg/m <sup>2</sup> )	26.4	(3.53)	25.4	(4.76)
Body weight	81.6	(11.9)	67.4	(12.7)
Socioeconomic status				
Low	15.0 %		24.3 %	
Middle	57.8 %		55.7 %	
High	27.3 %		20.0 %	
Place of residence				
< 5 000 inhabitants	16.7 %		16.0 %	
5 000-100 000 inhabitants	53.7 %		53.7 %	
≥ 100 000 inhabitants	29.6 %		30.3 %	
Smoking				
Never	27.8 %		51.5 %	
Former	29.5 %		18.4 %	
Current	42.7 %		30.1 %	

<sup>a</sup> If not specified otherwise, values are mean (sd)

<sup>b</sup> N=4 026 for men, n=4 183 for women, since measured in second and final survey only

The results of the models that simultaneously include sport intensity, duration and frequency are shown in Table 6.5. Sport intensity was significantly associated with diastolic blood pressure ( $p < 0.05$ ), heart rate ( $p < 0.01$ ), and peak expiratory flow ( $p < 0.05$ ) in men and with heart rate ( $p < 0.05$ ) and peak expiratory flow ( $p < 0.001$ ) in women, at constant levels of duration and frequency. Duration was significantly associated with HDL cholesterol ( $p < 0.05$ ), HDL/total cholesterol ratio ( $p < 0.05$ ), and heart rate ( $p < 0.01$ ) in men, and with systolic blood pressure and peak expiratory flow (both  $p < 0.05$ ) in women. Finally, frequency was significantly associated with total cholesterol ( $p < 0.05$ ), HDL/total cholesterol ratio ( $p < 0.01$ ), heart rate

( $p < 0.001$ ), and body mass index ( $p < 0.001$ ) in men, and with HDL cholesterol ( $p < 0.01$ ), HDL/total cholesterol ratio ( $p < 0.01$ ), triglycerides ( $p < 0.05$ ), heart rate ( $p < 0.001$ ), and body mass index ( $p < 0.05$ ) in women. Overall, the magnitude of association was strongest for frequency compared with intensity and duration (see standardized coefficients). Analyses with exclusion of users of blood pressure medication showed similar results.

Table 6.3 Percentage of the population spending different amounts of energy per week on activity intensity levels

	LTPA	Low	Moderate	High
<b>Men</b>				
No activity	16.4 %	23.4 %	69.1 %	70.1 %
0.1-10 kcal/kg	15.2 %	24.9 %	9.0 %	11.3 %
10-20 kcal/kg	18.2 %	21.9 %	10.4 %	8.7 %
20-30 kcal/kg	14.1 %	12.1 %	4.8 %	4.8 %
30-40 kcal/kg	11.1 %	7.4 %	3.4 %	2.0 %
40-50 kcal/kg	7.3 %	4.1 %	1.5 %	1.5 %
≥ 50 kcal/kg	17.7 %	6.2 %	1.9 %	1.7 %
Mean (SD) kcal/kg	27.8 (28.8)	15.8 (18.1)	6.4 (14.8)	5.7 (12.8)
<b>Women</b>				
No activity	12.4 %	15.0 %	78.5 %	76.8 %
0.1-10 kcal/kg	17.3 %	23.8 %	8.8 %	12.2 %
10-20 kcal/kg	20.0 %	22.7 %	6.4 %	6.3 %
20-30 kcal/kg	15.9 %	15.0 %	2.6 %	2.3 %
30-40 kcal/kg	12.1 %	10.4 %	1.9 %	1.0 %
40-50 kcal/kg	7.3 %	5.7 %	0.7 %	0.7 %
≥ 50 kcal/kg	15.0 %	7.3 %	1.2 %	0.8 %
Mean (SD) kcal/kg	26.2 (25.4)	19.0 (18.1)	3.9 (12.4)	3.4 (9.7)

## Discussion

Recent recommendations<sup>24</sup> suggest that a moderate amount and intensity of physical activity may be helpful in reducing coronary heart disease risk. In our study, all observed coronary risk factors showed associations with high intensity physical activity, for either one or both genders. Some risk factors also showed beneficial associations with moderate and even low intensity physical activity, at a constant level of energy spent on high intensity activities. In addition, higher frequency and duration of sport showed, independent of intensity, beneficial associations with risk factors, especially with serum lipids and body mass index. Therefore, moderate and even low intensity activities,

conducted frequently and long enough, may have beneficial effects on cardiovascular health. We observed these associations in a generally sedentary population. The cross-sectional design of our study makes it impossible to claim a causal direction although we excluded individuals with several diseases and disabilities and adjusted for several potential confounders. So it is unlikely that the observed associations were the result of inability to conduct physical activities because of pre-existing illness.

Table 6.4 Linear regression coefficients (and standard error) for the relationships of coronary risk factors and energy spent (in kcal/kg/week) on activity intensity levels<sup>a</sup>

	Serum lipids									
	Total cholesterol (10 <sup>-3</sup> mmol/l)		HDL cholesterol (10 <sup>-3</sup> mmol/l)		HDL/total cholesterol × 10 <sup>3</sup>		Triglycerides (10 <sup>-3</sup> mmol/l)			
	β	(SEE)	β	(SEE)	β	(SEE)	β	(SEE)		
<b>Men</b>										
Low	1.0	(0.9)	0.8	(0.3) **	0.1	(0.1) (*)	-0.3	(0.9)		
Moderate	-0.6	(1.0)	0.3	(0.3)	0.1	(0.1)	-1.6	(1.1)		
High	-3.6	(1.2)**	1.7	(0.4)***	0.5	(0.1)***	-3.3	(1.3) **		
<b>Women</b>										
Low	-0.3	(0.8)	0.2	(0.3)	0.1	(0.1)	-1.4	(0.6) *		
Moderate	-1.1	(1.2)	1.1	(0.5) *	0.3	(0.1) **	-2.0	(0.9) *		
High	-2.2	(1.5)	0.9	(0.6)	0.2	(0.1) (*)	-1.5	(1.2)		
	Other cardiovascular risk factors									
	Systolic blood pressure (10 <sup>-1</sup> mmHg)		Diastolic blood pressure (10 <sup>-1</sup> mmHg)		Heart rate (10 <sup>-1</sup> beats/min)		Peak exp. flow (l/min)		Body mass index (10 <sup>-2</sup> kg/m <sup>2</sup> )	
	β	(SEE)	β	(SEE)	β	(SEE)	β	(SEE)	β	(SEE)
<b>Men</b>										
low	0.2	(0.1)	-0.1	(0.1)	-0.0	(0.1)	-0.1	(0.1)	-0.6	(0.3) *
moderate	-0.1	(0.1)	0.1	(0.1)	-0.5	(0.1)***	0.2	(0.1) (*)	-0.2	(0.3)
high	-0.1	(0.2)	-0.3	(0.1) **	-1.0	(0.1)***	0.3	(0.1) **	-1.1	(0.4) **
<b>Women</b>										
low	0.0	(0.1)	-0.2	(0.1) *	-0.0	(0.1)	0.1	(0.1) (*)	-0.7	(0.3) *
moderate	-0.2	(0.2)	-0.1	(0.1)	-0.1	(0.1)	0.3	(0.1) **	-1.5	(0.5) **
high	-0.7	(0.2) **	-0.1	(0.1)	-0.6	(0.1)***	0.5	(0.1)***	-1.4	(0.6) *

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, monthly temperature, BMI (except for BMI as dependent variable), residence place, survey period, liquid index, alcohol index, saturated/total fat ratio and occupational activity

\* P < 0.05, \*\* p < 0.01, \*\*\* p < 0.001, and (\*) borderline significant (p < 0.10)

Table 6.5 Linear regression coefficients (standard error and standardized B) for the relationships of coronary risk factors with sport activity components<sup>a</sup>

	Serum lipids														
	Total cholesterol (10 <sup>-3</sup> mmol/l)		HDL cholesterol (10 <sup>-3</sup> mmol/l)		HDL/total cholesterol x10 <sup>3</sup>		Triglycerides (10 <sup>-3</sup> mmol/l)								
	β	(SEE)	B	β	(SEE)	B	β	(SEE)	B						
<b>Men</b>															
Intensity <sup>b</sup>	-4.1	(6.5)	-0.011	-0.6	(2.1)	-0.005	-0.0	(0.4)	-0.002	2.5	(6.9)	0.006			
Duration	-0.2	(6.1)	-0.001	3.7	(1.9)	0.036*	0.8	(0.4)	0.035*	-9.0	(6.5)	-0.025			
Frequency	-14.4	(7.1)	-0.035*	3.6	(2.2)	0.029	1.2	(0.5)	0.047**	-10.8	(7.5)	-0.025			
<b>Women</b>															
Intensity	-1.9	(7.3)	-0.004	2.2	(2.9)	0.014	0.6	(0.5)	0.016	-2.5	(5.5)	-0.008			
Duration	-4.3	(7.0)	-0.010	-0.0	(2.8)	-0.000	0.2	(0.5)	0.005	-4.5	(5.3)	-0.015			
Frequency	-4.7	(8.3)	-0.009	9.1	(3.3)	0.050**	1.7	(0.6)	0.046**	-13.5	(6.2)	-0.038*			
				Other cardiovascular risk factors											
	Systolic blood pressure (10 <sup>-1</sup> mmHg)		Diastolic blood pressure (10 <sup>-1</sup> mmHg)		Heart rate (10 <sup>-1</sup> beats/min)		Peak expiratory flow (l/min)		Body mass index (10 <sup>-2</sup> kg/m <sup>2</sup> )						
	β	(SEE)	B	β	(SEE)	B	β	(SEE)	B	β	(SEE)	B			
<b>Men</b>															
Intensity	-0.9	(0.9)	-0.016	-1.6	(0.6)	-0.040*	-1.7	(0.6)	-0.044**	1.6	(0.6)	0.047*	1.8	(1.9)	0.016
Duration	0.6	(0.9)	0.011	0.7	(0.6)	0.020	-1.8	(0.6)	-0.055**	0.2	(0.6)	0.008	-0.1	(1.8)	-0.001
Frequency	-1.3	(1.0)	-0.021	-1.3	(0.7)	-0.032*	-3.6	(0.7)	-0.092***	0.8	(0.7)	0.024	-9.3	(2.1)	-0.078***
<b>Women</b>															
Intensity	-0.3	(1.1)	-0.004	0.4	(0.7)	0.009	-1.4	(0.7)	-0.037*	1.8	(0.5)	0.067***	-4.1	(2.9)	-0.023
Duration	-2.3	(1.0)	-0.034*	-0.6	(0.7)	-0.016	0.3	(0.7)	0.008	1.3	(0.5)	0.048*	-4.9	(2.8)	-0.029*
Frequency	-1.3	(1.2)	-0.017	-1.4	(0.8)	-0.029*	-3.1	(0.8)	-0.073***	-0.0	(0.6)	-0.001	-9.8	(3.3)	-0.050**

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, monthly temperature, BMI, residence place, survey period, liquid index, alcohol index, saturated/total fat ratio and occupational activity

<sup>b</sup> Mean intensity in kcal/kg/hour, duration in hours/week, frequency in times/week; B gives unitless estimates

\* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001, and (\*) borderline significant (p < 0.10)

Beneficial associations of risk factors with light or moderate physical activity levels have major public health relevance. It will be easier to engage a large part of sedentary communities, especially elderly, in light or moderate rather than in vigorous physical activity. Such individuals who were originally sedentary will benefit the most from an enhancement of physical activity. Therefore, more evidence of the substantial impact of low intensity activity may stimulate more people to become active.

Assessment of physical activity based on questionnaires has a large potential for misclassification. Although the questionnaire included a broad spectrum of leisure-time physical activities, it did not include all. However, only a small percentage of participants reported other activities not listed in the questionnaire. We based the intensity level of activities on their MET values which are crude estimates of intensity. The physical activity questions consider the 3 months before the interview which should reflect the long term physical activity pattern; this, however, is not necessarily true for everyone. We did, however, exclude people who reported more than 35 hours per week of LTPA, spent more than 5 days in bed in the last 4 weeks before the interview, or had (prior) cardiovascular disease. We also conducted analyses including all participants; these gave essentially similar results, although the magnitude of association was generally lower. Because of other misclassifications, it is likely that the observed associations underestimate the real association between physical activity and risk factors. In spite of the limitations, we still observed several significant associations with different components of LTPA in this large sample of mainly sedentary people after adjustment for potential confounders.

Seasonal temperature was included as a confounder because participants were measured throughout the year. People are generally more active in summer, and risk factors like serum cholesterol, blood pressure, or body mass index may show seasonal fluctuations. We also adjusted for beverage and alcohol consumption and proportion of saturated fat in the diet, which showed associations with coronary risk factors and with physical activity levels as well in our population. Age, smoking, socioeconomic status, body mass index, occupational activity, place of residence, and survey period, also predictors of coronary risk factors, show associations with physical activity and were observed to be confounders. Oral contraceptive use did not confound the relationships among women. However, we observed different magnitude of associations with energy spent on moderate activity levels and HDL cholesterol ( $\beta$ : 3.3 for users, 1.3 for nonusers; not significant) and heart rate ( $\beta$ : 0.4 for users; not significant, -0.4 for nonusers) as well as high intensity levels and systolic blood pressure ( $\beta$ : -1.4 for users, -0.5 for nonusers).

Total serum cholesterol showed only a significant association with high intensity activity among men. For HDL cholesterol we observed significant associations with moderate (women), and low and high intensity (men) physical activity. Others observed associations of serum lipids with moderate and high intensity activity levels<sup>6,25</sup>. In a study among 537 healthy men aged 20-60 years, beneficial associations with HDL cholesterol and total/HDL cholesterol ratio were only observed for energy spent on intensity levels above 7 MET, whereas we observed associations for low and moderate levels. For total, non-HDL cholesterol and (logarithmized) triglycerides, they observed only preferable associations for intensity levels above 9 MET, which is in accordance with our observations<sup>18</sup>. Lipid metabolism is closely related to energy metabolism. The metabolic rate is enhanced for some time after exercise; therefore, more frequent exercise will have a larger impact on energy metabolism<sup>26</sup>. This would mean that both duration and frequency could be important for the impact of physical activity on both serum lipids and body mass.

For systolic blood pressure, we observed a significant association only with high intensity activity in women, and for diastolic with high intensity activity in men and low intensity in women. Only vigorous exercise was associated with a lower hypertension incidence among college graduates<sup>23</sup>. Others too, observed associations of blood pressure with less than vigorous exercise in training programs<sup>5</sup> as well as cross-sectionally<sup>27</sup>. Heart rate was previously associated with time spent on low, moderate and high intensity activities in elderly men<sup>3</sup>. We observed associations with energy spent on moderate and high, but not with low, intensity activity. Among men, all components showed strong significant associations with heart rate, which is closely related to cardiovascular fitness. In additional analyses with five level categories for each component, we observed no threshold level in the relationship with heart rate (not presented). Circulating catecholamine levels and therefore sympathetic activity seems to play a role in exercise-induced changes in blood pressure<sup>5,27</sup>. Achieving a certain stimulus may be necessary and the intensity level may be important. Compared with the other components, association of intensity was stronger for diastolic blood pressure among men, but not substantially stronger among women. Intensity also seems important for heart rate and peak expiratory flow.

In general, the results show stronger associations with risk factors for the amount of energy spent on high intensity activities. The way in which energy is spent seems to be important. We explored the associations of risk factors separating frequency, duration, and intensity of sport activity. We used an additive regression model to estimate associations of the components independent of each other, not to achieve a maximal fit. The components

showed highly significant associations with risk factors (except for systolic blood pressure in men and total serum cholesterol in women) in models where both other components were excluded (not presented). For example the effect of the difference in frequency (times/week) at constant level of both intensity and duration for each risk factor can be obtained from the regression coefficients ( $\beta$ ) in a similar manner as illustrated for Table 6.4. However, to compare the relative importance of each component with the others, the standardized regression coefficients are more appropriate. (These are only valid for comparison since they largely depend on the variance in this population) When entered simultaneously, the strongest and most significant associations were observed for sports frequency (at constant level of intensity and duration). This is remarkable since frequency correlates less with the amount of expended energy compared with intensity and duration. Nevertheless, it seems that frequency is an important dimension of physical activity in regard to health benefits. A high exercise frequency could be more effective because it enhances metabolic rate over a long period beyond actual exercise. Questions about frequency might be easier to answer compared with duration of activities and would therefore be less hampered by misclassification. Therefore, its relative importance should be confirmed by other studies. This importance of frequency is in line with the American College of Sports Medicine (ACSM) which recommends that every U.S. adult should accumulate 30 minutes or more of moderately intense activity on *most, preferably all days of the week*<sup>24</sup>. Maintenance of adequate physical activity levels throughout the year is also considered to be important<sup>17,22</sup>.

In summary, our results are in agreement with previously reported beneficial associations of LTPA and CHD risk factors. For the same amount of energy expended, high intensity activities showed a stronger association with beneficial levels of coronary risk factors than low intensity activities. Beneficial effects of low intensity activity may not be large enough to reach statistical significance. Benefits could exist, however, on an individual level. We observed significant associations of low intensity activities with HDL cholesterol and body mass index among men and with triglycerides, diastolic blood pressure, and body mass index among women. Most of the parameters were significantly associated with frequency of sports. Low intensity activities conducted frequently may contribute to a beneficial effect on these cardiovascular risk factors and cardiovascular health in general. Public health may profit the most when sedentary people become just a little more active<sup>24</sup>. For certain groups of people, for example the elderly and the ill, recommending light or moderate rather than vigorous exercise might be more appropriate,

because of the possible risks such as injuries, heart attacks and sudden death<sup>8</sup> involved with vigorous exercise.

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chapter **7**

**Benefits of Leisure-time Physical Activity on the  
Cardiovascular Risk Profile at Older Age**

*„Der große Sport fängt da an, wo er aufhört gesund zu sein.“*

Berthold Brecht

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*submitted*

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## ABSTRACT

*The relationship of frequency and duration of leisure-time physical activities with cardiovascular risk factors was studied in 4 942 male and 5 885 female participants, ages 50-69, of the German Cardiovascular Prevention Study (1984-1991). After adjustment for several possible confounders, women with modest levels (0.5-3 times, 0.5-2 hours per week) of moderate-to-vigorous activity ( $\geq 5$  kcal/kg/hour) had significantly lower systolic blood pressure (-1.8%), resting heart rate (-3.1%) and body mass index (-3.2%) values than sedentary. Beneficial differences increased with frequency and duration of activity. Light activities (3-4.5 kcal/kg/hour), conducted  $\geq 5$  times per week, were significantly associated with favorable lower diastolic blood pressure (-1.4%), resting heart rate (-2.3%) among women, and body mass index (women -2.9%, men -2.2%) among both genders. Recommended activity levels ( $\geq 5$  times,  $\geq 3.5$  hours weekly) were associated with a lower prevalence of multiple risk factors (odds ratio (OR) 0.55 (95% confidence interval (CI) 0.41-0.75) for men and 0.44 (95% CI 0.31-0.63) for women). For the elderly, even less physical activity than currently recommended, is likely to improve the cardiovascular risk profile.*

## Introduction

General agreement exists regarding the usefulness of enhancing physical activity as a preventive measure against cardiovascular disease<sup>1,2,3</sup>. The public health impact of physical activity may be especially important for older adults, who are at high risk of cardiovascular disease and are often sedentary<sup>4</sup>. Promoting vigorous activity in this age group seems inappropriate because of possible adverse effects, such as increased injuries and heart attacks<sup>3,5,6</sup>. Older individuals may prefer types of activity with lower intensities, such as walking, cycling or gardening. They are probably less motivated by competitive elements and more by health aspects of exercise compared to younger individuals. Possible benefits of modest physical activity in this age group have therefore a high relevance for public health.

We studied the relationship of leisure-time physical activity and cardiovascular risk factors among German adults, ages 50-69. Since current recommendations outline the importance of frequency, intensity and duration of activity, all three dimensions were focused on in the analyses.

## **Material and methods**

The population was derived from the German Cardiovascular Prevention Study, whose aim was to measure the effect of community-based intervention on cardiovascular risk factors and mortality in several regions of former West Germany<sup>7</sup>. Independent surveys representative of the West German population ages 25-69, were conducted from May 1984 until March 1986, from September 1987 until October 1988 and from April 1990 until May 1991. During approximately the same periods, additional regionally representative surveys were performed. The response rate for all samples was about 70 percent. The national samples were concipated as national health interview and examination surveys. A comprehensive spectrum of health behavior, medical history and sociodemographic information by a self-administered questionnaire as well as an extensive medical examination of all participants was obtained. Systolic and diastolic blood pressure were measured twice by trained physicians while participants were sitting. The second measurements obtained with a Hawksley random-zero sphygmomanometer were used in the analyses. Resting heart rate was measured by 30-second pulse rate counting. Body weight and height were measured while wearing light clothes. Participants were in a nonfasting state and lying down when blood samples were obtained. The serum lipid levels were analyzed in the former Institute for Social Medicine and Epidemiology of the Federal Health Office, now Robert Koch-Institute.

The physical activity questionnaire was adapted from the Minnesota leisure-time physical activity questionnaire<sup>8</sup>. It included questions about the frequency (categories never, once per month or less, 2-3 times per month, about 1 time per week, more often per week, almost daily) and time spent per week on 18 leisure-time activity categories during the previous 3 months. For most activity categories, a test-retest Pearson correlation of 0.5-0.8 was observed in a sample of 598 German men and women, ages 20-75<sup>9</sup>. Duration was reported in hours and minutes spent per week for activities conducted at least once a week. Intensity categorization was based on metabolic values (METs) obtained from available sources<sup>10</sup>, expressing the energy cost of an activity as a multiple of the resting metabolic rate which is about 1 kcal per kg per hour. Duration and frequency per week were cumulated for light (3-4.5 MET; walking/shopping, cycling, gymnastics) and moderate-to-vigorous (5-9 MET; hiking/mountain climbing, dancing/ballet/jazz dancing, fitness-gymnastics/aerobics, skating/rollerskating, soccer/basketball/handball/volleyball, rowing, alpine skiing, table tennis/badminton, home exercises,

swimming, long distance running, cross-country skiing, boxing/wrestling/fighting/judo/karate, tennis/squash) activities.

Subsequently, we categorized the levels of moderate-to-vigorous activities according to frequency (< 0.5, 0.5-< 3, 3-< 5 and  $\geq 5$  times per week) and time (< 0.5, 0.5-< 2, 2-< 3.5,  $\geq 3.5$  hours per week). The highest categories resemble the currently recommended activity levels. In addition, we compared different quantities of light activities. Energy spent on activities was estimated by multiplying the time spent on these activities by the corresponding MET as described previously<sup>11</sup>. To adjust for other activities, an occupational activity index was constructed from the reported sleeping time (0.6 MET) and the predominant occupational posture during the day with categories sitting (1 MET), standing (2 MET), moving (3 MET) or a mixture of sitting, standing and moving (2 MET). Socioeconomic status was assessed using information about education, income and occupation as described previously<sup>12</sup>. From the national and regional samples we selected individuals ages 50-69 (17 800), excluding those who had a history of cardiovascular or cerebrovascular diseases or diabetes (6 447). We also excluded participants who had spent 5 or more days in bed during the last 4 weeks (185) as well as those reporting more than 35 hours of leisure-time physical activity per week (341). This resulted in a net sample of 4 942 men and 5 885 women.

With multivariate ANOVA models (PROC GLM in SAS) we calculated the mean levels of several cardiovascular risk factors for activity groups, adjusted for age, smoking (current smoker), socioeconomic status (low, middle, high), monthly outdoor temperature, body mass index (kg/m<sup>2</sup>; except for body mass index as dependent variable), urbanization level (village, middle or large city), survey period and energy spent on other leisure-time and occupational activities. Additionally constructed indices of alcohol intake, total fluid intake, fat intake, former smoking and intervention region did not confound the observed relationships between activity groups and risk factors in this population. In addition, we calculated the odds ratios of the simultaneous prevalence of at least two of the risk factors: low high density lipoprotein (HDL) cholesterol (< 35 mg/dl; 0.91 mmol/l for men or < 45 mg/dl; 1.16 mmol/l for women), high diastolic blood pressure ( $\geq 95$  mmHg), high systolic blood pressure ( $\geq 160$  mmHg), high body mass index ( $\geq 30$  kg/m<sup>2</sup>), and high resting heart rate ( $\geq 80$  beats per minute) of activity groups (with the reference, < 0.5 times, < 0.5 hours per week). Analyses were conducted with the SAS version 6.11 package<sup>13</sup>.

## Results

Benefits of modest amounts of moderate-to-vigorous activity (0.5- < 3 times and 0.5- < 2 hours per week) are not apparent among men (see Table 7.1). Among women we observed substantially preferable levels of systolic blood pressure ( $p < 0.05$ ), heart rate ( $p < 0.001$ ) and body mass index ( $p < 0.001$ ) compared with sedentary women.

**Table 7.1** Adjusted mean risk factor levels (95% CI) for sedentary and modestly active individuals, ages 50-69<sup>a</sup>

	Sedentary	Modestly active <sup>b</sup>
<b>Men</b>	(n = 1 457)	(n = 309)
Total cholesterol (mmol/l)	6.33 (6.27-6.40)	6.27 (6.14-6.41)
HDL cholesterol (mmol/l)	1.34 (1.32-1.36)	1.31 (1.26-1.35)
Diastolic blood pressure (mmHg)	85.7 (85.1-86.3)	84.4 (83.1-85.7)
Systolic blood pressure (mmHg)	141.7 (140.7-142.8)	140.7 (138.5-142.9)
Heart rate (beats/min)	74.5 (73.9-75.2)	73.3 (72.0-74.6)
Body mass index (kg/m <sup>2</sup> )	27.3 (27.2-27.5)	27.5 (27.2-27.9)
<b>Women</b>	(n = 2 547)	(n = 439)
Total cholesterol (mmol/l)	6.73 (6.68-6.78)	6.76 (6.65-6.87)
HDL cholesterol (mmol/l)	1.67 (1.65-1.69)	1.71 (1.67-1.76)
Diastolic blood pressure (mmHg)	83.9 (83.5-84.4)	83.0 (82.0-84.0)
Systolic blood pressure (mmHg)	141.1 (140.3-141.9)	138.5 (136.6-140.4)*
Heart rate (beats/min)	74.4 (74.0-74.9)	72.1 (71.1-73.1)***
Body mass index (kg/m <sup>2</sup> )	27.7 (27.6-27.9)	26.8 (26.4-27.3)***

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, average outdoor temperature, body mass index, urbanization, survey period and occupational activity

<sup>b</sup> 0.5 - < 3 times and 0.5 - < 2 hours per week of moderate-to-vigorous activity

\* Significantly different from sedentary at \*  $p < 0.05$ , \*\*  $p < 0.01$ , and \*\*\*  $p < 0.001$

More hours spent per week on moderate-to-vigorous activity are beneficially associated with resting heart rate among both genders and systolic blood pressure and body mass index among women, at constant frequency (Table 7.2). Similarly, a higher frequency of activity (3-5 or  $\geq 5$  times), at constant duration per week, is associated with beneficial diastolic blood pressure, resting heart rate and body mass index and, among women, systolic blood pressure (Table 7.3).

Men reporting a high frequency ( $\geq 5$  times per week) of light leisure-time activities had, on average, a significantly lower body mass index (and a nonpreferable lower HDL cholesterol level) as compared to sedentary (Table 7.4).

Table 7.2 Benefits of duration, mean risk factor levels (95% CI) according to hours spent on moderate-to-vigorous activity, independent of frequency<sup>a</sup>

	Hours per week			
	0 - < 0.5	0.5 - < 2	2 - < 3.5	≥ 3.5
<b>Men</b>	(n = 1 491)	(n = 445)	(n = 491)	(n = 824)
Total cholesterol (mmol/l)	6.35 (6.28-6.42)	6.28 (6.17-6.40)	6.24 (6.13-6.35)	6.32 (6.22-6.42)
HDL cholesterol (mmol/l)	1.34 (1.32-1.37)	1.31 (1.28-1.35)	1.34 (1.31-1.38)	1.38 (1.35-1.41)
Diastolic BP (mmHg)	85.4 (84.7-86.2)	84.4 (83.3-85.5)	85.3 (84.2-86.3)	85.9 (85.0-86.9)
Systolic BP (mmHg)	141.4 (140.2-142.6)	140.3 (138.5-142.2)	141.5 (139.7-143.3)	141.7 (140.1-143.4)
Heart rate (beats/min)	73.8 (73.1-74.5)	73.4 (72.3-74.5)	72.4 (71.4-73.4)*	71.5 (70.6-72.5)**
Body mass index (kg/m <sup>2</sup> )	27.2 (27.0-27.4)	27.4 (27.1-27.8)	27.2 (26.9-27.5)	27.2 (26.9-27.5)
<b>Women</b>	(n = 2 601)	(n = 621)	(n = 497)	(n = 587)
Total cholesterol (mmol/l)	6.71 (6.66-6.77)	6.75 (6.65-6.85)	6.76 (6.65-6.87)	6.71 (6.59-6.82)
HDL cholesterol (mmol/l)	1.68 (1.66-1.70)	1.70 (1.66-1.74)	1.70 (1.66-1.74)	1.69 (1.65-1.74)
Diastolic BP (mmHg)	83.7 (83.2-84.2)	83.1 (82.2-84.0)	83.4 (82.4-84.4)	82.6 (81.6-83.7)
Systolic BP (mmHg)	140.7 (139.8-141.6)	138.5 (136.9-140.1)*	140.0 (138.2-141.9)	138.8 (136.9-140.8)
Heart rate (beats/min)	74.2 (73.7-74.7)	72.0 (71.2-72.9)***	73.4 (72.4-74.4)	72.4 (71.3-73.4)**
Body mass index (kg/m <sup>2</sup> )	27.7 (27.5-27.9)	26.9 (26.5-27.3)***	26.9 (26.5-27.3)**	26.3 (25.9-26.8)***

BP = blood pressure

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, average temperature, body mass index, urbanization, survey period, occupational activity and frequency of activity per week

\* Significantly different from sedentary at \* p < 0.05, \*\* p < 0.01, and \*\*\* p < 0.001

Table 7.3 Benefits of frequency, mean risk factor levels (95% CI) according to frequency of moderate-to-vigorous activity, independent of duration<sup>a</sup>

	Frequency per week				
	0 < 0.5	0.5 < 3	3 < 5	≥ 5 times	
<b>Men</b>	(n = 1 582)	(n = 910)	(n = 427)	(n = 332)	
Total cholesterol (mmol/l)	6.33 (6.26-6.40)	6.30 (6.22-6.38)	6.30 (6.18-6.42)	6.31 (6.16-6.45)	
HDL cholesterol (mmol/l)	1.35 (1.33-1.38)	1.34 (1.31-1.36)	1.38 (1.34-1.41)	1.32 (1.28-1.37)	
Diastolic BP (mmHg)	86.0 (85.3-86.6)	84.7 (83.9-85.5)*	85.7 (84.5-86.9)	84.3 (82.9-85.8)	
Systolic BP (mmHg)	142.0 (140.9-143.1)	140.7 (139.4-142.0)	141.7 (139.8-143.7)	139.6 (137.2-142.0)	
Heart rate (beats/min)	74.2 (73.5-74.8)	72.9 (72.1-73.7)*	70.7 (69.6-71.9)***	70.2 (68.8-71.6)***	
Body mass index (kg/m <sup>2</sup> )	27.3 (27.1-27.5)	27.2 (27.0-27.4)	27.3 (27.0-27.6)	26.6 (26.2-27.0)**	
<b>Women</b>	(n = 2 641)	(n = 1 011)	(n = 378)	(n = 276)	
Total cholesterol (mmol/l)	6.72 (6.67-6.77)	6.72 (6.64-6.80)	6.83 (6.71-6.96)	6.61 (6.45-6.77)	
HDL cholesterol (mmol/l)	1.67 (1.65-1.69)	1.70 (1.67-1.73)	1.71 (1.65-1.76)	1.70 (1.64-1.76)	
Diastolic BP (mmHg)	83.8 (83.4-84.3)	83.3 (82.6-84.0)	82.2 (81.0-83.4)*	81.8 (80.3-83.2)*	
Systolic BP (mmHg)	140.9 (140.1-141.8)	139.5 (138.2-140.8)	137.4 (135.2-139.5)**	137.2 (134.6-139.9)*	
Heart rate (beats/min)	74.3 (73.9-74.8)	72.6 (71.9-73.3)***	72.1 (70.9-73.2)***	71.6 (70.2-73.0)***	
Body mass index (kg/m <sup>2</sup> )	27.6 (27.4-27.8)	26.8 (26.5-27.1)***	26.6 (26.1-27.1)***	27.1 (26.5-27.7)	

BP = blood pressure

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, average temperature, body mass index, urbanization, survey period, occupational activity and duration of activities per week

\* Significantly different from sedentary at \*  $p < 0.05$ , \*\*  $p < 0.01$ , and \*\*\*  $p < 0.001$

Women had more beneficial levels of diastolic blood pressure, resting heart rate and body mass index. For women, significantly lower levels of resting heart rate and body mass index were already seen at a frequency of 3-5 times per week (not presented).

The prevalence odds ratios of multiple risk factors (2 or more) show a graded relationship with both frequency and time spent on moderate-to-vigorous activity among men (see Figure 7.1). A significant lower OR of 0.55 (95% CI 0.41-0.75) was seen at recommended levels ( $\geq 5$  times,  $\geq 3.5$  hours per week) as compared to the reference ( $< 0.5$  times,  $< 0.5$  hours per week). Women reporting some participation in moderate-to-vigorous activities ( $\geq 0.5$  hours;  $\geq 0.5$  times per week) already had a significantly lower prevalence of multiple risk factors as compared to sedentary women. A further benefit, though small, of higher activity levels was observed. Women with recommended levels had a prevalence OR of 0.44 (95% CI 0.31-0.63).

Table 7.4 Benefits of light activities, adjusted mean risk factor levels (95% CI) for individuals with low and high frequency of light activities<sup>a</sup>

	Frequency per week	
	< 1 time	$\geq 5$ times
<b>Men</b>	(n = 688)	(n = 1 935)
Total cholesterol (mmol/l)	6.27 (6.18-6.36)	6.31 (6.25-6.36)
HDL cholesterol (mmol/l)	1.38 (1.35-1.41)	1.34 (1.32-1.36)*
Diastolic blood pressure (mmHg)	85.4 (84.5-86.3)	85.1 (84.6-85.6)
Systolic blood pressure (mmHg)	140.7 (139.2-142.3)	140.8 (139.9-141.7)
Heart rate (beats/min)	73.4 (72.5-74.3)	73.0 (72.5-73.5)
Body mass index (kg/m <sup>2</sup> )	27.6 (27.4-27.9)	27.0 (26.8-27.1)***
<b>Women</b>	(n = 722)	(n = 3 006)
Total cholesterol (mmol/l)	6.67 (6.58-6.76)	6.74 (6.70-6.79)
HDL cholesterol (mmol/l)	1.66 (1.63-1.70)	1.70 (1.68-1.71)
Diastolic blood pressure (mmHg)	84.2 (83.4-85.0)	83.0 (82.6-83.4)**
Systolic blood pressure (mmHg)	140.3 (138.9-141.8)	139.4 (138.7-140.1)
Heart rate (beats/min)	74.9 (74.2-75.7)	73.2 (72.8-73.6)***
Body mass index (kg/m <sup>2</sup> )	27.7 (27.4-28.1)	26.9 (26.7-27.1)***

<sup>a</sup> Adjusted for age, smoking, socioeconomic status, average outdoor temperature, body mass index, urbanization, survey period and occupational activity

\* Significantly different from sedentary at \*  $p < 0.05$ , \*\*  $p < 0.01$ , and \*\*\*  $p < 0.001$

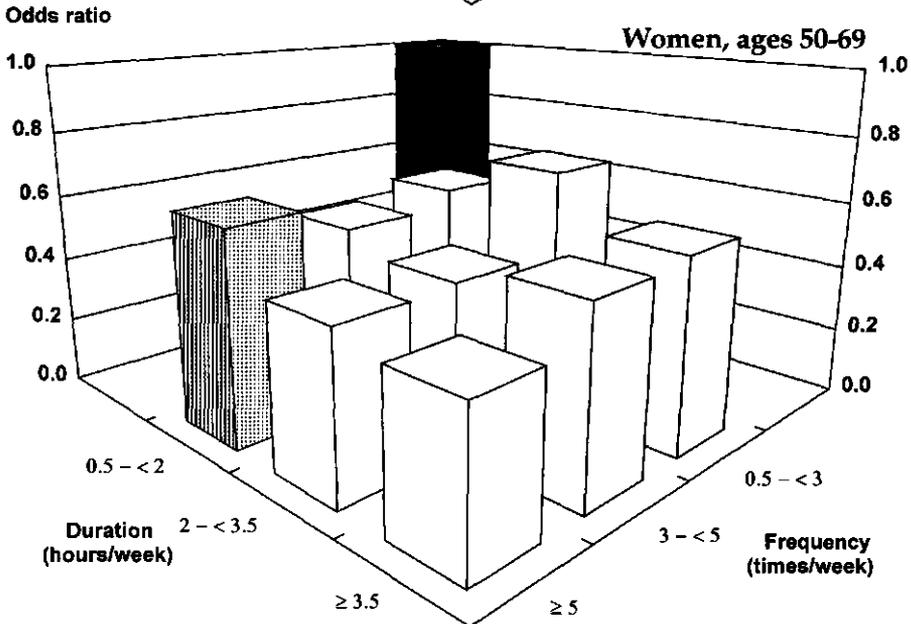
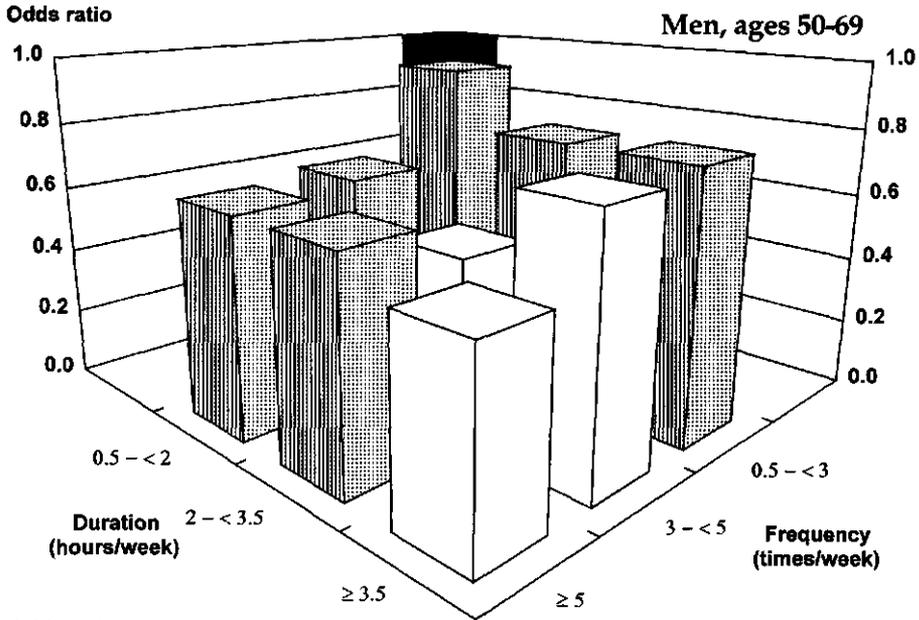


Figure 7.1 Odds ratios for prevalence of multiple risk factors by frequency and duration of moderate-to-vigorous leisure activity per week. These are adjusted for age, smoking, socioeconomic status, average outdoor temperature, body mass index, urbanization, survey period and occupational activity. Black bars are sedentary, white bars are significantly different from sedentary at  $p < 0.05$ .

## DISCUSSION

Engagement in moderate-to-vigorous leisure-time physical activities in amounts achievable for most older individuals (0.5-3 times, 0.5-2 hours per week) was beneficially associated with several risk factors among women but not among men. This was observed after adjustment for several possible confounders. Further analyses focused on the possible benefit of frequency and time of activity independent of each other. Both higher frequency and longer duration may contribute to a further reduction of these risk factors. A high frequency ( $\geq 5$  times per week) of moderate-to-vigorous activity was associated with a lower resting heart rate and body mass index among men. Even for light activities, conducted almost daily ( $\geq 5$  times per week) lower diastolic blood pressure and resting heart rate among women and body mass index among both genders were observed. Beneficial associations with light activities are important, since these activities seem to be preferred by older adults. Most individuals in our sample participated in such light activities.

We observed no substantial differences in serum lipid levels between activity groups, although this was observed in younger men<sup>14,15,16</sup>. A borderline significantly higher HDL cholesterol level was seen for modestly active women as compared to sedentary. A larger increase in HDL cholesterol of 0.06-0.08 mmol/l was observed for premenopausal women becoming more active independent of intensity level<sup>17</sup>. Lipid levels may be influenced mainly by total energy expenditure rather than frequency or intensity of activities. Older individuals spend considerably lower amounts of energy on leisure-time activities, which could explain the lack of association with serum lipids.

Currently adults are recommended to conduct at least 30 minutes of moderate-to-vigorous activity on most, preferably all days of the week<sup>2,3</sup>. These recommendations are reflected in the presented upper categories of moderate-to-vigorous activities (Table 7.2 and 7.3, Figure 7.1). Such activity levels are associated with substantially better risk factor levels, especially among women. Therefore, the elderly may improve their cardiovascular risk profile if these levels are achieved. For some risk factors, benefits seem to exist already at a lower than recommended intensity and duration of activity.

These results are based on cross-sectional observations, therefore a causal direction is not determinable. We excluded individuals with several prevalent diseases (although results were similar when they were included). Still, a generally better constitution resulting in higher activity levels may partly explain the observed associations. We adjusted for possible confounding influences of age, smoking, socioeconomic status, monthly outdoor temperature, urbanization, survey period, body mass index,

occupational activity index and energy spent on other activity intensity levels. Previous smoking, daily liquid intake, alcohol intake and ratio of saturated/total fat did not confound the observed relationships. Thus, it seems likely that the observed beneficial associations are directly related to enhanced physical activity. On the other hand, some overadjustment may have occurred. A high body mass index may be a result of low activity. Socioeconomic status, urbanization and occupational activity may influence leisure-time activity and may therefore, in part, show associations with the observed risk factors. Analyses without adjustments for these (possibly causal related) confounders gave similar results, although the favorable differences among women became stronger and more significant.

Activity assessment was based on self-report by questionnaire, which has a considerable potential for misclassification. Individuals reporting more than 35 hours of leisure time were excluded. Such high levels were mainly due to recent holidays or unemployment. Their reported activity may not reflect their long-term habits and we therefore excluded them from the analyses. Following similar considerations, those spending more than 5 days in bed during the last month were excluded. Nevertheless, misclassification is coherent with the assessment method and may not be totally excluded. Some individuals who appear to be inactive may participate in leisure activities not included in the questionnaire. Others may overestimate their activity, because an active lifestyle conforms to social norms. The use of average MET values for broad activity items may not reflect the intensity level of the individual. These sources of misclassification are not likely to correlate with the objectively measured risk factors (except possibly body mass index which was also considered as a confounder). Therefore, the remaining misclassification will be largely nondifferential and tend to dilute the relationships. Disturbing effects of remaining misclassification and confounding may be more important on the low side of physical activity levels, making it difficult to estimate the beneficial impact of light activities. The questionnaire included information about gardening activity. This broad category could include wood chopping or watering flowers with considerable different MET values. Therefore, we excluded it from the light activity category.

Frequency of activity may be easier to recall as total duration per week. This could explain the more significant associations with frequency compared to duration. This may also be due to the differences in categorization. For similar analyses using equal group sizes for frequency and duration categories, the stronger associations with frequency of activity persisted (not presented). Nevertheless, it seems that frequency is an important activity component for cardiovascular benefits. Gender differences in activities, not

reflected in the reported broad categories, may explain the apparent lower benefit of activity among men in this age group. In Germany, as in several other western societies, men at this age have a work schedule with a defined amount of leisure time, whereas women are mainly housewives. Therefore, the gender-specific intensity of some reported leisure-time activities may differ considerably. For women, walking could mean shopping, carrying heavy loads. For men, this could mainly include walking to and from work.

Differences in mean risk factor levels may not reflect the possible benefits of enhanced activity of those at high risk. We calculated the prevalence odds ratio of multiple (2 or more simultaneously) elevated risk factor levels. For both genders, a considerable lower prevalence of simultaneous risk factors was observed. For men, we observed a graded dose-response, whereas women at any activity level above sedentary had lower prevalence of multiple risk factors. Whereas several studies observed beneficial associations of cardiovascular risk factors with moderate or vigorous activities<sup>16,18,19</sup>, only few observed beneficial associations with light activities<sup>17,18,20</sup>. It appears that modest levels of moderate-to-vigorous activity or frequent participation in light activities has substantial benefits for the cardiovascular risk profile at an older age.

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**Chapter 8**

**General Discussion**

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For most people in Germany, only a minor part of their energy is spent on leisure activities. Nevertheless, enhanced levels of leisure activity observed in this general population, are associated with substantially preferable cardiovascular risk factor levels and, independent of these associations, with better survival rates for all-cause and cardiovascular disease mortality. These favorable associations were observed even after adjustment for health related demographic and behavioral characteristics.

These findings are based on cross-sectional and follow-up studies in representative samples of adults, ages 25-69, from former West Germany. During three periods, from 1984 to 1986, from 1987 to 1988 and from 1990 to 1991, comprehensive health information about 7 689 men and 7 747 women was gathered. For some analyses, we included comparable regional representative samples. The results reflect a „free living“ population with limited time to engage in low-to-moderate levels of physical activity during leisure time. These observed associations of physical activity with cardiovascular risk factors have high relevance for public health. The large sample sizes enabled us to investigate several aspects of physical activity, among them: frequency, duration and intensity. However, the results should be interpreted with caution. As far as the cross-sectional observations are concerned, it will be impossible to prove causality.

A causal inference may be performed by a thorough evaluation of possible non-causal explanations, such as chance and bias, and by integrating biological knowledge and results of other studies. These include experimental studies, which partly unraveled physiological mechanisms and generally conform to our findings. In the following chapter, the main findings are discussed and a brief review of previous findings and proposed biological pathways presented. Subsequently, methodological limitations in interpreting the results are considered. Finally, implications for public health and recommendations are provided.

## Main findings

### *Sociodemographic and lifestyle characteristics*

Several sociodemographic characteristics such as gender, age, and socioeconomic status, are associated with leisure activity. The physically active tend to be younger, single, urbanized, and have a higher socioeconomic status. A strong association was observed with socioeconomic status. Men and women with high socioeconomic status were, respectively, four and three times more

likely to engage in leisure activity than those with low socioeconomic status. After adjustment for sociodemographic determinants, a physically active lifestyle was associated with a lower propensity to smoke, leaner body mass, lesser need to sleep early, higher intakes of fruits, salads, whole grain breads, and amounts of vitamin supplements and fluids, routine breakfast consumption, and lower intake of white bread and meat (*Chapter 3*). Several observed behavioral aspects showed no substantial association with physical activity. Noteworthy is that all significant associations indicate a generally healthier lifestyle among the physically active. Other studies indicated similar associations, although a multivariate comparison was seldom made. These sociodemographic aspects and lifestyle habits were considered to be confounders in other analyses.

### *Risk factors and mortality*

Higher levels of physically intense and moderate leisure activity were associated with more favorable levels of serum cholesterol, HDL cholesterol, triglycerides, diastolic and systolic blood pressure, body mass index (BMI), heart rate and peak expiratory flow for both men and women, although not always statistically significant (*Chapters 4 and 6*). Among women we observed significant associations more often.

We estimated a relative risk (RR) of 0.33 with 95% confidence interval (CI) of 0.11-0.94 for cardiovascular disease mortality for men, ages 40-69, with high levels of conditioning physical activity and of 0.26 (95% CI 0.08-0.83) for men who play sports for more than 2 hours per week compared to men who do not play sports. Although only statistically significant for men, all-cause mortality showed a graded relationship with sport duration for both genders. For men and women who spent more than 2 hours per week on sports, we observed a RR of 0.36 (95% CI 0.16-0.79) and 0.28 (95% CI 0.07-1.17) respectively. A significant association with cardiovascular mortality among women could not be determined, probably because of the low occurrence among women in this age group. The estimates were adjusted for the baseline association of physical activity with age, blood pressure, serum cholesterol, BMI and smoking. Further adjustment for HDL cholesterol level and resting heart rate did not essentially change these results (presented in *Chapter 4*). The adjustments will have largely removed any confounding effects of other health behavior. The cardiovascular risk factors are also possible intermediates in the causal link between physical activity and cardiovascular disease (mortality). Our findings indicate that the beneficial effects of enhanced leisure activity go beyond a preferable effect on the classical cardiovascular risk factors. Conducting more

than 2 hours of sports per week may lower the cardiovascular mortality risk by a factor of about three to four compared to being sedentary. Other physiologic alterations as a result of regular physical activity such as enhanced blood flow, fibrinolytic activity and insulin resistance as well as a lower tendency for thrombosis<sup>1</sup>, may contribute to promote longevity.

### ***Resting heart rate***

The resting heart rate is a marker of cardiovascular fitness and is associated with habitual physical activity level. In a longitudinal study among 1 827 men and 2 929 women, ages 40-80, we observed a relative risk for all-cause mortality during 12 years of 1.7 (95% CI 1.4-2.2) for men and 1.4 (95% CI 1.1-1.8) for women with a 20 beats per minute higher heart rate. Similar risk estimates for cardiovascular disease mortality were 1.7 (95% CI 1.2-2.6) for men and 1.3 (95% CI 0.9-2.0) for women. These estimates were adjusted for age, serum cholesterol, BMI, systolic blood pressure, smoking and diabetes (*Chapter 5*). The heart rate is a long used, easily obtainable indicator of illness. Its sensitivity to actual conditions, such as infections or exhaustion, may have hampered its establishment as an independent predictor of cardiovascular disease. Large intra-individual fluctuations necessitate the investigation of its role in the etiology of cardiovascular disease in large samples or under strictly controlled conditions. We observed a graded association of the resting heart rate with all-cause and cardiovascular disease mortality and the same tendency for cancer mortality. Its causal role in the cardiovascular aging process is unclear. It is an indicator of overall good cardiovascular fitness which can be altered by physical activity. It may indicate disturbances in cardiovascular functioning which, on the long run, may have important influence on the process of atherosclerosis. Our results may give a new impetus to clarify the role of the resting heart rate as a long-term predictor of mortality.

### ***Frequency, intensity and duration***

Energy spent on vigorous (7.5-9.0 MET) leisure activities showed a stronger association with cardiovascular risk factors than the same amount of energy spent on moderate (5-7 MET) or low intensity (3-4.5 MET) leisure activities (*Chapter 6*). Each 100 kcal/kg/week spent on vigorous activities was associated with, among men: significant average differences of -0.36 mmol/l total cholesterol, +0.17 mmol/l HDL cholesterol, +0.05 HDL/total cholesterol, -0.33 mmol/l triglycerides, -3 mmHg diastolic blood pressure, -10 beats/min heart rate, +30 l/min peak flow, -1.1 kg/m<sup>2</sup> BMI, among women: -7 mmHg systolic blood pressure, -6 beats/min heart rate, +50 l/min peak flow and -1.4

kg/m<sup>2</sup> BMI. Either moderate or low intensity activity was significantly associated with HDL cholesterol, BMI, and, for men, heart rate, for women, HDL/total cholesterol, triglycerides, diastolic blood pressure and peak flow. With duration and intensity constant, increasing frequency by 1/week was significantly associated with -0.014 mmol/l total cholesterol, +0.001 HDL/total cholesterol, -0.36 beats/min heart rate, -0.093 kg/m<sup>2</sup> BMI among men, and +0.009 mmol/l HDL cholesterol, +0.001 HDL/total cholesterol, -0.014 mmol/l triglycerides, -0.31 beats/min heart rate and -0.098 kg/m<sup>2</sup> BMI among women.

Intensity and duration were significantly associated with some risk factors but, most obvious was that, at a constant level of intensity and duration, the frequency of leisure activity showed the stronger and more significant association with several risk factors such as serum lipids and BMI than both other activity components.

### ***Benefits for the elderly***

Our findings support the potential health benefit of regular physical activity for older adults, ages 50 to 69 (*Chapter 7*). Benefits were already observed for low amounts of moderate-to-vigorous activity as compared to a sedentary lifestyle and appeared to be stronger when these activities were conducted more frequently (with duration held constant) or at longer duration (with frequency held constant). Low intensity activities, such as walking and cycling were significantly associated with a lower resting heart rate and BMI, and among women, lower diastolic blood pressure levels. The prevalence of multiple risk factors was substantially lower among women with some participation in moderate-to-vigorous activities, as compared to sedentary women. We observed a graded decline in the prevalence of multiple risk factors with duration and frequency of activity for men. For those whose activity levels met the current recommendations ( $\geq 5$  times per week for a total of  $\geq 3.5$  hours), the prevalence odds ratio of multiple risk was 0.55 (95% CI 0.41-0.75) for men and 0.44 (95% CI 0.31-0.63) for women. Therefore benefits to cardiovascular health are likely to appear at recommended or even lower amounts of physical activity, which are achievable for most older adults.

### **Biologic plausibility**

The preventive effect of physical activity on cardiovascular disease is assumed to be largely due to physiologic adaptations to regular exercise. Health beneficial mechanisms have been postulated influencing atherosclerosis, coronary blood flow, blood coagulation, thrombosis, arrhythmia and the

tendency to develop non-insulin-dependent diabetes<sup>1</sup>. The mechanisms for the positive impact on major cardiovascular risk factors will be discussed in the following.

### *Serum lipids*

During exercise, energy metabolism and consequently the metabolism of serum lipids is enhanced. Lipids can be responsible for up to 90% of the oxidative metabolism during prolonged moderate exercise<sup>2</sup>. This affects acute lipid changes, but regular physical activity is also associated with preferable lipid profiles at rest<sup>3,4</sup>. However, reduced concentrations of several blood parameters may partly be the result of an increase in plasma volume among the regularly actives<sup>2</sup>.

### *Serum cholesterol*

In general, findings on the impact of physical activity on total serum cholesterol are inconsistent. While some studies observed lower total serum cholesterol levels<sup>5-7</sup>, others observed equal levels<sup>8-10</sup> among the regularly active as compared to sedentary individuals. An opposite effect on different lipoprotein fractions may be responsible for this inconsistency. Several studies observed a reduction of the atherogenic LDL cholesterol<sup>5,7,8</sup> and a favorable increase of HDL cholesterol among the physically active persons<sup>5-8,11</sup>. Since it has more power to predict atherosclerosis than other lipid fractions<sup>12</sup>, the (more often observed) increase in HDL cholesterol could be the most health-relevant. The findings of exercise intervention studies were less conclusive<sup>13,14</sup>. Exercise intervention studies generally reflect a short time period. Therefore, differences between study types may indicate that lipid profile changes in response to enhanced activity are slow. Changes in HDL cholesterol could not always be separated from dietary changes and weight loss<sup>4,15,16</sup>. In addition, physical activity could diminish the age and menopause related reduction of HDL cholesterol in middle-aged women<sup>17</sup>. Exercise may be more successful in increasing HDL cholesterol levels when initial levels are low (high atherogenic risk groups). Women have, on average, higher HDL cholesterol levels and lipolytic enzyme activity, which may explain the less pronounced alterations as compared to men<sup>16</sup>.

Exercise-induced adaptations in skeletal muscle could play a role in lipoprotein profile changes. An increased hydrolysis of very low density lipoprotein (VLDL) triglycerides, for use as a fuel, may promote the turnover of VLDL to HDL during exercise<sup>2</sup>. Changes in activity of lipoprotein lipase and hepatic lipase are assumed to regulate HDL cholesterol and HDL subfraction levels<sup>5</sup>.

### *Triglycerides*

Cross-sectional and training studies have related enhanced physical activity to lower serum triglyceride levels<sup>6,7,18,19</sup>. During exercise and after regular engagement in physical activity, lipoprotein lipase activity in skeletal muscles is increased. This enzyme will reduce triglyceride-rich lipoproteins. The deliverance of free fatty acids to muscle fibers during exercise is optimized and lipoprotein lipase may improve restoration of intramuscular triacylglycerol stores after exercise cessation. Endurance training also increases adipose tissue lipoprotein lipase, which may, together with changes in insulin sensitivity, improve the replenishment of triglyceride stores in adipose tissue after exercise. This is associated with a better clearance of diet-derived fats<sup>2</sup>. Since in our study nonfasting triglyceride levels were measured, the latter process may explain the major part of the observed differences.

In summary, changes in lipolytic enzyme activity may be responsible for alterations in lipid fractions. These alterations are closely related to energy metabolism. Consistent changes were observed more often for endurance exercise, although resistance exercise was also associated with lipid changes<sup>6,8</sup>. Since energy metabolism is relevant, lipid profile changes (as well as body mass changes) might be less related to intensity than to duration and frequency of physical activity. Regular, more frequent exercises may have a larger impact on total energy expenditure since the metabolic rate is enhanced for some time after exercise<sup>20</sup>. This is in correspondence with our observations (*Chapter 6*). Likewise, less pronounced associations with lipids among elderly may be due to the lower amount of energy spent on activities as compared to younger adults.

### *Blood pressure*

Many epidemiological and intervention studies observed an inverse relationship between physical activity and blood pressure<sup>21-24</sup>. This was generally observed for endurance but not for resistance training. The magnitude of effects seems to be dependent of initial blood pressure. An average reduction of 3/3 mmHg (systolic/diastolic) for the normotensive was observed, whereas for the borderline hypertensive a reduction of 6/7 mmHg and for the hypertensive a reduction of 10/8 mmHg were observed<sup>25</sup>.

The responsible mechanisms are largely unresolved. The decrease in blood pressure may be related to a lower cardiac output or to lower systemic vascular resistance and improved capillary blood flow<sup>26</sup>. Circulating catecholamine levels are an indication of sympathetic nervous system activity. The observed lower plasma noradrenaline levels, indicating a decrease in auto-

nostic activity, may play a role as well as changes in adrenaline<sup>27,28</sup>, receptor sensitivity<sup>29</sup>, and in the renin-angiotensin-aldosterone system<sup>30</sup>. Increased muscle building may also play a role in blood pressure changes<sup>21</sup>. Increased insulin resistance of tissues among sedentary individuals, which will increase plasma insulin levels and sympathetic nervous system activity, may additionally lead to increased sodium re-absorption by the kidney tubules and promote hypertension<sup>31</sup>.

Since sympathetic activity seems to play a central role, intensity of physical activity may be more important than duration or frequency for reducing blood pressure. We observed a significant association between male diastolic blood pressure and frequency, but not with other aspects, of physical activity.

### ***Resting heart rate***

An elevated resting heart rate, generally measured by pulse rate, is associated with higher cardiovascular disease risk and low levels of regular physical activity<sup>10,11,22,24</sup>. Beneficial effects are observed for both endurance<sup>11</sup> and resistance training<sup>32,33</sup>. Possible adaptations, resulting in a reduced resting heart rate, include enhanced parasympathetic tone, increased left ventricular stroke volume and longer diastolic filling time as well as reduced sympathetic discharge leading to lower impulse rates<sup>32</sup>. Of all observed parameters in our study, the resting heart rate showed the strongest correlation with physical activity. As with blood pressure, high intensity activities may have a larger impact<sup>10</sup> which is in accordance with our findings.

### ***Body mass index***

High body mass may influence other cardiovascular risk factors, but is independently associated with an increased cardiovascular risk<sup>34,35</sup>. Some studies observed an inverse association between physical activity and BMI<sup>11,36-38</sup>, whereas others did not<sup>5,10,24</sup>. Physical activity increases energy expenditure and fat metabolism and may optimize energy balance and body weight<sup>39</sup>. Higher caloric intakes may compensate for higher energy expenditure as observed among lean women but not among obese women<sup>40,41</sup>. Energy metabolism remains elevated for some time after exercise<sup>20</sup>. The impact of exercise on energy balance is observed to be small. Although exercise can contribute to a considerable part of total energy expenditure, differences may be compensated by increased energy intake<sup>42</sup>. A combination of enhanced physical activity and dietary changes are most effective in reducing body weight. Exercise may change fat distribution and reduce intra-abdominal fat depots which could be more relevant for cardiovascular disease risk<sup>37</sup>. Exercise is

associated with a reduction of fat mass<sup>9,43</sup> and an increase in muscle mass<sup>43</sup>. The BMI is generally used as an estimate of obesity, but it reflects both fat and muscle mass. The reduction in fat mass may be larger than observed through reduction of BMI. A less pronounced association of physical activity with BMI among men as compared to women may be related to their larger muscle mass and a higher impact of exercise on muscle growth. Larger differences among women may be associated with aspired weight reduction through both physical activity and dietary changes.

Exercise alone may produce small reductions in body mass. Lower turnover of free fatty acids and glycerol phosphate into triglycerides in adipose tissue will reduce lipogenesis. In addition, glucose uptake and oxidation in skeletal muscles are enhanced due to exercise<sup>39</sup>. Increased enzymatic activity, protein synthesis, hormone concentrations and replenishment of glycogen stores may also be important<sup>9</sup>. In summary, exercise may be helpful in maintaining lean body mass<sup>44,45</sup>. Similar to the considerations for serum lipids, duration and frequency may be more relevant than intensity to reduce body weight<sup>44</sup>.

### *Further beneficial mechanisms*

Regular exercise may induce other beneficial adaptations. Endurance training can help reduce the progression or the severity of atherosclerosis in the coronary arteries<sup>46</sup>. If the oxygen supply to the heart muscle is insufficient, clinical symptoms of atherosclerosis appear. The training effect on the heart muscle will improve coronary blood supply by development of new blood vessels<sup>47</sup> and increase in diameter of major coronary arteries<sup>48</sup>.

These processes together with reduced sympathetic nervous system activity may reduce the risk of ventricular fibrillation (arrhythmia)<sup>49</sup>. In addition, training reduces thrombosis through the improved enzymatic breakdown of blood clots (fibrinolysis) and reduced platelet aggregation<sup>50</sup>.

Physical activity can also increase insulin sensitivity and may therefore prevent or delay the onset of non-insulin-dependent-diabetes mellitus (NIDDM) which is also a risk factor for cardiovascular disease<sup>51</sup>.

## **Methodological considerations**

Our findings are consistent with the body of epidemiological and experimental studies and in line with biological considerations. However, our cross-sectional observations contain no information regarding time relationships, which complicates causal inference. Individuals with a better constitution may

have a higher tendency to engage in sports or other physical activities („healthy sportsman effect“), whereas certain diseases could be a hindrance to being active. In contrast, individuals who know that they have a cardiovascular disease may tend to follow advice to enhance their leisure activities. A cross-sectional comparison of physical activity and cardiovascular morbidity would partly reflect these pathways. Also, acute and fatal cases of cardiovascular disease are not assessed, which may lead to an underestimation of the impact of regular physical activity on cardiovascular disease. Therefore we focused on objectively measured cardiovascular risk factors, with the exclusion of several prevalent diseases. Except for the BMI, it is unlikely that risk factor levels have altered the previously reported physical activity.

The results of our prospective analyses (*Chapters 4 and 5*) may provide stronger evidence of causal relationships. The follow-up studies include a clear time sequence between exposure and outcome. The internal validity was improved by adjusting for major cardiovascular risk factors and using separate analyses which excluded early mortality cases.

Bias, resulting from differential or non-differential error, may modify existing and nonexistent relationships. An error is regarded as differential when it tends to vary across the true values of other variables. For continuous variables, differential error also occurs if the error distribution varies with the true value of the variable itself<sup>52</sup>. Errors are non-differential if they do not tend to vary with the true value of other variables (or the variable itself). Generally, non-differential error results in a dilution of existing relationships towards the null value<sup>52,53</sup>. However, this is not guaranteed for polytomous variables<sup>54,55</sup>. The effect of differential error is harder to predict.

Several sources of bias find their origin in failures of design or conduct of the study and should be carefully considered and omitted at that stage. These include selection and information bias which generally cannot be controlled for in the analyses. A theoretical judgment of their impact on the observed results can and should be performed. Confounding may be regarded as a special source of bias, although it can also interfere with other sources of bias and has different practical consequences. Confounding results from unequal distribution of naturally occurring factors (confounders) among exposure groups which, independent of exposure, are associated with the disease outcome<sup>52,53,56</sup>. Confounding can theoretically be omitted by perfect randomization. If confounders are appropriately assessed, they can be adjusted for in the analyses. In the following, we discuss the possible sources of bias relevant to our study. Subsequently, we make some considerations about external validity. Since several error sources may interfere, there will be some inevitable overlap in the discussion.

## *Internal validity*

### *Selection or response bias*

Our results are not likely to be affected by selection bias, since exposure comparisons are made within representative population samples, with the same selection criteria for all participants. The response rate for all samples was about 70%. Nonresponse analyses could not detect differences in smoking habits and BMI between respondents and nonrespondents<sup>57</sup>. It could be that sedentary individuals tend to refuse to participate, but this is not likely to be related to the observed risk factors, independent of the effect of a sedentary lifestyle (differential bias). Differential error could occur if physically active individuals with good cardiovascular health or sedentary individuals with bad health are systematically more frequently included than physically active individuals with bad health or sedentary individuals with good health, which is very unlikely.

For several multivariate analyses we excluded those with ill-health. This may have largely removed the possibility of an association between physical activity and health due to the impact of existing illnesses on physical activity habits. It was not possible to separate pre-existing illness from illness as a result of a sedentary lifestyle and therefore, the observed associations may be attenuated since they reflect a relatively healthy population. The observed magnitude of associations may therefore be smaller than the real impact of leisure activity on health. The results without exclusion of these individuals were, however, essentially similar.

### *Information bias*

Physical activity (the exposure variable) and several potential confounders were measured by questionnaire. Assessment by questionnaire has a large potential for misclassification. More accurate activity assessment methods do exist, such as the doubly labeled water method and pulse rate monitoring. In practice, these methods are not applicable to measure the long-term physical activity habits in a free-living population, and are expensive to apply to large population samples. They may also have a lower acceptance rate (because they require more time and cooperation from the participants) or can influence actual activity behavior. Our objective was to assess long-term physical activity habits, for which questionnaires are generally preferred. The leisure activity questionnaire was adapted from the Minnesota leisure-time activity questionnaire<sup>58</sup>, and the individual items showed reasonable repeatability<sup>59</sup>. Nevertheless, it is a crude measurement method and the use of MET

values for some indicators may be an additional source of misclassification. One MET reflects the energy expenditure at rest and is about 3.5 ml O<sub>2</sub> per minute. The MET has the advantage that it is almost independent of body weight and reflects 1 kcal per kilogram body weight per hour. MET values were assigned to activities to estimate expended energy and intensity level. People who reported never having participated in leisure activities were assumed to be sedentary. Still, they could participate in leisure activities not included in the questionnaire. This, however, also applies to the more active. The analyzed risk factors were unknown at the time of assessment. Misclassification is therefore mainly independent and non-differential. The possibility of detecting relationships despite the attenuation by misclassification is higher for large sample sizes.

For several reasons, it is unlikely that substantial bias from differential misclassification occurred. First, we constructed various indicators of physical activity, reflecting energy expenditure on total-, leisure time-, conditioning-, low-, moderate- and high-intensity physical activity as well as indicators of sport time and average frequency, intensity and duration of leisure activity. Their association with several cardiovascular risk factors did generally not result in spurious trends and all analyses consistently showed that higher levels of physical activity are beneficial to cardiovascular health. Second, although the definitions were not identical, the consistency was satisfactory between sport time from the single item question with the cumulative conditioning leisure time calculated from the leisure-time questionnaire. Third, to further eliminate the possibility of systematic error, we made exclusions for circumstances such as: a recent holiday (vacation), unemployment and retirement. Since under these circumstances the amount of leisure time may have changed, the reported leisure-time activity may differ substantially from long-term physical activity. This concerns most participants who reported more than 35 hours of leisure activity per week – they were therefore excluded from the analyses.

The questionnaire provided comprehensive information about frequency and time spent in leisure-time activities. If the frequency of some activity category was below „once a week“, participants did not have to report the time spent per week on this activity. This may result in misclassification, especially of those reporting many activities but all with a frequency below „once a week“. Therefore, individuals with reported frequency but no reported time were excluded from the analyses. Unfortunately, this exclusion made it impossible to further refine the analyses of the low frequency physical activity groups. Among those included, about 5% of reported frequencies were below 3 times per month. No systematic differences in the distribution of these fre-

quencies among groups could be detected. Therefore, it is not likely that individuals with many leisure activities but all with frequencies below 3 times per month will differ in their relationship of physical activity and risk factors.

The associations between physical activity and other healthy habits may be affected by a social desirability bias. Participants might report more physical activities during leisure time because this conforms to social norms. Since the questionnaire was self-administered and anonymous, this may be of minor relevance. However, certain participants who over-report physical activity may tend to over-report other healthy behavior. This bias could partly explain the observed association of other healthy lifestyle habits with physical activity.

In summary, we observed mainly objectively measured risk factors as dependent variables. Therefore, most of the described error sources will be non-differential and will tend to dilute the observed associations. So the „real effects“ of activity may be larger, but the large sample sizes may ensure detection of small effects.

#### *Specification bias*

The use of inappropriate statistical models can introduce specification bias in the estimates<sup>52</sup>. In our studies, we have carefully checked the assumptions allowing the use and ascertaining the correctness of the statistical models. Overall, we used a variety of statistical models, including: simple contingency tables, multiple linear regression, analysis of variance, logistic regression, and proportional hazard models. Cross-checking the obtained results from these models confirmed the dependability of our findings.

#### *Confounding*

Sociodemographic and behavioral characteristics are potential confounders in the relationship of leisure activity and cardiovascular risk factors. An overview of their relationship with leisure activity and possible explanations is given in *Chapter 3*. These characteristics show associations with risk factors independent of physical activity, and show associations with, but which are not necessarily explained by, physical activity. They were tested for confounding effects and, if appropriate, were controlled for in the analyses. In general, the unadjusted relationships showed similar trends as the adjusted. Still, undetected confounders as well as inadequate adjustments (due to e.g. measurement errors)<sup>60</sup> resulting in residual confounding may partly explain the observed relationships. Dietary habits, for instance, were based on a food frequency questionnaire, which is a semi-quantitative assessment method. The adjustments for BMI and socioeconomic status may largely account for resid-

ual confounding of unmeasured dietary differences. In the follow-up studies, the adjustment for cardiovascular risk factors (which are partly a consequence of dietary habits), will have a similar effect. In the analyses for older adults we observed no substantial confounding by dietary habits.

The BMI deserves special attention. A part of the association of physical activity with cardiovascular disease risk factors was supposed to be mediated by a regulating effect of physical activity on BMI. From an epidemiological perspective, this implies that the BMI is an intermediate factor beside its role as a confounder. Therefore, adjustment could introduce some over-adjustment bias. As observed by others, the direct effect of exercise or enhanced leisure-time activity on BMI is probably small<sup>43,44</sup>. Training as a measure to reduce body weight is only useful with simultaneous changes in diet. Several training hours may be necessary to compensate for the excess of energy intake of an opulent meal. So, by controlling for BMI, a correction for other health related behavior is performed indirectly. In addition, severe obesity may alter physically active behavior and would, in this sense, be a classical confounder. The association between physical activity and BMI is considered to be weak and variation in BMI is mainly due to other factors. Therefore, we assume that the relationships adjusted for BMI are the less biased ones. Moreover, we were interested in the effects of physical activity on risk factors, independent of its association with body mass. Of course, we also conducted similar analyses without a correction for BMI and, although the magnitude of some associations slightly improved, they were essentially the same.

Adjustment for socioeconomic status and probably the individual's residential surroundings (urbanization level) also indirectly adjusts for a wide variety of health related circumstances and habits. Individuals of high socioeconomic status as well as those living in a city might have better access to health information and medical resources and may differ in eating, smoking and drug consumption patterns. They could also have better access to a broad variety of leisure-time activities. In addition, physical and psychological stress at work and during leisure time could differ. Similar to BMI, some of these aspects may be dependent of leisure activity as related to cardiovascular risk factors. Therefore, a partial over-correction may have occurred and the real association of physical activity with risk factors might be stronger.

In the presented analyses, smoking and a history of smoking were included as binary variables. However, we conducted similar analyses with serum thiocyanate, which is a biomarker for cumulative smoking, and got similar results. Therefore, residual confounding due to tobacco consumption may be negligible.

Finally, total physical activity could confound the observed association between leisure activity and cardiovascular risk. Our total physical activity index showed only a weak association with mortality. Some analyses were adjusted for other activity which did not seriously confound the association of leisure activity and risk factors (perhaps due to the adjustment for socioeconomic status). This is in accordance with observations that current occupational levels of physical activity are not strongly and consistently related to cardiovascular health<sup>61</sup>. In summary, although leisure activity is associated with sociodemographic and behavioral parameters, these associations could not explain the observed relationship with cardiovascular risk factors.

### *External validity*

The representativeness of our samples and the similarity of leisure activity levels with those of other western populations advocate ready applicability. Several population-based studies were conducted in North America, but leisure activity levels may differ from Germany. When comparing German activity levels with levels found in North American population studies, it seems that the proportion of the extremely sedentary and the extremely active in Germany is lower<sup>1</sup>. In Germany we observed generally higher cardiovascular risk factor levels but lower cardiovascular mortality, as compared to North America<sup>62</sup>. Therefore, we wanted to estimate the public health impact of regular physical activity in Germany.

Some indicators of activity (energy expenditure, intensity) were calculated using MET values, which may not be appropriate for every individual and could hamper the applicability of absolute impact. The MET value is a relative ratio of the energy cost of an activity in units of the resting metabolic rate. This ratio is empirically observed to be relatively independent of body weight. It is measured as oxygen consumption, one MET being about 3.5 ml/min/kg. This is equivalent to approximately a 1 kcal/kg/hour energy cost. We regard our indices as indicators of physical activity and not as energy expenditure measures. Nevertheless, they were similar to other reported activity levels and energy requirements. The proportion of non-sporting individuals was similar to observations from another representative German sample<sup>63</sup>.

The larger amount of total activity and low intensity leisure activity observed among the subgroup of 60-69 year olds compared with the young (*Chapter 4*) may be surprising. This could indicate the inappropriateness of MET values for elderly. MET values are multiples of resting metabolic rate which may decline with age. However, the decline in energy expenditure was found to be small, after correction for fat and fat-free mass<sup>64</sup>. Energy expen-

ditures based on MET may not be comparable for different age groups, but within age groups they are useful to estimate activity levels. We observed an increased amount of leisure time due to retirement (especially for men) and decreased hours of sleeping among the elderly. These factors make the leisure-time spectrum for this group different which may explain the results. This increase in leisure time should be used to enlarge participation in moderate or intense activities.

### *Effect modification*

Effect modifiers may or may not be confounders<sup>56</sup>. Whereas confounding is not related to the causal pathways, studying effect modification may contribute to the understanding of etiology (which needs a different analysis concept). While confounding results from unequal distribution, the relationship between exposure and outcome is different among strata of the effect modifier. This may be of biological relevance for which documentation (separate analyses), rather than adjustment, is appropriate. Effect modification has important implications for the applicability of the results.

We have tested several parameters, each analyzed separately, but failed to detect any relevant effect modification in the relationships of interest, gender being the exception. The most prominent among possible effect modifiers, and a main focus point of current physical activity research, is age. In our context, it might be hard to define age as an effect modifier. Not age itself, but several circumstances changing with age, may cause effect modification in the observed relationships. An assumed different association among elderly might mainly be a result of alterations in physical activity (and a failure to measure those accurately with the questionnaire used) and higher risk factor levels. For the same recorded leisure activities, the intensity level of the elderly will probably be lower due to deterioration in physical condition, less competitive motivation, and absence of stimulation by a coach to reach exhaustive levels. In addition, the variation of both activity and some risk factor levels at older age might be diminished, which could result in the observed weaker associations. Older adults, however, are a major risk group for cardiovascular disease and should be a focus group for preventive programs. Except for total cholesterol, all risk factors showed preferable associations with regular physical activity in this age group. Effect modification in the relationship between resting heart rate and mortality is described in *Chapter 5*.

## Conclusion

The observed associations were achieved using large representative samples. This representativeness may be somewhat lost by exclusions and statistical adjustments. However, since the crude and adjusted relationships were similar, the presented results may closely reflect the situation in the West German population. The similarity between unadjusted and adjusted results convinced us that the reported impact closely reflects reality in Germany. Since physical activity, risk factor levels and cardiovascular disease in other West European countries are similar, it is very likely that the impact in these countries is comparable. In general, the separate relationships of physical activity with cardiovascular disease risk factors were weak but the magnitude of the association could be somewhat stronger if physical activity levels had been more accurately measured. The relative risk for cardiovascular mortality of the sedentary versus the regularly active was about 3-4 (depending on the definition of active), which is a fairly strong association. Our study supports the importance of regular physical activity for cardiovascular health.

## Public health relevance

The various perspectives under which we analyzed the association of leisure activity (energy expenditure, time, frequency and intensity) and cardiovascular risk (risk factors and mortality) consistently showed beneficial results from enhanced regular physical activity. Although other explanations for these results are largely ruled out, the ultimate evidence for a direct preventive impact of leisure activity on mortality is still outstanding. Final proof could only come from a longitudinal intervention experiment over a long period of time, which would be impractical and financially and ethically impossible to conduct. Studies of late<sup>65-67</sup> indicated a positive effect of recent increases in physical activity in the older population independent of physical activity levels during young adulthood. However, changes in constitution or health status may precede these physical activity changes and may be the underlying reason for a positive association, although this is not likely.

Nevertheless, we think that the presented associations will closely reflect the real impact of regular physical activity on cardiovascular health. Although the impact for the individual may appear small, enhancing regular physical activity on a societal level would have a large public health impact. Public health may benefit the most if sedentary people become modestly active<sup>68</sup>. As noted in the introduction, the impact of light activities is unclear, especially among older adults (who may prefer these levels more than moderate

activities). Frequent engagement in light or some engagement in moderate activities (1-3 times per week, 0.5-2 hours total) may have benefits compared to a sedentary lifestyle (*Chapter 7*). For the total population we observed beneficial associations for some risk factors with moderate and even light activities (HDL cholesterol, triglycerides, diastolic blood pressure, heart rate, peak expiratory flow and BMI) as presented in *Chapters 6 and 7*.

In Figure 8.1, we have summarized the difference in the adjusted mean risk factor levels between sedentary men and women and daily physically active (5 or more times per week, totaling at least 3.5 hours of moderate-to-vigorous activity) and regularly physically active (3 or more times per week totaling at least 2 hours of moderate-to-vigorous activity) men and women. The individuals who are active daily reflect the 12% most active men and 5% most active women of the 25-69 year old population. A cumulative impact of the presented differences can be estimated as the difference in expected all-cause mortality risk with the use of a multiple logistic function. We calculated multiple logistic functions of a regional sample (the same as described in *Chapter 4*) for the older population (ages 40-69) with a total of 8 years follow-up time for all-cause and cardiovascular mortality. These included the impacts of total serum cholesterol, HDL cholesterol, systolic blood pressure and heart rate, holding the effects of age and smoking constant. Since the risk functions were calculated for a population ages 40-69, it seems appropriate to apply them to the net differences observed for the same age group.

A male in this age group with reduced risk factors similar to the average reductions observed for daily active individuals will have a 30% lower all-cause mortality and a 41% lower cardiovascular mortality risk. The reductions for regularly moderate-to-vigorously active individuals would imply a 19% lower all-cause and an 28% lower cardiovascular disease mortality risk. For a female the risk reduction is relatively small (7-11% for all-cause, no function estimable for cardiovascular mortality), probably because of the low mortality risk for women in this age group. Of course, these are crude estimates with large confidence intervals (and even larger uncertainty intervals). It shows, that because of the broad impact of physical activity on cardiovascular risk factors, the expected overall reduction in mortality risk is impressive. Moreover, the reduction may be larger due to an effect on other risk factors not considered in the risk function. Using the RR estimates for cardiovascular mortality with sedentary living habits as an exposure variable (RR = 3 for sedentary; 1.4 for moderate actives compared to high actives; see *Chapter 4*), a population attributable risk of 56% for cardiovascular mortality was estimated for men in this age group. This percentage is larger than similar estimates for the North American population<sup>68</sup>.

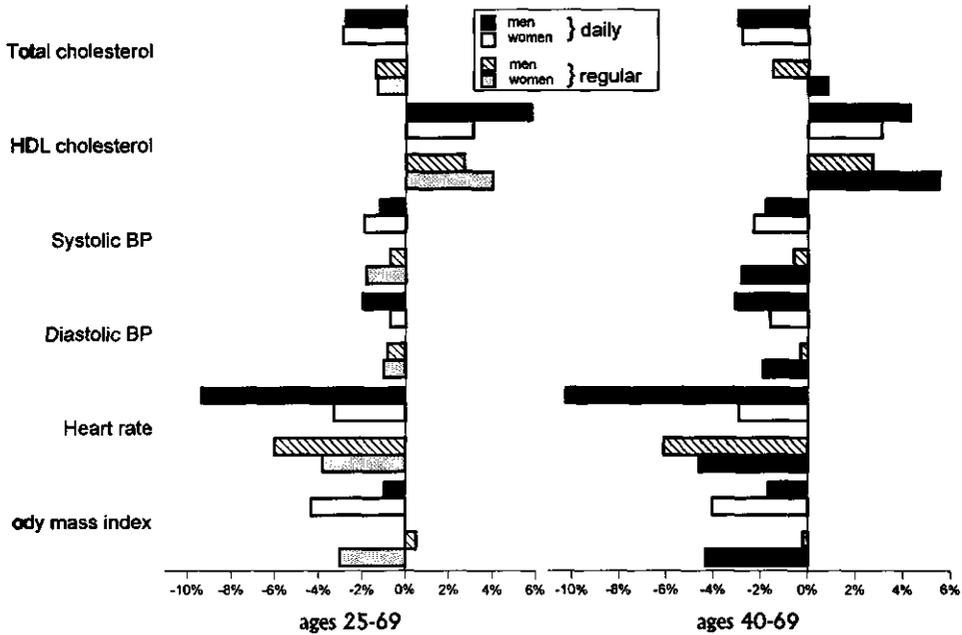


Figure 8.1 Net differences in adjusted means between sedentary and regularly moderate-to-vigorous physically active individuals. Adjusted for age, smoking, socioeconomic status, residential surroundings, weather, occupational activity, BMI, survey period, liquid, alcohol and fat intake. Daily is  $\geq 5$  times and  $\geq 3.5$  hours weekly; regular is  $\geq 3$  times and  $\geq 2$  hours but less than daily.

Considering the annual 55 794 cardiovascular deaths (1995) in this age group, approximately 31 000 cardiovascular deaths could theoretically be prevented, if all men became adequately active. Such an increase in activity levels may be unrealistic. Therefore we also estimated the number of cardiovascular deaths which could be prevented if 50 percent of sedentary men in this age group increased their activity level to moderate (up to 18 kcal/kg/week which, for example, could be 4 hours of brisk walking or cycling, 2.5 hours swimming or volleyball or 2 hours long distance running, tennis or squash). This would still mean that more than 6 500 of annual deaths among men ages 40-69, could be prevented. This may indicate the relevance of regular physical activity for public health and may give an impetus to health policy.

## Physical activity recommendations

Both extremely low and high levels of physical activity may severely stress the heart. The resting heart rate may substantially increase after 14 days absolute bed rest<sup>69</sup>. Myocardial infarction patients receive an exercise therapy as soon as possible after myocardial infarction, in contrast to some decades ago. On the other hand, an increased occurrence of myocardial infarcts was observed during vigorous activities such as marathon running. Several studies indicated that the actual risk during strenuous exercise is elevated (probably due to underlying cardiac disturbances), but the long-term risk of the regularly active individuals for myocardial infarction is far below that of sedentary individuals<sup>70</sup>. Individuals with advanced atherosclerosis but free of symptoms at rest may develop angina pectoris during exhaustive physical exercise. Sedentary persons should therefore start with a low-to-moderate activity level and gradually advance to the desired level.

The following recommendations are cross-checked with available literature and are in line with recent recommendations<sup>1,71,72</sup>. They focus on improvement in cardiovascular health but may not be adequate to improve body shape or physical performance.

The preferred type of exercise is decidedly endurance, including: swimming, jogging, running, brisk walking, hard cycling, and several ball games.

Regular activity sessions, lasting for 30 minutes, of moderate or vigorous exercise (resulting in enhanced sweating, breathing and heart rate; at least 50% of  $\text{VO}_2$  max), should be performed at least 3 times per week, preferably more often. If vigorous activity is preferred, a duration of 20 minutes conducted 3 times per week might be adequate. We observed beneficial associations of several cardiovascular risk factors with low intensity activity among elderly. Low or moderate intensity activity is a preferable starting level, which may progressively be increased, for older adults and those with prevailing high risk factor levels. These individuals as well as the long-term inactive, should consult a physician before they start an exercise program. However, it is important to have regular, sustained physical activity since several beneficial effects of exercise may diminish after some weeks and may disappear after some months<sup>1</sup>.

These recommended levels are feasible for almost all individuals. The achievement of cardiovascular health may be of minor importance for the trained athlete, but improving cardiovascular health, the enhancement of physical abilities, social contacts and simply pleasure, may well motivate elderly and high risk individuals. The expected benefits are important for public health but individual improvements may not be enough motivation in the long

run. Additional motivation, such as fun (by choosing a preferred sport), improved social contacts, well-being, functional capacity and stress reduction may improve compliance, especially among the elderly. Group activities are preferred because they are likely to improve compliance.

## Suggestions for future research

We observed a generally healthier lifestyle among the less sedentary. This cross-sectional observation makes it impossible to determine a causal direction, but an active lifestyle may stimulate other healthy habits. More insight into such interrelationships may be useful for more effective prevention and health promotion programs. Intervention studies which estimate the impact of enhancing physical activity on other health related behavior should be conducted in several (young and elderly) population samples. In addition, more research to better understand the reasons for becoming active as well as reasons for the failure to stay active would be important to refine prevention programs.

Our study indicates the importance of frequency, in addition to (but independently of) intensity and duration of physical activity. Further studies, preferably intervention experiments with different exercise frequencies, could support, and more accurately determine, the optimal frequency for maximal cardiovascular health benefits. In addition, the impact of light activities needs further clarification. Further clarification of biologic pathways responsible for the preventive effect of regular physical activity, independent of the major cardiovascular risk factors would be scientifically interesting, and may lead to a better understanding of the degenerating process of atherosclerosis. In addition, the interpretation of the resting heart rate as a predictor should be further investigated.

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## Summary

Most people in Germany and other western countries have a highly sedentary lifestyle. Low physical activity levels may contribute to the high prevalence of cardiovascular diseases, which is a major health problem in these societies. Enhanced physical activity during leisure time seems to be a perfect preventive measure against cardiovascular disease since it appears to have a beneficial impact on all major cardiovascular risk factors, such as hypertension, hypercholesterolemia and obesity. It is unlikely that the majority of the population will turn into athletes, therefore health benefits from moderate levels of leisure activity for the general population are highly relevant to public health.

The main objectives addressed in this thesis are: (1) to determine the relationship of leisure activity with serum total and HDL cholesterol, triglycerides, blood pressure, resting heart rate and body mass index in the German population; (2) to evaluate the interference from sociodemographics and health related lifestyles on these relationships; and (3) to estimate the impact of regular physical activity on mortality risk, independent of the baseline association with major cardiovascular risk factors (*Chapter 1*).

The major part of the presented analyses are based on three nationally representative samples of the West German population, each containing about 5 000 men and women, ages 25-69. As part of the German Cardiovascular Prevention Study, these surveys were conducted from 1984 to 1986, 1987 to 1988, and 1990 to 1991. A comprehensive description of this study and its main results is given in *Chapter 2*.

In the most recent sample (1990-1991) we analyzed the interrelationships of leisure activity, other health-related lifestyles and sociodemographic characteristics (*Chapter 3*). We observed that physically active individuals in general, were younger, more likely to be single and more likely to live in medium to large cities than sedentary individuals. Men and women of a high socioeconomic status were, respectively, four and three times more often engaged in leisure activity than those of a low socioeconomic status. Independent of these characteristics, physically active individuals were less likely to smoke, had a lower body mass index, ate breakfast more regularly, felt less need to sleep early, and consumed more frequently fruit, salad, wholemeal bread and vitamin supplements than sedentary individuals. They also consumed less frequently white bread and meat and consumed higher amounts of fluids. In summary, enhanced leisure activity was associated with a generally healthier lifestyle.

In the pooled samples we observed that active men (spending more than 18 kcal/kg/week on conditioning activities) had significantly favorable total serum cholesterol (-2.5%), HDL/total cholesterol ratios (+4.2%), resting heart rates (-4.3%) and peak expiratory flow (+4.2%) values than sedentary men (*Chapter 4*). Active women (spending more than 12 kcal/kg/week on conditioning activities) had significantly favorable levels of HDL cholesterol (+3.7%), HDL/total cholesterol ratio (+3.9%), triglycerides (-5.1%), diastolic (-1.3%) and systolic blood pressure (-1.6%), body mass index (-2.8%), resting heart rate (-2.5%) and peak expiratory flow (+5.0%). For a regional sample (1 061 men and 1 212 women, ages 40-69) we conducted a 5-8 year mortality follow-up. For active men a relative risk of 0.33 (95% CI 0.11-0.94) for cardiovascular disease mortality compared with sedentary men was estimated, independent of the baseline association with main cardiovascular risk factors. Men spending more than 2 hours per week on sports, had a relative risk of 0.36 (95% CI 0.16-0.79) for all-cause and of 0.26 (95% CI 0.08-0.83) for cardiovascular disease mortality, with sedentary men as a reference. Among women, the corresponding relative risk for total mortality was 0.28 (95% CI 0.07-1.17). The effect of physical activity on cardiovascular disease mortality among women was not clear owing to too few fatal cardiovascular events.

In a separate longitudinal study among 1 827 men and 2 929 women, ages 40-80, followed for 12 years, we analyzed the relationship of resting heart rate and mortality (*Chapter 5*). Among the measured risk factors, resting heart rate was the one most closely related to physical activity. We estimated a relative risk for all-cause mortality of 1.7 (95% CI 1.4-2.2) for men and of 1.4 (95% CI 1.1-1.8) for women for each 20 beats/min higher resting heart rate. Corresponding estimates of cardiovascular disease mortality were 1.7 (95% CI 1.2-2.6) for men and 1.3 (95% CI 0.9-2.0) for women, after adjusting for other cardiovascular risk factors.

The relative contribution of frequency, intensity and duration of leisure activities to the cardiovascular risk profile was studied in *Chapter 6*. For the same amount of energy expended, we observed stronger associations between cardiovascular risk factors and vigorous activity (7.5-9 MET) than with moderate (5-7 MET) or light activity (3-4.5 MET). Among men, each 100 kcal/kg/week spent on vigorous activities was associated with significant average differences of -0.36 mmol/l total serum cholesterol, +0.17 mmol/l HDL cholesterol, +0.05 HDL/total cholesterol ratio, -0.33 mmol/l triglycerides, -3 mmHg diastolic blood pressure, -10 beats/min resting heart rate, +30 l/min peak expiratory flow, and -1.1 kg/m<sup>2</sup> body mass index. Among women, such a level was associated with -7 mmHg systolic blood pressure, -6 beats/min resting heart rate, +50 l/min peak expiratory flow and -1.4 kg/m<sup>2</sup> body mass

index. Nevertheless, we observed significant and beneficial associations of light activity with HDL cholesterol and body mass index among men, and with triglycerides, diastolic blood pressure and body mass index among women. In similar multivariate models we studied the impact of the dimensions of activity: frequency, intensity and duration. With duration and intensity constant, increasing frequency by one time per week was significantly associated with  $-0.014$  mmol/l total cholesterol,  $+0.001$  HDL/total cholesterol ratio,  $-0.36$  beats/min heart rate,  $-0.093$  kg/m<sup>2</sup> body mass index among men, and  $+0.009$  mmol/l HDL cholesterol,  $+0.001$  HDL/total cholesterol ratio,  $-0.014$  mmol/l triglycerides,  $-0.31$  beats/min heart rate and  $-0.098$  kg/m<sup>2</sup> body mass index among women. The frequency of sport participation showed the strongest association with serum lipids and body mass index. Resting heart rate showed significant associations with all three dimensions among men (and with intensity and frequency among women). All three dimensions seem important for an overall better cardiovascular risk profile.

Finally (in *Chapter 7*), we studied the association of cardiovascular risk factors with different levels of light and moderate-to-vigorous activities among older adults, ages 50-69. Higher amounts generally showed greater benefits on the cardiovascular risk profile but moderate-to-vigorous activities conducted with a frequency of 0.5-3 times per week for a total of 0.5-2 hours, were already associated with significantly favorable risk factor levels. This was especially evident among modestly active women, who had significantly favorable systolic blood pressure ( $-1.8\%$ ), resting heart rate ( $-3.1\%$ ) and body mass index ( $-3.2\%$ ) values compared with sedentary women. For modestly active men we observed no substantial differences. Furthermore, both frequency and duration of activity have the potential to reduce risk factor levels independently. Activity levels according to the current recommendations may have considerable health benefits for older adults. We observed an odds ratio for the prevalence of multiple risk factors of 0.55 (95% CI 0.47-0.75) for men and of 0.44 (95% CI 0.31-0.63) for women following these recommendations (with sedentary individuals as a reference). In addition, we observed a beneficial association of light activities conducted frequently with diastolic blood pressure ( $-1.4\%$ ) and resting heart rate ( $-2.3\%$ ) among women, and body mass index among both men ( $-2.2\%$ ) and women ( $-2.9\%$ ).

In *Chapter 8* we discussed our findings in light of methodological limitations and coherence with previous findings and proposed mechanisms. Previous results generally support ours, and plausible mechanisms for the association between the risk factors of physical activity exist. It is unlikely that they are the result of bias, since the cross-sectional observed beneficial associations persisted after adjustment for age, smoking, socioeconomic status, season

(monthly outdoor temperature), body mass index, urbanization, alcohol and total liquid intake, ratio of saturated/total fat consumption, occupational activity and leisure activities with other intensity levels. The main contributions of this thesis to prevailing knowledge include the observation of the considerable cardiovascular benefits from moderate and even light activities. The reductions of cardiovascular risk factors associated with regular moderate-to-vigorous activity were estimated to result in a 19% lower all-cause and a 28% lower cardiovascular disease mortality risk among men, ages 40-69. Furthermore, we showed the importance of frequency next to intensity and duration. In addition, our results outline the prominence of physical inactivity as a major risk factor for cardiovascular disease mortality in the German population. Consequently, we recommend regular sessions of about 30 minutes of moderate leisure activities, preferably endurance types like cycling, swimming, running or brisk walking, performed at least 3 times per week, preferably daily. Persons with such activity levels may further improve their health by performing more frequent and more intense activities. Elderly persons, who previously were sedentary, should start to perform light activities (such as walking, cycling) on a daily base and, if they like, may gradually increase their activity level.

Since benefits of light activities may have the largest consequences for public health, further research should focus on the impact of such activities. Furthermore, the most effective ways to stimulate activity in the population should be determined.

## Zusammenfassung

Die meisten Menschen in Deutschland und anderen westlichen Ländern bewegen sich zu wenig. Das niedrige Niveau körperlicher Aktivität trägt zur hohen Prävalenz kardiovaskulärer Krankheiten bei und stellt ein bedeutendes Gesundheitsproblem dar. Körperliche Aktivität in der Freizeit erweist sich als ideale Prävention gegen kardiovaskuläre Krankheiten, da so eine positive Wirkung auf die wesentlichen kardiovaskulären Risikofaktoren wie z.B. Bluthochdruck, Hypercholesterolemie und Fettsucht erzielt werden kann. Es ist unwahrscheinlich, daß aus der Mehrheit der Bevölkerung Athleten werden. Daher ist der positive Effekt auch von mäßiger körperlicher Aktivität von großer Bedeutung für die Gesundheit der Bevölkerung.

In dieser Arbeit werden folgende Themenkomplexe behandelt: (1) die Beziehung zwischen körperlicher Freizeitaktivität der deutschen Bevölkerung und dem Serum-Gesamtcholesterin, dem HDL-Cholesterin sowie den Triglyceriden, dem Blutdruck, dem Ruhepuls und dem Body Mass Index, (2) der Einfluß von Gesundheitsverhalten und soziodemographischen Merkmalen auf diese Beziehungen und (3) Einschätzung der Auswirkungen regelmäßiger körperlicher Aktivität auf das Mortalitätsrisiko unter Berücksichtigung des Zusammenhangs mit den wichtigsten kardiovaskulären Risikofaktoren (*Kapitel 1*).

Der überwiegende Teil der dargestellten Analysen basiert auf drei bundesweiten repräsentativen Stichproben der westdeutschen Bevölkerung von jeweils ungefähr 5 000 Männern und Frauen im Alter von 25-69 Jahren. Im Rahmen der Deutschen Herz-Kreislauf-Präventionsstudie wurden von 1984 bis 1986, von 1987 bis 1988 und von 1990 bis 1991 Gesundheitssurveys durchgeführt. Eine ausführliche Beschreibung dieser Studie und seiner hauptsächlichen Ergebnisse wird in *Kapitel 2* dargestellt.

Anhand der Daten des letzten Surveys (1990-1991) analysierten wir die Wechselbeziehungen von Freizeitaktivitäten, anderen gesundheitsbezogenen Verhaltensweisen und soziodemographischen Merkmalen (*Kapitel 3*). Wir beobachteten, daß körperlich aktive Personen im allgemeinen jünger und öfter alleinstehend waren und eher in größeren Städten lebten als nichtaktive. Männer und Frauen aus hohen sozioökonomischen Schichten waren drei- bis viermal häufiger in ihrer Freizeit körperlich aktiv als Personen aus niedrigen. Unabhängig davon waren körperlich aktive Personen seltener Raucher, hatten einen niedrigeren Body Mass Index, frühstückten regelmäßiger, hatten seltener das Bedürfnis, früh schlafenzugehen, aßen häufiger Obst, Salat und Vollkornbrot und nahmen häufiger Vitaminpräparate als nichtaktive. Sie aßen seltener

Weißbrot und Fleisch und hatten einen höheren Flüssigkeitskonsum. Insgesamt wurde erhöhte körperliche Freizeitaktivität mit einem allgemein gesünderen Lebensstil assoziiert.

In der Gesamtstichprobe beobachteten wir, daß aktive Männer, deren Energieverbrauch bei konditionsfördernden Aktivitäten mehr als 18 kcal/kg/Woche betrug, signifikant günstigere Werte für Serum-Gesamtcholesterin (-2.5%), den Quotienten HDL-/Gesamtcholesterin (+4.2%), den Ruhepuls (-4.3%) und das maximale Atemstoßvolumen (+4.2%) hatten als nichtaktive (*Kapitel 4*). Bei den aktiven Frauen, deren Energieverbrauch bei konditionsfördernden körperlichen Aktivitäten höher als 12 kcal/kg/Woche war, wurden signifikant günstigere Werte für HDL-Cholesterin (+3.7%), den Quotienten HDL-/Gesamtcholesterin (+3.9%), Triglyceride (-5.1%), den diastolischen (-1.3%) und systolischen Blutdruck (-1.6%), Body Mass Index (-2.8%), Ruhepuls (-2.5%) und das maximale Atemstoßvolumen (+5.0%) gemessen. In einer regionalen Unterstichprobe (1 061 Männer und 1 212 Frauen im Alter von 40-69 Jahren) wurde die Mortalitätsrate über einen Zeitraum von 5-8 Jahren bestimmt. Bei körperlich aktiven Männern betrug das relative Risiko, an einer Herz-Kreislauferkrankung zu sterben, im Vergleich zu nichtaktiven 0.33 (95% Konfidenzintervall (KI) 0.11-0.94), unabhängig vom Zusammenhang mit den wichtigsten kardiovaskulären Risikofaktoren am Anfang der Studie. Männer, die mehr als zwei Stunden pro Woche Sport trieben, hatten ein relatives Risiko zu sterben von 0.36 (95% KI 0.16-0.79) und ein relatives Risiko, an einer Herz-Kreislauferkrankung zu sterben, von 0.26 (95% 0.08-0.83) im Vergleich zu nichtaktiven. Bei Frauen lag das relative Gesamtmortalitätsrisiko bei 0.28 (95% KI 0.07-1.17). Der Einfluß körperlicher Aktivität auf die Herz-Kreislaufmortalität bei Frauen konnte wegen der zu geringen Zahl von kardiovaskulären Todesfällen nicht untersucht werden.

In einer 12jährigen Longitudinalstudie mit 1 827 Männern und 2 929 Frauen im Alter von 40-80 Jahren analysierten wir die Beziehung zwischen Ruhepuls und Mortalität. Den deutlichsten Zusammenhang mit körperlicher Aktivität zeigte von allen beobachteten Risikofaktoren der Ruhepuls. Ein Unterschied von jeweils 20 Schlägen pro Minute führte in dieser Studie zu einem relativen Gesamtmortalitätsrisiko von 1.7 (95% KI 1.4-2.2) bei Männern bzw. von 1.4 (95% KI 1.1-1.8) bei Frauen. Entsprechend ergab sich für die Herz-Kreislaufmortalität ein Risiko von 1.7 (95% KI 1.2-2.6) für Männer und von 1.3 (95% KI 0.9-2.0) für Frauen bei konstanter Höhe der anderen kardiovaskulären Risikofaktoren (*Kapitel 5*).

Der relative Einfluß von Häufigkeit, Intensität und Dauer der körperlichen Freizeitaktivitäten auf das kardiovaskuläre Risikoprofil wird in *Kapitel 6* dargestellt. Bei gleichem Energieverbrauch wurden stärkere Zusammenhänge

zwischen kardiovaskulären Risikofaktoren und anstrengenden Aktivitäten (7.5-9 MET) beobachtet als bei mäßigen (5-7 MET) oder leichten Aktivitäten (7.5-9 MET). Bei Männern wurde jeder Energieverbrauch von 100 kcal/kg/Woche während anstrengender körperlicher Aktivitäten im Durchschnitt verbunden mit signifikanten Unterschieden der Werte beim Serum-Gesamtcholesterin (-0.36 mmol/l), beim HDL-Cholesterin (+0.17 mmol/l), beim Quotienten HDL-/Gesamtcholesterin (+0.05), bei den Triglyceriden (-0.33 mmol/l), dem diastolischen Blutdruck (-3 mmHg), dem Ruhepuls (-10 Schläge/min), dem maximalen Atemstoßvolumen (+30 l/min) und beim Body Mass Index (-1.1 kg/m<sup>2</sup>). Bei den Frauen wurden auf diesem Aktivitätsniveau signifikant bessere Werte des systolischen Blutdrucks (-7 mmHg), des Ruhepulses (-6 Schläge/min), des maximalen Atemstoßvolumens (+50 l/min) und des Body Mass Indexes (-1.4 kg/m<sup>2</sup>) gemessen. Weiterhin beobachteten wir auch signifikante positive Beziehungen zwischen leichter körperlicher Aktivität und HDL-Cholesterin sowie dem Body Mass Index bei Männern und Triglyceriden, diastolischem Blutdruck und Body Mass Index bei Frauen. In vergleichbaren multivariaten Modellen untersuchten wir den Einfluß der Häufigkeit, Intensität und Dauer von körperlicher Aktivität. Bei gleichbleibender Dauer und Intensität ergab eine Zunahme der Häufigkeit von jeweils einmal pro Woche eine signifikante Verbesserung der Werte von Gesamtcholesterin (-0.014 mmol/l), Quotient HDL-/Gesamtcholesterin (+0.001), Ruhepuls (-0.36 Schläge/min) und Body Mass Index (-0.093 kg/m<sup>2</sup>) bei Männern und bei Frauen von HDL-Cholesterin (+0.009 mmol/l), Quotient HDL-/Gesamtcholesterin (+0.001), Triglyceriden (-0.014 mmol/l), Ruhepuls (-0.31 Schläge/min) und Body Mass Index (-0.098 kg/m<sup>2</sup>). Im Vergleich mit Intensität und Dauer wurde deutlich, daß die Häufigkeit sportlicher Betätigung den stärksten Zusammenhang mit Serumlipidwerten und Body Mass Index zeigte. Der Ruhepuls bei Männern wies signifikante Zusammenhänge mit allen drei Aktivitätsgrößen und bei Frauen mit Intensität und Häufigkeit auf. Alle drei Aktivitätsgrößen scheinen für ein insgesamt besseres kardiovaskuläres Risikoprofil von Bedeutung zu sein.

Abschließend (*in Kapitel 7*) untersuchten wir die Beziehung zwischen kardiovaskulären Risikofaktoren und unterschiedlichen Graden leichter und mäßiger bis anstrengender körperlicher Aktivitäten Erwachsener im Alter von 50-69 Jahren. Eine höheres körperliches Aktivitätsniveau hatte im allgemeinen positive Auswirkungen auf das kardiovaskuläre Risikoprofil. Jedoch wiesen bereits mäßige bis anstrengende Aktivitäten, die 0.5-3mal pro Woche für 0.5-2 Stunden ausgeübt wurden, wesentlich günstigere Werte auf. Dies zeigte sich besonders bei mäßig aktiven Frauen, die im Vergleich zu nichtaktiven Frauen einen signifikant günstigeren systolischen Blutdruck (-1,8%), Ruhepuls

(-3.1%) und Body Mass Index (-3.2%) hatten. Bei gering aktiven Männern beobachteten wir keine wesentlichen Unterschiede. Aktivitätshäufigkeit als auch -dauer sind unabhängig voneinander geeignet, kardiovaskuläre Risikofaktoren zu senken. Körperliche Aktivität, die den aktuellen Empfehlungen entspricht, kann auch älteren Erwachsenen beträchtliche Gesundheitsvorteile bringen.

Wir beobachteten eine Odds Ratio für die Prävalenz multipler Risikofaktoren von 0.55 (95% KI 0.47-0.75) bei Männern und von 0.44 (95% KI 0.31-0.63) bei Frauen, die entsprechend den Empfehlungen aktiv waren (mit nichtaktiven Personen als Bezugsgröße). Zusätzlich beobachteten wir Zusammenhänge zwischen häufig ausgeübten leichten körperlichen Aktivitäten und diastolischem Blutdruck (-1.4%) sowie Ruhepuls (-2.3%) bei Frauen und dem Body Mass Index bei Männern (-2.2%) und Frauen (-2.9%).

In Kapitel 8 diskutieren wir unsere Ergebnisse im Hinblick auf methodologische Grenzen, auf ihre Übereinstimmung mit anderen Studienergebnissen und auf mögliche biologische Wirkmechanismen. Zuvor gewonnene Ergebnisse unterstützen unsere Befunde, und die plausiblen Wirkmechanismen für die Zusammenhänge zwischen Risikofaktoren und körperlicher Aktivität sind aus der Literatur bekannt. Es ist unwahrscheinlich, daß die Ergebnisse der Querschnittstudien auf Verzerrungen beruhen, da die positiven Zusammenhänge nach Anpassung für Alter, Rauchen, soziale Schicht, Jahreszeit (monatliche Außentemperatur), Body Mass Index, Wohnsitz Stadt/Land, Alkohol- und Flüssigkeitskonsum, Aufnahme von gesättigten Fettsäuren und Gesamtfettkonsum, körperliche Aktivität im Beruf und gegebenenfalls Freizeitaktivitäten auf anderem Intensitätsniveau weiterhin bestanden. Den Hauptbeitrag zum gegenwärtigen Wissensstand leistet diese Arbeit durch die beobachteten beträchtlichen kardiovaskulären Vorteile mäßiger und sogar leichter körperlicher Aktivitäten. Die günstigeren Werte der kardiovaskulären Risikofaktoren, die bei regelmäßig ausgeübten mäßigen bis anstrengenden körperlichen Aktivitäten beobachtet wurden, führen bei Männern im Alter von 40-69 Jahren schätzungsweise zu einem Rückgang der Gesamtmortalität um 19% und einem Rückgang der Herz-Kreislaufmortalität um 28%. Ferner wurde neben der Bedeutung von Intensität und Dauer die Regelmäßigkeit körperlicher Aktivität deutlich. Unsere Ergebnisse heben körperliche Untätigkeit als bedeutenden Risikofaktor für kardiovaskuläre Mortalität in der deutschen Bevölkerung hervor. Deshalb empfehlen wir die regelmäßige Ausübung mäßiger körperlicher Aktivitäten von jeweils ungefähr 30 Minuten Dauer, vorzugsweise Ausdauersportarten wie z.B. Radfahren, Schwimmen, Laufen, und zwar mindestens dreimal pro Woche, vorzugsweise täglich. Personen, die bereits ein derartiges Trainingsniveau erreicht haben, könnten ihre Gesundheit weiter fördern, indem sie ein noch häufigeres und intensiveres Trainings-

pensum leisteten. Ältere Personen, die zuvor nicht aktiv waren, sollten mit täglichen leichten körperlichen Aktivitäten wie z.B. Gehen, Radfahren anfangen. Falls sie mögen, könnten sie ihr Trainingspensum allmählich steigern. Da die Vorteile leichter körperlicher Aktivität großen Einfluß auf die Gesundheit in der Bevölkerung haben dürften, sollten künftige wissenschaftliche Untersuchungen vor allem die Auswirkungen von leichten körperlichen Aktivitäten untersuchen. Es müßten effektivere Möglichkeiten gefunden werden, die körperliche Aktivität in der Bevölkerung optimal zu fördern.

## Samenvatting

De meeste mensen in Duitsland en andere westerse landen hebben een overwegend inactieve levensstijl. Te weinig lichamelijke activiteit kan bijdragen tot een hoge prevalentie van hart- en vaatziekten, die in deze landen een belangrijk gezondheidsprobleem vormen. Een verhoging van de lichamelijke activiteit in de vrije tijd lijkt een perfecte preventieve maatregel tegen hart- en vaatziekten omdat dit een positief effect blijkt te hebben op alle belangrijke risicofactoren voor hart- en vaatziekten, zoals hoge bloeddruk, hoge cholesterolwaarden en overgewicht. Aangezien het onwaarschijnlijk is dat de meerderheid van de bevolking atleet wordt, zijn de voordelen van matige lichamelijke activiteit in de vrije tijd bijzonder relevant voor de gezondheid van de gemiddelde bevolking.

De belangrijkste doelen van dit proefschrift zijn: (1) het vaststellen van de relatie van lichamelijke activiteit in de vrije tijd met totaal serum cholesterol, HDL cholesterol, triglyceriden, bloeddruk, hartslag in rust en de body mass index in de Duitse bevolking; (2) het evalueren van de invloed van sociodemografische factoren en andere leefgewoonten op de onderzochte relaties; en (3) het schatten van het effect van regelmatige lichamelijke activiteit op het mortaliteitsrisico, onafhankelijk van de initiële samenhang met de belangrijkste risicofactoren voor hart- en vaatziekten (*hoofdstuk 1*).

Het merendeel van de analyses is gebaseerd op drie landelijk representatieve steekproeven uit de West-Duitse bevolking, die elk ongeveer 5000 mannen en vrouwen in de leeftijd van 25 tot 69 jaar omvatten. Deze werden van 1984 tot 1986, 1987 tot 1988 en 1990 tot 1991 onderzocht in het kader van de „Deutsche Herz-Kreislauf-Präventionsstudie“. De studie en haar belangrijkste uitkomsten zijn uitgebreid beschreven in *hoofdstuk 2*.

In de meest recente steekproef (1990-1991) hebben we de wisselwerking tussen lichamelijke activiteit in de vrije tijd, andere leefgewoonten en sociodemografische factoren onderzocht (*hoofdstuk 3*). We zagen dat lichamelijk actieve personen over het algemeen jonger en vaker alleenstaand zijn en vaker in een (middelgrote tot grote) stad wonen dan inactieve personen. Mannen en vrouwen met een hoge sociaal-economische status zijn met een vier, respectievelijk drie keer hogere waarschijnlijkheid actief in hun vrije tijd dan personen met een lage sociaal-economische status. Onafhankelijk van deze kenmerken waren lichamelijk actieve individuen vaker niet-rokers, hadden gemiddeld een lagere body mass index, ontbeten regelmatig, waren minder geneigd vroeg te gaan slapen en consumeerden vaker fruit, rauwkost, volkorenbrood en vitamine- preparaten dan inactieve individuen. Zij aten minder vaak wit

brood en vlees en namen gemiddeld meer vloeistof tot zich. Samengevat: een hogere lichamelijke activiteit kan worden geassocieerd met een over het algemeen gezondere levensstijl.

Analyse van de gepoolde steekproeven liet zien dat actieve mannen (die wekelijks meer dan 18 kcal/kg voor conditie-bevorderende activiteiten verbruiken) significant gunstiger waarden vertoonden voor totaal serum cholesterol (-2.5%), de verhouding HDL-totaal cholesterol (+4.2%), hartslag in rust (-4.3%) en expiratoire piekstroom (+4.2%) dan inactieve mannen (*hoofdstuk 4*). Actieve vrouwen (die wekelijk meer dan 12 kcal/kg voor conditie-bevorderende activiteiten verbruiken) vertoonden significant gunstiger waarden voor HDL cholesterol (-3.7%), de verhouding HDL- totaalcholesterol (+3.9%), triglyceriden (-5.1%), diastolische (-1.3%) en systolische bloeddruk (-1.6%), body mass index (-2.8%), hartslag in rust (-2.5%) en expiratoire piekstroom (+5.0%). Met een regionale steekproef (1 061 mannen en 1 212 vrouwen, leeftijd 40-69 jaar) werd een 5- tot 8-jarige mortaliteits follow-up uitgevoerd. Voor actieve mannen werd een relatief sterfte-risico aan hart- en vaatziekte van 0.33 (95% betrouwbaarheidsinterval (BI) 0.11-0.94) berekend, onafhankelijk van de samenhang met belangrijke risicofactoren voor hart- en vaatziekten aan het begin van de studie. Mannen die meer dan 2 uur per week aan sport deden, hadden een relatief risico van 0.36 (95% BI 0.16-0.79) voor totale mortaliteit en van 0.26 (95% BI 0.08-0.83) voor mortaliteit aan hart- en vaatziekten, met inactieve mannen als referentiegroep. Bij vrouwen was het corresponderende relatieve risico voor totale mortaliteit 0.28 (95% BI 0.07-1.17). Het effect van lichamelijke activiteit op mortaliteit aan hart- en vaatziekten bij vrouwen was niet duidelijk vanwege te weinig sterfgevallen door hart- en vaatziekten.

In een ander longitudinaal onderzoek bij 1 827 mannen en 2 929 vrouwen in de leeftijd van 40 tot 80 jaar die 12 jaar gevolgd werden, bestudeerden we de relatie tussen hartslag in rust en mortaliteit (*hoofdstuk 5*). Van de gemeten risicofactoren vertoonde de hartslag in rust de sterkste relatie met lichamelijke activiteit. We stelden een relatief risico voor totale mortaliteit voor mannen vast van 1.7 (95% BI 1.4-2.2) en voor vrouwen van 1.4 (95% BI 1.1-1.8), per 20 hartslagen per minuut méér in rust. Vergelijkbare schattingen voor sterfte aan hart- en vaatziekten waren, na correctie voor de versturende invloeden van andere risicofactoren, 1.7 (95% BI 1.2-2.6) voor mannen en 1.3 (95% BI 0.9-2.0) voor vrouwen.

De relatieve bijdrage van frequentie, intensiteit en duur van lichamelijke activiteit in de vrije tijd aan het risicoprofiel voor hart- en vaatziekten word gepresenteerd in *hoofdstuk 6*. Voor dezelfde hoeveelheid verbruikte energie, observeerden we een sterkere samenhang tussen risicofactoren voor hart- en vaatziekten en intensieve activiteit (7.5-9 kcal/kg/uur) dan tussen dezelfde

risicofactoren en matige (5-7 kcal/kg/uur) of lichte activiteit (3-4.5 kcal/kg/uur). Bij mannen werd elke 100 kcal/kg die per week werd verbruikt voor intensieve activiteit in verband gebracht met significante verschillen van gemiddeld -0.36 mmol/l totaal serum cholesterol, +0.17 mmol/l HDL cholesterol, +0.05 ratio HDL/totaal cholesterol, -0.33 mmol/l triglyceriden, -3 mmHg diastolische bloeddruk, -10 slagen/min hartslag in rust, +30 l/min expiratoire piekstroom en 1.1 kg/m<sup>2</sup> body mass index. Bij vrouwen werd een dergelijk activiteitsverschil in verband gebracht met significante verschillen van -7 mmHg systolische bloeddruk, -6 slagen/min hartslag in rust, +50 l/min expiratoire piekstroom en -1.4 kg/m<sup>2</sup> body mass index. We stelden ook significant gunstige associaties vast van lichte activiteit met HDL cholesterol en body mass index bij mannen en met triglyceriden, diastolische bloeddruk en body mass index bij vrouwen. In vergelijkbare modellen met meer variabelen bestudeerden we het effect van de verschillende dimensies van activiteit: frequentie, intensiteit en duur. Bij een constante duur en intensiteit van de activiteit, wordt een frequentieverhoging van een keer per week geassocieerd met een significant verschil van -0.014 mmol/l totaal serum cholesterol, +0.001 ratio HDL/totaal cholesterol, -0.36 slagen/min hartslag in rust en -0.098 kg/m<sup>2</sup> body mass index bij mannen en met +0.009 mmol/l HDL cholesterol, +0.001 ratio HDL/totaal cholesterol, -0.014 mmol/l triglyceriden, -0.31 slagen/min hartslag in rust en -0.098 kg/m<sup>2</sup> body mass index bij vrouwen. In vergelijking met intensiteit en duur vertoonde de frequentie van sportbeoefening de sterkste samenhang met serum lipiden en body mass index. De hartslag in rust vertoonde een significant verband met alle drie dimensies bij mannen en met intensiteit en frequentie bij vrouwen. Alle drie dimensies lijken belangrijk voor een gunstiger risicoprofiel voor hart- en vaatziekten.

Tenslotte (in hoofdstuk 7) werd het verband tussen risicofactoren voor hart- en vaatziekten en de verschillende niveaus van lichte en matige tot intensieve activiteiten onderzocht bij oudere mensen, in de leeftijd van 50 tot 69 jaar. In het algemeen gold: hoe hoger de activiteit, hoe gunstiger het risicoprofiel voor hart- en vaatziekten. Matige tot intensieve activiteiten met een frequentie van 0.5-3 keer en in totaal 0.5-2 uur per week zijn reeds geassocieerd met significant gunstiger risicofactoren. Dit is vooral te zien bij matig actieve vrouwen met een significant gunstiger systolische bloeddruk (-1.8%), hartslag in rust (-3.1%) en body mass index (-3.2%) dan inactieve vrouwen. Voor matig actieve mannen observeerden we geen duidelijke verschillen. Verder bleken zowel de frequentie als duur van de activiteit onafhankelijk van elkaar de risicofactoren te kunnen verlagen. Een activiteitsniveau volgens de huidige aanbevelingen kan aanzienlijke voordelen voor de gezondheid van oudere mensen opleveren. De odds ratio voor het gelijktijdig voorkomen van meerdere risicofactoren was

0.55 (95% BI 0.47-0.75) voor mannen en 0.44 (95% BI 0.31-0.63) voor vrouwen die al leefden volgens deze adviezen (met inactieven als referentie). Ook vonden we een gunstige samenhang tussen frequente lichte activiteit en diastolische bloeddruk (-1.4%) en hartslag in rust (-2.3%) bij vrouwen en body mass index bij zowel mannen (-2.2%) als vrouwen (-2.9%).

In *hoofdstuk 8* worden methodologische beperkingen van de resultaten alsmede overeenkomsten met vorige observaties en met veronderstelde mechanismen uitvoeriger besproken. Eerdere resultaten ondersteunen in het algemeen onze bevindingen en er zijn plausibele biologische mechanismen die de gevonden relaties tussen risicofactoren en lichamelijke activiteit kunnen verklaren. Het is onwaarschijnlijk dat de gevonden gunstige verbanden in het dwarsdoorsnede-onderzoek een vertekend beeld opleveren, omdat ze overeind bleven na correctie voor leeftijd, roken, sociaal-economische status, seizoen (gemiddelde buitentemperatuur van de maand), body mass index, woonomgeving (stad/platteland), alcohol- en totale vloeistofconsumptie, verhouding verzadigd/totale vetconsumptie, beroepsactiviteit en (bij intensiteitsanalyses) activiteit in de vrije tijd met een andere intensiteit. Onze analyses leveren voornamelijk een bijdrage aan de huidige inzichten door de constatering van aanmerkelijke voordelen van matige en zelfs van lichte activiteiten voor hart- en bloedvaten. De verlaging van risicofactoren voor hart- en vaatziekten, gerelateerd aan regelmatig bedreven matige tot intensieve activiteit, zou bij mannen in de leeftijd van 40 tot en met 69 jaar naar schatting resulteren in een 19% lagere totale mortaliteit en een 28% lagere mortaliteit aan hart- en vaatziekten. Verder toonden we het belang aan van de frequentie, naast de intensiteit en de duur van de activiteit. Onze resultaten maken tevens het belang duidelijk van lichamelijke inactiviteit als een belangrijke risicofactor voor de mortaliteit aan hart- en vaatziekten in de Duitse bevolking. Het is derhalve aan te raden regelmatig matig tot intensieve lichamelijke activiteit te bedrijven, bij voorkeur in de vorm van duursporten als fietsen, zwemmen, hardlopen of stevig wandelen met een duur van ongeveer 30 minuten, het liefst dagelijks maar zeker drie keer per week. De gezondheid van personen met een dergelijk activiteitsniveau kan verder profiteren van meer frequente en intensieve activiteit. Oudere personen, die voorheen weinig actief waren, doen er goed aan te beginnen met dagelijks lichte activiteiten (zoals wandelen en fietsen) en, desgewenst, het activiteitsniveau langzaam op te voeren.

Omdat de gezondheidsvoordelen van lichte activiteiten waarschijnlijk de grootste uitwerking op de volksgezondheid hebben, zou toekomstig onderzoek zich vooral op het effect van dergelijke activiteiten moeten richten. Verder zou gezocht moeten worden naar de meest effectieve manier om de activiteit in de bevolking te stimuleren.

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**Appendix**

**Leisure Activity Questions in the GCP  
Questionnaire**

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How often do you participate in sports?

- Regularly more than 2 hours per week
- Regularly 1-2 hours per week
- Less than 1 hour per week
- No sports activities

Do you play competitive sports (e.g. in a sports club) or do you take part in sports competitions?      Yes      No

How often have you been practising these sports or physical activities during the last 3 months, and (if you did at least once a week) how long per week?  
(see next page for original text).

During the last 3 months					Duration	
never	once per month or less	2-3 times per month	about once per week	several times per week	(almost) daily	Summarized per week

- Walking long distances (walking, going to work, shopping etc.)
- Hiking, mountain hiking, mountain climbing
- Cycling (incl. cycling to work, shopping etc.)
- Gardening
- Dancing, ballet, jazz dancing
- Gymnastics
- Fitness-gymnastics, aerobic
- Skating, roller-skating
- Swimming (not bathing)
- Jogging, sprinting, running
- Soccer, basketball, handball, volleyball
- Rowing
- Cross-country skiing
- Alpine skiing
- Boxing, wrestling, fencing, judo, karate
- Table tennis, badminton
- Tennis, squash
- Home exercise (ergometer, chest-expander, rowing, weight lifting)

Please indicate your physical activities which have not been mentioned above:

No physical activities during the last 3 months \_\_\_

**Wie oft haben Sie diese Sportarten oder körperlichen Betätigungen in den letzten 3 Monaten ausgeübt, und (falls mindestens 1mal pro Woche) wie lange pro Woche?**

	In den letzten 3 Monaten						Dauer	
	Nie	1mal im Monat oder seltener	2-3mal im Monat	Etwa 1mal in der Woche	Mehr-mals in der Woche	(Fast) täglich	Stunden	Minuten
Längere Wege zu Fuß gehen (Spazierengehen, Wege zur Arbeit, Einkaufen usw.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Wandern, Bergwandern, Bergsteigen	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fahrradfahren (einschl. Wege zur Arbeit, zum Einkaufen usw.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Gartenarbeit	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tanzen, Ballett, Jazz-Tanz	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Turnen, Gymnastik	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fitness-Gymnastik, Aerobic	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rollschuh-/Schlittschuhlaufen	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Schwimmen (nicht baden)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dauerlaufen, Trimmtrab, Jogging, Leichtathletik (Laufen)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fußball, Basketball, Handball, Volleyball	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rudern	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Skilanglauf	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Skilauf-Alpin (Abfahrtski)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Boxen, Ringen, Fechten, Judo, Karate u.ä.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tischtennis, Federball	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tennis, Squash	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Heimtraining (Heimfahrrad, Rudergeät, Expander u.ä.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Falls andere Bewegungsarten als oben genannt, bitte angeben:								
<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Keine Bewegungsarten in den letzten 3 Monaten	<input type="checkbox"/>							

Falls Sie hier ankreuzen, bitte auch rechte Seite ausfüllen!



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Bewegung gehört zum Leben und das Leben ist letztendlich das Wichtigste. Auf Griechisch heißt Leben Ζωή. So, du warst insgesamt die wichtigste Unterstützung. Dein großes Interesse, dein Mitleben und – falls nötig – die notwendige Ablenkung und die geduldige Anhörung der immer gleichen Themen hat dazu geführt, daß die Arbeit jetzt endlich fertig ist.

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## About the Author

Gert Mensink was born on March 1, 1961 in Almelo, The Netherlands. After completing secondary school (Pius X College, Almelo), he started his study on Human Nutrition at Wageningen Agricultural University in 1979. In 1986 he worked for several months at the Institute for Social Medicine and Epidemiology, Federal Health Office, Berlin, Germany. He graduated with majors in animal physiology, human nutrition and epidemiology in January 1987. Thereafter he attended his alternative service in the project „Dust exposure in the animal feed industry“ at the Department of Epidemiology and Public Health at the Wageningen Agricultural University. In 1988 he became researcher in the German National Nutrition Survey (VERA study) and from 1989 on in the German Cardiovascular Prevention Study at the Institute for Social Medicine and Epidemiology, Berlin. In 1991 he attended the Harvard Summer Course in epidemiology, held in Berlin. In 1993 he organized a GLIM course in Berlin in cooperation with the University of North London. In 1996 and 1997 he was involved in the European Union „Feasibility of a European health monitoring system“ study group. Since 1994, he is head of the Section for Methods of Risk Assessment and Epidemiology at the Robert Koch-Institute (former Federal Health Office), Berlin.