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Leisure-time Physical Activity Levels and Changes in Relation to Risk of Hip Fracture in Men and Women

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The authors prospectively studied the effect of leisure-time physical activity level on hip fracture risk along with the influence of within-subject changes in activity levels, while taking possible confounding by other health behaviors and poor health into account. Analyses were based on pooled data from three population studies conducted in Copenhagen, Denmark. Among 13,183 women and 17,045 men, 1,121 first hip fractures were identified during follow-up. In comparison with being sedentary, the relative risk (RR) of hip fracture associated with being moderately physically active 2–4 hours per week was 0.72 (95% confidence interval (CI): 0.59, 0.89) in women and 0.75 (95% CI: 0.55, 1.03) in men after adjustment for confounders. Being in the most active leisure activity category did not decrease the risk of hip fracture further. Adjustment for poor health affected the risk estimates only modestly. Subjects who, during follow-up, reduced their physical activity level from the highest or the intermediate activity level to a sedentary level had a higher risk of hip fracture than did those who remained moderately physically active at the intermediate level (multivariate adjusted RR = 2.19, 95% CI: 1.00, 4.84 and RR = 1.89, 95% CI: 1.21, 2.95, for reduction from the highest and intermediate levels, respectively). There was no evidence of a fracture-protective effect from increasing physical activity. In conclusion, moderate levels of physical activity appear to provide protection against later hip fracture. Decline in the physical activity level over time is an important risk factor for hip fracture. *Am J Epidemiol* 2001;154:60–8.

exercise; hip fractures; osteoporosis; prospective studies; risk factors

A general adaptation to a sedentary lifestyle during the past century is thought to be one of the causes responsible for the steep rise in hip fracture incidence observed in most Western countries during the last 5 decades (1–3). This assumption rests on the observation of an osteogenic effect of physical activity on human and animal bones (4–6) and on findings that physical activity improves muscle strength, balance, and physical function, thereby reducing the risk of falling (7–10). Furthermore, numerous epidemiologic studies seem to confirm the existence of an inverse relation between physical activity and hip fracture risk (11–26). Considering the observational design of these studies, selection bias, recall bias, and confounding by other health behaviors or by functional status cannot, however, be ruled out as alternative explanations of the apparent fracture-protective effect of physical activity. Intervention studies may clarify the existence of a causal relation between physical activity and hip fracture, but the long lag time to occurrence of hip fracture makes such studies difficult to conduct. Valuable information toward making causal inference as well as assessing public health implications may be obtained by observing the consequences of changes in physical activity level on hip fracture risk.

By using pooled data from three large, population-based follow-up studies, we evaluated the effect of leisure-time physical activity level on hip fracture risk while taking possible confounding introduced by other health behaviors and functional status into account. Furthermore, we assessed the influence of within-subject changes in physical activity level on hip fracture risk.

MATERIALS AND METHODS

Study population

This study is based on data from The Copenhagen Center for Prospective Population Studies, which compiles data

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Abbreviations: CCCPM, Copenhagen County Center for Preventive Medicine; CI, confidence interval; CMS, Copenhagen Male Study; ICD-8, *International Classification of Diseases*, Eighth Revision; RR, relative risk.

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The Copenhagen Center for Prospective Population Studies consists of the Copenhagen County Center for Preventive Medicine, the Copenhagen City Heart Study, and the Copenhagen Male Study.

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from three longitudinal population studies conducted in the Copenhagen, Denmark, area between 1964 and 1992: The Copenhagen County Center for Preventive Medicine (CCCPM) (formerly the Glostrup Population Study), with 10,191 randomly selected men and women from six birth cohorts from Copenhagen suburbs; the Copenhagen City Heart Study, with 15,786 randomly selected, age-stratified men and women from central Copenhagen; and the Copenhagen Male Study (CMS), which sampled 5,246 men from 14 major work sites in the Copenhagen area (27–30). The overall attendance rate at the first examination was 77 percent (range, 69–88 percent). After the exclusion of subjects with missing information on leisure-time physical activity, subjects with previous hip fracture, and double participants, 30,228 subjects were available for analysis of the effect of physical activity levels on hip fracture risk. Characteristics of the study population are outlined in table 1.

To study the influence of changes in physical activity levels on hip fracture risk, we selected subjects who attended the first and second examinations of the Copenhagen City Heart Study and the CCCPM. Because of a very short interval between the first and second examinations of the CMS and the lack of analog information on leisure-time physical activity from the third CMS examination, subjects who attended the first and the fourth examinations of this study were selected for the analysis of changes in physical activity. The combined population for the study of changes in physical activity levels totaled 17,285 subjects, of whom 15,498 (8,431 women and 7,067 men) gave information on their level of leisure-time physical activity at both examinations. A total of 13,487 subjects (45 percent of the entire study population) were not eligible for the analysis of changes in physical activity due to the following circumstances: 1,311 subjects (10 percent) died between the baseline examination and the time of the second (CMS: fourth) examination, 3,113 subjects (23 percent) did not respond the invitation to the second (CMS: fourth) examination, 3,416 subjects (25 percent) participated in a substudy in which no reexaminations were performed during follow-up, and 5,647 subjects (42 percent) were recruited and/or examined for the first time at one of the reexaminations.

Examination procedure and ascertainment of leisure-time physical activity

As part of a general health examination, all three population studies used a self-administered questionnaire with detailed questions regarding lifestyle habits and other health-related items. The phrasing of questions differed slightly in the various subcohorts, but the covariates used for this study could be harmonized without substantial loss of information.

Participants were asked to place themselves into one of the four following categories of leisure-time physical activity levels: 1) sedentary, i.e., physically inactive, performing mainly sedentary tasks such as watching television, reading, or performing moderate physical activities such as light housekeeping, light gardening, biking, or walking less than 2 hours per week; 2) moderately physically active 2–4 hours per week; 3) moderately physically active more than 4 hours per week or energetically physically active 2–4 hours per week, including energetic activities such as running, brisk walking or biking, heavy gardening, playing tennis etc.; and 4) energetically physically active more than 4 hours per week or participating in sports competitions. Owing to the small number of subjects in the last category, it was necessary to collapse physical activity levels 3 and 4 into a single category in all analyses. For the analyses of changes in physical activity levels, subjects were categorized into the nine combinations of physical activity for the first and second examinations.

TABLE 1. Characteristics of the study population, The Copenhagen Centre for Prospective Population Studies, Copenhagen, Denmark, 1964–1992

Substudy	No. of women*	No. of men*	Year of examination	Age (years) at first examination (mean)	No. of hip fractures
Copenhagen City Heart Study	8,460	7,155	1977, 1982	20–93 (52.7)	776
Copenhagen Male Study		5,174	1970, 1971, 1976, 1985	40–60 (48.8)	149
Copenhagen County Center of Preventive Medicine					
1897 cohort	228	239	1976, 1977	70	63
1914 cohort	573	657	1964, 1974, 1984, 1989	50	105
1936 cohort	584	517	1976, 1981, 1987	40	9
MONICA† I	1,837	1,932	1982, 1987	30–60 (45.5)	46
MONICA II	702	703	1987	30–60 (45.3)	7
MONICA III	1,009	1,002	1992	30–70 (50.0)	14
Total	13,393	17,379		20–93 (50.3)	1,169

* Subjects with hip fracture before entrance into the study ($n = 88$), double participants ($n = 246$), subjects with *International Classification of Diseases*, Eighth Revision, diagnosis code modifications indicating previous hip fracture ($n = 54$), and subjects lost to follow up ($n = 63$) were excluded.

† MONICA, monitoring of trends and determinants in cardiovascular disease (World Health Organization projects).

Other covariates

Physical activity at work. Physical activity levels at work was divided into four categories: 1) sedentary work; 2) standing and walking; 3) walking and lifting; and 4) physically exacting work.

Smoking habits. Tobacco exposure was divided into five categories: 1) never smokers; 2) ex-smokers; 3) current smokers of 1–14 g/day; 4) current smokers of 15–24 g/day; and 5) current smokers of 25 g/day or more.

Alcohol intake. Daily alcohol intake was divided into five categories: abstainers, and 1–2, 3–5, 6–10, and 11 or more drinks per day (one drink contained an average of 12 g of alcohol).

Educational level. Educational level was divided into three categories: 1) less than 8 years (completed primary school); 2) 8–11 years; and 3) 12 or more years.

Body mass index. Body mass index was calculated as measured weight (kg)/height (m^2) and divided into four categories: 1) less than 20; 2) 20–24; 3) 25–29; and 4) 30 or more kg/m^2.

Follow-up and assessment of prevalent and incident chronic disabling diseases

Subjects were followed from the date of the first examination to the date of their first hip fracture, death, disappearance, or emigration or until the end of follow-up, whichever occurred first. In the analyses of the influence of changes in physical activity level on hip fracture risk, the follow-up period started at the second examination. Vital status of the population samples was followed by using the unique person identification number in the Civil Registration System until December 31, 1997. Less than 1 percent of the subjects were lost in the follow-up period.

Information on incident hip fractures was obtained through individual-based linkage to the Danish National Hospital Register (31). Follow-up concerned the first occurrence of a cervical or trochanteric hip fracture (*International Classification of Diseases*, Eighth Revision (ICD-8), code 820 or *International Classification of Diseases*, Tenth Revision, codes S72.0–S72.2). A sample of 110 first-time registered hip fracture diagnosis codes identified in this study population was validated by reviewing hospital records. The validation showed that 93 percent of all first-time, registered hip fracture diagnosis codes in the hospital register represented low-energy, first-ever fractures. A more detailed description of our follow-up and validation procedure has been published elsewhere (32).

To ensure that the overall effect of physical activity and changes in physical activity level on hip fracture risk was unaffected by poor health, we repeated the analyses of the associations after the exclusion of subjects with prevalent and incident chronic disabling diseases, defined as diseases that potentially are associated with long-lasting effects on the physical ability of affected persons. Data on prevalent and incident cancers were obtained from the Danish Cancer Register. Similarly, data on prevalent and incident chronic diseases were obtained from the Danish National Hospital Register. The chronic, disabling diseases thus identified were all site cancers (ICD-8 codes 140–172, 174–209, and 230–239); diseases of the nervous system (ICD-8 codes 340–358); circulatory diseases, including myocardial infarction, stroke, and intermittent claudication (ICD-8 codes 393–458); chronic lung diseases (ICD-8 codes 490–493); locomotor system diseases (ICD-8 codes 710–738); chronic diseases of the gastrointestinal tract, liver, and pancreas (ICD-8 codes 530–537, 560–573, and 577); chronic kidney diseases (ICD-8 codes 580–584); chronic hematologic diseases (ICD-8 codes 280–289); endocrine diseases (ICD-8 codes 240–279); and various chronic infectious diseases (ICD-8 codes 40–46, 79, 83, 93–95, and 570).

In subjects examined before the onset of the Danish National Hospital Register in 1977, internal data on chronic disease were obtained from responses to questionnaires (answering questions such as, "Did a doctor ever tell you that you suffered from …?") and included information on heart disease, stroke, chronic pulmonary disease, intermittent claudication, and hypertension. Approximately one third of all subjects—those defined as having a baseline chronic disease in this study—had this information assessed by questionnaire, while the other two thirds had the information assessed through records from the Danish National Hospital Register and the Danish Cancer Register.

To eliminate the influence of subclinical, nondiagnosed disease on the risk estimates, we finally eliminated the first 5 years of follow-up from all analyses.

Statistical analyses

The data were analyzed by means of Cox proportional hazards regression models with age as underlying time scale and delayed entry accordingly. The models were estimated by the maximum likelihood method, and the effects of covariates and first-order interactions, all treated as categorical variables, were tested by using likelihood ratio tests. Relative risks for physical activity and changes in activity levels and other covariates did not differ significantly between the three substudies, allowing the final analyses to be based on the pooled data. All analyses were stratified by study of origin, which introduces assumption of equal effects of covariates in the three substudies but allows differences in baseline hazard between studies.

In analysis of the effect of leisure-time physical activity on hip fracture risk, subjects who were examined repeatedly contributed person-years to the physical activity level in which they had most recently described themselves. Thus, a given subject who changed his or her habits during follow-up contributed person-years to several physical activity levels. If values were missing at any reexamination, they were extrapolated forward from the last examination the subject had attended. In both sexes, the model describing the overall relation between physical activity during leisure time and hip fracture contained the following covariates: leisure-time physical activity (three levels), physical activity at work (four levels), smoking (five levels), alcohol intake (four levels), body mass index (four levels), and school education (three levels). Analyses were repeated after exclusion of subjects with prevalent disease at the time of the health examinations and after additional exclusion of the first 5 years of observation.

Changes in physical activity levels during follow-up were expressed as a combination of levels of activity at the first and second examinations. For retention of statistical power, the model describing the relation between changes in level of physical activity and hip fracture included men and women. There was no significant interaction between sex and changes in physical activity. Likewise, no significant interactions between sex and other covariates in the model were observed. Subjects with disease at baseline and those with incident disease between the two examinations were subsequently excluded, as were the first 5 years of observation.

RESULTS

Effect of leisure-time physical activity level on hip fracture risk

Approximately 55 percent of all men and women were moderately physically active 2–4 hours per day. More men than women were active at the highest levels, leaving a slightly higher proportion of women than men in the sedentary group (25 vs. 21 percent, respectively).

During follow-up, 688 first hip fractures were identified in women and 433 in men. In men, the age-adjusted relative risk of hip fracture gradually decreased by level of leisure-time activity compared with men who were sedentary: from relative risk (RR) = 0.70 (95 percent confidence interval (CI): 0.5, 0.90) in men who were moderately physically active 2–4 hours per week to RR = 0.59 (95 percent CI: 0.45, 0.77) in men who were moderately active more than 4 hours per week. The dose-response-like association diminished after adjustment for confounders, but a 25 percent borderline significant lower risk of hip fracture persisted among nonsedentary men (table 2). In women, no dose-response-like association between the level of physical activity and the risk of hip fracture was observed, but after adjustment for confounders, nonsedentary women had a significant 28 percent lower risk of hip fracture than did sedentary women (table 2). Exclusion of subjects with prevalent chronic disabling diseases (3,514 women and 3,523 men) slightly weakened the apparent protective effect of physical activity on hip fracture risk in men, while the association remained almost unaltered in women (table 2). Further exclusion of the first 5 years of follow-up strengthened the protective effect of a high physical activity level on hip fracture in women, while the risk estimates remained almost unaltered in men.

Changes in leisure-time physical activity level and hip fracture risk

Of the 15,498 subjects who reported their physical activity level during leisure time twice during follow-up, 607 sustained a first hip fracture after the second assessment of physical activity. The mean interval between the two examinations was 6.3 years (standard deviation, ±3 years).

The distribution of the subjects according to changes in physical activity level between the first and second examinations is shown in table 3. Disease status differed only a little among subjects with different patterns of physical activity changes, but a slightly higher proportion of baseline and incident disease was observed among subjects who were sedentary at both examinations and among subjects who became physically inactive between two examinations (table 3). Finally, a relatively high proportion of subjects who raised their activity from the sedentary level to the highest level of physical activity had a history of disease between the two examinations.

Subjects who reduced their physical activity during leisure time from being moderately active 2–4 hours per week to a sedentary level had a higher risk of subsequent hip fracture than did those who remained moderately physically active at this level (multivariate adjusted RR = 1.53, 95 percent CI: 1.12, 2.08) (table 4). Likewise, subjects who reduced their physical activity from the highest level to the sedentary level exhibited an elevated, but insignificant, risk of hip fracture compared with those who remained moderately physically active at the intermediate level (multivariate adjusted RR = 1.61, 95 percent CI: 0.97, 2.51). Sequential exclusion of subjects with baseline and incident disease and of the initial 5 years of follow-up further strengthened the association between decreased physical activity and hip fracture risk (table 4).

Generally, increments in the physical activity level between examinations did not influence the risk of hip fracture. However, subjects who increased their activity level from a sedentary state to the highest level of leisure-time activity exhibited an increased risk of hip fracture relative to those who remained physical active at the intermediate level (multivariate adjusted RR = 1.73, 95 percent CI: 1.10, 2.70), but the risk gradually diminished after the exclusion of subjects with baseline and incident disease and after exclusion of the first 5 years of follow-up (table 4).

Subjects who participated in the baseline examination and were alive and free of hip fracture at the time of the reexamination, but did not attend this examination ("nonresponders to reexamination"), were at a higher risk of hip fracture compared with those who participated in both examinations ("responders to reexamination") (multivariate adjusted RR = 1.57, 95 percent CI: 1.29, 1.90). At baseline, more nonresponders than responders were physically inactive during leisure time and were smoking, while only minor differences with respect to age, sex distribution, alcohol intake, physical activity at work, and body mass index were observed in the two groups (table 5). The elevated risk of hip fracture among nonresponders to reexamination was equal at all levels of baseline leisure-time activity (data not shown).

DISCUSSION

This large, prospective study of the influence of leisure-time physical activity levels and longitudinal changes on subsequent risk of hip fracture supports the existence of a causal relation between physical inactivity and hip fracture. Even a relatively low level of physical activity, corresponding to 2–4 hours of moderate physical activity per week,

TABLE 2. Relative risks of hip fracture according to physical activity level during leisure time among men and women in the Copenhagen Centre for Prospective Population Studies, Copenhagen, Denmark, 1964–1997

Physical activity during leisure time	Women					Men				
	No. of hip fractures	Age-adjusted relative risk*	95% CI†	Multivariate adjusted relative risk‡	95% CI	No. of hip fractures	Age-adjusted relative risk*	95% CI	Multivariate adjusted relative risk‡	95% CI
All subjects (13,183 women/17,045 men)										
Sedentary	203	1.00		1.00		99	1.00		1.00	
Moderate activity 2–4 hours/week	340	0.76	0.63, 0.91	0.72	0.59, 0.89	213	0.70	0.55, 0.90	0.75	0.55, 1.03
Moderate activity >4 hours week	145	0.74	0.59, 0.92	0.72	0.57, 0.92	121	0.59	0.45, 0.77	0.76	0.54, 1.07
After exclusion of subjects who had a history of chronic disease (3,514 women/3,523 men)										
Sedentary	123	1.00		1.00		51	1.00		1.00	
Moderate activity 2–4 hours/week	203	0.73	0.58, 0.92	0.69	0.52, 0.90	129	0.78	0.57, 1.09	0.77	0.50, 1.20
Moderate activity >4 hours week	96	0.73	0.55, 0.96	0.72	0.52, 0.98	73	0.64	0.45, 0.93	0.82	0.52, 1.32
After additional exclusion of initial 5 years of follow-up (637 women/1,078 men)										
Sedentary	89	1.00		1.00		37	1.00		1.00	
Moderate activity 2–4 hours/week	156	0.71	0.54, 0.93	0.64	0.47, 0.87	100	0.79	0.54, 1.16	0.69	0.42, 1.14
Moderate activity >4 hours week	76	0.69	0.51, 0.95	0.66	0.46, 0.94	56	0.63	0.41, 0.96	0.73	0.43, 1.24

* Stratified on study of origin.
† CI, confidence interval.
‡ Stratified on study of origin and adjusted for age, physical activity at work, smoking, alcohol intake, body mass index, and school education.

TABLE 3. Comorbid status of subjects included in the change of physical activity analysis according to the level of leisure-time physical activity level at the first and second examinations, The Copenhagen Centre for Prospective Population Studies, Copenhagen, Denmark, 1964–1997

Physical activity level at first examination	Physical activity level at second examination														
	Sedentary					Moderate activity 2–4 hours/week					Moderate activity >4 hours/week				
	No. of subjects	No. of hip fractures	Men (%)	Baseline disease* (%)	Incident disease† (%)	No. of subjects	No. of hip fractures	Men (%)	Baseline disease (%)	Incident disease (%)	No. of subjects	No. of hip fractures	Men (%)	Baseline disease* (%)	Incident disease† (%)
Sedentary	1,404	47	41	27	31	1,219	50	41	21	28	424	26	69	20	33
Moderate activity 2–4 hours/week	1,319	84	39	23	30	5,087	184	58	20	26	2,049	74	59	17	29
Moderate activity >4 hours week	342	18	65	24	37	1,584	56	52	17	29	1,998	68	62	14	26

* Percentage with prevalent chronic, disabling disease at first examination.
† Percentage with incident chronic, disabling disease between the two examinations.

appears to reduce the risk of hip fracture by approximately 25 percent, while higher levels of physical activity apparently exert no further notable risk reduction. Our study indicates that the inverse association between physical activity and hip fracture is not due to physical inability among inactive subjects. The association is independent of the inclusion of early endpoints and of confounding by otherwise healthy behavior among the physically active subjects. The observation that intraindividual reductions in physical activity levels are predictive of subsequent hip fracture suggests a causal interrelation and proposes that maintenance of moderate levels of physical activity at leisure time during aging provides protection against later hip fracture.

Consistent with our findings, three prospective studies observed a significantly lower risk of hip fracture among physically active subjects compared with physically inactive subjects (11–13). A Norwegian and a British cohort study also suggested an inverse relation between physical activity and hip fracture, but, due to low study power (few hip fracture cases), the risk estimates did not reach statistical significance (33, 34). In accordance with the findings of the prospective studies, several case-control studies reported an inverse relation between leisure-time activity and risk of hip fracture (14–26). Altogether, previous studies suggest that weight-bearing physical activities of relatively low intensity lower the risk of later hip fracture by 30–50 percent.

The inverse association between leisure-time activity and hip fracture in our study appeared to be only moderately confounded by tobacco smoking, alcohol intake, body mass index, and level of education. A slight positive confounding effect of these factors was evident in men at the highest level of physical activity, while the effect of adjustment for confounders in women was negligible. The modest influence of confounders on the association between physical activity and hip fracture in this study matches observations from several others (11, 12, 15, 16, 19, 20, 33, 34) and stresses that the inverse relation between physical activity and hip fracture is not likely to be explained by a healthier lifestyle among the most physically active subjects.

Among the elderly, measurement of physical activity is probably also a measure of disability or reduced function. Since reduced function is associated with increased risk of falls and, consequently, fractures (35–37), the elevated risk of hip fracture among the physically inactive may be interpreted as the effect of reduced ability rather than of a physically sedentary lifestyle. Previous studies that excluded subjects who reported discontinued or reduced physical activity due to injury or ill health observed only a modest influence of such exclusions on the risk estimates (11, 12). Similarly, we observed no notable change in risk estimates after our far-reaching exclusion of subjects with diagnosed chronic, disabling diseases. Furthermore, additional elimination of undiagnosed disabling disease by exclusion of early endpoints appeared to have only a negligible effect on risk estimates in our study. Altogether, these findings indicate that the inverse relation between physical activity and hip fracture is not confounded by disability or poor health among inactive subjects.

TABLE 4. Multivariate adjusted relative risk* of hip fracture and 95% confidence interval by leisure-time physical activity levels at first and second examinations, The Copenhagen Centre for Prospective Population Studies, 1964–1997†

Physical activity level at first examination	Physical activity level at second examination					
	Sedentary		Moderate activity 2–4 hours/week		Moderate activity >4 hours/week	
	RR	95% CI‡	RR	95% CI	RR	95% CI
All subjects						
Sedentary	1.22	0.83, 1.81	1.26	0.88, 1.81	1.73	1.10, 2.70
Moderate activity 2–4 hours/week	1.53	1.12, 2.08	1.00		0.97	0.72, 1.30
Moderate activity >4 hours week	1.61	0.97, 2.76	0.98	0.69, 1.38	1.16	0.85, 1.58
Exclusion of subjects with a history of chronic disease at baseline						
Sedentary	1.05	0.66, 1.69	1.25	0.83, 1.87	1.58	0.94, 2.65
Moderate activity 2–4 hours/week	1.65	1.17, 2.32	1.00		0.98	0.70, 1.35
Moderate activity >4 hours week	1.91	1.08, 3.34	0.99	0.68, 1.44	1.19	0.85, 1.67
Additional exclusion of subjects with a history of chronic disease between examinations 1 and 2						
Sedentary	1.02	0.55, 1.90	1.13	0.67, 1.89	1.36	0.72, 2.58
Moderate activity 2–4 hours/week	1.73	1.14, 2.63	1.00		0.89	0.59, 1.34
Moderate activity >4 hours week	2.46	1.26, 4.81	1.03	0.65, 1.63	1.20	0.80, 1.79
Further exclusion of initial 5 years of follow-up after examination 2						
Sedentary	1.16	0.61, 2.21	1.16	0.67, 2.02	1.24	0.59, 2.61
Moderate activity 2–4 hours/week	1.89	1.21, 2.95	1.00		0.91	0.59, 1.41
Moderate activity >4 hours week	2.19	1.00, 4.84	1.06	0.65, 1.76	1.10	0.70, 1.73

* Stratified by study of origin and adjusted for age, sex, physical activity at work, smoking, alcohol intake, body mass index, and school education measured at the second examination (Copenhagen Male Study fourth examination).
† Relative risk (RR) is set at 1.0 in subjects who were moderately physically active 2–4 hours/week at both examinations.
‡ CI, confidence interval.

This study expands previous research by evaluating the influence of intraindividual changes in leisure-time physical activity on fracture risk. We found that subjects who reduced their physical activity from the highest or the intermediate level to a sedentary level almost doubled their risk of hip fracture in comparison with those who remained moderately physically active at the intermediate level over time. This finding proposes that maintaining (not reducing) one's physical activity levels during aging may provide protection against hip fracture. The observation that exclusion of subjects with baseline and incident disabling disease further strengthened the association between decreased physical activity level and hip fracture was somewhat unexpected but may be explained by the relative high proportions of disabling disease in the comparison group (unchanged physical activity at the intermediate level) as noted in table 3.

We found no beneficial effect in improving one's leisure-time activity from a sedentary level to a higher level. In contrast, our results were suggestive of an excess risk among those who increased their activity level from the sedentary level to the highest activity group. The finding that the elevated risk among these subjects gradually disappeared after exclusion of prevalent disease, incident disease, and early endpoints, however, strongly suggests that this subgroup

TABLE 5. Baseline characteristics of responders and nonresponders to reexamination, The Copenhagen Centre for Prospective Population Studies, 1964–1997

	No. of subjects	Age (mean)	Men (%)	Sedentary at leisure time (%)	Sedentary at work (%)	Smokers (%)	Drinkers of ≥6 drinks per day (%)	<8 years education (%)	Body mass index ≥30 kg/m² (%)
Responders*	17,285	49.9	49	19	26	60	13	47	10
Nonresponders†	3,113	50.7	51	30	24	68	16	50	14

* Subjects who participated in the baseline examination and the second examination (Copenhagen Male Study fourth examination).
† Subjects who participated in the baseline examination and were alive and without hip fracture at the time of the second examination (Copenhagen Male Study fourth examination), but did not attend this examination.

included highly selected subjects who may have increased their activity levels with the purpose of preventing deterioration of preexisting disease (for example, on a doctors advice). The critical question of whether sedentary subjects do benefit from improving physical activity level with respect to hip fracture risk still remains to be answered, however.

In this study, information on physical activity at work was handled as a confounding factor in the association between leisure-time physical activity and hip fracture and not as an independent measurement of physical activity. We find physical activity at work to be a less useful measurement of physical activity, since subjects who perform heavy tasks are likely to be healthier than those who have more sedentary jobs, making this measurement very prone to bias.

Some methodological problems may influence the interpretation of our results. First, the self-reported categorization of leisure-time physical activity levels are crude, making the reliability and validity of the exposure questionable. In this context, it may be noted that similar versions of questionnaires on leisure-time physical activity level have been able to discriminate between sedentary and physically active subjects with respect to maximal oxygen uptake (38). Furthermore, physically active subjects tended to have a lower body mass index than did sedentary subjects in our study (data not shown). Finally, supplementary questions on engagement in sport activities in a subgroup of the study population gave a correlation of 0.36 with the four-point leisure-time activity scale. The completeness of hip fracture identification during the course of follow-up from the Danish National Hospital Register may also be questioned. The study period 1964–1977, representing 10 percent of the total person-years of follow-up, was not covered by the register. During this period, hip fracture cases from the CCCPM were identified from validated, self-reported diagnoses collected during successive examinations of the cohorts and by screening admissions at the regional hospitals for cohort members. During the first 7 years of follow-up (1970–1977), no fracture diagnoses were available from the CMS. Since this period represented only 5 percent of the total person-years of follow-up and since subjects were middle-aged men (mean age, 48.8 years at the start of the study), it is unlikely that any serious bias was introduced in this way.

Since nonresponse appeared to be linked to leisure-time inactivity and nonresponders per se were at higher risk of hip fracture, selection bias may potentially have influenced the estimates of the association between change in physical activity levels and hip fracture. On the other hand, we found that the increase in the risk of hip fracture among nonresponders was equal at all levels of baseline physical activity, indicating that nonresponse to reexamination is unlikely to have introduced bias in the analysis of the influence of change of physical activity on hip fracture risk.

Misclassification of leisure-time physical activity levels due to under- or overreporting is inevitable and may have led to incorrect classification of subjects with respect to decreased or increased activity levels over time. According to the prospective design of this study, this misclassification is likely to be random or unrelated to future fracture history and can therefore only serve to dilute any true association between changes in physical activity levels and hip fracture.

Some degree of residual confounding may be present in our study because of insufficient adjustment of time-dependent covariates. In the analysis of the association between physical activity and hip fracture, we eliminated some of this residual confounding by updating the individual exposure status according to the current status at successive reexaminations during follow-up. Furthermore, in the "change in physical activity analysis," we adjusted for confounders measured at the second examination in accordance with the closer time relation of these covariates to the start of the follow-up period.

In conclusion, this study substantiates that moderate levels of physical activity during leisure time provide protection against later hip fracture and that decline in physical activity levels is associated with increased risk of hip fracture. Recommendation of regular physical activity and maintenance of physical activity during the aging process should become an essential part of strategies aimed at controlling the alarming increase in hip fractures worldwide.

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