Effects of Physical Activity on Life Expectancy With Cardiovascular Disease

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Background: Physical inactivity is a modifiable risk factor for cardiovascular disease. However, little is known about the effects of physical activity on life expectancy with and without cardiovascular disease. Our objective was to calculate the consequences of different physical activity levels after age 50 years on total life expectancy and life expectancy with and without cardiovascular disease.

Methods: We constructed multistate life tables using data from the Framingham Heart Study to calculate the effects of 3 levels of physical activity (low, moderate, and high) among populations older than 50 years. For the life table calculations, we used hazard ratios for 3 transitions (healthy to death, healthy to disease, and disease to death) by levels of physical activity and adjusted for age, sex, smoking, any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema, or pulmonary disease), and examination at start of follow-up period.

Results: Moderate and high physical activity levels led to 1.3 and 3.7 years more in total life expectancy and 1.1 and 3.2 more years lived without cardiovascular disease, respectively, for men aged 50 years or older compared with those who maintained a low physical activity level. For women the differences were 1.5 and 3.5 years in total life expectancy and 1.3 and 3.3 more years lived free of cardiovascular disease, respectively.

Conclusions: Avoiding a sedentary lifestyle during adulthood not only prevents cardiovascular disease independently of other risk factors but also substantially expands the total life expectancy and the cardiovascular disease–free life expectancy for men and women. This effect is already seen at moderate levels of physical activity, and the gains in cardiovascular disease–free life expectancy are twice as large at higher activity levels.

Arch Intern Med. 2005;165:2355-2360

THE BENEFICIAL EFFECT OF physical activity in the prevention of cardiovascular disease is widely known and is supported by a large amount of evidence.[1,2] From the bus drivers described by Morris et al[3,4] to the Harvard alumni more recently described by Paffenbarger et al,[5,6] different studies have reported a protective effect of physical activity on total mortality, cardiovascular disease, and diabetes in the general population.[7-14] Through lowering the inflammatory response involved in atherogenesis and

modifying the traditional risk factors of cardiovascular disease, increasing physical activity reduces the rates of cardiovascular disease in the general population.[6,15] Expected effects are seen for different levels of intensity, from moderate to very high, different durations, and for different activity types.[11,16,17] However, it remains unclear whether physical activity levels have a sig-

nificant effect on life expectancy or on time spent with and without cardiovascular disease. This is crucial to assess the contribution of physical activity in cardiovascular risk management. In this study we calculated the effects of different levels of physical activity on life expectancy and years lived with and without cardiovascular disease at age 50 years or older.

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METHODS

Using data from the original Framingham Heart Study,[18] we built life tables to calculate the relation between different levels of physical activity and total life expectancy and life expectancy with and without cardiovascular disease at age 50 years in the general population.

DATA SOURCES

The Framingham cohort consisted of 5209 respondents residing in Framingham, Mass, between 1948 and 1951. The study included men (n=2336) and women (n=2873) aged 28 to 62 years. The cohort has been examined biannually for 46 years. Further description can be found elsewhere.[18]

STUDY SAMPLE

To calculate transition rates by levels of physical activity, we pooled 3 nonoverlapping follow-up periods of 12 years. Each period started with a measurement of physical activity. In the present investigation, the follow-up periods started at examinations 4, 11 (if present, otherwise 12), and 19 (if present, otherwise 20). Using the pooling of repeated observations method,[19] we pooled follow-up information over 3 follow-up periods, compiling a total of 9773 observation intervals. The same participant could thus be observed during 3 periods until the event (first onset of cardiovascular disease or death) occurred or the subject was censored. However, follow-up time and physical activity status were reevaluated in each interval. We used observation intervals of no more than 12 years to avoid overlapping periods of follow-up. After exclusion of participants with missing data on physical activity (n=592) and cardiovascular disease at baseline (n=148), 4121 subjects were available from examination 4, 3260 from examination 11 or 12, and 1652 from examination 19 or 20, yielding a total of 9033 observation intervals.

ASSESSMENT OF PHYSICAL ACTIVITY

Participants were asked to estimate how long they spent in a typical day at various levels of activity: sleeping, resting, or engaging in light, moderate, or heavy physical activity. The reported levels of activity were weighted based on the estimated oxygen consumption for each activity to reflect metabolic expenditure corresponding to metabolic equivalents. Weights used were as follows: for sleeping, 1; for being sedentary, 1.1; for light activity, 1.5; for moderate activity, 2.4; and for heavy activity, 5. Finally, a daily physical activity score was calculated by adding the sum of the weighted hours for each level of activity. The minimum possible score was 24 for a participant sleeping 24 hours a day. Further detail on the assessment of physical activity and calculation of the daily physical activity score can be found elsewhere.[12]

Based on tertiles of the physical activity score, we grouped the participants into 3 levels: low (<30), moderate (30-33), and high (>33) physical activity level.

OUTCOME ASSESSMENT

The primary outcome measure of our study is incident or fatal cardiovascular disease. Cardiovascular disease included coronary heart disease (angina, coronary insufficiency, myocardial infarction, and sudden or not-sudden death as a consequence of coronary disease), congestive heart failure, stroke, transient ischemic attack, and intermittent claudication. A panel of 3 physicians evaluated all events; agreement of all 3 was required. More detail on the evaluation of outcomes in the Framingham Heart Study is available elsewhere.[20]

POTENTIAL CONFOUNDERS

Potential confounders were measured at each baseline except for education, which was only measured once. All analyses were adjusted or stratified by age and sex. Potential confounders considered were as follows: education (eighth grade or less vs higher than eighth grade), smoking (never, ever, or current smoking), marital status (single, married, widowed, separated, or divorced), comorbidity present at baseline (any of the following diseases: cancer, left ventricular hypertrophy, diabetes, arthritis, ankle edema, or any pulmonary disease), total cholesterol level, and the start of the follow-up period (examination 4, 11/12, or 19/20). The examination at the start of the follow-up period was included to correct for a potential cohort and period effect, since the participants could belong to 3 different periods of follow-up and different birth cohorts. Intermediate variables considered were hypertension and body mass index (BMI) (calculated as weight in kilograms divided by the square of height in meters). Hypertension was defined as systolic blood pressure of 140 mm Hg or higher or diastolic blood pressure of 90 mm Hg or higher.[21] For BMI, 4 categories were defined: lower than 18.5; 18.5 to lower than 25; 25 to lower than 30; and 30 or higher.[22] For the final analysis, only participants who had information on the selected confounders were included.

DATA ANALYSIS

To calculate the life expectancy with and without cardiovascular disease, we created a period multistate life table, which combined information from people at different ages and from different birth cohorts and included 3 different states: "free of cardiovascular disease," "history of cardiovascular disease," and "death." The possible transitions were (1) from free of cardiovascular disease to history of cardiovascular disease, (2) from free of cardiovascular disease to death, and (3) from history of cardiovascular disease to death. No backflows were allowed, and only the first entry into a state was considered.[23]

To evaluate the differences in risk among persons 50 years or older for the 3 levels of activity, we first calculated the overall sex- and age-specific transition rates for each transition. Then we calculated hazard ratios by levels of activity using Poisson regression (Gompertz distribution) and adjusting for sex, age, potential confounders, and intermediate variables. Three final models were selected. One basic model adjusted for age and sex. The second model adjusted for confounders that substantially changed the effect of physical activity on cardiovascular disease or mortality (in addition to age and sex). The third model also included intermediate variables (BMI and hypertension).

Finally, the 3 sets of transition rates were calculated for each physical activity level using the overall transition rates, the adjusted hazard ratios of cardiovascular disease by activity level, and the prevalence of physical activity level by sex and presence of cardiovascular disease. Similar calculations have been described previously,[24,25] and the data spreadsheets are available on request.

Separate life tables were created for each sex and each level of physical activity incorporating each of the 3 transitions. The multistate life table was started at age 50 years and was closed at age 100 years. The measures available from the life table include total life expectancy and life expectancy with and without cardiovascular disease by levels of physical activity and sex.

All statistical analyses were performed using STATA version 8.2 for Windows (Stata Corp, College Station, Tex). We calculated confidence intervals for all life expectancies and their differences using Monte Carlo simulation (parametric bootstrapping).[26] To calculate the confidence intervals we used @RISK software (Anonymous 2000; MathSoft Inc, Cambridge, Mass), 10 000 runs.

SENSITIVITY ANALYSIS

Finally, since it has been reported that levels and effects of physical activity change with time,[27] in a sensitivity analysis we evaluated the effect of length of follow-up on the relation between physical activity and cardiovascular disease and/or mortality. All the analyses were repeated for different periods of follow-up: 12, 10, 8, and 6 years.

BASELINE CHARACTERISTICS

In general, participants in the low physical activity group tended to be older (mean age, 62 years) than the participants in the moderate and high activity groups (mean ages, 58 and 59 years, respectively). The levels of each of the comorbidities, mean systolic blood pressure, diastolic blood pressure, and total cholesterol were higher among the participants with low physical activity (**Table 1**). The low and moderate activity groups tended to have a higher proportion of women (63% and 62%, respectively) than the high physical activity group (46%).

RISK OF CARDIOVASCULAR DISEASE AND DEATH

All transition hazard ratios corrected for age and sex were inversely related to the level of physical activity (**Table 2**). Overall there was a dose-response protective relation between physical activity level and incident cardiovascular disease or death among participants free of cardiovascular disease and for mortality among participants with cardiovascular disease.

Selected confounders were smoking status, presence of comorbidity (cancer, left ventricular hypertrophy, diabetes, arthritis, ankle edema, or any pulmonary disease), and the starting date of the follow-up period. Other variables like education, marital status, and total cholesterol level were also tested but not included in the final model since they did not alter the relative risks for cardiovascular disease and mortality substantially. Information on the selected confounders was available for 9003 observation intervals (98%).

After adjustment for age, sex, and selected confounders, the effect of physical activity was significant (2-sided P value <.05) for a high level of physical activity with all transitions (incident cardiovascular disease, no cardiovascular disease to death, and cardiovascular disease to death). For the group with a moderate level of activity, the protective effect of physical activity was significant for the transition from no cardiovascular disease to death but not for the other 2 transitions. The directions and significance but not the magnitude—which was reduced—of these relations remained the same after adjusting for both confounders and intermediate variables (Table 2).

TOTAL LIFE EXPECTANCY AND LIFE EXPECTANCY WITH AND WITHOUT CARDIOVASCULAR DISEASE

Total life expectancy increased proportionally with higher levels of physical activity (**Figure**). After adjustment for the selected confounders, participants in the moderate and high activity groups, respectively, lived more than 1.3 and 3.5 years longer overall and more than 1.1 and 3.2 years longer free of cardiovascular disease than participants in the low activity group (**Table 3**). This longer total life expectancy for both sexes comprised more

Table 1. Baseline Characteristics by Physical Activity Level*

| Characteristic | Level of Physical Activity, Tertiles | | |
	Low (n = 2857)	Moderate (n = 3349)	High (n = 2975)
Age, mean (SD), y	61.6 (13.1)	57.6 (12.3)	59.1 (11.8)
Women	1790 (63)	2075 (62)	1366 (46)
PA score, mean (SD)	28.1 (1.15)	31.3 (0.97)	38.1 (5.37)
Marital status			
Single	279 (10)	279 (8)	177 (6)
Married	1944 (68)	2517 (76)	2410 (81)
Widowed	518 (18)	417 (13)	290 (10)
Divorced or separated	72 (3)	86 (3)	62 (2)
Education			
Eighth grade or less	709 (26)	855 (26)	743 (26)
Higher than eighth grade	2055 (74)	2416 (74)	2154 (74)
Smoking status			
Never smoker	1128 (39)	1223 (37)	871 (29)
Former smoker	667 (23)	752 (23)	865 (29)
Current smoker	1062 (38)	1364 (40)	1239 (42)
Any comorbidity†	1326 (47)	1213 (37)	1079 (37)
BMI, mean (SD)	26.2 (4.6)	25.9 (4.1)	26.1 (3.9)
SBP, mean (SD), mm Hg	140.3 (24.3)	137.2 (22.7)	136.2 (20.9)
DBP, mean (SD), mm Hg	88.9 (24.1)	84.7 (18.0)	84.3 (17.7)
Total cholesterol, mean (SD), mg/dL (mmol/L)	239.0 (46.8) (6.2 [1.2])	234.6 (43.4) (6.1 [1.1])	230.6 (41.6) (6.0 [1.1])

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); DBP, diastolic blood pressure; PA, physical activity; SBP, systolic blood pressure.

*Subjects included were alive and with no missing data on physical activity. Unless otherwise noted, data are reported as number (percentage) of subjects.

†Comorbidities include cancer, left ventricular hypertrophy, diabetes, arthritis, ankle edema, or pulmonary disease.

years lived without cardiovascular disease and also—although to a lesser degree and not statistically significant—more years lived with cardiovascular disease (Table 3).

SENSITIVITY ANALYSIS

The effect of physical activity on cardiovascular disease and mortality was consistent for all lengths of follow-up, although its magnitude increased as the period of follow-up was reduced; the shorter the period of follow-up, the higher the differences in life expectancies between physical activity groups (**Table 4**).

COMMENT

Life expectancy for sedentary people at age 50 years was found to be 1.5 years shorter than for people engaging in moderate daily physical activity and more than 3.5 years shorter than for people with high physical activity levels. These differences were similar for both sexes.

The longer total life expectancy measured for participants with higher levels of physical activity was the result of the larger number of years lived without cardiovascular disease and a slightly longer life expectancy with cardiovascular disease. The increased life expectancy with cardiovascular disease among participants at moderate and high physical activity levels compared with the group

Table 2. Hazard Ratios for Cardiovascular Disease and Death by Physical Activity Level*

Transition	Cases, No.	Person-Years	Physical Activity Level	HR† (95% CI)	HR‡ (95% CI)	HR§ (95% CI)
Incident CVD	1573	62 185	Low	1.00	1.00	1.00
			Moderate	0.92 (0.82-1.04)	0.94 (0.83-1.06)	0.95 (0.84-1.08)
			High	0.74 (0.65-0.84)	0.77 (0.67-0.87)	0.77 (0.68-0.89)
No CVD to death	629	62 185	Low	1.00	1.00	1.00
			Moderate	0.75 (0.62-0.91)	0.78 (0.64-0.94)	0.80 (0.66-0.98)
			High	0.63 (0.54-0.80)	0.68 (0.56-0.84)	0.72 (0.58-0.89)
CVD to death	1046	15 748	Low	1.00	1.00	1.00
			Moderate	0.91 (0.80-1.04)	0.94 (0.82-1.07)	0.97 (0.84-1.10)
			High	0.67 (0.58-0.77)	0.74 (0.64-0.86)	0.77 (0.65-0.89)

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio.
*All subjects 50 years or older at the start of follow-up period.
†Adjusted for age and sex.
‡Adjusted for age, sex, smoking, examination at start of follow-up period, and any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema, or pulmonary disease).
§Adjusted for age, sex, smoking, any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema or pulmonary disease), examination at start of follow-up period, body mass index, and hypertension.
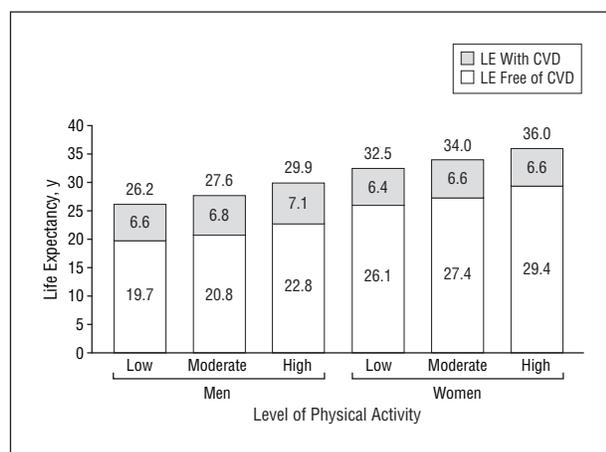

Figure. Effect of physical activity level on life expectancy (LE) at age 50 years. All LEs have been calculated with hazard ratios adjusted for age, sex, smoking, examination at start of follow-up period, and any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema, or pulmonary disease). CVD indicates cardiovascular disease.

at low physical activity level was not statistically significant. In all cases it was less than 0.5 years.

The longer cardiovascular disease–free life expectancy was due to a protective effect of physical activity on the incidence of cardiovascular disease combined with a protective effect of physical activity on mortality among participants free of cardiovascular disease. On the other hand, the slightly longer life expectancy with cardiovascular disease was caused by the effect of physical activity on mortality among participants with cardiovascular disease: people with cardiovascular disease at higher levels of physical activity lived longer and therefore experienced an increased burden of cardiovascular disease. Another reason for the increase in years with cardiovascular disease is that higher physical activity is associated with increased survival to advanced ages when the risks of cardiovascular disease are higher.

The diluting effect of increasing time of follow-up in the preventive role of physical activity on cardiovascular disease and mortality that we found in this study has been reported before.[27] This reduction or dilution of effect may be explained by misclassification of exposure: subjects tend to change their physical activity behaviors with time. However, the dilution may also be owing to less selection and reverse causation (although we corrected for known comorbidity in all analyses), which are the potential biases associated with shorter terms of follow-up. We chose 12 years of follow-up to maximize power and minimize the risks for selection and reverse causation. Importantly, in our study length of follow-up affected mainly the magnitude of effect. These observed differences in effects secondary to length of follow-up should not affect the interpretation of the results, though, because the direction of the relation we found between physical activity and cardiovascular disease and mortality was consistent over the different terms of follow-up.

The hazard ratios we found fall well within the range of the published measures of effect of physical activity on cardiovascular disease and total mortality.[3-5,9,10,12-17,27-31] While our results are similar to ratios reported in studies of non-Framingham populations, comparison is limited by the definition and classification of exposure that is unique to the Framingham Heart Study. In the case of primary prevention of cardiovascular disease, the protective effect of physical activity that we found is moderately higher than that found by past investigations of the Framingham population. However, the earlier studies used longer periods of follow-up (14-16 years), which could explain their lower effects.[12,28,31] To our knowledge, this is the first study to present the effect of physical activity on life expectancy with and without cardiovascular disease.

A strength of our study was the use of a well-organized historic cohort that has been observed biannually for decades (we used 36 years) with readily available upgraded information on covariates and outcomes.

Some limitations of this study must be considered. This is a prospective observational study in which no intervention was performed; therefore, it has the inherent weaknesses of all cohort studies and lacks the strength of causality that a randomized trial could offer.

Table 3. Subject Life Expectancy at Age 50 Years*

Sex	Physical Activity Level	Total LE	Difference in Total LE†	LE Free of CVD	Difference in LE Free of CVD†	LE With CVD	Difference in LE With CVD†
Men	Low	26.2 (25.4-27.1)	Ref	19.7 (18.7-20.6)	Ref	6.6 (6.0-7.2)	Ref
	Moderate	27.6 (26.6-28.7)	1.3 (0.3-2.3)	20.8 (19.6-21.9)	1.1 (−0.02-2.1)	6.8 (6.1-7.6)	0.2 (−0.5 to 1.0)
	High	29.9 (29.0-31.0)	3.7 (2.6-4.8)	22.8 (21.6-23.9)	3.2 (1.9-4.3)	7.1 (6.4-7.9)	0.5 (−0.3 to 1.4)
Women	Low	32.5 (31.7-33.3)	Ref	26.1 (25.3-27.0)	Ref	6.4 (5.8-7.0)	Ref
	Moderate	34.0 (33.0-35.0)	1.5 (0.4-2.5)	27.4 (26.4-28.5)	1.3 (0.1-2.4)	6.6 (5.8-7.3)	0.2 (−0.5 to 0.9)
	High	36.0 (35.0-37.1)	3.5 (2.4-4.6)	29.4 (28.2-30.6)	3.3 (2.0-4.5)	6.6 (5.8-7.4)	0.2 (−0.5 to 1.1)

Abbreviations: CVD, cardiovascular disease; LE, life expectancy; Ref, reference.
*All life expectancies were calculated with hazard ratios adjusted for age, sex, smoking, examination at start of follow-up period, and any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema, or pulmonary disease). Unless otherwise indicated, data are reported as mean (95% confidence interval) years.
†Differences are calculated using the low physical activity group as the reference: moderate vs low and high vs low.

Table 4. Life Expectancy at Age 50 Years Calculated at Different Lengths of Follow-up*

	Length of Follow-up, y											
	10				8				6			
Physical Activity Level	Total LE	Dif Total LE†	Dif LE Free of CVD†	Dif LE With CVD†	Total LE	Dif Total LE†	Dif LE Free of CVD†	Dif LE With CVD†	Total LE	Dif Total LE†	Dif LE Free of CVD†	Dif LE With CVD†
Men												
Low	26.6	Ref	Ref	Ref	25.9	Ref	Ref	Ref	25.3	Ref	Ref	Ref
Moderate	28.1	1.6	1.2	0.4	28.4	2.4	1.8	0.6	28.0	2.7	1.6	1.0
High	30.5	3.9	3.1	0.8	30.3	4.3	3.1	1.2	31.2	5.9	4.2	1.7
Women												
Low	32.7	Ref	Ref	Ref	32.8	Ref	Ref	Ref	32.4	Ref	Ref	Ref
Moderate	34.5	1.7	1.4	0.3	35.4	2.1	2.1	0.5	35.1	2.7	1.8	0.9
High	36.4	3.7	3.2	0.5	36.7	3.9	3.2	0.7	37.7	5.3	4.2	1.1

Abbreviations: CVD, cardiovascular disease; Dif, difference; LE, life expectancy; Ref, reference.
*All life expectancies have been calculated with hazard ratios adjusted for age, sex, smoking, examination at start of follow-up period, and any comorbidity (cancer, left ventricular hypertrophy, arthritis, diabetes, ankle edema, or pulmonary disease). Data are reported as mean years.
†Differences are calculated using the low physical activity group as the reference: moderate vs low and high vs low.

Reverse causation, which means that lower physical activity levels are caused by disease and not the other way around, is an important issue to consider because it could introduce bias in the evaluation of the effect of physical activity. Different approaches exist to reduce the effect of reverse causation, but there is no method to eliminate it completely. To correct for reverse causation, we adjusted our analyses for comorbidities at baseline instead of excluding the subjects with disease at the start of follow-up, since our original objective was to evaluate the effect of physical activity in the general population and not on selected healthy populations. Also we ran additional analyses excluding the participants with the lowest levels of physical activity who also represented the highest risk of reverse causation and found no substantial changes in our hazard ratios (data not shown).

Another limitation of our study is the way exposure was assessed in the Framingham study. During the Framingham Heart Study, physical activity levels were evaluated by self-report, which may introduce misclassification of exposure. However, this misclassification is likely to be nondifferential, which can only attenuate our results, making them less than the true association.

A relevant limitation of our study is that we could not evaluate the effect of physical activity levels completely independently of other risk factors of cardiovascular disease such as diet and alcohol and aspirin intake. Although we accounted in our analyses for some risk factors at baseline by correcting for BMI, blood pressure, education, cholesterol, smoking, sex, and comorbidities (cancer, left ventricular hypertrophy, diabetes, arthritis, ankle edema, or any pulmonary disease), the data for diet and alcohol and aspirin intake were incomplete, unreliable, or unavailable for a large proportion or all of our population. It is possible that part of the observed differences in life expectancy within the 3 physical activity groups might be explained by the differences in diet and alcohol and aspirin intake levels or that our results do not correspond fully to isolated differences in physical activity but to a more general effect of following a healthy lifestyle. However, the extent of this diet-intake effect cannot be calculated with the available data. Other important risk factors for cardiovascular disease were accounted for in our analysis: sex, age, BMI, smoking, blood pressure, left ventricular hypertrophy, diabetes, cholesterol, and education.

An added value of this study is the combination of assessing the relation between physical activity and onset

of cardiovascular disease and mortality in a large prospective study and the translation of these relations into life expectancy with and without cardiovascular disease. This study shows that higher levels of physical activity not only prolong total life expectancy but also life expectancy free of cardiovascular disease at age 50 years. This effect is already seen at moderate levels of physical activity, and the gains in cardiovascular disease–free life expectancy at higher levels are more than twice as large. Our results underline current recommendations for physical activity, which call for even moderate levels of activity to enjoy the benefits of a healthier and longer life. The protective effect of physical activity on cardiovascular disease is also significant in terms of life expectancy free of cardiovascular disease. The role that physical activity plays in cardiovascular risk management should be emphasized to achieve a worldwide implementation of an active pattern of life. Our study suggests that following an active lifestyle is an effective way to achieve healthy aging.

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