**Table 5. Multivariate Relative Risk of Mortality From Any Cause According to Joint Categories of Achievement of Recommendations for Activity of at Least Moderate Intensity and Vigorous Exercise in Subjects Defined by Selected Variables[a]**

| Variable | No. of Deaths | Inactive | Neither Recommendation | Recommendation for MPA Only[b] | Recommendation for VPA Only[c] | Recommendation for Both MPA and VPA |
|---|---|---|---|---|---|---|
| Sex | | | | | | |
| Women | 2661 | 1 [Reference] | 0.70 (0.61-0.79) | 0.65 (0.57-0.75) | 0.62 (0.53-0.73) | 0.53 (0.46-0.61) |
| Men | 5239 | 1 [Reference] | 0.70 (0.64-0.77) | 0.60 (0.54-0.67) | 0.60 (0.54-0.69) | 0.49 (0.44-0.54) |
| Age at baseline, y | | | | | | |
| <65 | 3454 | 1 [Reference] | 0.69 (0.62-0.77) | 0.64 (0.56-0.72) | 0.60 (0.53-0.69) | 0.50 (0.45-0.57) |
| ≥65 | 4446 | 1 [Reference] | 0.70 (0.63-0.78) | 0.60 (0.54-0.68) | 0.61 (0.54-0.68) | 0.49 (0.44-0.55) |
| Race/ethnicity | | | | | | |
| White | 7409 | 1 [Reference] | 0.70 (0.65-0.76) | 0.62 (0.57-0.68) | 0.62 (0.56-0.68) | 0.51 (0.45-0.55) |
| Black | 295 | 1 [Reference] | 0.67 (0.47-0.96) | 0.69 (0.46-1.05) | 0.45 (0.29-0.68) | 0.58 (0.39-0.86) |
| Hispanic | 105 | 1 [Reference] | 0.55 (0.30-0.99) | 0.44 (0.22-0.88) | 0.52 (0.26-1.03) | 0.18 (0.09-0.39) |
| Asian/Pacific Islander/Native American | 91 | 1 [Reference] | 0.43 (0.22-0.85) | 0.46 (0.22-0.96) | 0.39 (0.19-0.82) | 0.28 (0.14-0.57) |
| Education | | | | | | |
| <High school | 2371 | 1 [Reference] | 0.69 (0.60-0.78) | 0.61 (0.53-0.70) | 0.53 (0.46-0.62) | 0.48 (0.41-0.55) |
| College | 5529 | 1 [Reference] | 0.71 (0.64-0.78) | 0.63 (0.57-0.71) | 0.64 (0.57-0.72) | 0.51 (0.46-0.57) |
| Current smoking status | | | | | | |
| Smoker | 6081 | 1 [Reference] | 0.67 (0.61-0.73) | 0.60 (0.54-0.66) | 0.59 (0.53-0.65) | 0.48 (0.44-0.53) |
| Nonsmoker | 1819 | 1 [Reference] | 0.74 (0.64-0.86) | 0.64 (0.54-0.75) | 0.63 (0.53-0.76) | 0.54 (0.45-0.64) |
| BMI | | | | | | |
| <25 | 2876 | 1 [Reference] | 0.68 (0.59-0.77) | 0.58 (0.50-0.67) | 0.58 (0.49-0.67) | 0.45 (0.39-0.52) |
| ≥25 | 5024 | 1 [Reference] | 0.67 (0.61-0.74) | 0.60 (0.54-0.66) | 0.58 (0.52-0.65) | 0.48 (0.44-0.54) |
| Television or video watching, h/d | | | | | | |
| ≤2 | 2154 | 1 [Reference] | 0.71 (0.59-0.84) | 0.59 (0.49-0.72) | 0.67 (0.56-0.81) | 0.53 (0.44-0.63) |
| >2 | 5746 | 1 [Reference] | 0.70 (0.64-0.77) | 0.64 (0.58-0.70) | 0.59 (0.53-0.65) | 0.50 (0.45-0.55) |

Abbreviations: BMI (calculated as weight in kilograms divided by height in meters squared); MPA, moderate physical activity; VPA, vigorous physical activity.
[a] Data are given as relative risk (95% confidence interval) unless otherwise specified. The multivariate models were adjusted for the covariates listed in a footnote in Table 2. In each case, the stratification variable was excluded from the model. Within each stratum, the category of inactive subjects served as the reference group.
[b] Recommendation for MPA: more than 3 hours of activity of at least moderate intensity per week corresponding to 30 minutes of activity of moderate intensity on most days of the week.
[c] Recommendation for VPA: 20 minutes of continuous vigorous exercise 3 or more times per week.

support to current physical activity guidelines, which endorse 30 minutes of moderate activity on most days of the week or 20 minutes of vigorous exercise 3 or more times per week.[4,5,34]

Apart from the present study, only 1 previous investigation[39] has quantified both moderate and vigorous activity in a manner that facilitates a direct comparison with the physical activity guidelines. That modestly sized study from Germany[39] included 943 deaths and examined mortality from any cause and found a statistically significant inverse relation of recommended levels of activity of moderate activity to risk of mortality in women (RR, 0.65; 95% CI, 0.51-0.82) but not in men (RR, 0.90; 95% CI, 0.77-1.01). Conversely, vigorous activity at recommended levels was statistically significantly inversely related to mortality risk in men (RR, 0.74; 95% CI, 0.68-0.94) but not in women (RR, 0.78; 95% CI, 0.57-1.08).

Previous epidemiologic studies of physical activity and mortality generally presented data in study-specific categories that do not readily compare with the guidelines or provided estimates of energy expenditure that require conversion into units of time before they can be translated into levels that correspond to the guidelines.[2,9] In those studies, an activity energy expenditure of approximately 1000 kcal/wk—an amount that corresponds to minimal adherence to the physical activity guidelines—was associated with a 20% to 30% reduction in mortality risk.[16,18,40-43]

Our study has numerous important strengths, including the substantial cohort size yielding precise risk estimates, the uniform criteria for ascertaining deaths, and the evaluation of cause-specific mortality. Subjects with preexisting chronic disease were excluded at baseline, thereby reducing the potential influence of chronic disease on physical activity levels. In secondary analyses, we further minimized the potential for bias due to undiagnosed chronic disease by excluding the initial follow-up period and excluding subjects without regular screening examinations.

Inclusion of BMI and cardiovascular risk factors in the models had little impact on the physical activity and mortality relation, suggesting that regulation of these factors explains only a small portion of the benefit of physical activity. In contrast, adjustment for smoking had an appreciable impact on the association between vigorous exercise and cancer mortality, indicating the importance of considering both vigorous exercise and smoking levels in the assessment of cancer mortality risk.

Our study has certain limitations. Information on physical activity was self-reported, which invariably entails some degree of misclassification.[44] However, the large cohort size prohibited us from using more accurate measures, such as activity monitors.[45] In addition, validation studies comparing physical activity assessments similar to those used in this cohort with referent methods suggest that the reliability and validity of our instrument is comparable to self-reported measures used in other cohorts.[46] Moreover, our activity measures were associated with current smoking, BMI, television or video watching, and total energy intake in the hypothesized directions, providing evidence of construct validity of our physical activity assessment. Using activity of at least moderate intensity to approximate the guidelines for moderate activity may have overstated the potential benefits of moderate activity because it includes vigorous activities. Likewise, our measure of vigorous exercise may have included some moderate activities, which would have understated the apparent protection afforded by vigorous exercise. We were unable to adjust for family history of cardiovascular disease, which may partly explain the stronger observed effects of physical activity on cardiovascular mortality than on cancer mortality.

Engaging in some activity at less than recommended levels provided protection from mortality. One potential explanation is overreporting of physical activity levels among active individuals. Notwithstanding, data from other studies[14,22,26,28,47] suggesting that lower-than-recommended activity levels may suffice to achieve mortality benefits are intriguing and require further evaluation.

Our findings showing that vigorous exercise was associated with a striking reduction in mortality risk among individuals with high television or video watching indicates that vigorous activity has the greatest potential for health benefits among those who are physically inactive. That individuals with greater activity levels consumed more calories than their less active counterparts suggests that apart from dietary intake, being physically inactive represents an important determinant of positive energy balance.

Numerous governmental agencies and private organizations have made recommendations for the appropriate amount of physical activity. The OSG, the CDC, the ACSM, the Institute of Medicine of the National Academy of Sciences, and the joint US Department of Agriculture/Department of Health and Human Services Dietary Guidelines for Americans all endorse a minimum of 30 minutes of moderate activity on most days of the week for overall health benefits.[4,5,48-50] In addition, several agencies and organizations have formulated complementary physical activity recommendations targeted at specific health goals such as weight control, cancer prevention, or cardiorespiratory fitness. Specifically, the Institute of Medicine recommends at least 60 minutes of moderate activity each day,[49] and the US Dietary Guidelines advocate 60 minutes of moderate to vigorous activity on most days of the week to prevent unhealthy adult weight gain.[50] The American Cancer Society calls for 45 to 60 minutes of moderate to vigorous activity on most days of the week to reduce the risk of developing obesity-related malignant conditions such as colon and breast cancers.[51] The ACSM distinguishes between physical activity vs fitness and promotes vigorous activities for at least 20 minutes 3 times a week to improve cardiorespiratory fitness.[34] Thus, physical activity recommendations vary depending on the particular health issue of interest.

Mechanistic studies show that the beneficial effects of physical activity and fitness involve biological processes that primarily mediate risk for cardiovascular disease and cancer.[4] Many biological mechanisms are likely to operate both with moderate and vigorous activity levels.[4,52] One study suggests that genetic factors do not account for physical activity–related mortality differences.[53] The independent nature of the association between physical activity and mortality that we observed following adjustment for and stratification by body mass index indicates that the metabolic pathways by which physical activity reduces mortality risk are not mediated through its impact on weight control. This suggests the value of regular exercise in promoting longevity not just for normal weight individuals but also for those who are overweight or obese.

In summary, engaging in more than 3 hours of at least moderate intensity activity per week decreases the risk of mortality by 27%. Substantial reduction in mortality risk can also be accomplished by 20 minutes of vigorous exercise 3 times per week. We conclude that following physical activity recommendations is associated with lower risk of death. In addition, our findings suggest that engaging in any physical activity by those who are currently sedentary represents an important opportunity to decrease the risk of mortality.

**Accepted for Publication:** July 18, 2007.
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**Author Contributions:** Dr Leitzmann had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Leitzmann, Ballard-Barbash, Mouw, and Schatzkin. *Acquisition of data:* Ballard-Barbash, Hollenbeck, and Schatzkin. *Analysis and interpretation of data:* Leitzmann, Park, Blair, Ballard-Barbash, and Schatzkin. *Drafting of the manuscript:* Leitzmann and Ballard-Barbash. *Critical revision of the manuscript for important intellectual content:* Leitzmann, Park, Blair, Mouw, Hollenbeck, and Schatzkin. *Statistical analysis:* Leitzmann, Park, and Blair. *Obtained funding:* Schatzkin. *Administrative, technical, and material support:* Mouw, Hollenbeck, and Schatzkin. *Study supervision:* Schatzkin.
**Financial Disclosure:** None reported.
**Funding/Support:** This research was supported by the Intramural Research Program of the NIH National Cancer Institute.
**Role of the Sponsor:** The funding organization played no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.
**Additional Contributions:** We are indebted to the participants in the NIH-AARP Diet and Health Study for their outstanding cooperation. Leslie Carroll, MA, at Information Management Services and Sigurd Hermansen, MA, and Kerry Grace Morrissey, MPH, from Westat provided data support, and Tawanda Roy at the Nutritional Epidemiology Branch assisted in research.

## REFERENCES

1. Bauman AE. Updating the evidence that physical activity is good for health: an epidemiological review 2000-2003. *J Sci Med Sport.* 2004;7(1)(suppl):6-19.
2. Katzmarzyk PT, Janssen I, Ardern CI. Physical inactivity, excess adiposity and premature mortality. *Obes Rev.* 2003;4(4):257-290.
3. American College of Sports Medicine. American College of Sports Medicine position statement on the recommended quantity and quality of exercise for developing and maintaining fitness in healthy adults. *Med Sci Sports.* 1978;10 (3):vii-x.
4. US Department of Health and Human Services. *Physical Activity and Health: A Report of the Surgeon General.* Atlanta, GA: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion; 1996.
5. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *JAMA.* 1995;273(5):402-407.
6. Centers for Disease Control and Prevention. Adult participation in recommended levels of physical activity—United States, 2001 and 2003. *MMWR Morb Mortal Wkly Rep.* 2005;54(47):1208-1212.
7. Centers for Disease Control and Prevention. Physical activity trends—United States, 1990-1998. *MMWR Morb Mortal Wkly Rep.* 2001;50(9):166-169.
8. Trost SG, Owen N, Bauman AE, Sallis JF, Brown W. Correlates of adults' participation in physical activity: review and update. *Med Sci Sports Exerc.* 2002; 34(12):1996-2001.
9. Lee IM, Skerrett PJ. Physical activity and all-cause mortality: what is the dose-response relation? *Med Sci Sports Exerc.* 2001;33(6)(suppl):S459-S474.
10. Shephard RJ. What is the optimal type of physical activity to enhance health? *Br J Sports Med.* 1997;31(4):277-284.
11. Lee IM. No pain, no gain? thoughts on the Caerphilly study. *Br J Sports Med.* 2004;38(1):4-5.
12. Blair SN, LaMonte MJ. How much and what type of physical activity is enough? what physicians should tell their patients. *Arch Intern Med.* 2005;165(20):2324-2325.
13. Slattery ML, Jacobs DR Jr, Nichaman MZ. Leisure time physical activity and coronary heart disease death: the US Railroad Study. *Circulation.* 1989;79(2):304-311.
14. Lee IM, Hsieh CC, Paffenbarger RS Jr. Exercise intensity and longevity in men: the Harvard Alumni Health Study. *JAMA.* 1995;273(15):1179-1184.
15. Mensink GB, Deketh M, Mul MD, Schuit AJ, Hoffmeister H. Physical activity and its association with cardiovascular risk factors and mortality. *Epidemiology.* 1996; 7(4):391-397.
16. Lee IM, Paffenbarger RS Jr. Associations of light, moderate, and vigorous intensity physical activity with longevity: the Harvard Alumni Health Study. *Am J Epidemiol.* 2000;151(3):293-299.
17. Yu S, Yarnell JW, Sweetnam PM, Murray L. What level of physical activity protects against premature cardiovascular death? the Caerphilly study. *Heart.* 2003; 89(5):502-506.
18. Myers J, Kaykha A, George S, et al. Fitness versus physical activity patterns in predicting mortality in men. *Am J Med.* 2004;117(12):912-918.
19. Kampert JB, Blair SN, Barlow CE, Kohl HW III. Physical activity, physical fitness, and all-cause and cancer mortality: a prospective study of men and women. *Ann Epidemiol.* 1996;6(5):452-457.
20. Erikssen G, Liestol K, Bjornholt J, Thaulow E, Sandvik L, Erikssen J. Changes in physical fitness and changes in mortality. *Lancet.* 1998;352(9130):759-762.
21. Evenson KR, Stevens J, Thomas R, Cai J. Effect of cardiorespiratory fitness on mortality among hypertensive and normotensive women and men. *Epidemiology.* 2004;15(5):565-572.
22. Paffenbarger RS Jr, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med.* 1986;314(10):605-613.
23. Hakim AA, Petrovitch H, Burchfiel CM, et al. Effects of walking on mortality among nonsmoking retired men. *N Engl J Med.* 1998;338(2):94-99.
24. Wannamethee SG, Shaper AG, Walker M. Changes in physical activity, mortality, and incidence of coronary heart disease in older men. *Lancet.* 1998;351 (9116):1603-1608.
25. Lubin F, Lusky A, Chetrit A, Dankner R. Lifestyle and ethnicity play a role in all-cause mortality. *J Nutr.* 2003;133(4):1180-1185.
26. Kushi LH, Fee RM, Folsom AR, Mink PJ, Anderson KE, Sellers TA. Physical activity and mortality in postmenopausal women. *JAMA.* 1997;277(16):1287-1292.
27. Bath PA, Morgan K. Customary physical activity and physical health outcomes in later life. *Age Ageing.* 1998;27(suppl 3):29-34.
28. Rockhill B, Willett WC, Manson JE, et al. Physical activity and mortality: a prospective study among women. *Am J Public Health.* 2001;91(4):578-583.
29. Schatzkin A, Subar AF, Thompson FE, et al. Design and serendipity in establishing a large cohort with wide dietary intake distributions: the National Institutes of Health-American Association of Retired Persons Diet and Health Study. *Am J Epidemiol.* 2001;154(12):1119-1125.
30. Hill ME, Rosenwaike I. The Social Security Administration's Death Master File: the completeness of death reporting at older ages. *Soc Secur Bull.* 2001;64 (1):45-51.
31. Rich-Edwards JW, Corsano KA, Stampfer MJ. Test of the National Death Index and Equifax Nationwide Death Search. *Am J Epidemiol.* 1994;140(11):1016-1019.
32. Michaud DS, Midthune D, Hermansen S, et al. Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH-AARP Diet and Health Study. *J Registry Manage.* 2005;32:70-75.
33. Lee IM. Physical activity and cancer prevention—data from epidemiologic studies. *Med Sci Sports Exerc.* 2003;35(11):1823-1827.
34. American College of Sports Medicine. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. *Med Sci Sports Exerc.* 1990;22(2):265-274.
35. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol.* 1993;46 (2):153-162.
36. Schuit AJ, Schouten EG, Westerterp KR, Saris WH. Validity of the Physical Activity Scale for the Elderly (PASE): according to energy expenditure assessed by the doubly labeled water method. *J Clin Epidemiol.* 1997;50(5):541-546.
37. Cox DR. Regression models and lifetables. *J R Stat Soc (B).* 1972;34:187-220.
38. Ussher M. Exercise interventions for smoking cessation. *Cochrane Database Syst Rev.* 2005;(1):CD002295.
39. Bucksch J. Physical activity of moderate intensity in leisure time and the risk of all cause mortality. *Br J Sports Med.* 2005;39(9):632-638.
40. Leon AS, Connett J, Jacobs DR Jr, Rauramaa R. Leisure-time physical activity levels and risk of coronary heart disease and death: the Multiple Risk Factor Intervention Trial. *JAMA.* 1987;258(17):2388-2395.
41. Fried LP, Kronmal RA, Newman AB, et al. Risk factors for 5-year mortality in older adults: the Cardiovascular Health Study. *JAMA.* 1998;279(8):585-592.
42. Lee IM, Sesso HD, Oguma Y, Paffenbarger RS Jr. The "weekend warrior" and risk of mortality. *Am J Epidemiol.* 2004;160(7):636-641.
43. Lan TY, Chang HY, Tai TY. Relationship between components of leisure physical activity and mortality in Taiwanese older adults. *Prev Med.* 2006;43(1): 36-41.
44. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Sport.* 2000;71(2)(suppl):S1-S14.
45. LaMonte MJ, Ainsworth BE, Reis JP. Measuring physical activity. In: Zhu W, Woods T, eds. *Measurement Theory and Practice in Kinesiology.* Champaign, IL: Human Kinetics; 2006:237-272.
46. Pereira MA, FitzGerald SJ, Gregg EW, et al. A collection of Physical Activity Questionnaires for health-related research. *Med Sci Sports Exerc.* 1997;29 (6)(suppl):S1-S205.
47. Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? *Med Sci Sports Exerc.* 2001;33(6)(suppl):S379-S399.
48. Fletcher GF, Balady G, Froelicher VF, Hartley LH, Haskell WL, Pollock ML. Exercise standards: a statement for healthcare professionals from the American Heart Association Writing Group. *Circulation.* 1995;91(2):580-615.
49. Institute of Medicine of the National Academy of Science. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients).* Washington, DC: National Academy Press; 2002.
50. US Department of Health and Human Services and US Department of Agriculture. *Dietary Guidelines for Americans 2005.* 6th ed. Washington, DC: US Government Printing Office; 2005.
51. Kushi LH, Byers T, Doyle C, et al; American Cancer Society 2006 Nutrition and Physical Activity Guidelines Advisory Committee. American Cancer Society Guidelines on Nutrition and Physical Activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity [published correction appears in *CA Cancer J Clin.* 2007;57(1):66]. *CA Cancer J Clin.* 2006;56(5): 254-281.
52. Haskell WL. Physical activity and health: need to define the required stimulus. *Am J Cardiol.* 1985;55(10):4D-9D.
53. Kujala UM, Kaprio J, Sarna S, Koskenvuo M. Relationship of leisure-time physical activity and mortality: the Finnish twin cohort. *JAMA.* 1998;279(6):440-444.

| 論文名 | Physical activity recommendations and decreased risk of mortality |
|---|---|
| 著者 | Leitzmann MF, Park Y, Blair A, Ballard-Barbash R, Mouw T, Hollenbeck AR, Schatzkin A |
| 雑誌名 | Arch Intern Med |
| 巻・号・頁 | 167(22)　　2453-2460 |
| 発行年 | 2007 |
| PubMedリンク | http://www.ncbi.nlm.nih.gov/pubmed/18071167 |

**対象の内訳**

| | ヒト | 動物 | 地　域 | 欧米 | 研究の種類 | 縦断研究 |
|---|---|---|---|---|---|---|
| 対象 | 一般健常者 | 空白 | | (　　　) | | コホート研究 |
| 性別 | 男女混合 | (　　　) | | (　　　) | | (　　　) |
| 年齢 | 50-71歳 | | | (　　　) | | 前向き研究 |
| 対象数 | 10000以上 | | | (　　　) | | (　　　) |

| 調査の方法 | 質問紙 | (　　　) | | | | | |
|---|---|---|---|---|---|---|---|

**アウトカム**

| | | | | | | |
|---|---|---|---|---|---|---|
| 予　防 | 心疾患予防 | な し | ガン予防 | な し | 死亡 | (　　　) |
| 維持・改善 | な し | な し | な し | な し | (　) | (　　　) |

**図表**

Table 2. Relative Risk (RR) of Mortality From Any Cause and Mortality From Specific Causes According to Activity of at Least Moderate Intensity and Vigorous Exercise

| Type of Activity[a] | | | | | | P Value for Trend |
|---|---|---|---|---|---|---|
| **Mortality From Any Cause** | | | | | | |
| Activity of at least moderate intensity, h/wk | Inactive | <1 | 1-3 | 4-7 | >7 | |
| No. of deaths | 1683 | 937 | 1940 | 1794 | 1546 | |
| Person-years | 170 957 | 133 217 | 321 719 | 329 352 | 310 151 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.80 (0.74-0.87) | 0.72 (0.68-0.77) | 0.68 (0.63-0.73) | 0.61 (0.57-0.66) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.81 (0.75-0.88) | 0.74 (0.69-0.79) | 0.70 (0.65-0.75) | 0.63 (0.59-0.68) | <.001 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.82 (0.75-0.89) | 0.74 (0.70-0.80) | 0.70 (0.65-0.75) | 0.63 (0.59-0.68) | <.001 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.85 (0.79-0.93) | 0.79 (0.74-0.85) | 0.76 (0.71-0.82) | 0.68 (0.63-0.74) | <.001 |
| Vigorous exercise, times per week | Inactive | <1 | 1-2 | 3-4 | ≥5 | |
| No. of deaths | 2030 | 1109 | 1682 | 1775 | 1334 | |
| Person-years | 202 815 | 174 174 | 281 371 | 352 635 | 254 352 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.70 (0.65-0.75) | 0.66 (0.62-0.71) | 0.55 (0.51-0.59) | 0.58 (0.53-0.62) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.71 (0.66-0.77) | 0.68 (0.63-0.73) | 0.57 (0.53-0.61) | 0.59 (0.55-0.64) | <.001 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.72 (0.67-0.78) | 0.71 (0.66-0.76) | 0.61 (0.57-0.66) | 0.65 (0.60-0.70) | <.001 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.77 (0.71-0.83) | 0.77 (0.72-0.82) | 0.68 (0.63-0.73) | 0.71 (0.66-0.77) | <.001 |
| **Mortality From Cardiovascular Disease** | | | | | | |
| Activity of at least moderate intensity, h/wk | Inactive | <1 | 1-3 | 4-7 | >7 | |
| No. of deaths | 511 | 303 | 574 | 516 | 432 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.86 (0.75-1.00) | 0.71 (0.62-0.81) | 0.64 (0.56-0.73) | 0.56 (0.49-0.65) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.88 (0.76-1.02) | 0.74 (0.66-0.84) | 0.68 (0.60-0.78) | 0.60 (0.52-0.69) | <.001 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.88 (0.76-1.02) | 0.73 (0.65-0.83) | 0.67 (0.58-0.76) | 0.58 (0.50-0.67) | <.001 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.94 (0.81-1.08) | 0.80 (0.71-0.91) | 0.75 (0.66-0.86) | 0.65 (0.57-0.75) | <.001 |
| Vigorous exercise, times per week | Inactive | <1 | 1-2 | 3-4 | ≥5 | |
| No. of deaths | 611 | 316 | 491 | 521 | 397 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.65 (0.56-0.74) | 0.63 (0.56-0.71) | 0.53 (0.47-0.60) | 0.57 (0.50-0.65) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.66 (0.58-0.76) | 0.65 (0.58-0.74) | 0.56 (0.50-0.64) | 0.61 (0.53-0.70) | <.001 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.67 (0.58-0.77) | 0.67 (0.59-0.76) | 0.59 (0.52-0.67) | 0.64 (0.56-0.74) | <.001 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.72 (0.63-0.82) | 0.74 (0.66-0.84) | 0.66 (0.59-0.76) | 0.71 (0.62-0.82) | <.001 |
| **Mortality From Cancer** | | | | | | |
| Activity of at least moderate intensity, h/wk | Inactive | <1 | 1-3 | 4-7 | >7 | |
| No. of deaths | 645 | 392 | 884 | 894 | 818 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.84 (0.74-0.95) | 0.80 (0.72-0.89) | 0.81 (0.72-0.90) | 0.77 (0.68-0.86) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.84 (0.74-0.96) | 0.81 (0.73-0.90) | 0.82 (0.73-0.91) | 0.79 (0.69-0.87) | .002 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.86 (0.76-0.98) | 0.83 (0.75-0.93) | 0.84 (0.75-0.93) | 0.79 (0.71-0.89) | .003 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.88 (0.78-1.00) | 0.86 (0.78-0.96) | 0.88 (0.79-0.98) | 0.83 (0.74-0.93) | .02 |
| Vigorous exercise, times per week | Inactive | <1 | 1-2 | 3-4 | ≥5 | |
| No. of deaths | 754 | 506 | 811 | 854 | 706 | |
| Age- and sex-adjusted RR (95% CI) | 1 [Reference] | 0.84 (0.75-0.94) | 0.82 (0.74-0.91) | 0.66 (0.60-0.74) | 0.75 (0.67-0.84) | <.001 |
| Age- and sex-adjusted RR + BMI (95% CI) | 1 [Reference] | 0.85 (0.76-0.95) | 0.83 (0.75-0.92) | 0.67 (0.61-0.75) | 0.76 (0.68-0.86) | <.001 |
| Age- and sex-adjusted RR + smoking (95% CI) | 1 [Reference] | 0.87 (0.78-0.98) | 0.89 (0.80-0.99) | 0.76 (0.69-0.85) | 0.85 (0.76-0.95) | .008 |
| Full multivariate RR (95% CI)[b] | 1 [Reference] | 0.91 (0.81-1.02) | 0.94 (0.85-1.04) | 0.82 (0.74-0.92) | 0.95 (0.85-1.07) | .23 |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval.

[a] Activity of at least moderate intensity is defined as activities with an estimated energy expenditure of greater than 3 metabolic equivalents (METs). The MET is defined as the ratio of work to resting energy expenditure (1 MET=1 kcal/kg/h or 3.5-mL oxygen uptake/kg/min). Resting energy expenditure is assumed to be 1 MET. Vigorous exercise is defined as activities that lasted 20 minutes or more and caused either increases in breathing or heart rate or working up a sweat.

[b] The multivariate models used age as the underlying time metric and included the following covariates: sex (women; men), body mass index (<18.5; 18.5-24.9; 25.0-29.9; 30.0-34.9; 35.0-39.9; and ≥40.0), smoking (never smoking; past smoking of 1-19 cigarettes per day; past smoking of ≥20 cigarettes per day; current smoking of 1-19 cigarettes per day; and current smoking of ≥20 cigarettes per day), race/ethnicity (white; black; Hispanic; and Asian/Pacific Islander/Native American combined), education (<high school; high school; vocational school or some college; and college graduate), marital status (married or living as married; and divorced, separated, widowed, or never married), family history of cancer (yes; no), menopausal hormone therapy (never; current or former user of estrogen only; current user of estrogen and progestin combined; former user of estrogen and progestin combined; and not applicable), aspirin use (yes; no), multivitamin use (yes; no), intakes of vegetables (quintiles), fruit (quintiles), red meat (quintiles), and alcohol (0; 0.01-4.9; 5.0-14.9; 15.0-29.9; 30.0-49.9, and ≥50.0 g/d). The multivariate analyses of activity of at least moderate intensity and vigorous exercise were mutually adjusted.

| 図表掲載箇所 | P2456, Table2 |
|---|---|

**概　要（800字まで）**

本研究は、アメリカのThe NIH-AARP Diet and HealthStudyに参加した男女252,925名を対象に5年間の追跡調査を行い、国が定める身体活動指針で示される身体活動量と全死因死亡リスクとの関連を検討したものである。質問紙により、20分以上の高強度身体活動を行った週当たりの頻度と、週当たりに行った中強度身体活動の平均時間を尋ねた。高強度活動については、不活動、1回/週未満、1-2回、3-4回、5回/週以上の5群に、中強度活動については、不活動、1時間/週未満、1-3時間、4-7時間、7時間/週以上の5群に分類した。アメリカにおける全身持久力向上のための身体活動推奨量は、20分以上の高強度活動を週3回以上であり、健康増進のための身体活動推奨量は中強度活動をほぼ毎日30分以上行うことである(本研究の3時間/週とほぼ同等)。中強度身体活動に関して、不活動な集団と比較すると、全ての集団で全死因死亡リスクが有意に減少した。相対リスクは順に、0.85(95%信頼区間:0.79-0.93)、0.79(0.74-0.85)、0.76(0.71-0.82)、0.68(0.63-0.74)であった(Ptrend<0.001)。高強度活動に関して、同様に全ての集団で全死因死亡リスクが有意に減少した。相対リスクは順に、0.77(0.71-0.83)。0.77(0.72-0.82)、0.68(0.63-0.73)、0.71(0.66-0.77)であった(Ptrend<0.001)。心疾患発症リスクについては、中強度活動を1時間/週以上からリスク減少がみられ(Ptrend<0.001)、高強度活動については、全ての集団で有意なリスク減少がみられた(Ptrend<0.001)。がん発症リスクは、中強度活動については1時間/週以上で、高強度活動については3回/週以上で有意なリスク減少がみられた。

**結　論（200字まで）**

本研究のコホートに対して、アメリカの身体活動推奨量は妥当であり、推奨量を実施することで全死因死亡リスク、心疾患発症リスク、およびがん発症リスクを大いに低下させることが明らかとなった。また、推奨量に達していない者も、不活動でいるよりは少しでも身体活動量を増やすことでそれらのリスクが減少することが明らかとなった。

**エキスパートによるコメント（200字まで）**

身体活動基準の策定に使用された研究である。基準で定められた身体活動量を満たさなくても、少しでも身体活動を増やすことの価値を示した点に意義がある。

担当者　久保絵里子・村上晴香・宮地元彦

# WALKING COMPARED WITH VIGOROUS EXERCISE FOR THE PREVENTION OF CARDIOVASCULAR EVENTS IN WOMEN

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## ABSTRACT

*Background* The role of walking, as compared with vigorous exercise, in the prevention of cardiovascular disease remains controversial. Data for women who are members of minority racial or ethnic groups are particularly sparse.

*Methods* We prospectively examined the total physical-activity score, walking, vigorous exercise, and hours spent sitting as predictors of the incidence of coronary events and total cardiovascular events among 73,743 postmenopausal women 50 to 79 years of age in the Women's Health Initiative Observational Study. At base line, participants were free of diagnosed cardiovascular disease and cancer, and all participants completed detailed questionnaires about physical activity. We documented 345 newly diagnosed cases of coronary heart disease and 1551 total cardiovascular events.

*Results* An increasing physical-activity score had a strong, graded, inverse association with the risk of both coronary events and total cardiovascular events. There were similar findings among white women and black women. Women in increasing quintiles of energy expenditure measured in metabolic equivalents (the MET score) had age-adjusted relative risks of coronary events of 1.00, 0.73, 0.69, 0.68, and 0.47, respectively (P for trend, <0.001). In multivariate analyses, the inverse gradient between the total MET score and the risk of cardiovascular events remained strong (adjusted relative risks for increasing quintiles, 1.00, 0.89, 0.81, 0.78, and 0.72, respectively; P for trend <0.001). Walking and vigorous exercise were associated with similar risk reductions, and the results did not vary substantially according to race, age, or body-mass index. A brisker walking pace and fewer hours spent sitting daily also predicted lower risk.

*Conclusions* These prospective data indicate that both walking and vigorous exercise are associated with substantial reductions in the incidence of cardiovascular events among postmenopausal women, irrespective of race or ethnic group, age, and body-mass index. Prolonged sitting predicts increased cardiovascular risk. (N Engl J Med 2002;347:716-25.)



PHYSICAL activity has been associated with a reduced risk of cardiovascular disease in epidemiologic studies,[1,2] but data for women and members of minority ethnic groups have been sparse. Moreover, the specific role of walking, the most common form of exercise among women,[3] has been addressed only minimally. Federal guidelines from the Centers for Disease Control and Prevention and the American College of Sports Medicine,[4] as well as the Surgeon General's Report on Physical Activity and Health,[3] endorse at least 30 minutes of moderate-intensity physical activity on most, and preferably all, days of the week, in contrast to earlier guidelines that recommended vigorous endurance exercise for at least 20 minutes three or more times per week.[5] Although the federal guidelines encourage a level of activity that is safe, accessible, and feasible for most Americans[6] (at least 75 percent of whom have less than the recommended level of activity[3]), the potential benefits of moderate-intensity activity in preventing cardiovascular events remain uncertain. Moreover, the role of time spent in sedentary behavior, such as sitting, in predicting risk remains relatively unexplored.

We therefore compared the roles of walking and vigorous exercise in the prevention of coronary and cardiovascular events in a large, ethnically diverse cohort of postmenopausal women. Using detailed assessments of physical activity, we examined the magnitude of associations between each of the measures of physical activity (the total physical-activity score, the intensity of exercise [walking vs. vigorous exercise], and the hours spent sitting) and the incidence of cardiovascular events.

## METHODS

### Study Population

The study population consisted of 73,743 women who were enrolled in the Women's Health Initiative Observational Study, which

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involved a national, multicenter cohort of postmenopausal women who were 50 to 79 years of age at entry. The Women's Health Initiative is a prospective, ethnically and racially diverse, multicenter clinical trial and observational study designed to address the major causes of illness and death in postmenopausal women (see the Appendix for a list of study investigators). A total of 93,676 women were enrolled in the observational study at 40 clinical centers between 1994 and 1998. Criteria for exclusion from the study included the presence of any medical condition associated with predicted survival of less than three years (e.g., class IV congestive heart failure, obstructive lung disease requiring supplemental oxygen, or severe chronic liver or kidney disease), alcoholism, mental illness, or dementia. In addition, women were excluded from the present analyses if, at base line, they had a history of coronary heart disease, stroke, or cancer; were nonambulatory (unable to walk at least one block); or had missing data on the physical-activity questionnaire. After women had been excluded for these reasons, 73,743 women remained in the analysis. Of these women, 61,574 were non-Hispanic white, 5661 were non-Hispanic black, 2880 were Hispanic, 2288 were Asian or Pacific Islander, and 1340 were American Indian or of other racial or ethnic background. Race was self-assigned. Details of the scientific rationale, design, eligibility requirements, and base-line characteristics of the cohort have been published elsewhere.[7]

### Exposure Assessment

All women enrolled in the Observational Study were required to come for a clinic visit for base-line screening. At this visit, women completed self-administered questionnaires related to personal and family medical history, physical activity, smoking, diet, and other behavioral and lifestyle-related factors. Clinical measurements including height, weight, waist and hip circumferences, and blood pressure were obtained by trained staff members. All women provided written informed consent, and the study protocol was approved by the institutional review board of each center.

Recreational physical activity was assessed by a detailed questionnaire on the frequency and duration of walking and of several other types of activity (strenuous, moderate, and mild). Walking was assessed by a series of questions about the frequency of walks outside the home for more than 10 minutes without stopping, the average duration of each walk, and the usual walking pace. Vigorous exercise was defined as that in which "you work up a sweat and your heart beats fast," and examples included aerobics, aerobic dancing, jogging, tennis, and swimming laps. Moderate exercise was defined as that which was "not exhausting," and examples included biking outdoors, using an exercise machine (such as a stationary bicycle or a treadmill), calisthenics, easy swimming, and popular or folk dancing. Examples of mild exercise were slow dancing, bowling, and golf. Using a standardized classification of the energy expenditure associated with physical activities,[8] we calculated a weekly energy-expenditure score in metabolic equivalents (MET score) for walking and for total physical activity. Finally, participants were asked to estimate the number of hours per day they spent engaged in sedentary behavior, including time spent sitting as well as lying down or sleeping.

### Reproducibility and Validation of the Physical-Activity Assessment

A sample of participants in the Observational Study (1092 women) was recruited into a reliability study to assess the reproducibility of selected questionnaires, including the physical-activity assessment. The average time between base line and repeated assessments was three months. The test–retest reliability for recreational physical activity, including walking and strenuous activity, was assessed (weighted kappas among all women ranged from 0.67 to 0.71).[7] The intraclass correlation coefficient for the primary summary variable (total energy expenditure in MET from all recreational physical activity) was 0.77. A similar physical-activity questionnaire has been found to be correlated with physical-activity diaries (r=0.62) and with one-week recall of activity (r=0.79) in a cohort of female health professionals.[9]

### Ascertainment of End Points

The primary end points for this study were newly diagnosed coronary heart disease (nonfatal myocardial infarction or death from coronary causes) and total cardiovascular events (myocardial infarction, death from coronary causes, coronary revascularization, angina, congestive heart failure, stroke, or carotid revascularization) that occurred after the return of the base-line questionnaire but before August 27, 2000. Newly diagnosed cardiovascular events were identified on the basis of annual mailed follow-up questionnaires (response rates have been above 95 percent), and permission to review medical records was requested. Study physicians with no knowledge of the self-reported risk-factor status reviewed the records. The diagnosis of nonfatal myocardial infarction was confirmed if data in the hospital record met standardized criteria of diagnostic electrocardiographic changes, elevated cardiac-enzyme levels, or both.[10] Treatment with coronary or carotid revascularization was confirmed by documentation of the procedure in the medical record. The presence of angina was confirmed by hospitalization and confirmatory evidence on angiography, diagnostic stress test, or diagnosis by a physician and medical treatment. The occurrence of stroke was confirmed by documentation in the medical record of the rapid onset of a neurologic deficit consistent with stroke and lasting at least 24 hours or until death. The presence of congestive heart failure was confirmed by hospitalization and diagnostic confirmatory tests.

Fatal coronary disease was considered confirmed if there was documentation in the hospital or autopsy records or if coronary disease was listed as the cause of death on the death certificate and evidence of previous coronary disease was available. For deaths from other cardiovascular causes, a review of confirmatory evidence by physician-adjudicators was required.

### Statistical Analysis

Our primary analyses used the detailed physical-activity assessment at base line. Person-time for each woman was calculated from the date of return of the base-line questionnaire to the date of a confirmed cardiovascular event, death from any cause, or August 27, 2000, whichever came first. Age-adjusted relative risks were computed as the incidence rate in a specific category of activity divided by the incidence rate in the lowest quintile, with adjustment for one-year age categories. We conducted tests of linear trend by treating the categories as a continuous variable and assigning the median score for each category.[11] All tests of statistical significance were two-sided.

We used Cox proportional-hazards regression[12] to adjust simultaneously for potential confounding variables, including age, smoking status, body-mass index (the weight in kilograms divided by the square of the height in meters), the ratio of the waist circumference to the hip circumference, alcohol consumption, age at menopause, use of hormone-replacement therapy, parental history of premature myocardial infarction (before 55 years of age in the father or before 65 years of age in the mother), race or ethnic group, education, family income, and several dietary variables. Additional models controlled for history or absence of history of hypertension, diabetes, and high cholesterol levels, as well as for functional status and a summary score for mental and emotional health.[13] The total MET score, the MET score for walking, time spent in vigorous exercise, walking pace, and hours spent sitting and lying down or sleeping were analyzed separately. Differences in the results for activity according to race (white women vs. black women), age, and body-mass index were assessed. Secondary analyses excluded data for the first year of follow-up in order to minimize potential bias caused by the presence of subclinical disease.

## RESULTS

During up to 5.9 years of follow-up (mean, 3.2 years; total, 232,971 person-years), we documented 345 newly diagnosed cases of coronary disease (287 nonfatal myocardial infarctions and 58 deaths from coronary causes), 309 strokes, and 1551 first cardiovascular events among the 73,743 women 50 to 79 years of age who completed a detailed physical-activity questionnaire, were ambulatory, and were free of cardiovascular disease and cancer at base line. The base-line characteristics of the cohort and the distribution of physical-activity profiles and other risk factors have been described elsewhere.[7]

The total physical-activity score (in MET-hours per week) at base line had a strong inverse relation with the risk of coronary heart disease during the follow-up period (Table 1). In age-adjusted analyses, the relative risk declined with increasing quintiles of the total MET score (1.00, 0.73, 0.69, 0.68, and 0.47, respectively; P for trend <0.001). Risk reductions for increasing categories of walking (P for trend = 0.004) were similar to those for increasing categories of vig-

**TABLE 1.** RELATIVE RISKS OF CARDIOVASCULAR DISEASE ACCORDING TO QUINTILE OF TOTAL PHYSICAL-ACTIVITY SCORE AND CATEGORIES OF WALKING AND VIGOROUS EXERCISE.*

| CATEGORY | QUINTILE OF TOTAL MET-HR PER WK | | | | | P VALUE FOR TREND |
|---|---|---|---|---|---|---|
| | 1 (LOWEST) | 2 | 3 | 4 | 5 (HIGHEST) | |
| **Total exercise** | | | | | | |
| Total MET score (MET-hr/wk) | | | | | | |
| Median | 0 | 4.2 | 10.0 | 17.5 | 32.8 | |
| Range | 0–2.4 | 2.5–7.2 | 7.3–13.4 | 13.5–23.3 | ≥23.4 | |
| Coronary heart disease | | | | | | |
| No. of cases | 92 | 70 | 68 | 70 | 45 | |
| No. of person-years | 44,989 | 45,329 | 46,003 | 49,338 | 47,312 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 0.73 (0.53–0.99) | 0.69 (0.51–0.95) | 0.68 (0.50–0.93) | 0.47 (0.33–0.67) | <0.001 |
| Total cardiovascular disease | | | | | | |
| No. of cases | 396 | 342 | 304 | 281 | 228 | |
| No. of person-years | 44,448 | 44,836 | 45,550 | 48,948 | 46,972 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 0.83 (0.71–0.95) | 0.72 (0.62–0.84) | 0.63 (0.54–0.74) | 0.55 (0.47–0.65) | <0.001 |
| Multivariate relative risk (95% CI) | 1.00 | 0.89 (0.75–1.04) | 0.81 (0.68–0.97) | 0.78 (0.66–0.93) | 0.72 (0.59–0.87) | <0.001 |
| **Walking** | | | | | | |
| Energy expenditure (MET-hr/wk) | | | | | | |
| Median | 0 | 1.5 | 3.8 | 7.5 | 16.7 | |
| Range | None | 0.1–2.5 | 2.6–5.0 | 5.1–10.0 | >10.0 | |
| Coronary heart disease | | | | | | |
| No. of cases | 133 | 64 | 52 | 47 | 49 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 0.71 (0.53–0.96) | 0.60 (0.44–0.83) | 0.54 (0.39–0.76) | 0.61 (0.44–0.84) | 0.004 |
| Total cardiovascular disease | | | | | | |
| No. of cases | 550 | 322 | 249 | 236 | 194 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 0.88 (0.77–1.01) | 0.70 (0.60–0.81) | 0.66 (0.57–0.77) | 0.58 (0.49–0.68) | <0.001 |
| Multivariate relative risk (95% CI) | 1.00 | 0.91 (0.78–1.07) | 0.82 (0.69–0.97) | 0.75 (0.63–0.89) | 0.68 (0.56–0.82) | <0.001 |
| **Vigorous exercise** | | | | | | |
| Energy expenditure (min of strenuous exercise/wk) | | | | | | |
| Median | 0 | 30 | 90 | 140 | 210 | |
| Range | None | 1–60 | 61–100 | 101–150 | >150 | |
| Coronary heart disease | | | | | | |
| No. of cases | 269 | 35 | 13 | 14 | 14 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 1.12 (0.79–1.60) | 0.56 (0.32–0.98) | 0.73 (0.43–1.25) | 0.58 (0.34–0.99) | 0.008 |
| Total cardiovascular disease | | | | | | |
| No. of cases | 1220 | 125 | 78 | 61 | 67 | |
| Age-adjusted relative risk (95% CI) | 1.00 | 0.87 (0.72–1.04) | 0.73 (0.58–0.92) | 0.69 (0.53–0.89) | 0.60 (0.47–0.76) | <0.001 |
| Multivariate relative risk (95% CI) | 1.00 | 0.91 (0.73–1.12) | 0.81 (0.63–1.06) | 0.85 (0.64–1.13) | 0.76 (0.58–1.00) | 0.01 |

*Coronary heart disease includes nonfatal myocardial infarction and fatal coronary disease. Multivariate models included age (as a continuous variable), smoking status (0, 1 to 14, 15 to 24, or ≥25 cigarettes per day), race or ethnic group (non-Hispanic white, non-Hispanic black, Hispanic, Asian, or other), level of education (5 categories), family income (7 categories), body-mass index (<25.0, 25.0 to 29.9, or ≥30.0), waist-to-hip ratio (as a continuous variable), level of alcohol intake (0, 1 to 4, 5 to 14, or ≥15 g per day), parental history of premature myocardial infarction, age at menopause, use or nonuse of hormone-replacement therapy, percentage of calories from saturated fat, number of servings of fruit and vegetables per day, and dietary fiber intake (g per day). MET denotes metabolic equivalent, and CI confidence interval.

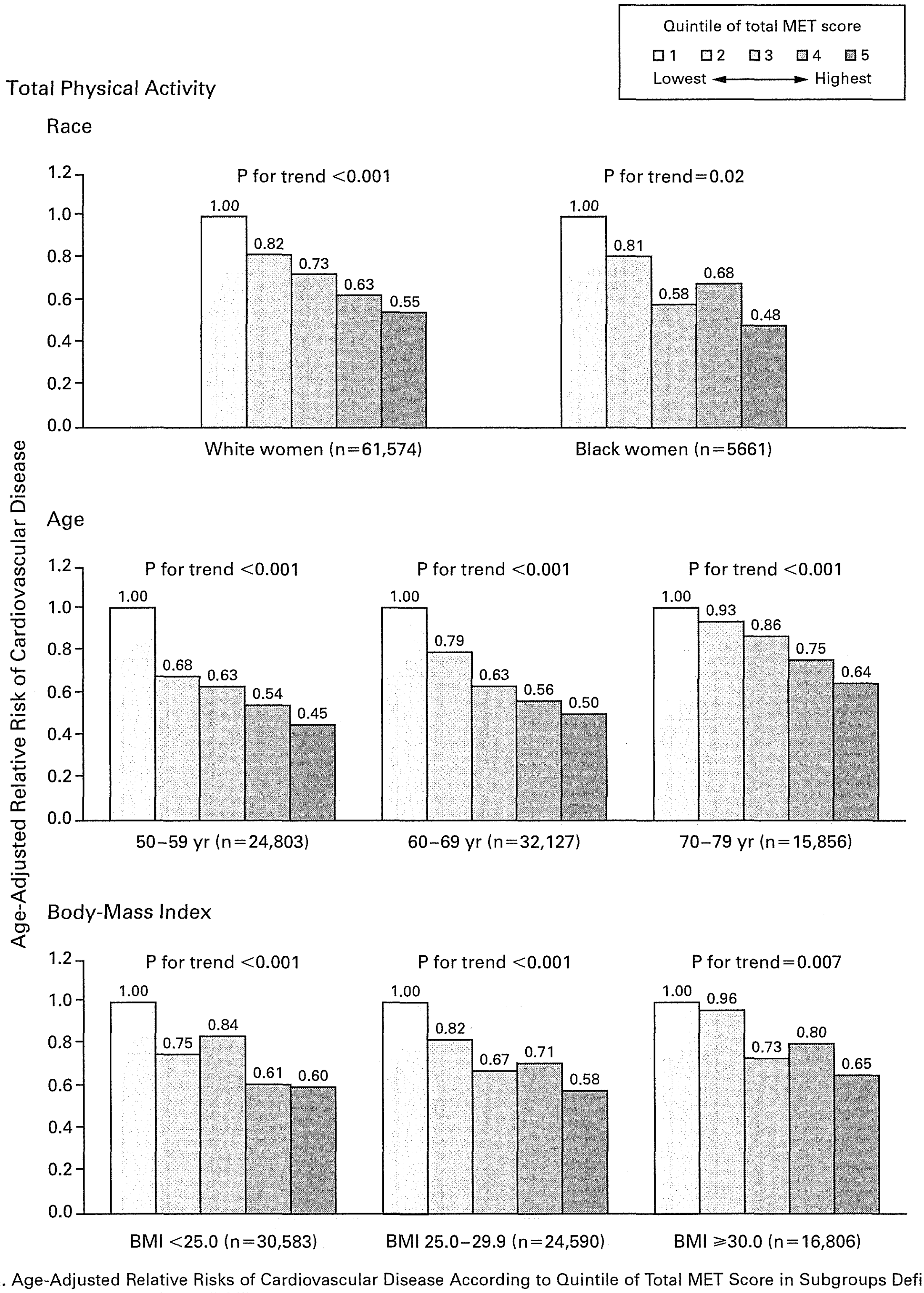


**Figure 1.** Age-Adjusted Relative Risks of Cardiovascular Disease According to Quintile of Total MET Score in Subgroups Defined by Race, Age, and Body-Mass Index (BMI).
The reference category is the lowest quintile of MET score.

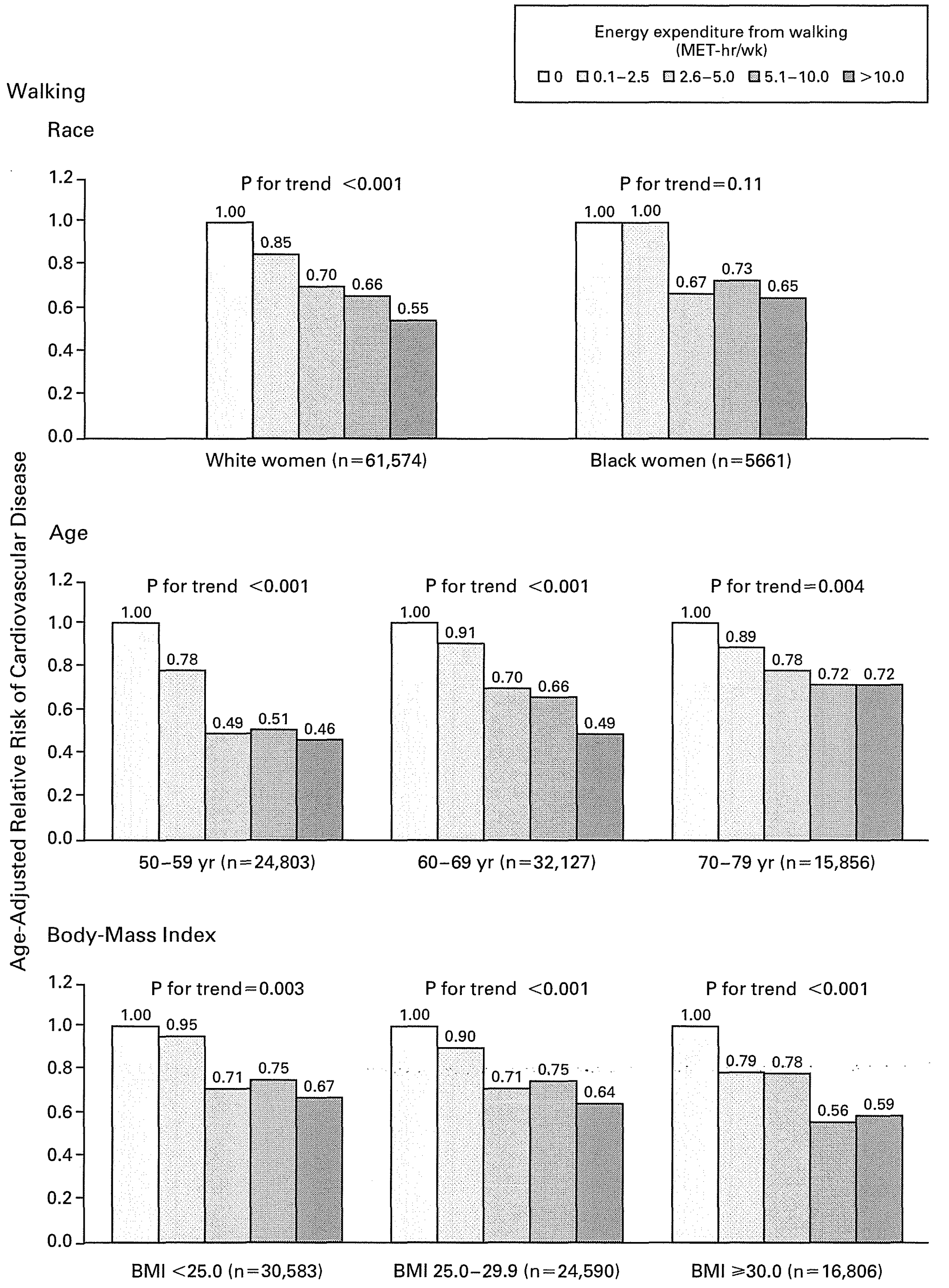


**Figure 2.** Age-Adjusted Relative Risks of Cardiovascular Disease According to Energy Expenditure from Walking (MET-Hr/Wk) in Subgroups Defined by Race, Age, and Body-Mass Index (BMI).
The reference category is the lowest category of energy expenditure from walking.

orous exercise (activities with MET scores of 6 or higher; P for trend = 0.008) (Table 1).

Reductions in the risk of total cardiovascular events with increasing categories of total MET scores, walking, and vigorous exercise were similar to those for the risk of coronary disease (Table 1). Women who either walked or exercised vigorously at least 2.5 hours per week had a risk reduction of approximately 30 percent. Similar reductions in the risk of cardiovascular events with an increasing MET score were observed for white women and for black women (for other racial and ethnic groups, the samples were not large enough to be analyzed separately), as well as for women in different categories of age or body-mass index (Fig. 1). The relative risk of cardiovascular disease in the highest quintile of MET score as compared with the lowest quintile was 0.55 (95 percent confidence interval, 0.47 to 0.65) among white women and 0.48 (95 percent confidence interval, 0.25 to 0.93) among black women. Moreover, increasing categories of walking were inversely associated with the risk of cardiovascular events in each of these subgroups (Fig. 2). Women who engaged in both walking and vigorous exercise had greater reductions in cardiovascular risk than those who did either one alone (the age-adjusted relative risk for those in the highest category of each was 0.37 [95 percent confidence interval, 0.25 to 0.57]) (Fig. 3).

In multivariate analyses, after simultaneous control for age, race or ethnic group, smoking status, body-mass index, waist-to-hip ratio, socioeconomic status, several dietary factors, and other covariates, physical activity remained a powerful predictor of the subsequent risk of cardiovascular events (Table 1). For increasing quintiles of the total MET score, the relative risks were 1.00, 0.89, 0.81, 0.78, and 0.72, respectively (P for trend <0.001). Increasing categories of walking were associated with similar reductions in risk (relative risks, 1.00, 0.91, 0.82, 0.75, and 0.68, respectively; P for trend <0.001), which were also similar to the risk reductions with vigorous exercise (Table 1) and remained unchanged after simultaneous inclusion of walking and vigorous exercise in the model. These results were not substantially altered after further control for biologic variables that could be considered to be in the causal pathway, such as hypertension, hypercholesterolemia, and diabetes, and for the summary score for mental and emotional health[13] (the relative risks of cardiovascular events with increasing total MET scores were 1.00, 0.92, 0.87, 0.83, and 0.77, respectively; P for trend = 0.008). When we excluded data from the first year of follow-up (to minimize potential bias caused by the influence of subclinical disease on the activity level), the results were not materially altered (the multivariate relative risk of car-

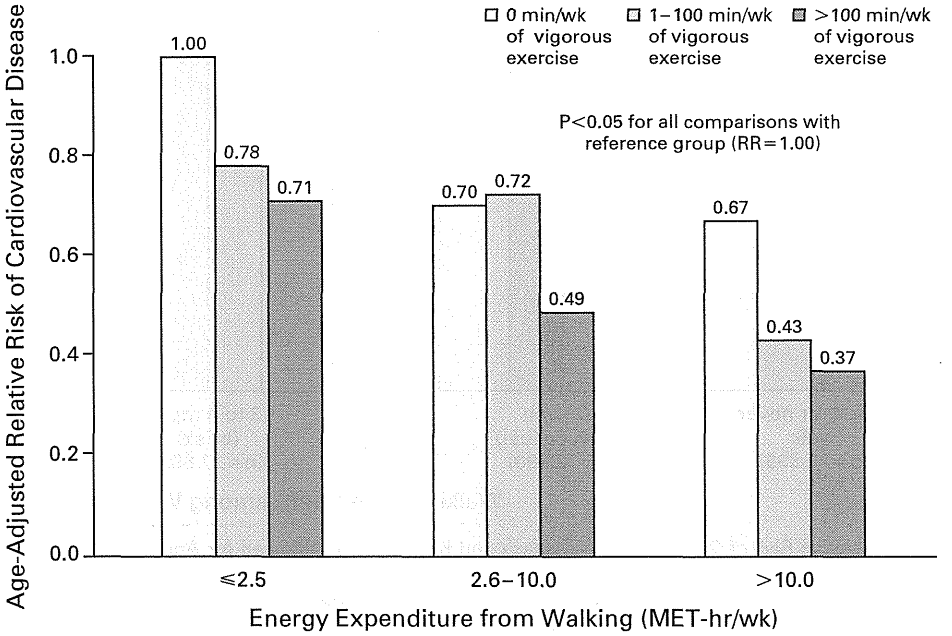


**Figure 3.** Joint Association of Walking and Vigorous Exercise with the Age-Adjusted Relative Risk of Cardiovascular Disease. RR denotes relative risk.

diovascular disease for women in the highest quintile of total MET score was 0.76 [95 percent confidence interval, 0.61 to 0.96; P for trend = 0.02]).

Walking pace was also an important determinant of reduction in cardiovascular risk (Fig. 4). As compared with women who never or rarely walked (the reference category, with a relative risk of 1.00), women who walked at faster paces of 2 to 3 miles per hour (mph) (3.2 to 4.8 km per hour), 3 to 4 mph (4.8 to 6.4 km per hour), and more than 4 mph had relative risks of cardiovascular disease of 0.86, 0.76, and 0.58, respectively (P for trend = 0.002), according to multivariate models that included control for time spent walking.

Finally, we assessed the relation between hours spent sitting, as well as hours spent lying down or sleeping, and the risk of cardiovascular events. After we accounted for age and recreational energy expenditure (total MET score), the relative risk of cardiovascular disease was 1.38 (95 percent confidence interval, 1.01 to 1.87) among women who spent 12 to 15 hours per day lying down or sleeping and 1.68 (95 percent confidence interval, 1.07 to 2.64) among women who spent at least 16 hours per day sitting, as compared with those who spent less than 4 hours per day. Other durations of sitting or lying down were not significantly associated with cardiovascular risk.

## DISCUSSION

These prospective data from an ethnically diverse cohort of postmenopausal women indicate that both walking and vigorous exercise are associated with substantial reductions in the incidence of cardiovascular events. In contrast, prolonged time spent sitting predicts increased risk. We observed similar magnitudes of risk reduction with walking and vigorous exercise, and the results were similar among white women and black women as well as among women in different age groups and categories of body-mass index. These findings extend those of previous analyses from predominantly white populations[14-17] to a racially and ethnically diverse cohort of women in the United States. The results also lend further support to current federal exercise guidelines that endorse moderate-inten-

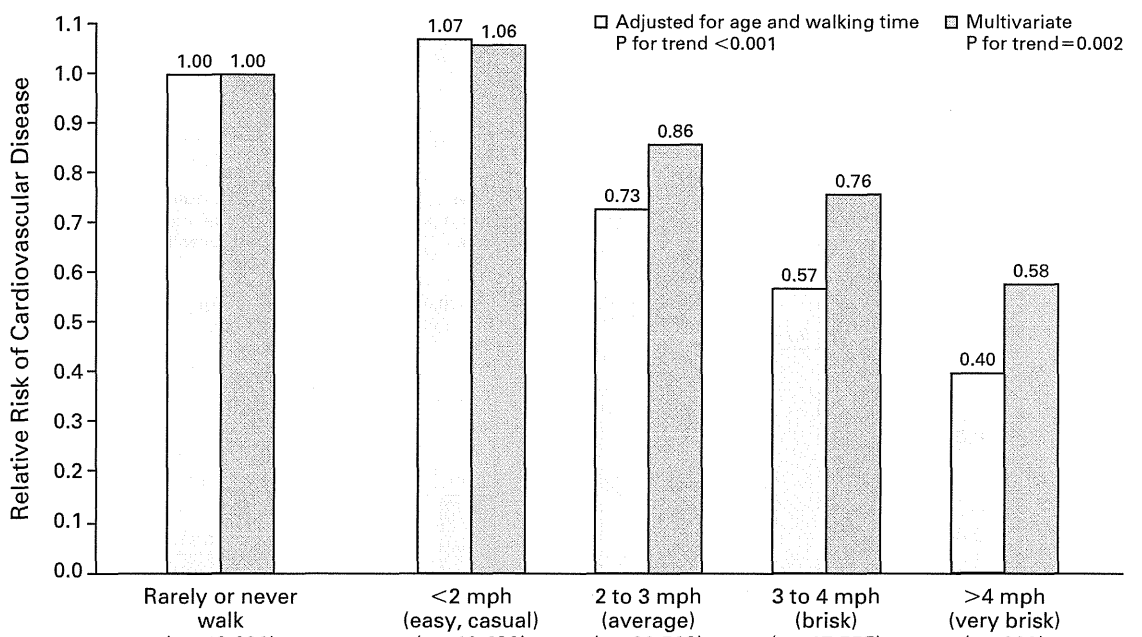


**Figure 4.** Multivariate Relative Risk of Cardiovascular Disease and Relative Risk Adjusted for Age and Walking Time, According to Walking Pace.

Multivariate relative risks were adjusted for age, time spent walking, smoking status (0, 1 to 14, 15 to 24, or ≥25 cigarettes per day), race or ethnic group, level of education, annual family income, body-mass index, waist-to-hip ratio, level of alcohol intake, parental history of premature myocardial infarction, age at menopause, use or nonuse of hormone-replacement therapy, percentage of calories from saturated fat, number of servings of fruit and vegetables per day, and dietary fiber intake. To convert values for distance to kilometers, multiply by 1.6.

sity exercise for at least 30 minutes on most, and preferably all, days of the week.[3,4] Women who either walked briskly or exercised vigorously at least 2.5 hours per week had a risk reduction of approximately 30 percent. Evidence of the applicability of these guidelines to nonwhite women is of particular importance because of the high prevalence of sedentary lifestyles, obesity, and related conditions in minority populations.[3]

Strengths of the present study include the prospective design, the large size, the racial and ethnic diversity of the cohort, the detailed assessment of physical activity as well as sedentary behavior, and the uniform and strict criteria for the coronary and cardiovascular end points. Women with diagnosed cardiovascular disease or cancer at base line and those who were nonambulatory (unable to walk at least one block) were excluded from the analyses. These exclusions and the prospective design minimized any influence of preexisting disease on the level of physical activity. Moreover, we performed secondary analyses excluding data from the first year of follow-up in order to minimize bias related to the presence of subclinical disease. The strong dose–response gradient observed between the physical-activity level and the reduced risk of cardiovascular disease and the consistency of the findings across strata of age, race, and body-mass index lend further credence to a causal interpretation. Other strengths of the study include the high follow-up rate and the detailed information about potential confounding variables.

Because our multivariate analyses controlled for several factors that could be considered to be intermediate biologic variables,[3] such as body-mass index and waist-to-hip ratio, and additional models controlled for history of hypertension, hypercholesterolemia, and diabetes, our analyses provide a conservative estimate of the relation between activity and cardiovascular disease. Physical activity may be associated with even greater reductions in cardiovascular risk — closer to the 50 percent reductions found in our age-adjusted analyses — given that the relative risks derived from the multivariate models estimate the effects of exercise without taking into account its favorable influence on adiposity and related morbidity.

Some limitations of our study also deserve attention. Physical activity was assessed by questionnaire, and some misclassification of exposure was inevitable. Nondifferential misclassification of exposure, however, would be expected to bias the risk estimate toward unity; thus, it cannot explain the strong inverse associations observed between the level of physical activity and the incidence of cardiovascular events. Despite the fact that we controlled for a large number of potentially confounding variables in our multivariate analyses, residual confounding by lifestyle-related factors cannot be excluded. Finally, our study population of volunteers in the Women's Health Initiative, although of more diverse racial and ethnic background and socioeconomic status than most previously studied cohorts, is not an entirely representative cross-section of women in the United States.

More than 40 epidemiologic studies have addressed the relation between exercise and cardiovascular disease,[1,2] but only one third of published studies have included women,[14-28] and few of these have specifically addressed the role of walking.[14-19] In previous studies, results for women have been generally similar to those for men, indicating that risk among both sexes is reduced by 30 to 50 percent with regular physical activity. Recent reports from several large-scale cohort studies involving women[14,15,20] have suggested that moderate and vigorous exercise have similar cardiovascular benefits, but these cohorts were predominantly white. Moreover, to our knowledge, no previous large-scale study has addressed the relation between walking and cardiovascular events in black women or the role of sitting after accounting for recreational energy expenditure in women. The evidence that moderate-intensity activity is associated with a similar magnitude of reduction in cardiovascular risk among white women and black women, among younger and older postmenopausal women, and across the spectrum of adiposity is important for the targeting of these diverse groups with health-promotion activities. The cardiovascular benefits of walking[29] and even moderate levels of physical fitness[27,30] also appear to apply to men.

An important role for both moderate and vigorous exercise in reducing cardiovascular risk is also biologically plausible. Increasing intensity or duration of exercise has a graded relation to improvements in lipid levels[3,31] and insulin sensitivity.[32] Moderate-intensity activity may produce reductions in diastolic blood pressure similar to those achieved with vigorous exercise and may produce even greater reductions in systolic blood pressure.[3] Moderate exercise coupled with modification of the diet led to a reduced risk of type 2 diabetes among subjects with impaired glucose tolerance.[33,34] Moreover, equivalent energy expenditure with moderate or vigorous exercise leads to similar reductions in adipose mass.[3] Finally, physical activity of any intensity has been linked to improvement in emotional well-being.[3]

In conclusion, these prospective data from a large and diverse cohort of postmenopausal women indicate that both walking and vigorous exercise are associated with substantial reductions in the risk of cardiovascular events. A graded inverse relation was observed among both white women and black women, lean women and obese women, and younger women and older women. Moreover, prolonged time spent sitting predicted increased risk. These findings lend support to current federal guidelines that endorse moderate-intensity activity, including walking. Although vigorous exercise should not be discouraged for those who choose a higher intensity of activity, our results indicate that moderate-intensity exercise confers substantial health benefits for postmenopausal women.

Supported by the National Heart, Lung, and Blood Institute and a research contract (N01-WH-3-2109) from the National Institutes of Health.

*We are indebted to the participants, investigators, and staff of the Women's Health Initiative for their outstanding dedication and commitment and to Philomena Quinn for her expert assistance.*

## APPENDIX

The following persons are members of the Women's Health Initiative Study Group. *Program office:* J.E. Rossouw, L. Pottern, S. Ludlam, J. McGowan, N. Morris (National Heart, Lung, and Blood Institute, Bethesda, Md.). *Clinical coordinating center:* R. Prentice, G. Anderson, A. LaCroix, R. Patterson, A. McTiernan (Fred Hutchinson Cancer Research Center, Seattle); S. Shumaker, P. Rautaharju (Bowman Gray School of Medicine, Winston-Salem, N.C.); E. Stein (Medical Research Labs, Highland Heights, Ky.); S. Cummings (University of California at San Francisco, San Francisco); J. Himes (University of Minnesota, Minneapolis); S. Heckbert (University of Washington, Seattle). *Clinical centers:* S. Wassertheil-Smoller (Albert Einstein College of Medicine, Bronx, N.Y.); J. Hays (Baylor College of Medicine, Houston); J. Manson (Brigham and Women's Hospital and Harvard Medical School, Boston); A.R. Assaf (Brown University, Providence, R.I.); L. Phillips (Emory University, Atlanta); S. Beresford (Fred Hutchinson Cancer Research Center, Seattle); J. Hsia (George Washington University Medical Center, Washington, D.C.); C. Ritenbaugh (Kaiser Permanente Center for Health Research, Portland, Oreg.); B. Caan (Kaiser Permanente Division of Research, Oakland, Calif.); J. Morley Kotchen (Medical College of Wisconsin, Milwaukee); B.V. Howard (Medstar Research Institute, Washington, D.C.); L. Van Horn (Northwestern University, Chicago and Evanston, Ill.); H. Black (Rush–Presbyterian–St. Luke's Medical Center, Chicago); M.L. Stefanick (Stanford Center for Research in Disease Prevention, Stanford University, Stanford, Calif.); D. Lane (State University of New York at Stony Brook, Stony Brook); R. Jackson (Ohio State University, Columbus); C.B. Lewis (University of Alabama at Birmingham, Birmingham); T. Bassford (University of Arizona, Tucson and Phoenix); M. Trevisan (State University of New York at Buffalo, Buffalo); J. Robbins (University of California at Davis, Sacramento); A. Hubbell (University of California at Irvine, Orange); H. Judd (University of California at Los Angeles, Los Angeles); R.D. Langer (University of California at San Diego, LaJolla and Chula Vista); M. Gass (University of Cincinnati, Cincinnati); M. Limacher (University of Florida, Gainesville and Jacksonville); D. Curb (University of Hawaii, Honolulu); R. Wallace (University of Iowa, Iowa City and Davenport); J. Ockene (University of Massachusetts, Worcester); N. Lasser (University of Medicine and Dentistry of New Jersey, Newark); M.J. O'Sullivan (University of Miami, Miami); K. Margolis (University of Minnesota, Minneapolis); R. Brunner (University of Nevada, Reno); G. Heiss (University of North Carolina, Chapel Hill); L. Kuller (University of Pittsburgh, Pittsburgh); K.C. Johnson (University of Tennessee, Memphis); R. Schenken (University of Texas Health Science Center, San Antonio); C. Allen (University of Wisconsin, Madison); G. Burke (Wake Forest University School of Medicine, Winston-Salem, N.C.); S. Hendrix (Wayne State University School of Medicine and Hutzel Hospital, Detroit).

## REFERENCES

1. Powell KE, Thompson PD, Caspersen CJ, Kendricks JS. Physical activity and the incidence of coronary heart disease. Annu Rev Public Health 1987;8:253-87.
2. Berlin JA, Colditz GA. A meta-analysis of physical activity in the prevention of coronary heart disease. Am J Epidemiol 1990;132:612-28.
3. Department of Health and Human Services. Physical activity and health: a report of the Surgeon General. Atlanta: Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
4. Pate RR, Pratt M, Blair SN, et al. Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 1995;273:402-7.
5. American College of Sports Medicine. Guidelines for exercise testing and prescription. 3rd ed. Philadelphia: Lea & Febiger, 1986.
6. Manson JE, Lee I-M. Exercise for women — how much pain for optimal gain? N Engl J Med 1996;334:1325-7.
7. Langer RD, White E, Lewis CE, et al. Baseline characteristics of the participants in the Observational Study of the Women's Health Initiative and reliability of baseline measures. Ann Epidemiol (in press).
8. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32:Suppl:S498-S504.
9. Wolf AM, Hunter DJ, Colditz GA, et al. Reproducibility and validity of a self-administered physical activity questionnaire. Int J Epidemiol 1994;23:991-9.
10. Curb D, McTiernan A, Heckbert SR, et al. Women's Health Initiative: outcomes. Ann Epidemiol (in press).
11. Kleinbaum DG, Kupper L, Morgenstern H, eds. Epidemiologic research: principles and quantitative methods. New York: Van Nostrand Reinhold, 1982.
12. SAS procedure guide, release 8.02 ed. Cary, N.C.: SAS Institute, 1999-2001.
13. Ware JE, Kosinski M, Keller SD. SF-36 physical and mental health summary scales: a user's manual. Boston: The Health Institute, 1994.
14. Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking compared with vigorous exercise in the prevention of coronary heart disease in women. N Engl J Med 1999;341:650-8.
15. Lee I-M, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: Is "no pain, no gain" passé? JAMA 2001;285:1447-54.
16. Sesso HD, Paffenbarger RS Jr, Ha CY, Lee I-M. Physical activity and cardiovascular disease risk in middle-aged and older women. Am J Epidemiol 1999;150:408-16.
17. LaCroix AZ, Leveille SG, Hecht JA, Grothaus LC, Wagner EH. Does walking decrease the risk of cardiovascular disease hospitalizations and death in older adults? J Am Geriatr Soc 1996;44:113-20.
18. Lemaitre RN, Heckbert SR, Psaty BM, Siscovick DS. Leisure-time physical activity and the risk of nonfatal myocardial infarction in postmenopausal women. Arch Intern Med 1995;155:2302-8.
19. Folsom AR, Arnett DK, Hutchinson RG, Liao F, Clegg LX, Cooper LS. Physical activity and incidence of coronary heart disease in middle-aged women and men. Med Sci Sports Exerc 1997;29:901-9.
20. Kushi LH, Fee RM, Folsom AR, Mink PJ, Anderson KE, Sellers TA. Physical activity and mortality in postmenopausal women. JAMA 1997;277:1287-92.
21. Brunner D, Manelis G, Modan M, Levin S. Physical activity at work and the incidence of myocardial infarction, angina pectoris and death due to ischemic heart disease: an epidemiologic study in Israeli collective settlements (Kibbutzim). J Chronic Dis 1974;27:217-33.
22. Salonen JT, Puska P, Tuomilehto J. Physical activity and risk of myocardial infarction, cerebral stroke and death: a longitudinal study in Eastern Finland. Am J Epidemiol 1982;115:526-37.
23. Lapidus L, Bengtsson C. Socioeconomic factors and physical activity in relation to cardiovascular disease and death: a 12 year follow up of participants in a population study of women in Gothenburg, Sweden. Br Heart J 1986;55:295-301.
24. Kannel WB, Sorlie P. Some health benefits of physical activity: the Framingham Study. Arch Intern Med 1979;139:857-61.
25. Magnus K, Matroos A, Strackee J. Walking, cycling, or gardening, with or without seasonal interruption, in relation to acute coronary events. Am J Epidemiol 1979;110:724-33.
26. Scragg R, Stewart A, Jackson R, Beaglehole R. Alcohol and exercise in myocardial infarction and sudden coronary death in men and women. Am J Epidemiol 1987;126:77-85.
27. Blair SN, Kohl HW III, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality: a prospective study of healthy men and women. JAMA 1989;262:2395-401.
28. Fraser GE, Strahan TM, Sabate J, Beeson WL, Kissinger D. Effects of traditional coronary risk factors on rates of incident coronary events in a low-risk population: the Adventist Health Study. Circulation 1992;86:406-13.
29. Hakim AA, Petrovitch H, Burchfiel CM, et al. Effects of walking on mortality among nonsmoking retired men. N Engl J Med 1998;338:94-9.
30. Ekelund L-G, Haskell WH, Johnson JL, Whaley FS, Criqui MH, Sheps DS. Physical fitness as predictor of cardiovascular mortality in asymptomatic North American men: the Lipid Research Clinics Mortality Follow-up Study. N Engl J Med 1988;319:1379-84.
31. Williams PT. High-density lipoprotein cholesterol and other risk factors for coronary heart disease in female runners. N Engl J Med 1996;334:1298-303.

**32.** Mayer-Davis EJ, D'Agostino R Jr, Karter AJ, et al. Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study. JAMA 1998;279:669-74.
**33.** Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.
**34.** Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.

# エキスパートレビューのフォーマット

| | |
|---|---|
| 論文名 | Walking compared with vigorous exercise for the prevention of cardiovascular events in women. |
| 著　者 | Manson JE, Greenland P, LaCroix AZ, Stefanick ML, Mouton CP, Oberman A, Perri MG, Sheps DS, Pettinger MB, Siscovick DS. |
| 雑誌名 | N Engl J Med. |
| 巻・号・頁 | 347(10)巻　　716-725ページ |
| 発行年 | 2002 |
| PubMedリンク | http://www.ncbi.nlm.nih.gov/pubmed/1221394 |

| 対象の内訳 | | ヒト | 動物 | 地　域 | 欧米 | 研究の種類 | 縦断研究 |
|---|---|---|---|---|---|---|---|
| | 対象 | 一般健常者 | 空白 | | (　　　) | | コホート研究 |
| | 性別 | 女性 | (　　　) | | (　　　) | | (　　　) |
| | 年齢 | 50-79歳 | | | (　　　) | | 前向き研究 |
| | 対象数 | 10000以上 | 空白 | | (　　　) | | (　　　) |

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| 調査の方法 | 質問紙 | (　　　) | | | | | |
| アウトカム | 予　防 | 心疾患予防 | な し | な し | な し | (　　) | (　　　) |
| | 維持・改善 | な し | な し | な し | な し | (　　) | (　　　) |

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| 図 表 | |
| 図表掲載箇所 | |
| 概 要<br>(800字まで) | 背景：活発な運動と比べて、歩行が心血管疾患の予防に役割をもつかという点については争点のままで残っている。特に、少数派の人種もしくは民族の女性に対するデータは乏しい。方法：我々は、Women's Health Initiative Observational Study における50～79歳の73743名の閉経後女性に対して、冠動脈および全心血管異常の発生の予測因子として、総身体活動スコア、歩行、活発な運動、および座業時間をプロスペクティブ(前向き)に調査した。ベースラインでは、参加者は心血管疾患とガンに罹患しておらず、すべての参加者が身体活動に関する詳細な質問紙を終了した。我々は冠動脈疾患(CHD)と1551回の全心血管異常と345の新たに診断された症例を記録した。結果：増加する身体活動スコアは、冠動脈の異常と全心血管異常の両方のリスクとの間に、格付けされ、強い負の相関がみられた。白人の女性と黒人の女性においては同様の知見がみられた。代謝当量(METs)で測定されたエネルギー消費の増加からみた5段階における年齢補正による相対リスクは、それぞれ1.00、0.73、0.69、0.68、および0.47(P < 0.001)であった。多変量解析においては、総METsと心血管異常のリスクの負の傾向は強い状態を維持した(5段階の増加に対する相対リスク、1.00、0.89、0.81、0.78、および0.72; P < 0.001)。歩行と活発な運動は同様のリスク減少に関連しており、その結果は、人種、年齢、またはBMIによって実質的に異なることはなかった。活発な歩行速度や少ない座業時間もリスクを低くすると予測される。結論：これらのプロスペクティブ(前向き)なデータは、両方の歩行および活発な運動が閉経後の女性における冠動脈および心血管の異常を実質的に減少させることに関係があり、人種もしくは民族、年齢、BMIにもかかわりがないことを示唆するものである。長時間の座業という予測因子は、心血管疾患のリスクを増加させた |
| 結 論<br>(200字まで) | ウォーキング、および激しい運動ともに、循環器病リスクを減らす。 |
| エキスパートによるコメント<br>(200字まで) | 日本人にとってポピュラーな歩行という活動が循環器疾患の発症を減らすことは、本邦の健康づくりを考える上で重要である。 |

担当者　宮地 劉

# Leisure-Time Physical Activity, Body Size, and Colon Cancer in Women

*María Elena Martínez, Edward Giovannucci, Donna Spiegelman, David J. Hunter, Walter C. Willett, Graham A. Colditz**

*For the Nurses' Health Study Research Group*

***Background:*** **Physical inactivity and high body mass index (weight in kilograms divided by height in square meters) have been linked to increased risk of colon cancer. However, none of the few prospective studies in women has shown a statistically significant reduction in colon cancer incidence or mortality associated with increased leisure-time physical activity.** ***Purpose:*** **In this prospective study, we asked whether leisure-time physical activity, body mass index, or body fat distribution could significantly influence the risk of colon cancer in women.** ***Methods:*** **The participants in this study were enrolled in the Nurses' Health Study, which began in 1976. Every 2 years, the women provided additional personal information and information on medical risk factors and major medical events. The time spent per week at a variety of leisure-time physical activities was determined, and the time spent at each activity was multiplied by its typical energy expenditure, expressed in terms of metabolic equivalents or METs. The resulting values for each woman were added to yield an MET-hours-per-week score. Reported diagnoses of colon cancer were confirmed by review of hospital records and pathology reports. Relative risks and associated 95% confidence intervals were calculated.** ***Results:*** **In multivariate analyses that included body mass index, women who expended more than 21 MET-hours per week on leisure-time physical activity had a relative risk of colon cancer of 0.54 (95% confidence interval [CI] = 0.33-0.90) in comparison with women who expended less than 2 MET-hours per week. Women who had a body mass index greater than 29 kg/m$^2$ had a relative risk of colon cancer of 1.45 (95% CI = 1.02-2.07) in comparison with women who had a body mass index less than 21 kg/m$^2$. A tendency toward higher colon cancer risk was observed for increasing waist-to-hip ratio (relative risk = 1.48 [95% CI = 0.88-2.49] for comparison of the highest quintile ratio [>0.833] to the lowest [<0.728]).** ***Conclusions and Implications:*** **The significant inverse association between leisure-time physical activity and incidence of colon cancer in women in this study is consistent with what has been found in men. Recommendations to increase physical activity and maintain lean body weight should receive greater emphasis as part of a feasible approach to the prevention of colon cancer. [J Natl Cancer Inst 1997;89:948-55]**

Physical inactivity has been related to a higher risk of colon cancer (*1-37*), which is the second most common cause of cancer mortality in the United States (*38*). However, of the few prospective studies of physical activity and colon cancer in women (*8,13,17,18,26,30,37*), none has shown a statistically significant reduction in cancer incidence or mortality associated with increased leisure-time activity. Furthermore, relatively few studies have assessed colon cancer risk by anatomic subsite (*3,5,6,9,10,14,15,27,29,32,37*). Additional data (*39-52*) also support a direct association between body mass index (BMI) and colon cancer in men, but the evidence is weaker for women.

The considerably stronger evidence relating physical inactivity to a higher risk of colon cancer in men than in women is enigmatic. This divergence may reflect the scarcity of data for women or the inappropriateness for women of the activity instruments used. It is also possible that the adverse effects of inactivity on colon cancer risk differ by sex. Because of the paucity of data on women, we examined prospectively the relationship between leisure-time physical activity and the risk of colon cancer in the Nurses' Health Study. We also examined whether abdominal fat distribution, absolute weight, and weight change from age 18 years to adulthood are associated with the risk of colon cancer. We have previously published results on BMI and colon cancer in this cohort on the basis of 191 cases of cancer that occurred from 1976 through 1984 (*44*). Because of previous reports, we hypothesized that any influence of physical activity, body size, and fat distribution would be strongest for the distal colon.

## Subjects and Methods

### Nurses' Health Study Cohort

In 1976, 121 701 female registered nurses 30-55 years of age were enrolled in the Nurses' Health Study by return of a mailed questionnaire. Every 2 years, follow-up questionnaires are mailed to the participants to update information on risk factors and major medical events. The participants in the present study were women who were free of cancer (except non-melanoma skin cancer), ulcerative colitis, or Crohn's disease at the beginning of the follow-up period and who provided information on the risk factors of interest. The protocol for the study

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*See* "Notes" following "References."

was approved by the Human Research Committee of the Brigham and Women's Hospital in Boston, MA.

### Assessment of Physical Activity

On the 1986 questionnaire, we included a section on recreational or leisure-time physical activity during the past year. Participants reported the average time per week spent for each of the following activities: walking or hiking outdoors (including walking while playing golf); jogging (slower than 10 minutes per mile); running (10 minutes per mile or faster); bicycling (including use of a stationary machine); lap swimming; playing tennis; playing squash or racquet ball; and calisthenics, aerobics, aerobic dance, or use of a rowing machine. In addition, each woman reported the number of flights of stairs that she climbed daily and her usual walking pace. The reported time spent at each activity per week was multiplied by its typical energy expenditure requirements expressed in metabolic equivalents (METs) (*53*) and added together to yield an MET-hours-per-week score. One MET, the energy expended while sitting quietly, is equivalent to 3.5 mL of oxygen uptake per kilogram of body weight per minute for a 70-kg adult. Body weight was not included in the derivation of energy expenditure of physical activity to avoid confounding the energy expenditure variable by body weight. We used the following MET values for each activity: jogging, 7.0; running, 12.0; bicycling, 7.0; swimming, 7.0; playing tennis, 7.0; playing squash or racquet ball, 9.0; calisthenics, aerobics, aerobic dance, or use of a rowing machine, 6.5; and climbing stairs, 8.0. Walking was assigned an MET value correspondent to the reported pace: easy, 2.5; normal, 3.0; brisk, 4.0; or very brisk, 4.5.

Several groups (*54-56*) have investigated the reliability and validity of questionnaires designed to assess physical activity, and instruments such as ours appear to be acceptably valid. We assessed the validity of the self-reported physical activity questionnaire in a sample of 147 nurses from another, similar cohort study by comparing this questionnaire with the average of four, 7-day activity diaries recorded over a 1-year period (*57*). The Pearson correlation coefficient between the MET-hour score measured by the questionnaire and the average of the diaries was .46. After adjustment for within-person variation in the diaries, the deattenuated correlation was .56.

### Assessment of Body Size Parameters

In 1976, women reported their height. Body weight was reported in each biennial questionnaire. In 1980, 80% of the participants recorded their weight at age 18. In 1986, the nurses were instructed to measure (to the nearest quarter of an inch) their waist at the umbilicus and their hips at the largest circumference between the waist and thighs; the women took these measurements while they were standing and without bulky clothing (*58*). Sixty-nine percent of the participants provided circumference measures. This low response was due to the fact that the response to these questions was optional.

We used BMI (weight in kilograms divided by height in square meters) as the primary measure of adiposity, waist-to-hip ratio as the measure of relative distribution of fat, and waist circumference as an estimate of abdominal fat. BMI is minimally correlated with height in this population ($r = -.03$) and highly correlated with weight ($r = .86$) (*59*). We categorized women into groups with BMI corresponding to less than 21, 21-22.9, 23-24.9, 25-28.9, and 29 or more kg/m$^2$. We also calculated weight change from 18 years of age to 1980.

We evaluated the precision of self-reported anthropometric measures in a sample of 140 cohort members (*58*). Trained technicians visited the substudy participants twice, approximately 6 months apart, to measure current weight and waist and hip circumferences. The Pearson correlation between self-report and the average of the technicians' two measurements was .97 for weight, .87 for waist circumference, .81 for hip circumference, and .66 for waist-to-hip ratio.

### Identification of Cases

The ascertainment of cases of colorectal cancer has been detailed elsewhere (*60*). On each biennial follow-up questionnaire, we asked whether cancer of the colon or rectum had been diagnosed during the previous 2 years. We also used the National Death Index and the U.S. Postal Service to identify fatalities; we estimate that more than 98% of deaths were ascertained (*61*). When a participant (or the next of kin for decedents) reported a diagnosis of cancer of the colon or rectum on our follow-up questionnaire, we asked her (or the next of kin) for permission to obtain hospital records and pathology reports pertaining to this diagnosis. A study physician blinded to the exposure information reviewed the medical records to extract information on the histologic type, the anatomic location, and the stage of the cancer. Proximal colon cancers were defined as those from the cecum to and including the splenic flexure, and distal colon cancers were defined as those in the descending and sigmoid colon. Cancers other than adenocarcinoma were excluded. In the analysis of colon cancer overall, we included cases lacking information for anatomic location, since analyses limited to cases with complete information yielded results virtually identical to those of analyses excluding these cases.

### Statistical Analysis

Physical activity, waist circumference, and waist-to-hip ratio were analyzed in quintiles according to the distribution of the study population. BMI was categorized as described earlier, and change in weight from 18 years of age to 1980 was divided into informative increments on the basis of an examination of the distribution of values. Person-years of follow-up were computed from the date of return of the 1980 questionnaire (for BMI and change in weight from age 18 to 1980) or the 1986 questionnaire (for physical activity, waist circumference, and waist-to-hip ratio) to the date of colorectal cancer diagnosis, death from any cause, or May 31, 1992, whichever came first. Relative risks (RRs) and their 95% confidence intervals (CIs) were calculated with the lowest quintile as the reference for all variables except change in weight from age 18 to 1980, for which women with stable weight (±5 kg) were used as the reference group. A limited assessment of physical activity obtained in the 1980 questionnaire was used in the analysis of BMI.

We used the Mantel–Haenszel estimator and logistic regression models to adjust for age (across 5-year categories) and potentially confounding variables (*62*). A priori potential risk factors for colorectal cancer included in the models were age (in six categories), history of colorectal cancer in a parent or sibling, smoking (pack-years of smoking after smoking for a period of 35 years), aspirin use (times per week), intake of red meat, and alcohol consumption. We also included use of postmenopausal hormones (premenopausal status, never use, past use, or current use) in the models because these hormones are related to body fat distribution (*63*) and to colorectal cancer in this cohort. We used the median of each category as a continuous variable to calculate the tests for trend; the $P$ values for these tests are two-sided.

## Results

The 1980-1992 cohort for this study comprised 89 448 eligible women; 396 cases of colon cancer (185 distal, 159 proximal, and 52 unknown site) were identified during 1 012 375 person-years of follow-up. During 1986-1992, we identified 212 cases of colon cancer (97 distal, 88 proximal, and 27 unknown site) among 67 802 eligible participants who accrued 385 819 person-years of follow-up.

Compared with women who were less physically active, those who were more active consumed more energy, less total and animal fat, and more dietary fiber; they were also leaner and had a lower waist-to-hip ratio (Table 1). The most active group also included a lower proportion of women who were current smokers, a lower proportion of aspirin users, and a higher proportion of multivitamin users and users of postmenopausal hormones. There was no appreciable difference across physical activity quintiles for alcohol consumption, family history of colorectal cancer in first-degree relatives, previous endoscopy, or previous colorectal polyps.

### Physical Activity

Walking, the most common type of leisure-time physical activity, was reported by 70% of the respondents. In multivariate analysis, the risk of colon cancer was inversely related to leisure-time physical activity (Table 2). Compared with women who expended less than 2 MET-hours per week, those who expended more than 21 MET-hours had an RR of 0.54 (95% CI = 0.33-

**Table 1.** Characteristics of the study population according to quintiles of MET-hours* per week

| Characteristic† | MET-hours per week <2 | 2-4 | 5-10 | 11-21 | >21 |
|---|---|---|---|---|---|
| Participants, No. | 11 264 | 9032 | 11 651 | 10 641 | 10 287 |
| Mean daily intake‡ | | | | | |
| Energy, kcal | 1710 | 1763 | 1787 | 1792 | 1804 |
| Total fat, g | 60.3 | 59.3 | 58.7 | 57.6 | 56.3 |
| Animal fat, g | 34.5 | 33.8 | 33.1 | 32.3 | 31.7 |
| Dietary fiber, g | 16.0 | 16.8 | 17.3 | 18.0 | 18.7 |
| Alcohol, g | 6.1 | 5.9 | 5.9 | 6.4 | 6.9 |
| Mean body mass index, kg/m²§ | 26.0 | 25.3 | 25.0 | 24.5 | 24.0 |
| Mean waist-to-hip ratio | 0.796 | 0.788 | 0.783 | 0.778 | 0.773 |
| Current smoker, % | 26.4 | 22.5 | 19.6 | 16.4 | 16.8 |
| History of colorectal cancer,‖ % | 8.0 | 7.9 | 8.3 | 8.5 | 8.2 |
| Aspirin use,¶ % | 15.6 | 15.7 | 17.4 | 16.1 | 14.8 |
| Multivitamin use, % | 38.4 | 39.6 | 41.3 | 44.2 | 46.1 |
| Postmenopausal hormone use, % | 14.7 | 15.9 | 16.7 | 17.6 | 18.4 |
| Previous endoscopy, % | 17.2 | 17.2 | 17.2 | 17.9 | 17.8 |
| Previous colorectal polyp, % | 1.1 | 1.0 | 1.0 | 1.0 | 0.9 |

*Metabolic equivalent (MET)-hours = sum of the average time per week spent in each leisure-time physical activity multiplied by the MET value for each activity; MET value = (caloric need/kilogram body weight per hour activity)/(caloric need/kilogram body weight per hour at rest).

†Standardized for age at baseline.

‡Adjusted to total energy intake by regression analysis (except for alcohol).

§Weight in kilograms/height in square meters.

‖History of colorectal cancer in a parent or sibling.

¶Regular use of aspirin from 1980 to 1984.

0.90; *P* for trend = .03). This inverse association was essentially limited to cancer of the distal colon; women in the highest quintile were approximately 70% less likely to develop cancer at this site (RR = 0.31; 95% CI = 0.12-0.77; *P* for trend = .01) than women in the lowest quintile. No significant trend was found for cancer of the proximal colon. Excluding BMI from the multivariate models had no appreciable effect on the results.

We assessed the relationship between colon cancer and the intensity of activity by looking at the amount of time spent doing activities of low, moderate, or high intensity. The intensity cat-

**Table 2.** Relative risk (RR) of colon cancer according to level of leisure-time physical activity (in MET-hours*) in 1986,† Nurses' Health Study, 1986-1992

| | MET-hours per week <2 | 2-4 | 5-10 | 11-21 | >21 | Two-sided *P* for trend‡ |
|---|---|---|---|---|---|---|
| Person-years | 63 734 | 51 413 | 66 435 | 60 769 | 58 817 | |
| Colon cancer§ | | | | | | |
| No. of cases | 47 | 26 | 36 | 29 | 23 | |
| Age-adjusted RR | 1.00 (referent) | 0.69 | 0.74 | 0.65 | 0.52 | |
| Multivariate RR‖ | 1.00 (referent) | 0.71 | 0.78 | 0.67 | 0.54 | .03 |
| 95% CI¶ | — | 0.44-1.15 | 0.50-1.20 | 0.42-1.07 | 0.33-0.90 | |
| Distal colon cancer | | | | | | |
| No. of cases | 21 | 15 | 17 | 14 | 6 | |
| Age-adjusted RR | 1.00 (referent) | 0.89 | 0.78 | 0.70 | 0.31 | |
| Multivariate RR‖ | 1.00 (referent) | 0.92 | 0.81 | 0.71 | 0.31 | .01 |
| 95% CI¶ | — | 0.48-1.79 | 0.43-1.55 | 0.36-1.41 | 0.12-0.77 | |
| Proximal colon cancer | | | | | | |
| No. of cases | 19 | 8 | 15 | 11 | 13 | |
| Age-adjusted RR | 1.00 (referent) | 0.53 | 0.76 | 0.61 | 0.73 | |
| Multivariate RR‖ | 1.00 (referent) | 0.54 | 0.79 | 0.62 | 0.77 | .67 |
| 95% CI¶ | — | 0.23-1.22 | 0.40-1.56 | 0.30-1.32 | 0.38-1.58 | |

**See* footnote to Table 1 for definition and calculation of MET-hours.

†Data were based on 67 802 respondents. Data on leisure-time physical activity were missing for 51 case patients and 84 651 person-years.

‡Test for trend was calculated by use of the median of each MET-hours per week category as a continuous variable in the multiple regression model.

§Includes 22 cases lacking data on anatomic site.

‖Adjusted for age, cigarette smoking, family history of colorectal cancer, body mass index, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

¶CI = confidence interval.

egories were first created by including those activities corresponding to the range in METs for each category (<3 for low, 3-6 for moderate, and >6 for high). The amount of time spent in these activities was then categorized for the analyses. The multivariate RR for colon cancer for women who engaged in activities of moderate intensity for 1 hour or more per day was 0.69 (95% CI = 0.52-0.90) relative to women who participated in these activities for less than 1 hour per day. A similar reduction in risk was observed for activities of high intensity (RR = 0.61 [95% CI = 0.43-0.86] for ≥30 minutes per day compared with <30 minutes per day). There was no reduction in risk for activities of low intensity (RR = 1.54 [95% CI = 0.94-2.50] for ≥1 hour per day compared with <1 hour). When these variables were included in one multivariate model simultaneously, the RRs were only slightly attenuated.

Using data from our validation study (*57*), we corrected the estimated RRs and their respective 95% CIs for bias due to measurement error (*64*). For a difference of 30 MET-hours per week (approximately equal to 1 hour of brisk walking or 30 minutes of jogging or biking every day), the corrected RR adjusted for age, family history, and BMI was 0.38 (95% CI = 0.09-1.63) compared with the uncorrected value of 0.77 (95% CI = 0.52-1.13).

### BMI and Weight Change From Age 18 Years to Adulthood

The RR for colon cancer associated with a BMI of greater than 29 kg/m$^2$ was 1.45 (95% CI = 1.02-2.07; *P* for trend = .04) (Table 3). Similar to the observation for physical activity, this increase in risk was due largely to a strong association with cancer of the distal colon. Women in the upper category of BMI were at almost twice the risk of developing cancer of the distal colon as those in the lower category (RR = 1.96; 95% CI = 1.18-3.25; *P* for trend = .004). The RR for proximal colon cancer associated with BMI was weaker, and no significant trend was observed. Excluding physical activity from the multivariate models made no appreciable difference in the overall results. When we conducted analyses for BMI excluding current smokers, the results were not appreciably altered. In these analyses, the RRs for the upper compared with the lower quintile of BMI were 1.48 (95% CI = 0.95-2.31) for colon cancer overall, 2.04 (95% CI = 1.14-3.69) for distal colon cancer, and 1.28 (95% CI = 0.56-2.92) for proximal colon cancer.

After adjustment for BMI at age 18, weight gain from 18 years of age to 1980 was not appreciably associated with a higher risk of colon cancer overall. For colon cancer overall, women who gained 20 kg or more from age 18 to 1980 had an RR of 1.08 (95% CI = 0.79-1.48) compared with those with stable weight (±5 kg); however, the corresponding RR for distal colon cancer was stronger (RR = 1.56; 95% CI = 0.97-2.49).

### Waist-to-Hip Ratio and Waist Circumference

A tendency toward higher risk of colon cancer with increasing waist-to-hip ratio was observed (Table 4). Women in the highest quintile of waist-to-hip ratio had an RR for colon cancer of 1.48 (95% CI = 0.88-2.49) compared with women in the lowest quintile; however, the trend was not statistically significant (*P* = .16). The corresponding RR for distal colon cancer was stronger but less precise (RR = 1.79; 95% CI = 0.82-3.90; *P* for trend = .11). Although a positive association was also seen for cancer of the proximal colon, the point estimates were imprecise and no monotonic trend was observed. After adjustment for BMI, the results for waist-to-hip ratio were essentially unchanged.

Waist circumference was also positively, but not signifi-

**Table 3.** Relative risk (RR) of colon cancer according to body mass index (BMI*) in 1980,† Nurses' Health Study, 1980-1992

| | BMI, kg/m$^2$ | | | | | |
|---|---|---|---|---|---|---|
| | <21 | 21-22.9 | 23-24.9 | 25-28.9 | ≥29 | Two-sided *P* for trend‡ |
| Person-years | 215 722 | 246 238 | 203 842 | 200 472 | 140 048 | |
| Colon cancer§ | | | | | | |
| No. of cases | 57 | 94 | 78 | 91 | 73 | |
| Age-adjusted RR | 1.00 (referent) | 1.32 | 1.21 | 1.35 | 1.58 | |
| Multivariate RR‖ | 1.00 (referent) | 1.31 | 1.16 | 1.29 | 1.45 | .04 |
| 95% CI¶ | — | 0.94-1.82 | 0.82-1.63 | 0.92-1.80 | 1.02-2.07 | |
| Distal colon cancer | | | | | | |
| No. of cases | 25 | 38 | 39 | 41 | 41 | |
| Age-adjusted RR | 1.00 (referent) | 1.25 | 1.43 | 1.48 | 2.16 | |
| Multivariate RR‖ | 1.00 (referent) | 1.24 | 1.37 | 1.40 | 1.96 | .004 |
| 95% CI¶ | — | 0.75-2.04 | 0.83-2.27 | 0.85-2.31 | 1.18-3.25 | |
| Proximal colon cancer | | | | | | |
| No. of cases | 23 | 39 | 33 | 37 | 25 | |
| Age-adjusted RR | 1.00 (referent) | 1.33 | 1.27 | 1.34 | 1.28 | |
| Multivariate RR‖ | 1.00 (referent) | 1.33 | 1.20 | 1.29 | 1.26 | .54 |
| 95% CI¶ | — | 0.79-2.22 | 0.71-2.05 | 0.76-2.18 | 0.71-2.23 | |

**See* Table 1 and text for definition and calculation of BMI.

†Data were based on 89 448 respondents; BMI data were missing for three case patients and 6053 person-years.

‡Test for trend was calculated by use of the median of each BMI category as a continuous variable in the multiple regression model.

§Includes 52 cases lacking data on anatomic site.

‖Adjusted for age, cigarette smoking, family history of colorectal cancer, leisure-time physical activity, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

¶CI = confidence interval.

cantly, associated with the risk of colon cancer. The RR for colon cancer overall was 1.48 (95% CI = 0.89-2.46) for women whose waist circumference was greater than 34 inches compared with women whose waist circumference was 27.5 inches or less; for distal colon cancer, the RR was 1.47 (95% CI = 0.71-3.06). After adjustment for BMI, the corresponding RRs were 1.16 (95% CI = 0.61-2.21) for colon cancer overall and 1.09 (95% CI = 0.42-2.79) for distal colon cancer.

Using validation data on waist and hip circumference (*58*), we corrected the estimated RRs and their CIs for bias due to measurement error. After adjustment for age, family history of colorectal cancer, and physical activity, the corrected RR for colon cancer overall associated with a difference in waist-to-hip ratio of 0.20 (approximately equal to the difference between the medians of the upper and lower quintiles) was 2.84 (95% CI = 0.39-20.51) compared with the uncorrected RR of 1.31 (95% CI = 0.91-1.90).

## Discussion

In these prospective data, an increasing level of leisure-time physical activity was associated with a decrease in the incidence of colon cancer. As noted earlier, to our knowledge, none of the published prospective studies of women has reported a significant association between colon cancer incidence or mortality and recreational physical activity (*8,13,18,26,30,37*). It is difficult to address the discrepancy between the findings in these other studies and ours because of the wide variation in methodology. Some studies used colorectal cancer incidence as an end point (*8,18,37*), one focused on fatal colon cancer and considered a combination of activity at work and play (*26*), one suffered from a lack of power due to a small sample size (*13*), and one did not specifically target physical activity in the report (*30*). As shown in previous studies of men (*5,15*), including our own study (*29*), and in studies of men and women (*10,14,32*), the protective effect was stronger for cancer of the distal colon than for cancer of the proximal colon; however, in one study (*37*), the association was stronger for cancer of the proximal colon. These findings are also consistent with those for distal colon adenomas in this cohort (*65*), where stronger effects were seen for large adenomas, suggesting that physical inactivity promotes the growth of these polyps. A higher BMI was also associated with a 50% increase in the risk of colon cancer and an almost doubled risk of distal colon cancer. In addition, waist-to-hip ratio, used as a measure of the relative distribution of body fat, was positively, but not significantly, associated with the risk of colon cancer.

Most published studies of physical activity and colon cancer in women (*4,10,12-14,17,20-22,25,31,34-37*) have used a measure of occupational activity or a combination of occupational and leisure-time activities. It is possible that ascertainment of occupational physical activity is better in men than in women. Slattery et al. (*22*) noted that the activities of housewives are usually excluded from this assessment. Since there are sometimes fewer women in jobs having higher occupational activity levels, these women are statistically uninformative or usually combined with those in lower activity levels because of small numbers (*4,12,30*), thus providing narrow levels of activity. In addition, to our knowledge, only five of the published studies assessing recreational activities (*20,24,28,29,36*) have applied a factor of energy expenditure, such as MET equivalents, which takes into account the intensity of the activities measured. We observed a reduction in the risk of colon cancer for women who engaged in moderate or vigorous activity, but no reduction was seen for activities of low intensity, such as easy-paced walking.

Several mechanisms for a protective effect of physical activity have been proposed (*66*). They include decreased gastroin-



**Table 4.** Relative risk (RR) of colon cancer according to waist-to-hip ratio in 1986,* Nurses' Health Study, 1986-1992

| | Waist-to-hip ratio | | | | | |
|---|---|---|---|---|---|---|
| | <0.728 | 0.728-0.758 | 0.759-0.790 | 0.791-0.833 | >0.833 | Two-sided *P* for trend† |
| Person-years | 54 893 | 56 555 | 51 681 | 48 387 | 54 886 | |
| Colon cancer‡ | | | | | | |
| No. of cases | 21 | 29 | 24 | 38 | 49 | |
| Age-adjusted RR | 1.00 (referent) | 1.19 | 0.99 | 1.46 | 1.59 | |
| Multivariate RR§ | 1.00 (referent) | 1.18 | 0.97 | 1.51 | 1.48 | .16 |
| 95% CI‖ | — | 0.67-2.07 | 0.54-1.74 | 0.88-2.58 | 0.88-2.49 | |
| Distal colon cancer | | | | | | |
| No. of cases | 9 | 17 | 9 | 17 | 24 | |
| Age-adjusted RR | 1.00 (referent) | 1.64 | 0.90 | 1.55 | 1.91 | |
| Multivariate RR§ | 1.00 (referent) | 1.64 | 0.87 | 1.64 | 1.79 | .11 |
| 95% CI‖ | — | 0.73-3.69 | 0.35-2.20 | 0.73-3.71 | 0.82-3.90 | |
| Proximal colon cancer | | | | | | |
| No. of cases | 7 | 12 | 11 | 18 | 19 | |
| Age-adjusted RR | 1.00 (referent) | 1.48 | 1.38 | 2.01 | 1.71 | |
| Multivariate RR§ | 1.00 (referent) | 1.45 | 1.30 | 2.06 | 1.66 | .34 |
| 95% CI‖ | — | 0.57-3.68 | 0.50-3.35 | 0.86-4.96 | 0.69-3.99 | |

*Results based on 52 687 respondents to questionnaire on waist and hip circumference.

†Test for trend was calculated by use of the median of each waist-to-hip ratio category as a continuous variable in the multiple regression model.

‡Includes 18 cases lacking data on anatomic site.

§Adjusted for age, cigarette smoking, family history of colorectal cancer, leisure-time physical activity, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

‖CI = confidence interval.