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Physical Activity and Colorectal Cancer Risk by Sex, Race/Ethnicity, and Subsite: The Multiethnic Cohort Study

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Abstract

Physical activity has been associated with a lower risk of colorectal cancer. However, data is lacking on whether the association is consistent between sexes and across different races/ethnicities and anatomical subsites of tumors. We analyzed data from the Multiethnic Cohort in Hawaii and California, consisting of mostly African Americans, Native Hawaiians, Japanese Americans, Latinos, and whites aged 45–75 years at recruitment. During a mean follow-up of 16.8 years, 4,430 invasive adenocarcinoma cases of the colorectum were identified among 172,502 eligible participants. Cox proportional hazards models were used to estimate the hazard ratio (HR) and 95% confidence interval (CI). The multivariate-adjusted HR (95% CI) for the highest vs. lowest quintiles of physical activity (metabolic equivalent hours of moderate or vigorous activities per day) was 0.76 (0.66, 0.87) in men (*P* for trend <0.001) and 0.94 (0.80, 1.11) in women (*P* for trend = 0.53, *P* for heterogeneity by sex = 0.07). Sleeping and sitting hours were not associated with colorectal cancer risk both in men and women. In men, the inverse association was statistically significant among African Americans and Japanese Americans, for right colon and rectal cancer, and in all body mass index (BMI) groups, although heterogeneity tests were not significant across race/ethnicity or anatomical subsite of tumors. The findings confirm the inverse association between physical activity and colorectal cancer, which appears to be stronger in men, and suggest possible differences in the strength of the association by race/ethnicity and anatomical subsite of tumors.

Keywords

Colorectal cancer; Ethnic groups; Physical activity; Sex; Sitting time

Introduction

Past studies have provided consistent evidence that physical activity is associated with a lower risk of colorectal cancer (1–3). A meta-analysis of 12 prospective studies, conducted by the World Cancer Research Fund (WCRF)/American Institute for Cancer Research

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(AICR) Continuous Update Project (CUP) in 2017, showed a 20% (95% CI: 0.72, 0.88) decreased risk of colon cancer comparing the highest and lowest levels of total activity levels when including activities of various intensity levels (1).

However, data is lacking on whether the association is consistent between sexes and across different races/ethnicities and anatomical subsites of tumors. Given that incidence rates of colorectal cancer vary widely by sex and race/ethnicity, and that biological mechanisms may differ by anatomical subsite, the beneficial effects of physical activity may be greater for certain populations and subsites. To address this gap, we analyzed data from the Multiethnic Cohort Study, which mostly consists of African Americans, Native Hawaiians, Japanese Americans, Latinos, and whites living in Hawaii and California.

Materials and Methods

Study population

The design and characteristics of the Multiethnic Cohort Study (MEC) have been described in detail elsewhere (4). In brief, the MEC is a prospective cohort study designed to examine the relation of lifestyle and genetic factors with cancer among representative population groups of five races/ethnicities: African American, Native Hawaiian, Japanese American, Latino, and white in Hawaii and Los Angeles (4). Between 1993 and 1996, more than 215,000 men and women aged 45–75 years entered the cohort by completing a comprehensive questionnaire that included sections on physical activity, body weight and height, eating habits, and medication history. The study was approved by the review boards of the University of Hawaii and University of Southern California. For the current analyses, we excluded participants who were not in one of the targeted racial/ethnic groups (n=13,987), who had previous colorectal cancer reported on the baseline questionnaire (n=2,251) or identified from the tumor registries (n=301), or who reported implausible diet based on macronutrients (n=8,116) (5). We also excluded participants with missing information on physical activity variables (n=18,483). These were more likely to be women than men and African American or Latino, compared to the other three racial/ethnic groups. As a result, the analyses included 172,502 participants.

Assessment of physical activity

The physical activity questions were designed to reflect a participant's behavior over an average 24-hour period during the previous year and inquired about time spent sleeping, in various sitting activities, and in strenuous sports, vigorous work, and moderate activities. Sleep duration, including naps, was asked using six categories: ≤5, 6, 7, 8, 9, and ≥10 hours per day. Five categories of sitting activities were asked, including sitting in car or bus, sitting at work, watching TV, sitting at meals, and other sitting activities (such as reading, playing cards, sewing), each in seven categories: never, <1, 1−2, 3−4, 5−6, 7−10, and ≥11 hours per day. Total daily sitting hours per day was calculated as the sum of the midpoints of the sitting categories, using 0, 0.5, 1.5, 3.5, 5.5, 8.5, and 11, respectively. Strenuous sports (such as jogging, bicycling on hills, tennis, racquetball, swimming laps, aerobics), vigorous work (such as moving heavy furniture, loading or unloading trucks, shoveling, weight lifting, or equivalent manual labor), and moderate activity (such as housework, brisk walking, golfing, bowling, bicycling on level ground, gardening) were asked in eight categories: never, ½–1, 2–3, 4–6, 7–10, 11–20, 21–30, and ≥31 hours per week. Hours in each activity level per day was calculated using the midpoint of the categories: 0, 0.75/7, 2.5/7, 5/7, 8.5/7, 15/7, 25.5/7, and 31/7. Light physical activity was calculated by subtracting the total time spent in all activities (sleeping, sitting, or in moderate and vigorous activity) from 24 hours.

The metabolic equivalents (METs) for a 24-hour day were created using the following formula: (hours in sleep×0.91 + hours in sitting×1.0 + hours in light activity×2.4 + hours in moderate activities×4.0 + hours in vigorous activity×7.2)/24. MET-hours of moderate and vigorous activity per day were calculated as the sum of hours in moderate activities×4.0 and hours in vigorous activity×7.2. The physical activity questionnaire used in the MEC has been validated against the objective measure of total energy expenditure based on doubly labeled water in 230 adults (6). The correlation between the objective and self-reported values was reasonable with r=0.29 for METs.

The same questions on physical activity were asked in a 10-year follow-up survey (2003–2007) except for moderate activity, which separated recreational (such as brisk walking, golfing, bicycling on level ground, gardening, dancing, softball) and work activities (such as housework, yard work, restaurant work, sales work or equivalent moderate physical activity). Total recreational activity was calculated as the sum of hours in strenuous sports and moderate recreational activities. Total work-related activity was calculated as the sum of hours in vigorous work and moderate work.

Case ascertainment

Incident cases of colorectal cancer were identified by linking the cohort to the tumor registries in Hawaii and California through December 31, 2013. Cases in this study were limited to participants diagnosed with invasive adenocarcinoma of the large bowel with International Classification of Disease (ICD)-O2 codes of C180-C18.9, C19.9, and C20.9. For anatomical subsite-specific analyses, cases were categorized using ICD-O2 codes: C18.0-C18.5 for right colon, C18.6-C18.7 for left colon, and C19.9 and C20.9 for rectum, excluding multisite cases. Deaths were identified by linkage to death files in Hawaii and California and the National Death Index through December 31, 2013.

Statistical analyses

Cox proportional hazards models of colorectal cancer with age as the time metric were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for men and women separately. Colorectal cancer cases other than adenocarcinoma were censored at the date of diagnosis. Physical activity variables were parameterized as quintiles or quartiles, based on the overall distributions of the variables in men and women combined. Tests of proportional hazards assumption were based on the Schoenfeld residual method and found to be met (7). Trend tests were conducted by modeling a continuous variable assigned the sex/ethnic-specific median values within the quantile categories. All models were adjusted for race/ethnicity as a strata variable and age at cohort entry as a covariate. Multivariate models were further adjusted for family history of colorectal cancer (yes, no), history of intestinal polyps (yes, no), BMI (<25, 25–<30, ≥30 kg/m^2), pack-years of cigarette smoking, multivitamin use (yes, no), non-steroidal anti-inflammatory drug use (yes, no), daily intake of total energy (log transformed kcal), alcohol (g), red meat (g/1,000kcal), dietary fiber (g/1,000kcal), calcium (mg), folate (dietary folate equivalents), and vitamin D (IUs), and for women, menopausal hormone therapy (MHT) use (never, former, current use of estrogen). These covariates were chosen since they are established risk factors or were found to be associated with risk of colorectal cancer in the MEC. In the multivariate models, participants with missing data on covariates (n=11,145) were excluded, resulting in 161,357 participants. For subgroup analyses, we only presented the variable of MET-hours of moderate/vigorous activity since this variable showed the strongest association. The models were run separately by race/ethnicity and anatomical subsite of tumors (right colon, left colon, and rectum). We ran the models for combined association of physical activity and BMI with a group of the lowest level of moderate/vigorous activity and the highest BMI category (≥30 kg/m^2) as the reference. We also ran the models for combined association of physical activity and sitting time with a group of the lowest level of physical activity and the longest sitting hour (≥10 hours/day) as a reference. Among postmenopausal women, the models were run for MHT never and ever users, separately. Heterogeneity was tested by Wald statistics for cross-product terms of trend variables and subgroup membership. Heterogeneity by anatomical subsite was tested by Wald statistics using competing risk methodology (7).

For analyses of recreational and work-related physical activity, we repeated the models in the 76,010 men and women who participated in 10-year follow-up survey and met the inclusion criteria at the time of follow-up. Physical activity variables and covariates were from the 10-year follow-up survey and outcome was incident colorectal cancer occurring after the 10-year follow-up. For all analyses, we used SAS version 9.4 (SAS Institute). All P values were two-sided.

Results

Table 1 presents baseline characteristics by physical activity level in men and women. Men and women who had higher MET-hours of moderate or vigorous activity were more likely to be younger, Native Hawaiian or white, to have family history of colorectal cancer, to have higher education, to use multivitamin supplements, to have higher intakes of energy, calcium, folate, vitamin D, and alcohol, while they were less likely to be obese and NSAID users. Women with higher physical activity tended to be current users of MHT at baseline.

A total of 4,430 incident colorectal cancer cases (2,341 men and 2,089 women) were identified in the study population during an average follow-up of 16.8 years. Table 2 shows the association of sleep, sitting hours, and various types of physical activity with colorectal cancer risk in men and women. Sleep and total sitting hours were not related to colorectal cancer risk in either men or women. Sitting time watching TV was associated with an increased risk especially in women; however, this association was no longer significant after adjustment for covariates. In men, moderate activity (HR = 0.83, 95% CI: 0.72, 0.95 for the highest vs. lowest quintile, *P* for trend = 0.01) was associated with a decreased risk in multivariate-adjusted models. MET-hours of moderate and vigorous activity showed a stronger association (HR = 0.76, 95% CI: 0.66, 0.87 for the highest vs. lowest quintile, *P* for trend <0.001), compared with each activity type, total hours spent in three types of physical activity, and total METs (HR = 0.88, 95% CI: 0.77, 1.00; *P* for trend = 0.05). When considering Bonferroni correction for multiple comparisons ($P < 0.005$), the associations for moderate and vigorous activity in men both as hours and MET-hours were still statistically significant. In women, however, no association was found. There was a suggestion for heterogeneity by sex for strenuous sports ($P = 0.07$) and MET-hours of moderate/vigorous activity ($P = 0.07$), but not for the other types (*P*'s ≥ 0.13). In the sensitivity analysis excluding the cases diagnosed within the first 2 years of follow-up, the findings remained similar (in men: HR=0.76, 95% CI: 0.66, 0.87 for the highest vs. lowest quintile of MET-hours of moderate/vigorous activity, *P* for trend <0.001).

In racial/ethnic-specific analyses (Table 3), all HRs in the upper quintiles were below 1 across the five groups in men (*P* for heterogeneity = 0.36), with an inverse trend in African Americans (*P* for trend = 0.003) and Japanese Americans (*P* for trend = 0.02). Among women, only whites show a decrease in risk (HR = 0.64, 95% CI: 0.45, 0.90 for the highest vs. lowest quintile; *P* for trend = 0.08), but no indication was seen for racial/ethnic differences (*P* for heterogeneity = 0.36).

The inverse association with moderate/vigorous activity was more apparent for right colon and rectal cancer than for left colon in men (*P* for heterogeneity = 0.55) (Table 4). In women, decreases in risk for right colon cancer were shown (P for heterogeneity = 0.36).

In joint analyses of physical activity and BMI (Table 5), no difference in the association between moderate/vigorous activity on colorectal cancer risk was found across the BMI groups in either men or women (*P* for heterogeneity = 0.62 and 0.19, respectively), although among women, an inverse trend with physical activity was suggestive in the BMI ≥30 group. The BMI <30 groups were at lower risk regardless of physical activity levels in both men and women, compared with the reference group (BMI ≥30 and least physically active). There was further decrease in risk with physical activity in the BMI <25 group among men but not among women.

In combined analyses of physical activity and sitting time (Table 6), the inverse association with moderate/vigorous activity was seen in men with total sitting time longer than 6 hours per day, but not in those with 6 or less hours (*P* for heterogeneity = 0.06). When examining sitting time watching TV, the inverse association was significant in men watching TV for 3 hours or longer, but not in those with less than 3 hours (P for heterogeneity = 0.52). Among women, no association was found compared to those with the lowest physical activity level and the longest sitting time. In stratified analyses by MHT use at baseline among postmenopausal women (Table 7), MHT ever users who were at lower risk of colorectal cancer than never users showed further decrease in risk with physical activity, while no association was found in never users (*P* for heterogeneity = 0.03).

A total of 34,089 men (mean age: 69.0 ± 8.3 years) and 41,921 women (mean age: 68.6 ± 8.4 years) were included in the analysis conducted among participants who returned the 10-year follow-up questionnaire, (mean follow-up: 8.0 ± 2.1 years). In men, both recreational and work-related activities in the 10-year follow-up survey were associated with a lower risk of subsequent colorectal cancer (Table 8). The decrease in risk was seen for all 4 upper quintiles without further decrease in the highest quintile. No significant association was found in women. Similarly, moderate/vigorous activity measured in MET-hours and calculated from the 10-year follow-up was inversely associated with colorectal cancer risk in men but not in women.

Discussion

In this large multiethnic population, physical activity was associated with a lower incidence of colorectal cancer; this association was more apparent in men than in women. Sleep and sitting durations were not associated with colorectal cancer risk either in men or women. The association did not vary by race/ethnicity, anatomical subsite, and BMI group. The inverse trend was seen among men with longer sitting time (>6 hours per day) but not among those with short sitting time, while no association was found across all sitting time categories among women.

In the CUP meta-analysis based on the literature published up to April 2015, total physical activity in a comparison of the highest vs. lowest levels was consistently associated with a 20% lower risk of colon cancer (95% CI: 0.72, 0.88) but was not associated with rectal cancer (relative risk (RR)=1.04, 95% CI: 0.92, 1.18). Similarly, recreational physical activity was related to a 16% lower risk of colon cancer (95% CI: 0.78, 0.91) but not to rectal cancer (RR=0.95, 95% CI: 0.85, 1.07). Prospective studies published since the CUP have generally supported the conclusions of the CUP, with some differences. A report from the Women's Health Initiative Observational Study (WHI-OS) found an inverse association between leisure time physical activity and colorectal cancer risk, particularly for rectal cancer in postmenopausal women (8), which was not consistent with the CUP results. The Singapore Chinese Healthy Study found that strenuous-vigorous physical activity (sports and work) was associated with a lower risk of colorectal cancer in men and women combined, which was similar for colon and rectum tumors (9). In the AARP Diet and Health Study, physical activity (mostly recreational) was related to a lower risk of colon cancer among nondiabetic, but not diabetic, participants (10). In the current study, we found a lower risk of colon cancer with physical activity in both groups of men with and without a history of diabetes at baseline (*P* for heterogeneity = 0.93 for MET-hours of moderate/vigorous activity). A UK cohort study also reported that total physical activity was associated with a lower risk of colon cancer (11).

Although recent prospective studies and a meta-analysis (12) have supported similar strengths of association between men and women, the inverse association between physical activity and colorectal cancer risk in the MEC appears to be stronger in men than in women. The difference in benefits from physical activity between the sexes may reflect hormonal differences (13). However, when we examined the associations among MHT ever users and never users in postmenopausal women, the inverse association was only found among MHT ever users. As a group, MHT users were at lower risk of colorectal cancer than MHT never users or men. In addition to the possibility of biologically distinct responses to exercise between men and women (13), the potential for gender differences of physical activity levels and types even within the same category (e.g., moderate activity) should be also considered as a potential explanation for our findings (14,15).

In another recent meta-analysis of 17 cohort and 21 case-control studies (16), occupational, recreational, and transportation-related physical activity were related to a 26% (95% CI: 0.67, 0.82), 20% (95% CI: 0.71, 0.89), and 34% (95% CI: 0.45, 0.98) decrease in risk of colon cancer, and a 12% (95% CI: 0.79, 0.98), 13% (95% CI: 0.75, 1.01), and 12% (95% CI: 0.70, 1.12) decrease in risk of rectal cancer, respectively, comparing the highest vs. lowest levels. In the MEC, we found a similar risk reduction for colon (19%) and rectal cancer (21%) in men. We found similar HRs for right and left colon tumors, which was also reported by two meta-analyses (17,18). Although we were not able to examine domain-specific physical activity at baseline, a 10-year follow-up survey in the MEC asked separate questions for recreational and work-related activities. We found a decreased colorectal cancer risk with both recreational and work-related activity among men. This is consistent with the World Health Organization recommendation that moderate or vigorous activity can be accumulated in any domain for health benefits (2,19).

In the current study, the inverse association of physical activity and colorectal cancer risk appeared to be stronger in African American men, compared with the other racial/ethnic groups, although there was no indication for heterogeneity overall across races. Racial/ethnic differences have been reported regarding types of exercise and sports participation, which might not be captured by the MEC questionnaire but be related to colorectal cancer risk (20). However, in addition to the relatively small number of African Americans in the MEC, they tended to be less physically active than the other racial/ethnic groups and thus the group with the highest level of physical activity was small. Therefore, caution needs to be exercised when interpreting these findings.

A meta-analysis of 15 case-control and cohort studies found a stronger relative risk for physical activity and colorectal cancer risk in the higher BMI group (21). Although in our study women with higher BMI showed a suggestive inverse association, we found no evidence for an interaction between BMI and physical activity in relation to colorectal cancer risk. One of the potential mechanisms by which physical activity may lower colorectal cancer risk is through a reduction in insulin resistance and inflammation, which have been related to colorectal tumor development (1). However, it is not clear whether physical activity without weight loss has a significant impact on these pathways (1).

An interaction between physical activity and sitting time has previously been reported in relation to colorectal cancer risk. In the Singapore Chinese Health Study, inverse associations between physical activity and colorectal cancer risk were the clearest among those with longer sitting time (9). No such interaction was found in the WHI-OS (8). In the MEC, we found a greater decrease in risk among men with longer sitting hours. Thus, our findings suggest that moderate/vigorous physical activity may be particularly beneficial for colorectal cancer prevention among people with longer sitting times.

Strengths of our study include the prospective design, the large study population with various racial/ethnic backgrounds, and the comprehensive information collected. However, several limitations need to be taken into account when interpreting our findings. In the validation study of the physical activity questionnaire used in the MEC, the correlation with the doubly-labeled water standard was modest (6). Although we considered a wide range of confounding factors, there might still be uncontrolled factors related to colorectal cancer risk. For example, information on colorectal cancer screening was not available at baseline. However, using data from a 5-year follow-up survey that were available for 80% of the participants, we found that further adjustment for colorectal cancer screening did not change the associations with subsequent colorectal cancer. For the current analysis, we used physical activity measured once either at baseline or in the 10-year follow-up survey. When analyzing data with updated physical activity information from the 10-year follow-up survey, we found a similar inverse association of physical activity with subsequent colorectal cancer. In addition, we were only able to distinguish recreational activity from work-related activity based on the 10-year follow-up, but not the baseline questionnaire. Also, we were not able to distinguish type of activity within an intensity level.

In summary, our findings confirm the inverse association between physical activity and colorectal cancer; this association appears to be stronger in men, especially those with longer sitting time, and suggest possible differences in the strength of the association by race/ethnicity and anatomical subsite of the tumor.

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Table 1.

Baseline characteristics of participants by physical activity

	Physical activity (MET-hours/day)[a]				
	0–<1.42	**1.42–<2.86**	**2.86–<4.86**	**4.86–<9.14**	**≥9.14**
Men (n= 79,033)					
No. of participants	13,743	11,861	16,303	18,148	18,978
Age at cohort entry (y)	61.2 ± 8.5	61.3 ± 8.8	59.8 ± 8.9	59.8 ± 8.8	58.1 ± 8.8
Ethnicity (%)					
African American	19.9	16.4	13.0	10.4	9.5
Native Hawaiian	4.9	5.8	7.0	7.0	9.8
Japanese American	25.5	30.8	34.3	34.0	27.7
Latino	31.7	24.4	20.3	19.5	21.5
White	18.0	22.6	25.5	29.1	31.5
Family history of colorectal cancer (%)	6.4	7.4	7.3	7.9	7.6
History of intestinal polyps (%)	6.4	7.0	7.3	8.0	6.1
BMI (kg/m^2)					
<25	32.9	34.7	36.0	37.4	38.2
25–29.9	45.2	46.8	47.5	47.8	46.3
≥30	21.9	18.5	16.6	14.9	15.5
Smoking status (%)					
Never	27.3	28.7	30.9	31.3	31.4
Former	50.9	52.6	52.4	52.6	51.1
Current	21.7	18.7	16.7	16.1	17.5
Pack years among ever smokers	22.0 ± 17.4	21.6 ± 17.0	20.3 ± 16.4	20.6 ± 16.4	19.7 ± 16.1
Education					
≤12th grade	53.1	43.6	36.0	33.9	36.6
Vocational school/some college	26.1	29.0	29.8	29.6	33.1
≥Graduate college	20.8	27.4	34.2	36.5	30.3
Multivitamin use (%)	43.8	46.4	48.1	49.0	48.7
NSAID use (%)	53.7	51.8	49.4	49.9	48.7
Daily intake					
Energy (kcal)	2318.1 ± 1168.1	2319.9 ± 1091.7	2347.3 ± 1069.0	2426.1 ± 1074.9	2657.0 ± 1147.9
Red meat (g/1000kcal)	21.7 ± 14.2	20.4 ± 12.7	19.9 ± 12.2	19.3 ± 12.2	19.1 ± 12.2
Dietary fiber (g/1000kcal)	10.6 ± 4.1	10.6 ± 3.9	10.6 ± 3.9	10.8 ± 4.0	10.9 ± 4.1
Calcium (mg)[b]	974.7 ± 633.3	971.3 ± 596.2	986.3 ± 595.8	1026.4 ± 599.3	1114.7 ± 638.7
Folate (μg DFE)[b]	903.1 ± 616.0	937.5 ± 601.1	968.7 ± 620.9	1015.2 ± 627.0	1073.2 ± 657.1
Vitamin D (IU)[b]	303.1 ± 320.0	326.0 ± 329.5	343.9 ± 348.6	360.7 ± 353.1	371.9 ± 361.2
Alcohol (g)	14.1 ± 37.6	13.9 ± 32.2	14.1 ± 30.6	15.1 ± 30.5	16.5 ± 32.7
Women (n= 93,469)					
No. of participants	16,780	21,029	20,968	20,740	13,952

	Physical activity (MET-hours/day)[a]				
	0−<1.42	**1.42−<2.86**	**2.86−<4.86**	**4.86−<9.14**	**≥9.14**
Age at cohort entry (y)	59.9 ± 8.6	59.9 ± 8.9	59.0 ± 8.8	59.0 ± 8.8	58.2 ± 8.7
Ethnicity (%)					
African American	22.9	23.7	18.4	14.9	12.0
Native Hawaiian	5.3	7.3	8.2	7.9	10.0
Japanese American	24.8	31.2	30.4	30.6	23.9
Latino	32.4	18.1	18.1	14.7	17.0
White	14.5	19.7	24.9	31.9	37.1
Family history of colorectal cancer (%)	7.4	9.1	9.0	9.2	8.9
History of intestinal polyps (%)	4.0	4.5	4.7	4.5	4.3
BMI (kg/m^2)					
<25	37.3	44.0	47.6	52.2	54.4
25−29.9	33.9	32.0	32.0	29.9	29.2
≥30	28.7	24.1	20.5	17.8	16.4
Smoking status (%)					
Never	58.5	56.1	56.0	54.3	51.8
Former	28.2	28.7	29.8	31.7	32.4
Current	13.3	15.2	14.2	14.0	15.8
Pack years among ever smokers	15.4 ± 14.8	15.5 ± 14.2	15.2 ± 14.2	16.0 ± 14.6	16.0 ± 14.7
Education					
≤12th grade	57.7	46.7	41.0	37.0	37.8
Vocational school/some college	24.4	30.4	32.0	32.9	33.1
≥Graduate college	17.9	22.9	27.0	30.1	29.1
Multivitamin use (%)	51.2	51.8	54.2	54.8	56.8
NSAID use (%)	57.7	53.3	51.3	51.0	51.7
MHT use (%)					
Never	58.6	54.3	51.9	49.8	51.2
Past	18.2	18.5	17.3	17.1	16.9
Current	23.2	27.2	30.8	33.2	31.9
Daily intake					
Energy (kcal)	1978.9 ± 1048.6	1926.3 ± 937.3	1955.8 ± 920.3	1969.8 ± 893.6	2105.5 ± 952.1
Red meat (g/1000kcal)	18.5 ± 13.0	17.7 ± 11.9	17.0 ± 11.7	16.2 ± 11.3	15.9 ± 11.8
Dietary fiber (g/1000kcal)	12.3 ± 4.3	12.1 ± 4.1	12.4 ± 4.1	12.6 ± 4.2	13.0 ± 4.3
Calcium (mg)[b]	1052.9 ± 724.1	1042.6 ± 708.8	1109.4 ± 725.6	1166.9 ± 756.0	1244.0 ± 781.0
Folate (μg DFE)[b]	874.0 ± 605.9	872.4 ± 578.7	918.3 ± 589.7	957.7 ± 601.3	1018.8 ± 629.2
Vitamin D (IU)[b]	310.5 ± 333.1	324.3 ± 334.5	350.4 ± 346.1	368.4 ± 359.1	387.6 ± 370.9
Alcohol (g)	3.2 ± 14.0	3.7 ± 13.6	4.4 ± 15.2	5.1 ± 14.8	6.2 ± 17.7

Abbreviations: DFE, dietary folate equivalent; MET, metabolic equivalent; MHT, menopausal hormone therapy; NSAID, nonsteroidal anti-inflammatory drug.

[a]MET-hours for moderate and vigorous activity per day.

[b] From foods and supplements.

Table 2.

Association between physical activity and colorectal cancer risk in the Multiethnic Cohort, 1993–2013

Hours/day	Men (n = 79,033)				Women (n = 93,469)				P for heterogeneity[d]
	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	
Sleep									
≤5	205	1.00 (ref)	190	1.00 (ref)	226	1.00 (ref)	190	1.00 (ref)	
6	549	0.89 (0.76–1.05)	528	0.93 (0.78–1.09)	556	1.06 (0.91–1.24)	525	1.17 (0.99–1.39)	
7	713	0.89 (0.76–1.04)	679	0.91 (0.77–1.07)	608	0.91 (0.78–1.07)	562	1.00 (0.85–1.18)	
8	629	0.96 (0.82–1.13)	591	0.97 (0.82–1.14)	505	0.98 (0.84–1.15)	469	1.07 (0.90–1.27)	
≥9	245	1.01 (0.84–1.22)	237	1.01 (0.83–1.22)	194	1.11 (0.91–1.34)	181	1.20 (0.98–1.47)	
P for trend		0.31		0.54		0.93		0.67	0.78
Total sitting									
<5	493	1.00 (ref)	463	1.00 (ref)	420	1.00 (ref)	377	1.00 (ref)	
5–<7	508	0.95 (0.84–1.08)	483	0.93 (0.82–1.06)	437	0.99 (0.87–1.14)	402	0.98 (0.85–1.12)	
7–<9	478	0.95 (0.84–1.08)	456	0.92 (0.81–1.05)	435	1.03 (0.90–1.18)	405	1.00 (0.87–1.16)	
9–≤11	434	1.04 (0.91–1.18)	412	1.00 (0.87–1.14)	395	1.07 (0.93–1.23)	360	1.01 (0.87–1.17)	
>11	428	1.00 (0.87–1.14)	411	0.96 (0.84–1.10)	402	0.96 (0.83–1.10)	383	0.92 (0.80–1.07)	
P for trend		0.60		0.95		0.84		0.39	0.71
Sitting watching TV									
<1	262	1.00 (ref)	252	1.00 (ref)	245	1.00 (ref)	226	1.00 (ref)	
1–<3	883	1.05 (0.92–1.21)	838	1.01 (0.88–1.16)	749	1.02 (0.89–1.18)	687	0.98 (0.84–1.14)	
3–<5	902	1.08 (0.94–1.24)	864	0.99 (0.86–1.14)	823	1.14 (0.99–1.32)	765	1.04 (0.90–1.21)	
≥5	256	1.16 (0.98–1.38)	238	0.98 (0.82–1.18)	231	1.19 (0.99–1.43)	213	1.02 (0.84–1.24)	
P for trend		0.10		0.72		0.006		0.3634	0.42
Moderate activity									
<0.14	699	1.00 (ref)	654	1.00 (ref)	441	1.00 (ref)	391	1.00 (ref)	
0.14–<0.43	613	0.88 (0.79–0.98)	584	0.90 (0.80–1.00)	614	0.95 (0.84–1.08)	565	0.97 (0.86–1.11)	
0.43–<0.86	469	0.87 (0.77–0.98)	445	0.88 (0.78–1.00)	456	0.91 (0.80–1.04)	425	0.95 (0.83–1.09)	
0.86–<1.43	257	0.83 (0.72–0.96)	246	0.84 (0.73–0.98)	250	0.86 (0.74–1.01)	241	0.92 (0.78–1.09)	
≥1.43	303	0.81 (0.70–0.93)	296	0.83 (0.72–0.95)	328	0.91 (0.78–1.05)	305	0.94 (0.80–1.09)	
P for trend		0.004		0.01		0.24		0.41	0.25

Hours/day	Men (n = 79,033)				Women (n = 93,469)				P for heterogeneity[d]
	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	
Vigorous work									
0	1120	1.00 (ref)	1059	1.00 (ref)	1614	1.00 (ref)	1495	1.00 (ref)	
>0−<0.14	548	0.91 (0.82–1.01)	518	0.91 (0.82–1.01)	277	1.03 (0.90–1.17)	254	1.03 (0.90–1.18)	
0.14−<0.43	271	0.81 (0.71–0.93)	255	0.82 (0.72–0.94)	81	0.81 (0.65–1.02)	76	0.84 (0.66–1.05)	
≥0.43	371	0.92 (0.82–1.04)	364	0.94 (0.83–1.06)	72	1.00 (0.79–1.27)	65	1.01 (0.79–1.30)	
P for trend		0.26		0.42		0.75		0.86	0.96
Strenuous sports									
0	1512	1.00 (ref)	1438	1.00 (ref)	1533	1.00 (ref)	1413	1.00 (ref)	
>0−<0.14	419	0.91 (0.82–1.02)	399	0.97 (0.87–1.08)	276	0.90 (0.79–1.03)	255	0.96 (0.84–1.10)	
0.14−<0.43	194	0.78 (0.67–0.90)	184	0.85 (0.73–1.00)	151	0.96 (0.82–1.14)	139	1.05 (0.88–1.25)	
≥0.43	192	0.79 (0.68–0.92)	184	0.89 (0.76–1.04)	106	0.93 (0.76–1.14)	99	1.05 (0.85–1.29)	
P for trend		<0.001		0.05		0.39		0.56	0.07
Vigorous activity									
0	882	1.00 (ref)	828	1.00 (ref)	1300	1.00 (ref)	1198	1.00 (ref)	
>0−<0.21	407	0.93 (0.82–1.04)	384	0.94 (0.83–1.06)	366	1.07 (0.96–1.21)	342	1.12 (0.99–1.27)	
0.21−<0.46	391	0.91 (0.80–1.02)	378	0.96 (0.85–1.09)	197	0.86 (0.74–1.00)	176	0.88 (0.75–1.03)	
0.46−<0.71	287	0.82 (0.71–0.94)	272	0.86 (0.75–0.99)	128	0.94 (0.78–1.13)	121	1.02 (0.84–1.23)	
≥0.71	374	0.80 (0.70–0.90)	363	0.86 (0.75–0.97)	98	0.92 (0.75–1.13)	90	1.01 (0.81–1.26)	
P for trend		<0.001		0.02		0.19		0.83	0.32
Moderate/vigorous activity									
0−<0.32	516	1.00 (ref)	481	1.00 (ref)	402	1.00 (ref)	359	1.00 (ref)	
0.32−<0.71	456	0.92 (0.81–1.04)	430	0.92 (0.81–1.05)	543	0.99 (0.87–1.12)	498	0.99 (0.87–1.14)	
0.71−<1.07	419	0.83 (0.73–0.94)	393	0.84 (0.73–0.96)	434	0.93 (0.81–1.06)	398	0.95 (0.82–1.09)	
1.07−<1.79	455	0.76 (0.67–0.86)	440	0.80 (0.70–0.92)	325	0.82 (0.71–0.95)	313	0.89 (0.76–1.04)	
≥1.79	495	0.77 (0.68–0.87)	481	0.80 (0.70–0.91)	385	0.91 (0.79–1.05)	359	0.95 (0.82–1.11)	
P for trend		<0.001		0.003		0.15		0.45	0.25
Moderate/vigorous activity (MET-hours)									
<1.42	454	1.00 (ref)	423	1.00 (ref)	394	1.00 (ref)	353	1.00 (ref)	
1.42−<2.86	401	0.95 (0.83–1.09)	379	0.96 (0.83–1.10)	503	0.94 (0.83–1.08)	461	0.95 (0.82–1.09)	

Hours/day	Men (n = 79,033)				Women (n = 93,469)				P for heterogeneity[d]
	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	
2.86−<4.86	485	0.83 (0.73–0.95)	454	0.85 (0.74–0.97)	476	0.92 (0.81–1.06)	436	0.94 (0.82–1.08)	
4.86−<9.14	537	0.82 (0.72–0.93)	519	0.86 (0.76–0.98)	419	0.81 (0.71–0.93)	403	0.87 (0.75–1.00)	
≥9.14	464	0.72 (0.63–0.82)	450	0.76 (0.66–0.87)	297	0.90 (0.78–1.05)	274	0.94 (0.80–1.11)	
P for trend		<0.001		<0.001		0.17		0.53	0.07
Total METs									
<1.38	416	1.00 (ref)	394	1.00 (ref)	410	1.00 (ref)	384	1.00 (ref)	
1.38−<1.55	446	0.87 (0.76–1.00)	426	0.91 (0.79–1.04)	427	1.04 (0.91–1.20)	396	1.07 (0.93–1.23)	
1.55−<1.68	493	0.90 (0.79–1.03)	465	0.94 (0.82–1.08)	461	1.05 (0.92–1.20)	433	1.11 (0.97–1.28)	
1.68−<1.83	469	0.82 (0.72–0.94)	445	0.87 (0.76–1.00)	449	1.01 (0.88–1.16)	412	1.07 (0.92–1.23)	
≥1.83	517	0.81 (0.71–0.93)	495	0.88 (0.77–1.00)	342	0.99 (0.86–1.15)	302	1.03 (0.89–1.21)	
P for trend		0.001		0.05		0.80		0.61	0.13

Abbreviation: MET, metabolic equivalent.

[a]Adjusted by Cox proportional hazards regression for age at cohort entry and race/ethnicity.

[b]Excluding participants with missing information on covariates.

[c]Further adjusted for family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

[d]Tests for heterogeneity between men and women were performed based on the multivariate-adjusted models.

Table 3.

Association between physical activity and colorectal cancer risk by race/ethnicity in the Multiethnic Cohort, 1993–2013

Moderate/ vigorous activity (MET-hours/day)	African American		Native Hawaiian		Japanese American		Latino		White		P for heterogeneity
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	
Men											
<1.42	87	1.00 (ref)	20	1.00 (ref)	145	1.00 (ref)	105	1.00 (ref)	66	1.00 (ref)	
1.42–<2.86	58	0.82 (0.59–1.14)	23	1.01 (0.56–1.85)	136	0.86 (0.68–1.09)	91	1.18 (0.89–1.56)	71	0.99 (0.71–1.38)	
2.86–<4.86	62	0.82 (0.59–1.13)	27	0.73 (0.41–1.30)	192	0.82 (0.66–1.02)	81	0.92 (0.69–1.23)	92	0.85 (0.62–1.17)	
4.86–<9.14	65	0.93 (0.67–1.29)	33	0.79 (0.45–1.38)	230	0.88 (0.71–1.08)	80	0.84 (0.63–1.12)	111	0.80 (0.59–1.09)	
≥9.14	32	0.49 (0.33–0.74)	46	0.75 (0.44–1.29)	162	0.72 (0.58–0.91)	93	0.91 (0.69–1.21)	117	0.80 (0.59–1.09)	
P for trend		0.003		0.37		0.02		0.27		0.15	0.36
Women											
<1.42	99	1.00 (ref)	11	1.00 (ref)	109	1.00 (ref)	75	1.00 (ref)	59	1.00 (ref)	
1.42–<2.86	121	0.89 (0.68–1.16)	33	1.66 (0.84–3.29)	163	0.91 (0.71–1.16)	71	1.22 (0.88–1.69)	73	0.71 (0.50–1.00)	
2.86–<4.86	98	0.91 (0.69–1.21)	31	1.42 (0.71–2.83)	152	0.90 (0.71–1.16)	62	1.06 (0.76–1.49)	93	0.76 (0.54–1.05)	
4.86–<9.14	68	0.75 (0.55–1.03)	18	0.85 (0.40–1.82)	143	0.83 (0.65–1.07)	58	1.25 (0.88–1.77)	116	0.73 (0.53–1.00)	
≥9.14	54	1.14 (0.82–1.60)	26	1.50 (0.73–3.06)	91	1.01 (0.76–1.34)	28	0.82 (0.53–1.28)	75	0.64 (0.45–0.90)	
P for trend		0.40		0.89		0.73		0.29		0.08	0.36

Abbreviation: MET, metabolic equivalent.

[a]Adjusted by Cox proportional hazards regression for age at cohort entry, family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

Table 4.

Association between physical activity and colorectal cancer risk by anatomical subsite in the Multiethnic Cohort, 1993–2013

Moderate/vigorous activity (MET-hours/day)	Right colon		Left colon		Rectum		P for heterogeneity
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	
Men							
<1.42	187	1.00 (ref)	119	1.00 (ref)	109	1.00 (ref)	
1.42−<2.86	169	0.97 (0.79–1.19)	110	0.99 (0.76–1.28)	93	0.90 (0.68–1.19)	
2.86−<4.86	178	0.78 (0.63–0.96)	147	0.97 (0.76–1.24)	119	0.83 (0.64–1.08)	
4.86−<9.14	227	0.88 (0.72–1.07)	136	0.80 (0.62–1.03)	148	0.92 (0.71–1.18)	
≥9.14	183	0.72 (0.59–0.89)	138	0.83 (0.65–1.07)	120	0.73 (0.56–0.96)	
P for trend		0.004		0.09		0.04	0.55
Women							
<1.42	206	1.00 (ref)	79	1.00 (ref)	63	1.00 (ref)	
1.42−<2.86	216	0.76 (0.63–0.92)	131	1.22 (0.92–1.61)	103	1.19 (0.87–1.63)	
2.86−<4.86	239	0.88 (0.73–1.06)	116	1.14 (0.85–1.52)	75	0.90 (0.64–1.26)	
4.86−<9.14	222	0.81 (0.67–0.99)	104	1.04 (0.77–1.40)	69	0.81 (0.57–1.15)	
≥9.14	132	0.77 (0.62–0.97)	78	1.27 (0.92–1.75)	56	1.02 (0.70–1.48)	
P for trend		0.18		0.41		0.62	0.36

Abbreviation: MET, metabolic equivalent.

[a]Adjusted by Cox proportional hazards regression for age at cohort entry, race/ethnicity, family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

Table 5.

Combined association of physical activity and body mass index with colorectal cancer risk in the Multiethnic Cohort, 1993–2013

Moderate/vigorous activity (MET-hours/day)	Body mass index ≥30 kg/m²		25−<30 kg/m²		<25 kg/m²		P for heterogeneity
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	
Men							
<1.42	105	1.00 (ref)	177	0.72 (0.57–0.92)	141	0.73 (0.57–0.95)	
1.42−<2.86	71	0.88 (0.65–1.18)	181	0.76 (0.59–0.96)	127	0.66 (0.51–0.86)	
2.86−<4.86	69	0.71 (0.52–0.96)	211	0.64 (0.51–0.81)	174	0.64 (0.50–0.82)	
4.86−<9.14	76	0.77 (0.57–1.04)	240	0.65 (0.51–0.81)	203	0.64 (0.51–0.82)	
≥9.14	73	0.72 (0.53–0.97)	215	0.60 (0.48–0.76)	162	0.51 (0.40–0.66)	
P for trend		0.06		0.05		0.006	0.62
Women							
<1.42	121	1.00 (ref)	94	0.60 (0.46–0.79)	138	0.74 (0.58–0.95)	
1.42−<2.86	127	0.91 (0.71–1.16)	157	0.76 (0.60–0.97)	177	0.58 (0.46–0.74)	
2.86−<4.86	106	0.91 (0.70–1.19)	126	0.63 (0.49–0.81)	204	0.66 (0.52–0.83)	
4.86−<9.14	78	0.77 (0.58–1.02)	137	0.72 (0.56–0.92)	188	0.55 (0.43–0.70)	
≥9.14	45	0.77 (0.54–1.08)	87	0.73 (0.55–0.97)	142	0.64 (0.50–0.82)	
P for trend		0.06		0.44		0.86	0.19

Abbreviation: MET, metabolic equivalent.

[a]Adjusted by Cox proportional hazards regression for age at cohort entry, race/ethnicity, family history of colorectal cancer, history of colorectal polyp, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

Table 6.

Combined association of physical activity and sitting time with colorectal cancer risk in the Multiethnic Cohort, 1993–2013

Moderate/vigorous activity (MET-hours/day)	Sitting time						P for heterogeneity
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	Cases	HR (95% CI)	
	Total sitting						
	≥10 hours		>6−<10 hours		≤6 hours		
Men							
<1.42	124	1.00 (ref)	135	1.01 (0.79–1.29)	164	0.89 (0.71–1.13)	
1.42−<2.86	116	0.97 (0.76–1.25)	129	0.91 (0.71–1.17)	134	0.88 (0.69–1.12)	
2.86−<4.86	135	0.80 (0.63–1.03)	169	0.82 (0.65–1.04)	150	0.81 (0.63–1.03)	
4.86−<9.14	154	0.82 (0.65–1.04)	201	0.84 (0.67–1.06)	164	0.81 (0.64–1.02)	
≥9.14	88	0.67 (0.51–0.88)	162	0.66 (0.52–0.84)	200	0.82 (0.66–1.03)	
P for trend		0.02		<0.001		0.60	0.06
Women							
<1.42	94	1.00 (ref)	106	1.21 (0.91–1.59)	153	1.06 (0.81–1.37)	
1.42−<2.86	131	0.92 (0.71–1.20)	159	1.08 (0.84–1.40)	171	1.06 (0.82–1.37)	
2.86−<4.86	155	1.08 (0.83–1.39)	146	0.98 (0.76–1.27)	135	0.99 (0.76–1.29)	
4.86−<9.14	133	0.96 (0.74–1.25)	153	0.95 (0.74–1.24)	117	0.90 (0.68–1.18)	
≥9.14	59	0.95 (0.69–1.32)	108	1.02 (0.77–1.35)	107	1.06 (0.80–1.40)	
P for trend		0.64		0.70		0.70	0.89
	Sitting watching TV						
	≥3 hours		1−<3 hours		<1 hour		
Men							
<1.42	219	1.00 (ref)	144	0.96 (0.78–1.19)	50	0.82 (0.60–1.12)	
1.42−<2.86	191	0.90 (0.74–1.10)	144	0.97 (0.79–1.20)	40	0.91 (0.65–1.28)	
2.86−<4.86	223	0.81 (0.67–0.98)	173	0.82 (0.67–1.00)	52	0.88 (0.65–1.19)	
4.86−<9.14	269	0.85 (0.71–1.02)	184	0.79 (0.65–0.96)	59	0.93 (0.69–1.24)	
≥9.14	200	0.68 (0.56–0.83)	193	0.80 (0.66–0.97)	51	0.71 (0.52–0.97)	
P for trend		<0.001		0.10		0.39	0.52
Women							
<1.42	171	1.00 (ref)	133	1.02 (0.81–1.28)	41	0.67 (0.48–0.94)	
1.42−<2.86	225	0.88 (0.72–1.07)	165	0.85 (0.68–1.05)	62	1.17 (0.87–1.57)	
2.86−<4.86	238	0.96 (0.79–1.17)	143	0.79 (0.63–0.99)	44	0.84 (0.60–1.17)	
4.86−<9.14	217	0.85 (0.70–1.04)	128	0.73 (0.58–0.92)	54	1.03 (0.76–1.40)	
≥9.14	127	0.90 (0.72–1.14)	118	0.97 (0.76–1.23)	25	0.64 (0.42–0.98)	
P for trend		0.57		0.71		0.24	0.52

Abbreviation: MET, metabolic equivalent.

[a]Adjusted by Cox proportional hazards regression for age at cohort entry, race/ethnicity, family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

Table 7.

Combined association of physical activity and MHT use with colorectal cancer risk among postmenopausal women in the Multiethnic Cohort, 1993–2013

Moderate/vigorous activity (MET-hours/day)	MHT never users (n=30,182)		MHT ever users (n=38,349)		P for heterogeneity
	Cases	HR (95% CI)[a]	Cases	HR (95% CI)[a]	
<1.42	177	1.00 (ref)	142	0.89 (0.71–1.11)	
1.42−<2.86	206	0.90 (0.74–1.10)	194	0.79 (0.64–0.97)	
2.86−<4.86	180	0.90 (0.73–1.11)	193	0.77 (0.62–0.94)	
4.86−<9.14	184	0.95 (0.77–1.17)	180	0.67 (0.54–0.82)	
≥9.14	128	1.06 (0.84–1.34)	116	0.70 (0.55–0.88)	
P for trend		0.36		0.13	0.03

Abbreviations: MET, metabolic equivalent; MHT, menopausal hormone therapy.

[a]Adjusted for age at cohort entry, race/ethnicity, family history of colorectal cancer, history of colorectal polyp, BMI, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

Table 8.

Association between physical activity at 10-year follow-up and risk of subsequent colorectal cancer in the Multiethnic Cohort, 2003–2013

Hours/day	Men (n=34,089)				Women (n = 41,921)				P for heterogeneity[d]
	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	Cases	HR (95% CI)[a]	Cases[b]	HR (95% CI)[c]	
Recreational activity									
<0.21	158	1.00 (ref)	135	1.00 (ref)	171	1.00 (ref)	154	1.00 (ref)	
0.21–<0.46	71	0.61 (0.46–0.80)	57	0.59 (0.43–0.81)	96	0.99 (0.77–1.28)	84	1.05 (0.80–1.37)	
0.46–<0.82	98	0.75 (0.58–0.97)	86	0.79 (0.60–1.05)	80	0.95 (0.73–1.24)	73	1.09 (0.82–1.45)	
0.82–<1.32	63	0.71 (0.53–0.96)	58	0.81 (0.59–1.12)	40	0.87 (0.62–1.24)	35	0.97 (0.66–1.42)	
≥1.32	63	0.62 (0.46–0.84)	55	0.67 (0.48–0.92)	34	0.95 (0.65–1.37)	29	1.06 (0.70–1.60)	
P for trend		0.01		0.09		0.55		0.88	0.38
Work-related activity									
<0.21	134	1.00 (ref)	119	1.00 (ref)	79	1.00 (ref)	71	1.00 (ref)	
0.21–<0.46	119	0.85 (0.67–1.09)	102	0.83 (0.64–1.09)	144	1.16 (0.88–1.52)	129	1.18 (0.88–1.57)	
0.46–<0.82	89	0.75 (0.57–0.98)	74	0.71 (0.53–0.95)	95	1.11 (0.83–1.50)	83	1.13 (0.82–1.55)	
0.82–<1.43	55	0.71 (0.52–0.97)	47	0.69 (0.49–0.97)	50	0.98 (0.69–1.40)	45	1.04 (0.71–1.51)	
≥1.43	56	0.74 (0.54–1.02)	49	0.71 (0.50–1.00)	53	1.11 (0.78–1.58)	47	1.16 (0.80–1.69)	
P for trend		0.07		0.06		0.99		0.78	0.18
Moderate/vigorous activity (MET-hours)									
<1.86	115	1.00 (ref)	100	1.00 (ref)	96	1.00 (ref)	86	1.00 (ref)	
1.86–<3.34	74	0.67 (0.50–0.90)	63	0.66 (0.48–0.90)	105	0.94 (0.71–1.24)	95	1.00 (0.74–1.34)	
3.34–<5.71	76	0.65 (0.49–0.88)	62	0.61 (0.44–0.85)	75	0.92 (0.68–1.25)	64	0.96 (0.69–1.33)	
5.71–<10.3	98	0.66 (0.51–0.87)	87	0.69 (0.51–0.92)	79	0.90 (0.67–1.22)	72	1.02 (0.74–1.41)	
≥10.29	90	0.61 (0.46–0.81)	79	0.62 (0.45–0.84)	66	0.94 (0.68–1.30)	58	1.05 (0.74–1.49)	
P for trend		0.01		0.04		0.76		0.69	0.19

[a] Adjusted by Cox proportional hazards regression for age at 10-year follow-up and race/ethnicity.

[b] Excluding participants with missing information on covariates at 10-year follow-up.

[c] Further adjusted for family history of colorectal cancer, history of colorectal polyp, body mass index, pack-years of cigarette smoking, multivitamin use, non-steroidal anti-inflammatory drug use, menopausal hormone therapy use for women only, and intake of alcohol, total energy, red meat, dietary fiber, calcium, folate, and vitamin D.

[d] Tests for heterogeneity between men and women were performed based on the multivariate-adjusted models.