Physical activity, sedentary behavior, and the risk of colon and rectal cancer in the NIH-AARP Diet and Health Study

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Abstract

Objective—In order to prospectively investigate physical activity at varying intensities and sedentary behavior in relation to colorectal cancer.

Methods—We considered 488,720 participants of the NIH-AARP Diet and Health Study who were aged 50–71 years at baseline in 1995–1996. Through 31 December, 2003, we identified 3,240 and 1,482 colorectal cancers among men and women, respectively. We estimated multivariable relative risks (RR) and 95% confidence intervals (CI) of colorectal cancer using Cox regression.

Results—Engaging in exercise/sports five or more times per week compared to never or rarely exercising was associated with a reduced risk of colon cancer among men (*p*=0.001; RR=0.79, 95% CI=0.68–0.91) and a suggestive decrease in risk among women (*p*=0.376; RR=0.85, 95% CI=0.70–1.04). Engaging in exercise/sports was also associated with a decreased risk of rectal cancer in men (*P*=0.074; RR comparing extreme categories=0.76, 95% CI=0.61–0.94). In men, we observed inverse relations of both low intensity (*p*=0.017; RR=0.81, 95% CI=0.65–1.00 for ≥7 h/week) and moderate to vigorous intensity activity (*p*=0.037; RR=0.82, 95% CI=0.67–0.99 for =7 h/week) to colon cancer risk. In contrast, sedentary behavior (time spent watching television/videos) was positively associated with colon cancer (*p*<0.001; RR=1.61, 95% CI=1.14–2.27 for ≥9 h/day) among men. Similar, but less pronounced relations were observed in women.

Conclusion—Engaging in physical activity of any intensity is associated with reductions in colon and rectal cancer risk. Conversely, time spent sedentary is associated with increased colon cancer risk.

Keywords

Colon cancer; Rectal cancer; Physical activity; Cohort studies

INTRODUCTION

Colon cancer is the third most common cancer among both men and women and it currently accounts for approximately 10% of all cancer deaths in the United States [1]. Increased physical activity has been consistently associated with decreased risk of colon cancer [2–5], with both

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prospective [6–18] and case-control studies [19–27] reporting risk reductions of about 40% with high versus low levels of physical activity, particularly among men. Studies of physical activity and colon cancer among women have been much less consistent, with no statistically significantly association reported in most [6,8,10,11,15,16,28–34], but not all studies [12,13, 16,35]. Further, site-specific associations between physical activity and colon cancer have been largely inconclusive, with relatively few cohort studies reporting results by anatomical sub-site [12,13,16,18,33,36,37]. It is also unclear how physical activity performed during different age periods may affect colon cancer risk since many studies have been unable to detect associations with past physical activity [9,14,16,18,34,35,38]. In order to address these issues, in a large prospective study we examined in detail the relations of physical activity at varying intensities and sedentary behavior to colon and rectal cancer according to gender, colorectal sub-site, and age period of activity.

MATERIALS AND METHODS

The NIH-AARP Diet and Health Study

The NIH-AARP Diet and Health Study was established in 1995–1996 when 567,169 men and women responded to a mailed baseline questionnaire that requested information on diet, family history of cancer, physical activity, anthropometry, and other lifestyle factors [39]. Respondents were members of AARP between the ages of 50–71 years old at baseline and residing in one of eight study areas (California, Florida, Pennsylvania, New Jersey, North Carolina, Louisiana, and metropolitan Atlanta and Detroit). In 1996–1997, a second questionnaire was sent to respondents who did not have self-reported prostate, breast, or colorectal cancer at baseline to collect more detailed information on physical activity and sedentary behavior. A total of 334,908 respondents completed the second questionnaire. The NIH-AARP Diet and Health Study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute and all participants provided written informed consent.

Study population

Among baseline questionnaire respondents, we excluded 179 duplicate questionnaires, 15,760 individuals whose questionnaires were completed by proxies for the intended respondents, 582 persons who died or moved out of the study area before study entry, and 6 people who withdrew from the study. We also excluded 51,193 persons with a previous cancer diagnosis, 997 persons reporting end-stage renal disease, 5,711 subjects with missing information on physical activity, and 4,021 persons who were statistical outliers on reported energy intake. After exclusions, a total of 488,720 subjects (292,069 men and 196,651 women) remained for analysis of the baseline questionnaire. The same exclusion criteria were applied to persons responding to the second questionnaire resulting in 300,673 (175,600 men and 125,073 women) subjects available for the analyses regarding that questionnaire.

Cohort maintenance

Participants of the NIH-AARP cohort are followed annually for change of address by matching the cohort database to that of the National Change of Address maintained by the U.S. Postal Service (USPS). Information on address changes is also obtained through receipt of USPS processing of undeliverable mail, from other address change update services, and directly from participants who report address changes in response to study mailings such as questionnaires, newsletters, sample kits, etc. Vital status is ascertained by annual linkage of the cohort to the Social Security Administration Death Master File (SSA DMF) on deaths in the U.S., follow-up searches of the National Death Index for subjects that match to the SSA DMF, cancer registry linkage, questionnaire responses, and responses to other mailings.

Assessment of physical activity

The baseline questionnaire asked participants to provide information about the number of times per week during the last 12 months they engaged in periods of physical activity or sports that lasted at least 20 min and caused increases in breathing or heart rate, or caused them to work up a sweat (i.e., current exercise/sports). There were six possible response options: never; rarely; 1–3 times per month; 1–2 times per week; 3–4 times per week; and 5 or more times per week. Subjects were also asked to indicate which of the following categories best described their routine throughout the day at home or work (i.e., daily routine activity): sitting, sitting and walking, standing or walking but not lifting or carrying things, carrying light loads or climbing stairs, and carrying heavy loads or doing heavy work.

The second questionnaire inquired about physical activity during different ages (15–18 years, 19–29 years, 35–39 years, and in the past 10 years). For each age period, subjects were asked to report the average number of hours per week spent at low intensity activities (e.g., slow walking, bowling, light calisthenics, light gardening, light housework) and at moderate to vigorous activities (e.g., brisk walking, jogging, aerobics, heavy gardening, heavy housework). Response options for each of those items were as follows: never; rarely; weekly, but less than 1 h per week; 1–3 h per week; 4–7 h per week; and more than 7 h per week. A median value for the number of hours per week of physical activity was assigned and multiplied by the estimated metabolic equivalent task (MET) value specific to that intensity level. One MET is defined as the energy expended while sitting quietly and is approximately equal to 3.5 ml of oxygen uptake per kilogram of body weight per minute for a 70-kg adult [40]. The estimated MET values used for the two intensity categories (low intensity activity and moderate to vigorous activity) were created by averaging individual MET values from all specific activities included in that category. A total physical activity score was created by summing the MET-hours per week of low intensity activity and moderate to vigorous activity reported during each age period. A lifetime physical activity score was created by averaging the total physical activity scores calculated for each age period.

The second questionnaire also requested information on sedentary behavior by asking about the average number of hours per day currently spent watching television or videos, and the average number of hours per day spent sitting. The response options for those items were as follows: none; less than 1 h; 1–2 h; 3–4 h; 5–6 h; 7–8 h; and 9 or more hours. The reliability and validity of questionnaires to assess physical activity similar to the ones used in this study have been evaluated in similar U.S. cohorts and found to provide useful information [41].

Identification of cases

Histologically confirmed incident colon and rectal cancer cases through 31 December, 2003, were ascertained through probabilistic linkage to the eight state cancer registries serving our cohort and three additional states (AZ, NV, and TX), all of which met the certification requirements defined by the North American Association of Central Cancer Registries, which are estimated to have 90% case ascertainment within 24 months [42]. For matching purposes, we have virtually complete data on first and last name, address history, gender, and date of birth. All suspected matches underwent a process that rejects those with insufficient degree of similarity to confirm a true match (approximately 4%); uncertain matches underwent final manual review. We conducted a validation study of cancer endpoint ascertainment by linking a subset of our cohort (n=12,000) to the cancer registries and comparing the data to self-reports and subsequent medical record confirmation of incident cancer in this sub-cohort. We found that approximately 90% of all incident cancers were accurately identified using the registries included in this cohort as the gold standard [42].

We used the International Classification of Diseases for Oncology, 3rd edition, to classify incident cases of colon cancer (C180–189) and rectosigmoid and rectal cancer (C199 and C209). Colon cancers were further subdivided into cancers of the proximal colon (C180-184) and distal colon (C185–187). Participants diagnosed simultaneously with a colon and rectal cancer were included in both colon and rectal cancer analyses. Deaths due to colorectal cancer were, in addition, identified through linkage to the National Death Index Plus. We estimate that ascertainment of deaths in our cohort is more than 93% complete [43].

Statistical analysis

We used Cox proportional hazards regression to estimate relative risks (RR) and 95% confidence intervals (CI) of colon or rectal cancer using age as the underlying time metric [44]. We tested and verified that the proportional hazards assumption was not violated for our main exposures and the covariates by including appropriate cross product terms with age and testing that all coefficients equaled zero. Analyses were stratified by gender and conducted separately for colon and rectal cancers because of an a priori hypothesis that the association between physical activity and colorectal cancer may vary by tumor sub-site and gender. Person-time began from the age at which a questionnaire was returned and ended at the age of diagnosis of colon or rectal cancer, death, move out of cancer registry catchment area, or the end of the study follow-up (31 December, 2003), whichever occurred first. Since information on sedentary behavior and more detailed information on physical activity was first reported in the second questionnaire, follow-up in analyses involving these more extensive assessments began in 1996–1997. Total person-time may vary between analyses due to exclusion of subjects with missing physical activity data.

Three models were used to evaluate the relationship between physical activity and colon or rectal cancer. The first model adjusted for age only. The second model, in addition, included smoking (never, quit ≤20 cigarettes/day, quit 20+ cigarettes/day, currently smoking ≤20 cigarettes/day, currently smoking 20+ cigarettes/day, unknown), alcohol consumption (grams/ day: 0, <5, 5–15, 15–30, 30–50, 50+), education (<12 years, high school graduate, post-high school, any college and post-graduate, unknown), race (white, black, other, unknown), family history of colon cancer (yes, no, unknown), total energy, and energy-adjusted intakes (quintiles) of red meat, calcium, whole grains, fruits, and vegetables. We also adjusted for menopausal hormone therapy in women (never, former user, current user, unknown). The third model, in addition, adjusted for body mass index (BMI) (kg/m^2: <20.0, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, 30.0–31.9, 32.0–33.9, 34.0+, unknown). Since BMI is potentially in the causal pathway between physical activity and colon cancer, we evaluated risks adjusted for BMI separately. We created missing indicator variables to reflect missing data for each covariate. Variables representing activity intensity and sedentary behavior were mutually adjusted. Additional variables evaluated for potential confounding included screening for colorectal cancer, aspirin/NSAID use, oral contraceptive use, marital status, multivitamin use, and energy-adjusted total intakes of total fat, dietary fiber, vitamin C, vitamin D, vitamin E, folate, and iron. The results were similar to those from the parsimonious model and were not included in final models.

Linear trend tests were conducted by modeling the median value of each category as a single continuous variable. We examined effect modification by including a cross-product interaction term between the physical activity variable and the covariate of interest along with the main effects terms in the appropriate multivariable model. The coefficient of the interaction term was assessed using a Wald test. Effect modification was evaluated both using the full cohort and separately among men and women. Statistical analyses were conducted using the SAS Statistical Software, version 9.1. All *P* values were two-sided and considered statistically significant at an a level of <0.05.

RESULTS

The 488,720 participants contributed 3,355,603 person-years of follow-up during a mean follow-up of 6.9 years. Among men, a total of 2,298 colon and 942 rectal cancers were identified and among women 1,112 colon and 370 rectal cancers were identified. Baseline participant characteristics by frequency of current exercise/sports activity are shown in Table 1. Men and women who were more physically active tended to have a lower BMI, they were less likely to smoke, and they reported consuming less red meat than those who were less physically active. In addition, physically active participants had a higher level of education and they consumed more fruits, vegetables, calcium, and folate than less physically active subjects. Women with greater physical activity were more likely to be currently taking menopausal hormone therapy than their less active counterparts.

Among men and women, participants who engaged in exercise/sports 5 or more times per week had an 18% reduced risk of colon cancer (RR=0.82; 95% CI=0.73-0.92) compared to those who reported never or rarely exercising. In addition, colon cancer risk was inversely related to increasing level of daily routine activity (*p*=0.003), with the lowest risk observed for participants reporting climbing stairs or lifting light loads as part of their daily routine (RR=0.73; 95% CI=0.63–0.85). We next stratified the cohort according to gender in order to examine more closely the effect of physical activity in men and women, although the formal test for interaction was not statistically significant (*p*=0.322). In men, increasing frequency of current exercise/sports participation was associated with a graded, statistically significant decrease in colon cancer risk in both age and multivariable-adjusted models (Table 2). Men who reported engaging in exercise/sports 5 or more times per week had a 21% lower risk of colon cancer than men who reported never or rarely exercising (RR=0.79; 95% CI=0.68–0.91). Additional adjustment for BMI had limited impact, thus subsequent results in the text are presented for multivariable-adjusted models without BMI unless otherwise stated. Among women, current exercise/sports was inversely associated with colon cancer in age-adjusted analyses, but showed no statistically significant trend with colon cancer after adjustment for covariates. However, the multivariable-adjusted relative risks were decreased for women who reported exercising 1–3 times per month or 3–4 times per week compared to women who never or rarely exercised.

We next investigated daily routine activity in relation to colon cancer risk. As compared with men who reported mostly sitting throughout the day, men who reported engaging in a combination of sitting and walking, walking and standing, and climbing stairs, or hills, or lifting, or carrying light loads had a statistically significant decreased risk of colon cancer (Table 2). Risk did not further decrease among men in the top category of daily routine activity which comprised heavy work or carrying heavy loads, although case numbers were small in that category (*n*=82 cases). Similarly, among women all but the highest level of daily routine activity were statistically significantly associated with reduced risk of colon cancer in age-adjusted analyses. Associations in women became statistically nonsignificant in multivariable-adjusted models.

We next evaluated the relation of physical activity to colorectal cancer according to anatomic sub-site (Table 3). Among men, inverse associations with current exercise/sports activity were seen for proximal and distal colon cancers and for rectal cancers. Sub-site results showed some similarities among women, with statistically significant age-adjusted associations for both proximal and distal colon cancers and a significant test for trend for distal colon cancers and rectal cancers, all of which, however, became nonsignificant after multivariable adjustment. Among men, inverse associations were found between daily routine activity and proximal (*p*=0.028) and distal colon cancers (*p*=0.008) but not rectal cancers (*p*=0.163). Among women, a suggestive inverse relation was noted between increasing level of daily routine activity and

proximal cancers. Associations with distal colon cancers and rectal cancers showed no consistent patterns among women. For both men and women, risk estimates for rectal cancer did not differ appreciably from cancers of the rectosigmoid junction (data not shown).

We assessed the time spent at low intensity activity, moderate to vigorous intensity activity, and sedentary behavior in relation to risk of colon cancer (Table 4). As compared with men never or rarely engaging in low intensity activity (such as walking), men reporting more than 7 h per week of low intensity activity had a RR of colon cancer of 0.81 (95% CI=0.65–1.00), even after adjustment for moderate to vigorous intensity activity. Similarly, our assessment of moderate to vigorous activity demonstrated an inverse dose-response relationship for colon cancer in men (p=0.037), independent of time spent in low intensity activity, although the relation appeared to level off in the highest category of moderate to vigorous activity. When we examined the combination of low intensity activity and moderate to vigorous activity (i.e., total activity) in men, the RR comparing extreme quintiles was 0.76 (95% CI=0.63–0.90). With regards to sedentary behavior in men, 9 or more hours versus less than 3 h per day of watching television or videos was associated with a RR of colon cancer of 1.61 (95% CI=1.14–2.27). Overall time spent sitting was also suggestively associated with colon cancer in men (p=0.050). Among women, no statistically significant relations with colon cancer were observed for low intensity activity, moderate to vigorous activity, and the combination of low intensity activity and moderate to vigorous activity, or time spent sitting. However, increasing time spent watching television was statistically significantly associated with increased colon cancer risk in age-adjusted models among women. Multivariable risks for sedentary behavior among men and women were similar with or without adjustment for physical activity.

We investigated colon cancer risk according to total physical activity during different age periods of life. Physical activity variables for different age periods were positively correlated with one another; the correlation coefficients ranged from 0.30 to 0.91 and values decreased with increasing time between age periods. Among men, total physical activity at ages 15–18 and ages 19–29 years was not associated with colon cancer, whereas a decrease in colon cancer risk was observed with increasing levels of total physical activity at ages 35–39 years and increasing levels of total lifetime physical activity (Table 5). The RR comparing extreme quintiles of total lifetime activity was 0.82 (95% CI=0.69–0.98). In contrast, among women no relations of total physical activity at ages 15–18, ages 19–29, ages 35–39, or total lifetime physical activity to colon cancer were observed. In further analyses of past activity, we in addition adjusted for total current activity. No appreciable differences in risk estimates emerged, indicating that observed relations with past activity were independent of current activity (data not shown).

The associations of physical activity and sedentary behavior to colon cancer risk were not modified by age, body mass, education, race, family history of colon cancer, history of colorectal cancer screening, alcohol consumption, smoking status, aspirin/NSAID use, or menopausal hormone therapy (women only).

DISCUSSION

In this large prospective investigation, we observed inverse associations between various indices of physical activity and risk of colon cancer. In men, both low intensity activities such as walking and more vigorous forms of activity appeared to protect against colon cancer, and risk reduction associated with physical activity was apparent for proximal, distal, and rectal cancers. In addition, reported recent physical activity among men was associated with greater benefit than activity at earlier periods in life, and sedentary behavior was independently associated with increased risk. In women, physical activity was less strongly associated with

colon and rectal cancers. However, risk estimates were generally in the same direction as observed in men.

Our finding of an inverse association between physical activity and colon and rectal cancer risk is largely consistent with evidence from previous studies [3–5]. Findings from available epidemiologic studies of women have been less conclusive, with results from several prospective studies observing no association [6,8,15,32] and others reporting statistically nonsignificant risk reductions [33,34]. Few studies found a statistically significant inverse association between physical activity and colorectal cancer in women [13,16,35]. Although we cannot entirely dismiss the possibility that men and women have biologically distinct responses to exercise, we must also consider the potential for misclassification of physical activity due to the difficulties inherent in measuring physical activity in women. Data derived from physical activity diaries [45,46] suggest that women spend between 30 minutes to 6 hours per day doing household chores and family care activities with time spent in occupational activities ranging from 4 to 16 h per day [47]. Thus, the variable nature of women's lives makes it challenging to accurately assess their physical activity. This increases the difficulty in detecting a modest association, such as between physical activity and colon cancer, for women.

In this study, the inverse dose-response relationship between current exercise/sports activity and colon cancer risk did not appear to vary appreciably between proximal and distal colon cancers for men or women. Few cohort studies of physical activity and colon cancer have conducted analyses stratified by tumor sub-site [6,12,13,16–18,32–34,36,37,48,49], with those that did yielding conflicting results. Some studies reported stronger inverse findings for the proximal colon [12,16,17,33,48], while others observed stronger inverse associations for distal colon sites [6,13,18,36,37]. Observed differences may be due to varying etiologies between tumors of the proximal and distal colon [50].

We observed a decreased risk of rectal cancer among vigorously active men in our study, which is in agreement with several recent investigations [16,18,51,52]. In the Cancer Prevention Study II Cohort, a 30% lower risk of rectal cancer was observed among both men and women who reported any versus no physical activity in the year preceding study enrollment [16]. Results of the Fukuoka Colorectal Cancer Study showed that job-related as well as total and moderate leisure-time physical activity were associated with a significant reduction of rectal cancer risk in men only [51]. In contrast, several cohort studies [12,17,33] have failed to detect an association between physical activity and rectal cancer.

The intensity of physical activity required to reduce colon cancer risk is an important public health issue. We found that both low intensity and moderate to vigorous intensity activity was independently associated with decreased colon cancer risk to similar magnitudes in men. Most previous studies reporting on physical activity intensity suggest that vigorous exercise is more strongly associated with colon cancer risk reduction than light or moderate activity [3]. However, in the California Teachers Study moderate physical activity was associated with a stronger colon cancer risk reduction than strenuous physical activity among women [34].

Most previous studies examining the association between sedentary behavior and physical activity have done so within the context of occupational activity [21,31,37,53]. Le Marchand et al. [53] presented evidence that the number of years spent in sedentary or light work only was directly associated with cancer of the proximal colon in both men and women. A case-control study conducted by Whittemore et al. [21] observed that the risk for colon and rectal cancer increased with increasing time spent sitting and for those reporting an overall sedentary lifestyle. To our knowledge, ours is the first large cohort study to document risk of colon cancer associated specifically with time spent in sedentary activities outside of an occupational setting. Our results indicate that sedentary behavior, in particular television watching among men, is

independently associated with an increased risk of colon cancer, even after adjustment for time spent participating in physical activity and body mass index.

Few studies have investigated the association between lifetime physical activity and colon cancer. Most previous studies report on adult physical activity often recording activity occurring close in time to study baseline. Results of our study suggest that physical activity associations with colon cancer are stronger for activity reported at recent ages than activity at earlier times. This finding is consistent with most previous reports of lifetime activity [9,14, 16,18,38], although data should be interpreted cautiously since subjects may less accurately recall past activities, particularly past light activities [54].

Our study has several strengths, including its prospective design, large cohort size with many incident cancer cases, and wide variety of physical activity indices including those for sedentary behavior. We also had extensive information on many known or suspected colon cancer risk factors, which reduced potential confounding and allowed us to evaluate effect modification. Potential limitations of this study result from the use of self-reported as opposed to objective assessments of physical activity. However, studies comparing physical activity measures similar to ours with validation instruments indicate that our instrument provides useful information [41]. Moreover, our activity data were associated with body mass and total energy intake in the hypothesized directions, further suggesting construct validity of our physical activity assessment.

Hypothesized mechanisms through which physical activity may protect against colon cancer include reduced gastrointestinal transit time, avoidance of positive energy balance, decreased levels of insulin and insulin-like growth factors (IGFs), and enhanced immune function [3]. It remains unclear what role these mechanisms may have for regulating rectal cancer risk. Previous research suggests that the risk factors for colon and rectal cancer sites may differ [55].

Our study is among the largest investigations to date to examine physical activity in relation to colorectal cancer and it confirms previously documented inverse associations between physical activity and colorectal cancer risk. Our findings add support to the limited available evidence that recent physical activity is more strongly associated with risk reduction than distant past activity, and that increased vigorous activity may protect against rectal cancer, particularly in men. Further, our results suggest that engaging in physical activity of any intensity is associated with reductions in colon and rectal cancer risk. In addition, we present novel findings, requiring replication, that recreational time spent sedentary, such as television or video watching, is associated with increased risk of colon cancer, independent of physical activity and body mass.

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Table 1

Baseline characteristics of the NIH-AARP study population according to frequency of current exercise and/or sports

Characteristic	Frequency of current exercise/sports				
	Never/Rarely	1–3 times/month	1–2 times/week	3–4 times/week	≥5 times/week
MEN					
Number of participants	44,072	38,433	64,426	82,450	62,688
Mean age (years)	62.2	61.4	61.7	62.4	62.6
Mean body mass index (kg/m^2)	28.4	28.0	27.5	26.9	26.4
White (%)	91.8	93.7	94.3	93.7	94.3
Black (%)	3.7	2.7	2.4	2.8	2.3
Hispanic (%)	2.6	2.0	1.7	1.8	1.7
Asian (%)	1.9	1.6	1.6	1.7	1.7
Family history of colorectal cancer (%)	8.3	8.8	8.8	8.7	8.7
History of colorectal cancer screening (%)[a]	50.9	52.5	54.0	56.2	54.9
Education (% college education)	57.2	66.9	70.0	72.5	70.5
Currently married (%)	80.5	85.6	87.1	86.6	85.8
Currently smoker (%)	18.0	14.2	11.5	7.9	7.2
Mean daily intakes					
Total energy (kcal)	2037.9	1958.2	1997.9	1987.9	2098.8
Whole grains (servings)[b]	1.2	1.2	1.3	1.4	1.5
Fruits (servings)[b]	2.7	2.8	2.9	3.3	3.6
Vegetables (servings)[b]	2.8	3.0	3.1	3.4	3.6
Red meat (g/day)[b]	84.6	82.5	79.9	71.9	67.2
Calcium (mg/day)[bc]	837.4	851.0	876.4	923.3	953.3
Folate (μg/day)[bc]	552.9	573.8	598.5	641.2	667.3
Alcohol (grams/day)	18.5	17.4	16.7	16.0	16.5
WOMEN					
Number of participants	44,539	28,472	41,736	49,704	32,200
Mean age (years)	62.2	61.0	61.5	62.0	62.2
Mean body mass index (kg/m^2)	28.6	27.6	26.8	25.9	25.2
White (%)	89.3	91.2	91.5	90.9	91.8
Black (%)	6.8	5.7	5.1	5.5	4.9
Hispanic (%)	2.4	1.8	1.9	1.9	1.5
Asian (%)	1.5	1.3	1.5	1.7	1.7
Family history of colorectal cancer (%)	9.3	10.0	10.2	10.3	9.8
History of colorectal cancer screening (%)[a]	31.6	32.6	34.2	36.2	35.2
Education (% college education)	46.5	55.7	58.2	61.0	61.6
Currently married (%)	41.7	42.7	43.7	47.3	48.2
Current smoker (%)	20.4	17.6	14.8	10.9	9.9
Menopausal hormone therapy, current use (%)	37.8	43.6	45.2	48.6	46.9
Mean daily intakes					
Total energy (kcal)	1591.0	1536.7	1565.2	1559.3	1608.2
Whole grains (servings)[b]	1.2	1.3	1.4	1.5	1.5
Fruits (servings)[b]	3.3	3.5	3.8	4.2	4.5
Vegetables (servings)[b]	3.6	3.9	4.1	4.5	4.9
Red meat (g/day)[b]	67.2	63.5	60.4	53.6	49.7
Calcium (mg/day)[bc]	1056.2	1116.8	1175.0	1263.2	1320.7
Folate (μg/day)[bc]	594.6	626.0	654.6	688.5	713.9
Alcohol (grams/day)	5.7	5.9	5.6	5.9	6.2

[a]Variables derived from second questionnaire.

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[b] Adjusted for total energy intake.

[c] Accounts for reported dietary intake as well as intake derived from supplements.

Table 2

Relative risk of colon cancer according to frequency of current exercise/sports and daily routine activity

| | Current exercise/sports | | | | | | Daily routine activity | | | | | |
	Never/Rarely	1–3 times/month	1–2 times/week	3–4 times/week	≥5 times week	P_{trend}	Mostly sitting	Combination of sitting and walking	Combination of walking and standing	Climbing stairs or hills or lifting or carrying light loads	Heavy work or carrying heavy loads	P_{trend}
MEN												
No. cases	411	312	492	611	431		203	711	909	352	82	
Person-years[a]	283,006	257,707	434,539	554,527	420,314		145,785	638,048	742,091	349,495	74,675	
Age-adjusted RR (95% CI)	1.0	0.87 (0.76–1.01)	0.80 (0.70–0.91)	0.74 (0.65–0.84)	0.68 (0.59–0.78)	<0.001	1.0	0.75 (0.64–0.88)	0.75 (0.64–0.87)	0.62 (0.52–0.74)	0.80 (0.62–1.03)	<0.001
Multivariable RR[b] (95% CI)	1.0	0.94 (0.81–1.09)	0.89 (0.78–1.02)	0.86 (0.76–0.98)	0.79 (0.68–0.91)	0.001	1.0	0.80 (0.68–0.93)	0.79 (0.68–0.93)	0.66 (0.56–0.79)	0.83 (0.63–1.08)	0.001
Multivariable RR[b] + BMI (95% CI)	1.0	0.94 (0.81–1.09)	0.90 (0.79–1.03)	0.88 (0.77–1.01)	0.82 (0.71–0.95)	0.013	1.0	0.81 (0.69–0.95)	0.82 (0.70–0.96)	0.70 (0.58–0.83)	0.86 (0.66–1.12)	0.007
WOMEN												
No. cases	314	129	221	256	170		99	339	439	196	17	
Person-years[a]	298,084	195,941	286,320	341,386	220,515		113,470	443,708	529,595	231,817	23,654	
Age-adjusted RR (95% CI)	1.0	0.69 (0.56–0.84)	0.77 (0.65–0.91)	0.71 (0.60–0.84)	0.72 (0.60–0.87)	0.004	1.0	0.78 (0.62–0.98)	0.75 (0.60–0.93)	0.76 (0.59–0.96)	0.74 (0.44–1.24)	0.077
Multivariable RR[b,c] (95% CI)	1.0	0.73 (0.60–0.90)	0.85 (0.71–1.02)	0.83 (0.70–0.99)	0.85 (0.70–1.04)	0.376	1.0	0.86 (0.69–1.08)	0.86 (0.69–1.08)	0.88 (0.68–1.13)	0.82 (0.49–1.38)	0.509
Multivariable RR[b,c] + BMI (95% CI)	1.0	0.73 (0.60–0.90)	0.86 (0.72–1.03)	0.84 (0.71–1.01)	0.87 (0.71–1.06)	0.536	1.0	0.88 (0.70–1.10)	0.89 (0.71–1.12)	0.91 (0.70–1.17)	0.84 (0.50–1.42)	0.714

[a] Person-years may not sum to totals due to rounding.

[b] Multivariable models are adjusted for age, smoking, alcohol consumption, education, race, family history of colon cancer, total energy and energy-adjusted intake of red meat, calcium, whole grains, fruit and vegtables. Models are mutually adjusted for frequency of vigorous activity and daily routine activity.

[c] Also adjusted for menopausal hormone therapy use.

Table 3

Relative risk of colorectal cancer by anatomic site according to frequency of current exercise/sports and daily routine activity

Variable	Frequency of current exercise/sports						Daily routine activity					
	Never/Rarely	1–3 times month	1–2 times/ week	3–4 times/ week	≥5 times/ week	P_{trend}	Mostly sitting	Combination of sitting and walking	Combination of walking and standing	Climbing stairs or hills or lifting or carrying light loads	Heavy work or arrying cheavy loads	P_{trend}
MEN												
Proximal colon												
No. cases	207	169	261	326	227		102	370	483	203	32	
Age-adjusted RR (95% CI)	1.0	0.95 (0.78–1.16)	0.85 (0.70–1.01)	0.78 (0.65–0.93)	0.70 (0.58–0.85)	<0.001	1.0	0.77 (0.62–0.95)	0.77 (0.62–0.95)	0.69 (0.54–0.88)	0.62 (0.42–0.93)	0.008
Multivariate-adjusted RR[a] (95% CI)	1.0	1.01 (0.82–1.24)	0.93 (0.77–1.12)	0.88 (0.74–1.06)	0.80 (0.65–0.97)	0.009	1.0	0.80 (0.64–1.00)	0.81 (0.65–1.00)	0.74 (0.58–0.94)	0.65 (0.44–0.98)	0.028
Multivariate-adjusted RR[a] + BMI (95% CI)	1.0	1.01 (0.82–1.24)	0.94 (0.78–1.13)	0.90 (0.75–1.08)	0.83 (0.68–1.02)	0.033	1.0	0.82 (0.66–1.02)	0.84 (0.67–1.04)	0.77 (0.60–0.99)	0.68 (0.45–1.02)	0.070
Distal colon												
No. cases	185	131	205	266	184		95	309	388	134	45	
Age-adjusted RR (95% CI)	1.0	0.81 (0.65–1.01)	0.74 (0.60–0.90)	0.72 (0.60–0.87)	0.65 (0.53–0.80)	<0.001	1.0	0.70 (0.56–0.89)	0.70 (0.56–0.88)	0.52 (0.40–0.67)	0.94 (0.66–1.33)	0.004
Multivariate-adjusted RR[a] (95% CI)	1.0	0.88 (0.70–1.10)	0.84 (0.69–1.03)	0.88 (0.72–1.07)	0.79 (0.64–0.98)	0.107	1.0	0.75 (0.60–0.95)	0.75 (0.59–0.94)	0.55 (0.42–0.73)	0.94 (0.65–1.36)	0.008
Multivariate-adjusted RR[a] + BMI (95% CI)	1.0	0.87 (0.70–1.10)	0.85 (0.69–1.04)	0.90 (0.74–1.10)	0.83 (0.67–1.03)	0.285	1.0	0.77 (0.61–0.98)	0.78 (0.62–0.99)	0.59 (0.45–0.77)	0.98 (0.68–1.42)	0.027
Rectosigmoid and rectum												
No. cases	174	124	189	254	182		58	271	378	178	38	
Age-adjusted RR (95% CI)	1.0	0.81 (0.65–1.03)	0.72 (0.58–0.88)	0.73 (0.60–0.88)	0.68 (0.55–0.84)	0.003	1.0	1.01 (0.76–1.35)	1.12 (0.85–1.48)	1.12 (0.83–1.51)	1.29 (0.86–1.95)	0.094
Multivariate-adjusted RR[a] (95% CI)	1.0	0.85 (0.67–1.07)	0.77 (0.62–0.95)	0.82 (0.67–1.00)	0.76 (0.61–0.94)	0.074	1.0	1.09 (0.82–1.46)	1.18 (0.89–1.56)	1.19 (0.88–1.61)	1.25 (0.82–1.90)	0.163
Multivariate-adjusted RR[a] + BMI (95% CI)	1.0	0.85 (0.67–1.07)	0.77 (0.62–0.95)	0.82 (0.67–1.00)	0.76 (0.61–0.95)	0.093	1.0	1.10 (0.82–1.46)	1.19 (0.90–1.58)	1.20 (0.88–1.63)	1.26 (0.82–1.92)	0.144
WOMEN												
Proximal colon												
No. cases	190	77	134	162	107		61	200	284	119	6	

Variable	Frequency of current exercise/sports						Daily routine activity					
	Never/Rarely	1–3 times month	1–2 times/ week	3–4 times/ week	≥5 times/ week	P_{trend}	Mostly sitting	Combination of sitting and walking	Combination of walking and standing	Climbing stairs or hills or lifting or carrying light loads	Heavy work or carrying cheavy loads	P_{trend}
Age-adjusted RR (95% CI)	1.0	0.68 (0.52–0.89)	0.77 (0.62–0.96)	0.74 (0.60–0.92)	0.75 (0.59–0.95)	0.069	1.0	0.74 (0.55–0.98)	0.77 (0.58–1.02)	0.73 (0.53–0.99)	0.42 (0.18–0.98)	0.095
Multivariable-adjusted RR[a,b] (95% CI)	1.0	0.73 (0.56–0.95)	0.86 (0.68–1.07)	0.87 (0.70–1.09)	0.89 (0.69–1.15)	0.857	1.0	0.81 (0.61–1.08)	0.88 (0.66–1.17)	0.83 (0.60–1.15)	0.46 (0.20–1.07)	0.398
Multivariable-adjusted RR[a,b] + BMI (95% CI)	1.0	0.73 (0.56–0.96)	0.86 (0.69–1.09)	0.88 (0.71–1.10)	0.91 (0.70–1.17)	0.969	1.0	0.83 (0.62–1.11)	0.91 (0.68–1.21)	0.86 (0.62–1.19)	0.47 (0.20–1.09)	0.497
Distal colon												
No. cases	115	49	81	86	58		37	131	138	72	11	
Age-adjusted RR (95% CI)	1.0	0.70 (0.50–0.98)	0.76 (0.57–1.01)	0.65 (0.49–0.86)	0.68 (0.49–0.93)	0.018	1.0	0.83 (0.57–1.19)	0.66 (0.46–0.95)	0.78 (0.52–1.16)	1.31 (0.67–2.56)	0.372
Multivariable–adjusted RR[a,b] (95% CI)	1.0	0.75 (0.54–1.05)	0.85 (0.64–1.14)	0.76 (0.57–1.02)	0.78 (0.56–1.09)	0.208	1.0	0.91 (0.63–1.32)	0.76 (0.52–1.10)	0.91 (0.60–1.38)	1.47 (0.74–2.92)	0.861
Multivariable-adjusted RR[a,b] + BMI (95% CI)	1.0	0.75 (0.54–1.05)	0.86 (0.64–1.15)	0.78 (0.58–1.05)	0.82 (0.58–1.14)	0.336	1.0	0.94 (0.65–1.36)	0.80 (0.55–1.17)	0.97 (0.64–1.47)	1.54 (0.77–3.08)	0.868
Rectosigmoid and rectum												
No. cases	83	51	102	75	50		31	115	152	57	6	
Age-adjusted RR (95% CI)	1.0	0.99 (0.70–1.41)	1.32 (0.99–1.77)	0.79 (0.58–1.08)	0.81 (0.57–1.15)	0.028	1.0	0.88 (0.59–1.31)	0.90 (0.61–1.33)	0.77 (0.49–1.19)	0.87 (0.36–2.08)	0.337
Multivariable-adjusted RR[a,b] (95% CI)	1.0	1.06 (0.74–1.51)	1.47 (1.09–1.98)	0.92 (0.66–1.28)	0.95 (0.65–1.37)	0.235	1.0	0.90 (0.60–1.34)	0.95 (0.64–1.41)	0.80 (0.51–1.26)	0.89 (0.37–2.16)	0.479
Multivariable-adjusted RR[a,b] + BMI (95% CI)	1.0	1.07 (0.75–1.52)	1.49 (1.10–2.01)	0.94 (0.68–1.31)	0.97 (0.67–1.41)	0.290	1.0	0.91 (0.61–1.36)	0.96 (0.64–1.43)	0.82 (0.52–1.29)	0.89 (0.36–2.16)	0.525

[a] Multivariable models are adjusted for age, smoking, alcohol consumption, education, race, family history of colon cancer, total energy and energy-adjusted intake of red meat, calcium, whole grains, fruit and vegtables. Models are mutually adjusted for frequency of vigorous activity and daily routine activity.

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[b] Also adjusted for menopausal hormone therapy use.

Table 4

Relative risk of colon cancer according to time spent in sedentary behavior and time spent in low intensity and moderate to vigorous intensity activity[a]

Variable	No. cases	Person-years	Age-adjusted RR(95% CI)	Multivariable-adjusted RR[d] (95% CI)	Multivariable-adjusted RR[d] + BMI (95% CI)
MEN					
Low intensity (hours/week)[b]					
Never/Rarely	145	108,102	1.0	1.0	1.0
<1	121	95,136	0.96 (0.75–1.22)	0.98 (0.76–1.25)	0.97 (0.76–1.25)
1–3	337	276,424	0.89 (0.74–1.09)	0.97 (0.79–1.19)	0.97 (0.79–1.19)
4–7	332	290,830	0.80 (0.66–0.98)	0.92 (0.75–1.13)	0.92 (0.75–1.13)
≥7	329	311,098	0.71 (0.59–0.87)	0.81 (0.65–1.00)	0.81 (0.65–1.00)
P Trend			<0.001	0.017	0.017
Moderate to vigorous intensity (hours/week)[b]					
Never/Rarely	233	150,931	1.0	1.0	1.0
<1	149	114,170	0.86 (0.70–1.06)	0.90 (0.73–1.11)	0.91 (0.73–1.12)
1–3	313	272,964	0.74 (0.63–0.88)	0.82 (0.68–0.98)	0.83 (0.69–1.00)
4–7	282	281,835	0.64 (0.54–0.76)	0.74 (0.61–0.89)	0.76 (0.63–0.92)
≥7	287	261,689	0.67 (0.57–0.80)	0.82 (0.67–0.99)	0.86 (0.71–1.04)
P Trend			<0.001	0.037	0.135
Total physical activity score (median MET-hours/week)[b]					
Q1 (5.53)	301	205,246	1.0	1.0	1.0
Q2 (16.52)	238	189,079	0.84 (0.70–0.99)	0.86 (0.73–1.02)	0.87 (0.74–1.04)
Q3 (29.97)	270	252,045	0.70 (0.60–0.83)	0.75 (0.64–0.89)	0.77 (0.65–0.91)
Q4 (45.43)	224	233,310	0.61 (0.52–0.73)	0.66 (0.55–0.79)	0.68 (0.57–0.81)
Q5 (66.08)	231	201,909	0.70 (0.59–0.84)	0.76 (0.63–0.90)	0.79 (0.66–0.94)
P Trend			<0.001	<0.001	0.001
Time spent watching TV or videos (hours/day)[c]					
<3	368	394,573	1.0	1.0	1.0
3–4	594	484,242	1.24 (1.09–1.41)	1.16 (1.02–1.33)	1.14 (1.00–1.30)
5–6	227	155,500	1.42 (1.20–1.68)	1.26 (1.06–1.49)	1.22 (1.03–1.45)
7–8	35	24,535	1.40 (0.99–1.97)	1.19 (0.84–1.69)	1.15 (0.81–1.63)
≥9	37	19,997	1.90 (1.36–2.67)	1.61 (1.14–2.27)	1.56 (1.11–2.20)
P Trend			<0.001	<0.001	0.002
Time spent sitting (hours/day)[c]					
<3	201	199,334	1.0	1.0	1.0
3–4	391	315,575	1.22 (1.03–1.44)	1.21 (1.02–1.44)	1.20 (1.01–1.43)
5–6	375	306,848	1.24 (1.04–1.47)	1.23 (1.03–1.46)	1.21 (1.02–1.44)
7–8	191	162,098	1.28 (1.05–1.56)	1.24 (1.02–1.52)	1.23 (1.01–1.50)
≥9	106	94,621	1.32 (1.04–1.68)	1.24 (0.98–1.57)	1.22 (0.96–1.55)
P Trend			0.011	0.050	0.073
WOMEN					
Low intensity (hours/week)[b]					
Never/Rarely	31	37,417	1.0	1.0	1.0
<1	37	45,275	1.01 (0.63–1.62)	1.02 (0.63–1.65)	1.02 (0.63–1.65)
1–3	141	165,947	1.03 (0.70–1.52)	1.14 (0.76–1.71)	1.14 (0.76–1.71)
4–7	185	218,764	0.97 (0.67–1.42)	1.15 (0.77–1.72)	1.15 (0.77–1.72)
≥7	278	323,641	0.96 (0.66–1.39)	1.15 (0.77–1.71)	1.15 (0.77–1.71)
P Trend			0.520	0.543	0.553
Moderate to vigorous intensity (hours/week)[b]					
Never/Rarely	106	111,416	1.0	1.0	1.0
<1	80	83,921	1.04 (0.78–1.39)	1.05 (0.78–1.41)	1.05 (0.78–1.41)
1–3	171	201,933	0.90 (0.71–1.15)	0.93 (0.72–1.20)	0.93 (0.72–1.20)
4–7	154	203,716	0.79 (0.62–1.01)	0.84 (0.64–1.09)	0.84 (0.64–1.10)
≥7	161	190,058	0.87 (0.68–1.11)	0.93 (0.70–1.22)	0.93 (0.70–1.23)

Variable	No. cases	Person-years	Age-adjusted RR(95% CI)	Multivariable-adjusted RR^d (95% CI)	Multivariable-adjusted RR^d + BMI (95% CI)
P Trend			0.079	0.311	0.327
Total physical activity score (median MET-hours/week)^b					
Q1 (8.07)	122	128,895	1.0	1.0	1.0
Q2 (20.99)	173	200,328	0.88 (0.70–1.11)	0.94 (0.74–1.19)	0.94 (0.74–1.18)
Q3 (35.72)	83	110,649	0.77 (0.58–1.01)	0.85 (0.64–1.13)	0.85 (0.64–1.13)
Q4 (53.43)	168	202,644	0.82 (0.65–1.04)	0.92 (0.73–1.17)	0.92 (0.73–1.17)
Q5 (66.08)	126	148,528	0.82 (0.64–1.05)	0.92 (0.71–1.18)	0.92 (0.71–1.18)
P Trend			0.124	0.540	0.555
Time spent watching TV or videos (hours/day)^c					
<3	200	277,226	1.0	1.0	1.0
3–4	279	336,214	1.02 (0.85–1.23)	0.94 (0.78–1.13)	0.94 (0.78–1.13)
5–6	131	127,839	1.20 (0.96–1.49)	1.03 (0.82–1.30)	1.03 (0.82–1.30)
7–8	26	24,295	1.25 (0.83–1.89)	1.04 (0.69–1.58)	1.04 (0.68–1.58)
≥9	33	22,789	1.82 (1.26–2.63)	1.45 (0.99–2.12)	1.45 (0.99–2.13)
P Trend			0.002	0.174	0.180
Time spent sitting (hours/day)^c					
<3	148	173,280	1.0	1.0	1.0
3–4	194	228,658	0.97 (0.78–1.20)	0.96 (0.77–1.19)	0.96 (0.77–1.19)
5–6	188	211,665	1.08 (0.87–1.34)	1.04 (0.84–1.30)	1.04 (0.84–1.30)
7–8	83	111,851	1.02 (0.78–1.33)	0.96 (0.73–1.26)	0.96 (0.73–1.26)
≥9	54	62,322	1.34 (0.98–1.83)	1.24 (0.90–1.70)	1.23 (0.89–1.70)
P Trend			0.128	0.361	0.382

[a] Variables derived from the second questionnaire

[b] Refers to how often subjects participated during the last 10 years

[c] Refers to the time spent during the last 12 months

[d] Multivariable models are adjusted for age, smoking, alcohol consumption, education, race, family history of colon cancer, total energy and energy-adjusted intake of red meat, calcium, whole grains, fruit and vegetables. Models for women are adjusted for menopausal hormone therapy. Low intensity and moderate to vigorous intensity physical activity are mutally adjusted and sedentary behavior variables are adjusted for total physical activity.

Table 5

Relative risk of colon cancer in relation to total physical activity at ages 15–18, 19–29, 35–39, and over the lifetime[a]

Variable	Quintile of total physical activity					P_{trend}
	Q1	Q2	Q3	Q4	Q5	
MEN						
Total activity ages 15–18 years						
No. cases	288	221	254	143	335	
Person-years	230,444	188,030	240,891	123,471	276,163	
Age-adjusted RR (95% CI)	1.0	0.95 (0.79–1.13)	0.86 (0.73–1.02)	0.93 (0.76–1.14)	0.97 (0.83–1.13)	0.537
Multivariable-adjusted RR[b] (95% CI)	1.0	0.96 (0.81–1.15)	0.88 (0.74–1.04)	0.95 (0.78–1.16)	0.97 (0.83–1.14)	0.581
Multivariable-adjusted RR[b] + BMI (95% CI)	1.0	0.96 (0.81–1.15)	0.88 (0.74–1.04)	0.94 (0.77–1.15)	0.96 (0.82–1.13)	0.533
Total activity ages 19–29 years						
No. cases	233	287	279	201	241	
Person-years	191,596	236,257	257,044	171,761	202,340	
Age-adjusted RR (95% CI)	1.0	0.99 (0.84–1.18)	0.89 (0.75–1.06)	0.95 (0.79–1.15)	0.94 (0.78–1.12)	0.303
Multivariable-adjusted RR[b] (95% CI)	1.0	1.01 (0.85–1.20)	0.90 (0.76–1.07)	0.95 (0.79–1.15)	0.93 (0.77–1.11)	0.246
Multivariable-adjusted RR[b] + BMI (95% CI)	1.0	1.01 (0.85–1.20)	0.90 (0.75–1.07)	0.95 (0.79–1.15)	0.92 (0.77–1.11)	0.227
Total activity ages 35–39 years						
No. cases	304	197	279	247	214	
Person-years	223,716	159,019	254,831	224,600	196,833	
Age-adjusted RR (95% CI)	1.0	0.90 (0.76–1.08)	0.80 (0.68–0.94)	0.79 (0.67–0.93)	0.76 (0.64–0.91)	<0.001
Multivariable-adjusted RR[b] (95% CI)	1.0	0.91 (0.76–1.09)	0.83 (0.70–0.97)	0.80 (0.68–0.95)	0.76 (0.64–0.91)	0.001
Multivariable-adjusted RR[b] + BMI (95% CI)	1.0	0.91 (0.76–1.09)	0.83 (0.70–0.97)	0.80 (0.68–0.95)	0.76 (0.64–0.91)	0.001
Total activity over the lifetime						
No. cases	285	254	254	203	245	
Person-years	211,501	212,135	211,516	210,651	213,197	
Age-adjusted RR (95% CI)	1.0	0.89 (0.75–1.05)	0.89 (0.75–1.05)	0.70 (0.58–0.84)	0.81 (0.68–0.96)	0.001
Multivariable-adjusted RR[b] (95% CI)	1.0	0.91 (0.77–1.08)	0.91 (0.77–1.08)	0.72 (0.60–0.86)	0.82 (0.69–0.98)	0.003
Multivariable-adjusted RR[b] + BMI (95% CI)	1.0	0.91 (0.77–1.08)	0.90 (0.76–1.07)	0.71 (0.59–0.85)	0.82 (0.69–0.97)	0.002
WOMEN						
Total activity ages 15–18 years						
No. cases	131	124	128	87	177	
Person-years	149,820	158,128	160,226	117,518	184,718	
Age-adjusted RR (95% CI)	1.0	0.88 (0.69–1.12)	0.91 (0.71–1.16)	0.83 (0.64–1.09)	1.06 (0.85–1.33)	0.607
Multivariable-adjusted RR[b] (95% CI)	1.0	0.89 (0.69–1.13)	0.92 (0.72–1.18)	0.84 (0.64–1.10)	1.04 (0.83–1.31)	0.696
Multivariable-adjusted RR[b,c] + BMI (95% CI)	1.0	0.89 (0.69–1.14)	0.93 (0.73–1.19)	0.84 (0.64–1.11)	1.05 (0.84–1.32)	0.640
Total activity ages 19–29 years						
No. cases	138	111	104	119	175	
Person-years	157,524	146,787	140,876	121,561	203,662	
Age-adjusted RR (95% CI)	1.0	0.85 (0.66–1.09)	0.82 (0.64–1.06)	1.07 (0.84–1.36)	0.91 (0.72–1.13)	0.778
Multivariable-adjusted RR[b,c] (95% CI)	1.0	0.87 (0.68–1.11)	0.84 (0.65–1.08)	1.09 (0.85–1.39)	0.90 (0.72–1.13)	0.754

Variable	Q1	Q2	Q3	Q4	Q5	P_{trend}
			Quintile of total physical activity			
Multivariable-adjusted RR[b,c] + BMI (95% CI)	1.0	0.87 (0.68–1.12)	0.84 (0.65–1.09)	1.09 (0.85–1.40)	0.91 (0.73–1.14)	0.805
Total activity ages 35–39 years						
No. cases	138	118	93	102	196	
Person-years	154,977	150,823	144,954	124,699	194,956	
Age-adjusted RR (95% CI)	1.0	0.86 (0.67–1.10)	0.70 (0.54–0.91)	0.86 (0.67–1.12)	1.01 (0.81–1.26)	0.980
Multivariable-adjusted RR[b,c] (95% CI)	1.0	0.89 (0.69–1.14)	0.73 (0.56–0.95)	0.90 (0.70–1.17)	1.04 (0.83–1.30)	0.785
Multivariable-adjusted RR[b,c] + BMI (95% CI)	1.0	0.89 (0.70–1.14)	0.73 (0.56–0.96)	0.91 (0.70–1.18)	1.05 (0.84–1.31)	0.713
Total activity over the lifetime						
No. cases	129	125	111	158	124	
Person-years	153,807	154,203	154,536	153,601	154,262	
Age-adjusted RR (95% CI)	1.0	0.96 (0.75–1.22)	0.84 (0.65–1.08)	1.16 (0.92–1.46)	0.88 (0.69–1.13)	0.874
Multivariable-adjusted RR[b,c] (95% CI)	1.0	1.00 (0.78–1.28)	0.88 (0.68–1.14)	1.20 (0.95–1.52)	0.92 (0.72–1.18)	0.907
Multivariable-adjusted RR[b,c] + BMI (95% CI)	1.0	1.00 (0.78–1.28)	0.88 (0.68–1.14)	1.20 (0.95–1.52)	0.93 (0.72–1.19)	0.881

[a] Variables derived from the second questionnaire. Specific quintile ranges vary across variables.

[b] Multivariable models are adjusted for age, smoking, alcohol consumption, education, race, family history of colon cancer, total energy and energy-adjusted intake of red meat, calcium, whole grains, fruit and vegetables.

[c] Also adjusted for menopausal hormone therapy.