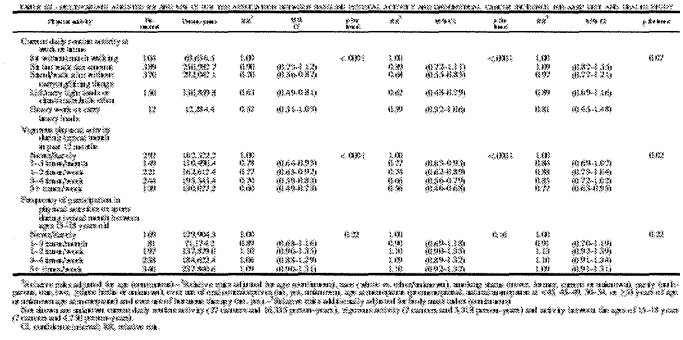
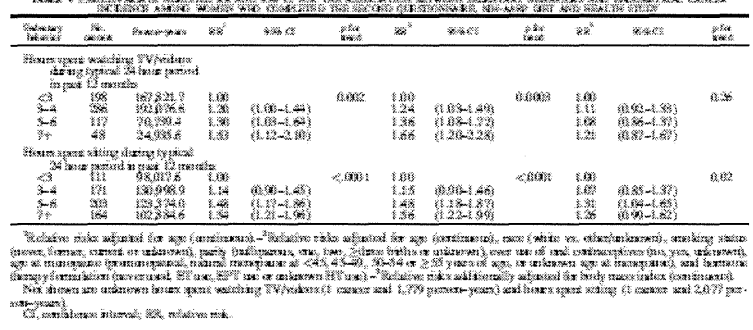
論文名	Physical activity, sedentary behavior, and endometrial cancer risk in the NIH-AARP Diet and Health Study
著 者	Gierach GL, Chang SC, Brinton LA, Lacey JV, Jr., Hollenbeck AR, Schatzkin A, Leitzmann MF
雑誌名	Int J Cancer
巻・号・頁	124 2139-2147
発行年	2009
PubMedリンク	http://www.ncbi.nlm.nih.gov/pubmed/19123463

対象の内訳	ヒト	動物	地 域	欧米	研究の種類	縦断研究
対象	一般健常者	空白		( )		コホート研究
性別	女性	( )		( )		( )
年齢	50-71歳	[redacted]		( )		前向き研究
対象数	10000以上			( )		( )

調査の方法	質問紙	( )				
アウトカム	予 防	な し	な し	ガン予防	な し	( ) ( )
	維持・改善	な し	な し	な し	な し	( ) ( )

図 表





図表掲載箇所	P2144, Table3, P2145, Table5
概 要 (800字まで)	本研究は、アメリカのThe NIH-AARP Diet and Health Studyに参加した閉経後の女性109,621名を対象に約8年間追跡調査し、身体活動や不活動と子宮内膜がん発症との関連を検討したものである。質問紙により、1)余暇身体活動を除く日常活動、2)高強度身体活動、3)職業活動や徒歩・自転車による通勤、4)余暇身体活動や家事活動、5)不活動についてそれぞれの頻度を尋ねた。過去1年間の典型的な月における高強度身体活動について、ほとんどない、1-3回/月、1-2回/週、3-4回/週、5回/週以上の5群に分類した。また、過去1年間の典型的な日における不活動について、テレビ視聴時間および座位時間が3時間未満、3-4時間、5-6時間、7時間以上の4群に分類した。高強度身体活動をほとんど行わない集団と比較すると、量反応的に子宮内膜がん発症リスクが減少し(Ptrend=0.02)、週当たり5回以上行う集団ではがん発症リスクが0.77(95%信頼区間:0.63-0.95)と有意に減少した。テレビ視聴時間と子宮内膜がん発症リスクとの関連については有意な差はみられなかったものの、座位時間とがん発症リスクについては、1日当たり3時間未満の集団と比較すると、量反応的にリスクが上昇し(Ptrend=0.02)、1日当たり5-6時間の集団で1.31(1.04-1.65)と有意にリスクの上昇がみられた。その
結 論 (200字まで)	閉経後の女性コホートにおける身体活動と子宮内膜がんの関連について、高強度身体活動の頻度が高い集団で発症リスクが抑えられ、特に肥満女性(BMI>25)における強力な保護効果が明らかとなった。また、肥満度とは独立して座位時間の延長ががん発症リスクを上昇させることが明らかとなった。
エキスパートによるコメント (200字まで)	身体活動基準の策定に用いられた研究の1つである。子宮内膜がんの発症と身体活動、不活動との関係を大規模な集団で検討した非常に重要な論文であり、高強度の身体活動の増大と座位時間の短縮の重要性を示唆している。座位時間は職業等によって大きく影響され、それは個人の意思に関わらないため、個人で改善可能な高強度の身体活動との相互作用についても今後検討されることが望まれる。

担当者:久保絵里子・村上晴香・宮地元彦

Cancer Causes Control (2008) 19:939–953
DOI 10.1007/s10552-008-9159-0

ORIGINAL PAPER

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

Regan A. Howard · D. Michal Freedman · Yikyung Park · Albert Hollenbeck · Arthur Schatzkin · Michael F. Leitzmann

Received: 17 January 2008 / Accepted: 8 April 2008 / Published online: 25 April 2008

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

R. A. Howard (✉) · D. M. Freedman
Division of Cancer Epidemiology and Genetics, Radiation Epidemiology Branch, National Cancer Institute, NIH, DHHS, Executive Plaza South, Suite 7091, Bethesda, MD 20892, USA
e-mail: reganho@mail.nih.gov

Y. Park · A. Schatzkin · M. F. Leitzmann
Division of Cancer Epidemiology and Genetics, Nutritional Epidemiology Branch, National Cancer Institute, Bethesda, MD, USA

A. Hollenbeck
AARP, Washington, DC, USA

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 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 α 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 non-significant 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

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
Current 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
Vegtables (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)[b,c]	837.4	851.0	876.4	923.3	953.3
Folate (μg/day)[b,c]	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
Vegtables (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)[b,c]	1056.2	1116.8	1175.0	1263.2	1320.7
Folate (μg/day)[b,c]	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

[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

Variable	Current exercise/sports					p_{trend}	Daily routine activity					p_{trend}
	Never/ rarely	1–3 times/ month	1–2 times/ week	3–4 times/ week	≥5 times/ week		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	
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, fruits, 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 carrying heavy 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	
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

Table 3 continued

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 heavy loads	p_{trend}
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, fruits, and vegtables. Models are mutually adjusted for frequency of vigorous activity and daily routine activity

[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-hrs/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 (0.78–1.72)	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)

Table 4 continued

Variable	No. cases	Person-years	Age-adjusted RR (95% CI)	Multivariable-adjusted RR[d] (95% CI)	Multivariable-adjusted RR[d] + BMI (95% CI)
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)
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 vegtables. 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

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

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					
	Q1	Q2	Q3	Q4	Q5	p_{trend}
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,c] (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
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	

Table 5 continued

Variable	Quintile of total physical activity					
	Q1	Q2	Q3	Q4	Q5	p_{trend}
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 vegtables

[c] Also adjusted for menopausal hormone therapy

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.

References

1. American Cancer Society (2007) Cancer facts and figures 2007. American Cancer Society, Atlanta, GA
2. Friedenreich CM (2001) Physical activity and cancer prevention: from observational to intervention research. Cancer Epidemiol Biomarkers Prev 10:287–301
3. Slattery ML (2004) Physical activity and colorectal cancer. Sports Med 34:239–252
4. Samad AKA, Taylor RS, Marshall T, Chapman MAS (2005) A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. Colorectal Dis 7:204–213
5. Harriss DJ, Cable NT, George K, Reilly T, Renehan AG, Haboubi N (2007) Physical activity before and after diagnosis of colorectal cancer: disease risk, clinical outcomes, response pathways and biomarkers. Sports Med 37:947–960
6. Wu AH, Paganini-Hill A, Ross RK, Henderson BE (1987) Alcohol, physical activity and other risk factors for colorectal cancer: a prospective study. Br J Cancer 55:687–694
7. Albanes D, Blair A, Taylor PR (1989) Physical activity and risk of cancer in the NHANES I population. Am J Public Health 79:744–750
8. Ballard-Barbash R, Schatzkin A, Albanes D et al (1990) Physical activity and risk of large bowel cancer in the Framingham study. Cancer Res 50:3610–3613

9. Lee IM, Paffenbarger RS, Hsieh CC (1991) Physical activity and risk of developing colorectal cancer among college alumni. J Natl Cancer Inst 83:1324–1329
10. Thun MJ, Calle EE, Namboodiri MM et al (1992) Risk factors for fatal colon cancer in a large prospective study. J Natl Cancer Inst 84:1491–1500
11. Bostick RM, Potter JD, Kushi LH et al (1994) Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). Cancer Causes Control 5:38–52
12. Thune I, Lund E (1996) Physical activity and risk of colorectal cancer in men and women. Br J Cancer 73:1134–1140
13. Martinez ME, Giovannucci E, Spiegelman D, Hunter DJ, Willett WC, Colditz GA (1997) Leisure-time physical activity, body size, and colon cancer in women. J Natl Cancer Inst 89:948–955
14. Lee IM, Manson JE, Ajani U, Paffenbarger RS, Hennekens CH, Buring JE (1997) Physical activity and risk of colon cancer: the Physician's Health Study (United States). Cancer Causes Control 8:568–574
15. Nilsen TI, Vatten LJ (2001) Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: exploring the hyperinsulinaemia hypothesis. Br J Cancer 84:417–422
16. Chao A, Connell CJ, Jacobs EJ et al (2004) Amount, type, and timing of recreational physical activity in relation to colon and rectal cancer in older adults: the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiol Biomarkers Prev 3:2187–2195
17. Friedenreich C, Norat T, Steindorf K et al (2006) Physical activity and risk of colon and rectal cancers: The European prospective investigation into cancer and nutrition. Cancer Epidemiol Biomarkers Prev 15:2398–2407
18. Larsson SC, Rutegard J, Bergkvist L, Wolk A (2006) Physical activity, obesity, and risk of colon and rectal cancer in a cohort of Swedish men. Eur J Cancer 42:2590–2597
19. Slattery ML, Schumacher MC, Smith KR, West DW, Abd-Elghany N (1988) Physical activity, diet, and risk of colon cancer in Utah. Am J Epidemiol 128:989–999
20. Gerhardsson de Verdier M, Steineck G, Hagman U, Rieger A, Norell SE (1990) Physical activity and colon cancer: a case-referent study in Stockholm. Int J Cancer 46:985–989
21. Whittemore AS, Wu-Williams AH, Lee M et al (1990) Diet, physical activity, and colorectal cancer among Chinese in North America and China. J Natl Cancer Inst 82:915–926
22. Longnecker MP, Gerhardsson de Verdier M, Frumkin H, Carpenter C (1995) A case-control study of physical activity in relation to risk of cancer of the right colon and rectum in men. Int J Epidemiol 24:42–50
23. White E, Jacobs EJ, Daling JR (1996) Physical activity in relation to colon cancer in middle-aged men and women. Am J Epidemiol 144:42–50
24. Levi F, Pasche C, Lucchini F, Tavani A, La Vecchia C (1999) Occupational and leisure-time physical activity and the risk of colorectal cancer. Eur J Cancer Prev 8:487–493
25. Tavani A, Braga C, La Vecchia C et al (1999) Physical activity and risk of cancers of the colon and rectum: an Italian case-control study. Br J Cancer 79:1912–1916
26. Steindorf K, Tobiasz-Adamczyk B, Popiela T et al (2000) Combined risk assessment of physical activity and dietary habits on the development of colorectal cancer. A hospital-based case-control study in Poland. Eur J Cancer Prev 9:309–316
27. Steindorf K, Jedrychowski W, Schmidt M et al (2005) Case-control study of lifetime occupational and recreational physical activity and risks of colon and rectal cancer. Eur J Cancer Prev 14:363–371
28. Pukkala E, Poskiparta M, Apter D, Vihko V (1993) Life-long physical activity and cancer risk among Finnish female teachers. Eur J Cancer Prev 2:369–376
29. Steenland K, Nowlin S, Palu S (1995) Cancer incidence in the National Health and Nutrition Survey I. Follow-up data: diabetes, cholesterol, pulse and physical activity. Cancer Epidemiol Biomarkers Prev 4:807–811
30. Schnohr P, Gronbaek M, Petersen L, Hein HO, Sorensen TI (2005) Physical activity in leisure-time and risk of cancer: 14-year follow-up of 28,000 Danish men and women. Scand J Public Health 33:244–249
31. Johnsen NF, Christensen J, Thomsen BL et al (2006) Physical activity and risk of colon cancer in a cohort of Danish middle-aged men and women. Eur J Epidemiol 21:877–884
32. Calton BA, Lacey JV, Schatzkin A et al (2006) Physical activity and the risk of colon cancer among women: a prospective cohort study (United States). Int J Cancer 119:385–391
33. Lee KJ, Inoue M, Otani T, Iwasaki M, Sasazuki S, Tsugane S (2007) Physical activity and risk of colorectal cancer in Japanese men and women: the Japan Public Health Cancer-based prospective Study. Cancer Causes Control 18:199–209
34. Mai PL, Sullivan-Halley J, Ursin G et al (2007) Physical activity and colon cancer risk among women in the California Teachers Study. Cancer Epidemiol Biomarkers Prev 16:517–525
35. Wolin KY, Lee IM, Colditz GA, Glynn RJ, Fuchs C, Giovannucci E (2007) Leisure-time physical activity patterns and risk of colon cancer in women. Int J Cancer 121:2776–2781
36. Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC (1995) Physical activity, obesity, and risk for colon cancer and adenoma in men. Ann Intern Med 122: 327–334
37. Colbert LH, Hartman TJ, Malila N et al (2001) Physical activity in relation to cancer of the colon and rectum in a cohort of male smokers. Cancer Epidemiol Biomarkers Prev 10:265–268
38. Marcus PM, Newcomb PA, Storer BE (1994) Early adulthood physical activity and colon cancer risk among Wisconsin women. Cancer Epidemiol Biomarkers Prev 3:641–644
39. Schatzkin A, Subar AF, Thompson FE et al (2001) Design and serendipity in establishing a large cohort with wide dietary intake distributions: the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol 154:371–374
40. Ainsworth BE, Haskell WL, Leon AS et al (1993) Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 25:71–80
41. Pereira MA, FitzerGerald SJ, Gregg EW et al (1997) A collection of physical activity questionnaires for health-related research. Med Sci Sports Exerc 29(6 Suppl):S1–205
42. Michaud DS, Midthune D, Hermansen S et al (2005) Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH-AARP Diet and Health Study. J Regist Manag 32:70–75
43. Rich-Edwards JW, Corsano KA, Stampfer MJ (1994) Test of the National Death Index and Equifax Nationwide Death Search. Am J Epidemiol 140:1016–1019
44. Korn EL, Graubard BI, Midthune D (1997) Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. Am J Epidemiol 145:72–80
45. Ainsworth BE, Irwin ML, Addy CL, Whitt MC, Stolarczyk LM (1998) Moderate physical acitivity patterns of minority women: The Cross-Cultural Activity Participation Study. J Womens Health Gend Based Med 8:805–813
46. Schor JB (1992) The overworked American. Harper Collins, New York
47. Ainsworth BE (2000) Challenges in measuring physical activity in women. Exerc Sport Sci Rev 28:93–96
48. Gerhardsson de Verdier M, Norell SE, Kiviranta H, Pedersen NL, Ahlbom A (1986) Sedentary jobs and colon cancer. Am J Epidemiol 123:775–780

49. Severson RK, Nomura AM, Grove JS, Stemmermann GN (1989) A prospective analysis of physical activity and cancer. Am J Epidemiol 130:522–529
50. Iacopetta B (2002) Are there two sides to colorectal cancer? Int J Cancer 101:403–408
51. Isomura K, Kono S, Moore MA et al (2006) Physical activity and colorectal cancer: the Fukuoka Colorectal Cancer Study. Cancer Sci 97:1099–1104
52. Slattery ML, Edwards S, Curtin K et al (2003) Physical activity and colorectal cancer. Am J Epidemiol 158:214–224
53. Le Marchand L, Wilkens LR, Kolonel LN, Hankin JH, Lyu LC (1997) Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. Cancer Res 57:4787–4794
54. Slattery ML, David R, Jacobs J (1995) Assessment of ability to recall physical activity of several years ago. Ann Epidemiol 5:292–296
55. Wei EK, Giovannucci E, Wu K et al (2004) Comparison of risk factors for colon and rectal cancer. Int J Cancer 108:433–442

論文名	Physical activity, sedentary behavior, and the risk of colon and rectal cancer in the NIH-AARP Diet and Health Study
著　者	Howard RA, Freedman DM, Park Y, Hollenbeck A, Schatzkin A, Leitzmann MF
雑誌名	Cancer Causes Control
巻・号・頁	19　　939-953
発行年	2008
PubMedリンク	http://www.ncbi.nlm.nih.gov/pubmed/18437512

		ヒト	動物	地　域	欧米	研究の種類	縦断研究
対象の内訳	対象	一般健常者	空白		( )		コホート研究
	性別	男女混合	( )		( )		( )
	年齢	50-71歳			( )		前向き研究
	対象数	10000以上			( )		( )
調査の方法	質問紙	( )					
アウトカム	予　防	なし	なし	ガン予防	なし	( )	( )
	維持・改善	なし	なし	なし	なし	( )	( )

図　表

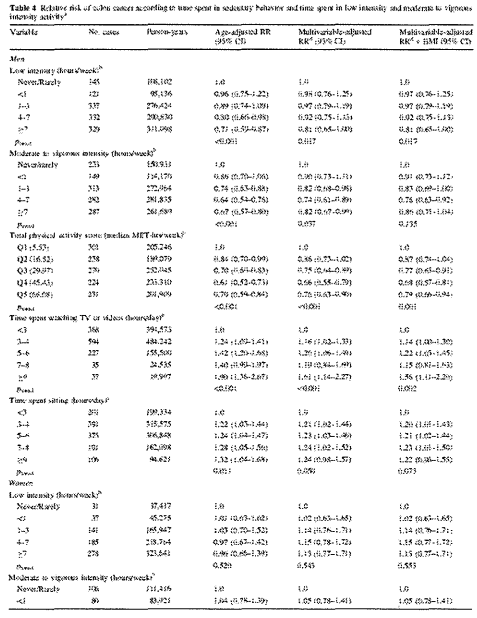


Table 4 Relative risk of colon cancer according to time spent in sedentary behavior and time spent in low intensity and moderate to vigorous intensity activity[a]

Variable	No. cases	Person-years	Age-adjusted RR (95% CI)	Multivariable-adjusted RR[b] (95% CI)	Multivariable-adjusted RR[b] + BMI (95% CI)
Men					
Low intensity (hours/week)[c]					
Never/Rarely	145	198,102	1.0	1.0	1.0
<3	122	95,136	0.96 (0.75–1.22)	0.94 (0.76–1.25)	0.97 (0.76–1.25)
3–3	337	279,424	0.99 (0.74–1.09)	0.97 (0.79–1.19)	0.97 (0.79–1.19)
4–7	332	200,830	0.80 (0.66–0.98)	0.92 (0.75–1.13)	0.92 (0.75–1.13)
≥7	329	311,998	0.77 (0.53–0.87)	0.81 (0.65–1.00)	0.81 (0.65–1.00)
*P*trend			<0.001	0.017	0.019
Moderate to vigorous intensity (hours/week)[c]					
Never/Rarely	253	150,933	1.0	1.0	1.0
<2	149	134,179	0.86 (0.70–1.06)	0.90 (0.73–1.11)	0.91 (0.73–1.12)
1–3	313	272,964	0.76 (0.63–0.88)	0.82 (0.68–0.98)	0.83 (0.69–1.00)
4–7	282	291,855	0.64 (0.53–0.76)	0.74 (0.62–0.89)	0.75 (0.63–0.92)
≥7	287	261,989	0.67 (0.53–0.80)	0.82 (0.67–0.99)	0.80 (0.71–1.04)
*P*trend			<0.001	0.037	0.135
Total physical activity score (median MET-hrs/week)[d]					
Q1 (5.57)	303	205,246	1.0	1.0	1.0
Q2 (16.52)	258	199,079	0.86 (0.70–0.99)	0.86 (0.73–1.02)	0.87 (0.70–1.04)
Q3 (29.07)	270	232,945	0.78 (0.65–0.83)	0.75 (0.64–0.90)	0.77 (0.65–0.91)
Q4 (45.43)	224	233,310	0.61 (0.52–0.71)	0.66 (0.55–0.79)	0.68 (0.57–0.81)
Q5 (66.05)	270	304,909	0.79 (0.54–0.84)	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)[e]					
<3	368	299,573	1.0	1.0	1.0
3–4	594	484,242	1.24 (1.03–1.43)	1.16 (1.02–1.33)	1.16 (1.00–1.30)
5–6	227	155,500	1.42 (1.23–1.64)	1.26 (1.06–1.49)	1.23 (1.03–1.45)
7–8	35	26,535	1.40 (0.98–1.97)	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)[e]					
<3	301	199,334	1.0	1.0	1.0
3–4	591	515,575	1.22 (1.03–1.44)	1.21 (1.02–1.44)	1.20 (1.01–1.43)
5–6	375	306,848	1.36 (1.04–1.47)	1.23 (1.03–1.46)	1.21 (1.02–1.44)
7–8	101	162,898	1.28 (1.05–1.56)	1.24 (1.02–1.52)	1.23 (1.01–1.50)
≥9	109	98,623	1.32 (1.04–1.69)	1.34 (0.98–1.57)	1.32 (0.98–1.55)
*P*trend			0.013	0.050	0.073
Women					
Low intensity (hours/week)[c]					
Never/Rarely	31	37,417	1.0	1.0	1.0
<5	37	45,275	1.02 (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 (0.78–1.72)	1.15 (0.77–1.72)
≥7	278	323,643	0.96 (0.66–1.39)	1.13 (0.77–1.71)	1.13 (0.77–1.71)
*P*trend			0.820	0.545	0.555
Moderate to vigorous intensity (hours/week)[c]					
Never/Rarely	106	131,316	1.0	1.0	1.0
<3	80	89,921	1.04 (0.78–1.39)	1.05 (0.78–1.41)	1.05 (0.78–1.41)

Table 4 continued

Variable	No. cases	Person-years	Age-adjusted RR (95% CI)	Multivariable-adjusted RR[b] (95% CI)	Multivariable-adjusted RR[b] + BMI (95% CI)
3–3	171	201,913	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)
*P*trend			0.079	0.311	0.327
Total physical activity score (median MET-hours/week)[d]					
Q1 (5.07)	122	126,995	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	110,969	0.77 (0.58–1.03)	0.85 (0.64–1.13)	0.85 (0.64–1.13)
Q4 (53.63)	168	202,644	0.82 (0.65–1.04)	0.92 (0.73–1.17)	0.92 (0.73–1.17)
Q5 (86.05)	126	168,028	0.92 (0.68–1.05)	0.92 (0.71–1.18)	0.92 (0.71–1.19)
*P*trend			0.124	0.540	0.555
Time spent watching TV or videos (hours/day)[e]					
<3	200	277,226	1.0	1.0	1.0
3–4	279	336,216	1.02 (0.85–1.23)	0.96 (0.78–1.18)	0.94 (0.76–1.15)
5–6	131	127,859	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	35	22,789	1.82 (1.26–2.63)	1.45 (0.99–2.12)	1.45 (0.99–2.13)
*P*trend			0.002	0.154	0.185
Time spent sitting (hours/day)[e]					
<3	148	173,280	1.0	1.0	1.0
3–4	394	428,558	0.97 (0.78–1.20)	0.96 (0.77–1.19)	0.96 (0.77–1.19)
5–6	198	213,695	1.05 (0.83–1.34)	1.04 (0.84–1.30)	1.04 (0.83–1.30)
7–8	85	141,851	1.02 (0.78–1.33)	0.96 (0.73–1.26)	0.96 (0.73–1.26)
≥9	54	62,122	1.34 (0.98–1.83)	1.21 (0.89–1.72)	1.21 (0.89–1.70)
*P*trend			0.129	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 mutually adjusted and sedentary behavior variables are adjusted for total physical activity

図表掲載箇所	P947-948, Table4
概　要 (800字まで)	本研究は、アメリカのThe NIH-AARP Diet and Health Studyに参加した男女488,720名を対象に平均6.9年間の追跡調査を行い、身体活動量や不活動と大腸がんや結腸がん発症との関連を検討したものである。質問紙によって、過去1年間の20分以上継続して行った身体活動の量(回数/週)や、日常活動、テレビ視聴時間や座位時間を尋ねた。また、過去10年間を年齢別に分けその期間で行った強度別(低・中・高強度)の平均身体活動量(時間/週)を合計し、総身体活動量を算出し、少ない順に下から5群(Q1～Q5)に分類した。男性で、総身体活動量の最も少ない集団(Q1)と比較すると、Q3,Q4,Q5で大腸がん発症リスクがそれぞれ0.75(95%信頼区間:0.64-0.89)、0.66(0.55-0.79)、0.76(0.63-0.90)と量反応的に有意に減少した。また、テレビ視聴時間が3時間/日未満の集団と比較すると、3-4時間/日、5-6時間/日、9時間/日以上の集団で大腸がん発症リスクがそれぞれ1.16(1.02-1.33)、1.26(1.06-1.49)、1.61(1.14-2.27)と有意に上昇した。女性においては、いずれも有意な差はみられなかった。20分以上継続した身体活動を全く行わない集団と比較すると、男性で週当たり3-4回以上、女性で1-3回以上行う集団で大腸がん発症リスクが有意に減少した。結腸直腸がん発症については、男性で週当たり5回以上行う集団で有意なリスク低下がみられた。女性では有意な差はみられなかったものの、リスクの減少傾向は男性と同様であった。
結　論 (200字まで)	身体活動を行うことは、その強度に関わらず大腸がんや結腸がん発症のリスクを低下させ、不活動でいることでそれらがんの発症リスクが増加することが明らかとなった。またそれら因子は互いに独立してリスクに関連していることが明らかとなった。
エキスパートによるコメント (200字まで)	身体活動基準の策定に用いられた研究の1つである。大腸がんと身体活動との関係は、様々な研究によって支持されている。本研究のような約50万人を対象にした研究でもそれらの関係が認められていることから、身体活動は大腸がんの予防に効果的であると言える。また本研究ではテレビ視聴時間との関係も検討しており、その時間を短縮することが重要であることを示した点で意義ある研究である。

担当者:久保絵里子・村上晴香・宮地元彦

American Journal of Epidemiology

Vol. 168, No. 4
DOI: 10.1093/aje/kwn146
Advance Access publication July 2, 2008

Original Contribution

Daily Total Physical Activity Level and Total Cancer Risk in Men and Women: Results from a Large-scale Population-based Cohort Study in Japan

Manami Inoue[1], Seiichiro Yamamoto[2], Norie Kurahashi[1], Motoki Iwasaki[1], Shizuka Sasazuki[1], and Shoichiro Tsugane[1] for the Japan Public Health Center-based Prospective Study Group

[1] Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, Japan.
[2] Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan.

Received for publication January 22, 2008; accepted for publication May 2, 2008.

The impact of total physical activity level on cancer risk has not been fully clarified, particularly in non-Western, relatively lean populations. The authors prospectively examined the association between daily total physical activity (using a metabolic equivalents/day score) and subsequent cancer risk in the Japan Public Health Center-based Prospective Study. A total of 79,771 general-population Japanese men and women aged 45–74 years who responded to a questionnaire in 1995–1999 were followed for total cancer incidence (4,334 cases) through 2004. Compared with subjects in the lowest quartile, increased daily physical activity was associated with a significantly decreased risk of cancer in both sexes. In men, hazard ratios for the second, third, and highest quartiles were 1.00 (95% confidence interval (CI): 0.90, 1.11), 0.96 (95% CI: 0.86, 1.07), and 0.87 (95% CI: 0.78, 0.96), respectively (p for trend = 0.005); in women, hazard ratios were 0.93 (95% CI: 0.82, 1.05), 0.84 (95% CI: 0.73, 0.96), and 0.84 (95% CI: 0.73, 0.97), respectively (p for trend = 0.007). The decreased risk was more clearly observed in women than in men, especially among the elderly and those who regularly engaged in leisure-time sports or physical exercise. By site, decreased risks were observed for cancers of the colon, liver, and pancreas in men and for cancer of the stomach in women. Increased daily physical activity may be beneficial in preventing cancer in a relatively lean population.

cohort studies; exercise; Japan; neoplasms; physical fitness

Abbreviations: CI, confidence interval; MET(s), metabolic equivalent(s).

A number of investigators have reported beneficial effects of physical activity on the risk of cancer at certain specific sites, and physical activity is now regarded as an important target for cancer prevention. The second report of the World Cancer Research Fund/American Institute for Cancer Research recently concluded that all forms of physical activity protect against some cancers, including colon cancer, postmenopausal breast cancer, and endometrial cancer, in relation to or independently of weight gain, overweight, and obesity (1).

To date, however, the association between physical activity and total cancer risk has been relatively poorly investigated. Given that exercise and physical activity probably affect cancer development at different sites via the same mechanism or closely similar mechanisms, at least to some degree, it is reasonable to assess the preventive effect of physical activity not only on cancer at specific sites but also on all cancers in aggregate. Further, from a public health point of view, an understanding of the preventive effect of physical activity on total cancer risk will provide concrete

Correspondence to Dr. Manami Inoue, Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan (e-mail: mnminoue@gan2.res.ncc.go.jp).

TABLE 1. Baseline characteristics of study subjects according to daily total physical activity level (n = 79,771), Japan Public Health Center-based Prospective Study, 1995–2004

Characteristic	Quartile of physical activity level (quartile of METs*/day score)†			
	Lowest	Second	Third	Highest
Men (n = 37,898)				
No. of subjects	12,966	7,822	7,579	9,531
Quartile median value (METs/day score)	25.45 (21.60–27.10)‡	31.85 (27.25–31.85)	34.25 (32.40–36.05)	42.65 (36.25–46.25)
Mean age (years)	56.7	56.4	56.9	56.1
Mean body mass index§	23.66	23.62	23.56	23.49
History of diabetes mellitus (%)	10.1	8.6	8.3	7.6
History of liver disease (%)	3.7	2.9	2.7	2.6
Current smoking (%)	47.2	46.9	47.2	48.8
Regular alcohol drinking (≥1 day/week) (%)	64.6	68.0	68.1	71.0
Regular leisure-time sports or physical exercise (≥3–4 days/week) (%)	9.0	10.8	13.1	12.0
Mean total energy intake¶ (kcal/day)	2,040.8	2,141.5	2,168.6	2,299.5
Women (n = 41,873)				
No. of subjects	13,277	10,838	9,663	8,095
Quartile median value (METs/day score)	26.10 (21.60–27.10)	31.85 (27.25–31.85)	34.25 (32.75–34.25)	42.65 (35.45–46.25)
Mean age (years)	57.3	56.4	56.5	56.0
Mean body mass index	23.58	23.41	23.40	23.49
History of diabetes mellitus (%)	5.0	3.8	3.5	3.9
History of liver disease (%)	1.3	1.3	1.5	1.0
Current smoking (%)	5.9	5.8	5.6	5.5
Regular alcohol drinking (≥1 day/week) (%)	12.8	13.4	13.7	13.2
Regular leisure-time sports or physical exercise (≥3–4 days/week) (%)	9.4	9.7	11.5	14.6
Mean total energy intake¶ (kcal/day)	1,840.3	1,886.4	1,882.3	1,972.2

* METs, metabolic equivalents.
† Sum of the scores for reported amount of time per day spent in each physical activity multiplied by the MET value for each activity.
‡ Numbers in parentheses, range.
§ Weight (kg)/height(m)^2.
¶ Adjusted for age.

clues in estimating the effect of physical activity measures in health policy planning. For the latter case, evidence from populations with similar general lifestyle backgrounds is indispensable. Evidence for an association between physical activity and total cancer risk is limited (2–10), however; most studies have targeted mortality (4–10) rather than incidence (2, 3) and have been carried out in Western populations (2–8). Evidence from other populations is sparse (9, 10).

Here, we examined the association between daily total physical activity and risk of all types of cancer in the Japan Public Health Center-based Prospective Study. Our main purpose was to estimate the magnitude of the effect of overall physical activity, including exercise and nonexercise physical activities, on total cancer risk among Japanese, a population characterized as non-Western and relatively lean. To date, physical activity has been assessed using various types of activity categories, such as leisure-time and non-leisure-time activity, physical exercise or sports, and nonexercise activities, such as occupational activity and household work. However, given recognition of the need for comprehensive evaluation of these physical activities in the aggregate, particularly with regard to nonexercise physical activity (11), here we attempted a quantitative approach to assessment using a common scale for all activities (namely, metabolic equivalents (METs)) to estimate the effect of total physical activity level.

MATERIALS AND METHODS

Study population

The Japan Public Health Center-based Prospective Study was started in 1990–1994. It targeted all registered Japanese inhabitants in 11 public health center areas who were aged 40–69 years at the beginning of the baseline survey (12).

The study protocol was approved by the institutional review board of the National Cancer Center, Japan. In the present analysis, one public health center area was excluded, since data on cancer incidence were not available.

The participants in the present study were subjects in the Japan Public Health Center-based Prospective Study who responded to a self-administered 5-year follow-up questionnaire

TABLE 2. Hazard ratios for total cancer incidence according to daily total physical activity level (n = 79,771), Japan Public Health Center-based Prospective Study, 1995–2004

Quartile of physical activity level (quartile of METs*/day score)	No. of subjects	Person-years of follow-up	Total					Excluding cases diagnosed within first 3 years				
			No. of cases	HR1*,†	95% CI*	HR2‡	95% CI	No. of cases	HR1	95% CI	HR2	95% CI
Men (n = 37,898)					(n = 2,704)					(n = 1,804)		
Lowest	12,966	92,421	921	1.00	Reference	1.00	Reference	604	1.00	Reference	1.00	Reference
Second	7,822	57,957	575	1.00	0.90, 1.10	1.00	0.90, 1.11	381	0.98	0.86, 1.11	0.98	0.86, 1.11
Third	7,579	56,512	574	0.96	0.86, 1.06	0.96	0.86, 1.07	386	0.95	0.83, 1.08	0.95	0.83, 1.08
Highest	9,531	72,841	634	0.87	0.79, 0.96	0.87	0.78, 0.96	433	0.86	0.76, 0.97	0.86	0.76, 0.98
p for trend					0.006		0.005			0.015		0.017
Per 1-MET increase				0.99	0.99, 0.998	0.99	0.99, 0.998		0.99	0.99, 0.999	0.99	0.99, 0.999
Per 10-MET increase				0.93	0.88, 0.99	0.93	0.88, 0.99		0.93	0.87, 0.996	0.93	0.87, 0.997
Women (n = 41,873)					(n = 1,630)					(n = 1,056)		
Lowest	13,277	99,385	569	1.00	Reference	1.00	Reference	368	1.00	Reference	1.00	Reference
Second	10,838	83,644	428	0.92	0.81, 1.04	0.93	0.82, 1.05	290	0.94	0.81, 1.10	0.94	0.81, 1.10
Third	9,663	74,073	350	0.84	0.73, 0.96	0.84	0.73, 0.96	222	0.80	0.68, 0.95	0.79	0.67, 0.94
Highest	8,095	62,284	283	0.83	0.72, 0.96	0.84	0.73, 0.97	176	0.78	0.65, 0.93	0.78	0.65, 0.94
p for trend					0.004		0.007			0.002		0.002
Per 1-MET increase				0.99	0.98, 0.997	0.99	0.98, 0.997		0.98	0.97, 0.995	0.98	0.97, 0.995
Per 10-MET increase				0.89	0.82, 0.97	0.90	0.82, 0.98		0.85	0.77, 0.95	0.85	0.77, 0.95

* MET(s), metabolic equivalent(s); HR, hazard ratio; CI, confidence interval.

† Adjusted for age (stratified, 5-year categories) and area (stratified, 10 public health center areas).

‡ Adjusted for age (stratified, 5-year categories), area (stratified, 10 public health center areas), total energy intake (stratified, quintiles), history of diabetes (no, yes), smoking status (never smoking, past smoking, or 1–19, 20–29, or ≥30 cigarettes/day), alcohol intake status (almost none, occasional, or regular), body mass index (weight (kg)/height (m)^2; <20, 20–<27, or ≥27), and leisure-time sports or physical exercise (<1, 1–2, or ≥3–4 days/week).

in 1995–1999 at age 45–74 years. Initially, at baseline, 133,323 subjects were identified as being in the study population. After excluding 241 persons with non-Japanese nationality (n = 51), duplicate enrollment (n = 4), a late report of emigration occurring before the start of the follow-up period (n = 180), or ineligibility due to an incorrect birth date (n = 6), a population-based cohort of 133,082 subjects was established. After exclusion of the 13,663 persons who had died, moved out of the study area, or been lost to follow-up before the starting point, the remaining 119,419 subjects were considered eligible for the present study. A total of 96,566 subjects responded to the questionnaire, yielding a response rate of 81 percent.

Questionnaire

The questionnaire included items on demographic factors, personal medical history, physical activity, smoking and alcohol drinking, other lifestyle factors, and diet (via a validated food frequency questionnaire containing questions on 138 food items and 14 supplementary questions (13)). Persons who had been diagnosed with cancer before the starting point (n = 2,153) or who had missing data for physical activity-related factors (n = 6,346) or other factors included in the multivariate model (n = 8,296) were excluded. Finally, 79,771 eligible subjects (37,898 men and 41,873 women) were included in the analysis.

Follow-up

Subjects were followed from the starting point until December 31, 2004. Residence status, including survival, was confirmed through the residential registry. Inspection of the resident registry is available to anyone under the resident registration law. Among the study subjects, 5,271 died, 3,166 moved out of the study area, one withdrew from the study, and 239 (0.3 percent) were lost to follow-up within the follow-up period. Information on the cause of death for deceased subjects was obtained from death certificates (provided by the Ministry of Health, Labour, and Welfare with the permission of the Ministry of Internal Affairs and Communications), on which cause of death is defined according to the *International Classification of Diseases*, Tenth Revision (14). Resident registration and death registration are required by law in Japan, and the registries are believed to be complete.

Incident cancers were identified through notification from the major hospitals in the study area and through data linkage with population-based cancer registries. Death certificates were used as a supplementary information source. The site and histology of each case were coded using the *International Classification of Diseases for Oncology*, Third Edition (15). In our cancer registry system, the proportion of cases for which information was available from death certificates only was 3.7 percent. For the present analysis, the