

# Associations of Recreational Physical Activity and Leisure Time Spent Sitting With Colorectal Cancer Survival

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## ABSTRACT

### Purpose

Little is known about the association of recreational physical activity or leisure time spent sitting with survival after colorectal cancer diagnosis. This study examined the associations of prediagnosis and postdiagnosis recreational physical activity and leisure time spent sitting with mortality among patients with colorectal cancer.

### Patients and Methods

From a cohort of adults without colorectal cancer at baseline in 1992-1993, we identified 2,293 participants who were diagnosed with invasive, nonmetastatic colorectal cancer up to mid-2007. At baseline, before their cancer diagnosis, and again after their cancer diagnosis, participants completed detailed questionnaires that included information concerning recreational physical activity and leisure time spent sitting.

### Results

During a maximum follow-up of 16.1 years after colorectal cancer diagnosis, 846 patients with colorectal cancer died, 379 of them from colorectal cancer. Engaging in 8.75 or more metabolic equivalent (MET) hours per week of recreational physical activity (equivalent to approximately 150 minutes per week of walking) compared with fewer than 3.5 MET hours per week was associated with lower all-cause mortality (prediagnosis physical activity: relative risk [RR], 0.72; 95% CI, 0.58 to 0.89; postdiagnosis physical activity: RR, 0.58; 95% CI, 0.47 to 0.71). Spending 6 or more hours per day of leisure time sitting compared with fewer than 3 hours per day was associated with higher all-cause mortality (prediagnosis sitting time: RR, 1.36; 95% CI, 1.10 to 1.68; postdiagnosis sitting time: RR, 1.27; 95% CI, 0.99 to 1.64).

### Conclusion

More recreational physical activity before and after colorectal cancer diagnosis was associated with lower mortality, whereas longer leisure time spent sitting was associated with higher risk of death.

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## INTRODUCTION

There is growing evidence from randomized, clinical trials that exercise is safe and well-tolerated by patients with cancer during and after treatment.<sup>1,2</sup> Exercise also enhances quality of life and improves physical functioning among colorectal cancer survivors.<sup>3-5</sup> The association between recreational physical activity and mortality among colorectal cancer survivors is unclear.<sup>6-9</sup> Of three studies with prediagnosis assessments of recreational physical activity, two assessed activity approximately 6 months to 2 years before colorectal cancer diagnosis and reported no association with mortality,<sup>7,9</sup> whereas the third study evaluated activity an average of 5 years before colorectal cancer diagnosis and reported a modest inverse association.<sup>6</sup> In contrast, studies of postdiagnosis recreational physical activ-

ity among colorectal cancer survivors have consistently shown markedly lower risks of mortality among more-active relative to less-active patients.<sup>7-9</sup> No study has yet assessed the association of sitting time on mortality among colorectal cancer survivors, although data suggest positive associations of sitting time with colorectal cancer incidence<sup>10-12</sup> and all-cause mortality.<sup>13-16</sup>

Several expert committees have provided physical activity guidelines for cancer survivors.<sup>1,17-19</sup> These recommendations are similar to guidelines for primary cancer prevention and include the accumulation of 150 or more minutes per week of moderate-to-vigorous intensity physical activity and the avoidance of inactivity. Given the current absence of data from randomized controlled trials, studies drawn from well-characterized prospective cohort studies are needed to help establish the

evidence base for physical activity and sitting time recommendations among cancer survivors. In this study, we assessed the association of recreational physical activity and leisure time spent sitting, before and after cancer diagnosis, on all-cause and cause-specific mortality among patients with invasive, nonmetastatic colorectal cancer.

## PATIENTS AND METHODS

### Study Cohort

Men and women in this study were identified from among the 184,194 participants in the Cancer Prevention Study-II (CPS-II) Nutrition Cohort. The CPS-II Nutrition Cohort is a prospective study of cancer incidence that was initiated in 1992.<sup>20,21</sup> The CPS-II Nutrition Cohort is approved by the Emory University institutional review board. At enrollment onto the Nutrition Cohort, participants completed a 10-page epidemiologic questionnaire. Follow-up questionnaires were mailed in subsequent years to update information and to learn of newly diagnosed cancers.

Among participants with no history of colorectal cancer at baseline, we identified 3,491 participants diagnosed with invasive colon or rectal cancer by the end of incidence accrual in June 2007. Colorectal cancer diagnoses were verified through medical records or linkage with state cancer registries when medical records could not be obtained. Among the 3,491 identified patients with colorectal cancer, exclusions were based on cancer identified through the National Death Index (NDI)<sup>22</sup> that could not be verified with cancer registries ( $n = 211$ ); prior diagnosis of cancer at baseline, other than nonmelanoma skin cancer ( $n = 367$ ); implausible diagnosis date ( $n = 8$ ); nonadenocarcinoma histology ( $n = 46$ ); missing or implausible body mass index (BMI) at baseline ( $n = 36$ ); missing recreational physical activity and leisure time spent sitting at baseline ( $n = 15$ ); diagnosis and death dates on the same day ( $n = 2$ ); unknown stage at diagnosis ( $n = 129$ ); and metastatic disease on diagnosis ( $n = 384$ ). Consistent with previous survival studies from this cohort,<sup>23,24</sup> patients with metastatic colorectal cancer were excluded. These patients are generally excluded from prognosis studies of lifestyle factors because of the potential for overt illness to have an impact on both mortality and the lifestyle factor of interest and because few patients with advanced disease would be able to return a postdiagnosis questionnaire. Thus, 2,293 men and women were included in analyses of prediagnosis physical activity.

In analyses of postdiagnosis recreational physical activity and leisure time spent sitting, patients who died within 6 months of returning their first postdiagnosis questionnaire were excluded because their activity and sitting time would have been plausibly affected by occult disease or overt illness (45 deaths for sitting time, 32 deaths for physical activity; no patients died within 6 months of returning the prediagnosis survey). Of the 2,262 patients with prediagnosis assessments of recreational physical activity, 1,800 (80%) also reported their postdiagnosis activity levels. Likewise, of the 2,236 patients with prediagnosis assessments of leisure time spent sitting, 1,656 (74%) also reported their postdiagnosis sitting time.

### Assessment of Recreational Physical Activity, Leisure Time Spent Sitting, and Relevant Covariables

Self-reported recreational physical activity was recorded on the baseline questionnaire (1992-1993) and updated on follow-up surveys in 1997, 1999, 2001, and 2005. On each survey that included physical activity questions, the same modes of physical activity were queried (ie, walking, jogging, lap swimming, tennis, cycling, aerobics, and dancing); however, the categories for "hours per week" sometimes differed. On the 1992-1993 baseline survey, the check-box categories for weekly duration of physical activities were "none," "1 to 3 hours," "4 to 6 hours," and "7+ hours." On the 1997 follow-up survey, the corresponding categories were "none," "1 hour," "2 to 3 hours," and "4+ hours." On the 1999, 2001, and 2005 surveys, the categories were "none," "1 to 19 minutes," "20 to 59 minutes," "1 hour," "1 to 1.5 hours," "2 to 3 hours," "4 to 6 hours," "7 to 10 hours," and "11+ hours." In this analysis, the categories from the more detailed surveys were combined to reflect the categories from the less detailed 1997 survey.

Recreational physical activity was categorized in this analysis as less than 3.5 (referent group), 3.5 to 8.74, and 8.75 or more metabolic equivalent (MET) hours per week. Detailed calculations for MET hours per week have been described previously.<sup>14,25</sup> The MET hours per week categories in this study translate to less than 1 hour of walking per week, 1 hour to less than 2.5 hours of walking per week, and 2.5 hours or more of walking per week (ie, meeting the physical activity recommendation for cancer survivors<sup>1,17-19</sup>), respectively.

Self-reported leisure time spent sitting was recorded on the 1992-1993 baseline and on the 1999, 2001, and 2005 surveys with questions that included daily time (in minutes or hours) in the past year spent driving or sitting in a car, sitting on a bus, or sitting on a train; sitting and watching television; and sitting at home reading. Sitting time categories in this analysis were defined as less than 3 hours per day, 3 to less than 6 hours per day, and 6 or more hours per day.

For this analysis, the 1992-1993 physical activity and sitting time questions served as the prediagnosis assessments at a mean of 7 years before cancer diagnosis (median, 6.8 years). The first surveys completed after the patients' colon or rectal cancer diagnoses were used for the postdiagnosis assessment. The postdiagnosis assessments occurred 1.7 and 2.3 years (means) after cancer diagnosis for physical activity and sitting time, respectively (physical activity median, 1.4 years; sitting time median, 1.9 years).

Information on first course of cancer treatment was obtained by self-reported questionnaires that were mailed to participants after their initial report of colorectal cancer. A participant could report surgery, chemotherapy, or radiation, or any combination thereof as a first course of cancer treatment. No data on treatment could be obtained from the approximately one third of participants who did not return this questionnaire.

### Study Outcomes

Vital status, cause of death, and date of death were ascertained through linkage to the NDI for deaths up to December 31, 2008.<sup>22</sup> Cause of death has been obtained for 99.3% of all known deaths in the CPS-II Nutrition Cohort. The primary outcome in this study was all-cause mortality. The secondary outcome was colorectal cancer-specific mortality (International Classification of Diseases, 9th Revision [ICD-9]: 153, 154; ICD, 10th Revision [ICD-10]: C18, C19, C20). Tertiary outcomes were cardiovascular disease (CVD)-specific mortality (ICD-9: 390-459; ICD-10: I00-199) and deaths from all noncolorectal and non-CVD causes combined (eg, all other causes of death). The cause-specific outcomes were mutually exclusive, defined according to the singular underlying cause of death on the NDI record.

### Statistical Analysis

Age-adjusted and multivariable-adjusted relative risks (RRs) and 95% CIs were calculated by using Cox proportional hazards models to estimate the associations of recreational physical activity and leisure time spent sitting with all-cause, colorectal cancer-specific, CVD-specific, and all other causes of death. The stratified Cox procedure was used to adjust for age at diagnosis within 1-year strata. The multivariable Cox models included recreational physical activity, leisure time spent sitting, BMI, education, red meat intake, smoking status, tumor stage, and sex. Recreational physical activity and leisure time spent sitting were mutually adjusted. Further adjustment for other variables (eg, time elapsed from baseline to colorectal cancer diagnosis, nonrecreational physical activity, family history of colorectal cancer, prevalent CVD or respiratory disease, aspirin or nonsteroidal anti-inflammatory drugs, and first-course cancer treatment) made no appreciable difference to the RR estimates and were not included in the final models.

Follow-up time for prediagnosis recreational physical activity and leisure time spent sitting began on the date of colon or rectal cancer diagnosis and ended on the date of death or December 31, 2008, whichever came first. Follow-up time for postdiagnosis recreational physical activity and leisure time spent sitting began on the date the postdiagnosis questionnaire was returned.

Whether the associations of physical activity or sitting time with mortality differed by sex, age, subsite in the colorectum, stage, BMI, education, smoking status, and red meat intake was examined via the likelihood ratio test. In sensitivity analyses, we excluded deaths that occurred within 2 years of colorectal cancer diagnosis, deaths that occurred within 2 years of returning a

survey, participants who were still employed, and participants whose postdiagnosis surveys were returned within 1 year of cancer diagnosis. All *P* values are two-sided; *P* values less than .05 are considered statistically significant.

## RESULTS

### Participant Characteristics at Baseline

The distributions of baseline characteristics by MET hours of recreational physical activity are provided in Table 1. There were no marked differences across recreational physical activity categories for age at colorectal cancer diagnosis, self-reported race, family history of colorectal cancer, leisure time spent sitting, hypertension, diabetes, or any of the pathologic or clinical characteristics, including stage. Differences across recreational physical activity categories were noted for sex, education, smoking, red meat intake, and BMI.

### Follow-Up Time and Mortality Outcomes

There were 2,293 men and women included in this analysis with Surveillance, Epidemiology, and End Results (SEER)–staged localized or regional colorectal adenocarcinoma, and the mean follow-up time from cancer diagnosis to death or end-of-study was 6.8 years (minimum, 2 days; maximum, 16.1 years). Among the participants who were alive at the end of follow-up, the mean follow-up time was 8.1 years (minimum, 1.5 years; maximum, 16.1 years). By the end of the follow-up period, 846 deaths occurred from all causes, of which 379 were attributed to colorectal cancer, 152 to CVD, 127 to other cancers, 49 to respiratory disease, and 139 to all remaining causes combined.

### Recreational Physical Activity Before and After Colorectal Cancer Diagnosis and Mortality

As delineated in Table 2, the highest prediagnosis recreational physical activity category (8.75 or more MET hours per week) compared with the lowest category (< 3.5 MET hours per week) was associated with a 28% lower risk of all-cause mortality. The same comparison for postdiagnosis recreational physical activity resulted in an RR of 0.58. In cause-specific mortality analyses, only the results for CVD mortality were statistically significant (prediagnosis RR, 0.60; postdiagnosis RR, 0.36). Recreational physical activity was modestly inversely associated with colorectal cancer mortality in both pre- and postdiagnosis assessments, but the CIs overlapped with 1 in the multivariable analysis.

### Leisure Time Spent Sitting Before and After Colorectal Cancer Diagnosis and Mortality

Leisure time spent sitting of 6 or more hours per day on the prediagnosis survey was associated with a statistically significant 36% higher risk of all-cause mortality (Table 3). The RRs for the associations of prediagnosis sitting time with colorectal cancer mortality and CVD mortality were nearly similar in magnitude but were not statistically significant. Postdiagnosis sitting time was associated with a 27% higher risk of all-cause mortality, although the lower limit of the CI was 0.99 (*P* = .06). Postdiagnosis sitting time was associated with a statistically significant 62% higher risk of colorectal cancer–specific mortality and a nonstatistically significant higher risk of CVD mortality.

### Recreational Physical Activity and Leisure Time Spent Sitting Stratified by Other Variables

As shown in Figures 1A and 1B, there was no evidence of heterogeneity for the associations of prediagnosis recreational physical activity (Fig 1A) or leisure time spent sitting (Fig 1B) with all-cause mortality by strata of sex, age, subsite in the colorectum, SEER summary stage, BMI, education, smoking, or red meat intake. Associations with postdiagnosis physical activity and sitting time were also largely consistent across subgroups (data not shown). In post hoc analysis among patients with distant metastatic disease, associations of prediagnosis physical activity and sitting time with all-cause mortality were similar to the reported associations among patients with non-metastatic disease (data not shown).

### Sensitivity Analyses

In sensitivity analyses, no substantive differences were noted for associations of recreational physical activity or leisure time spent sitting with all-cause mortality after excluding deaths that occurred within 2 years of colorectal cancer diagnosis; deaths that occurred within 2 years of returning the relevant survey; participants who were still employed; and, in analyses of postdiagnosis activity, participants whose postdiagnosis surveys were returned within 1 year of cancer diagnosis (data not shown).

## DISCUSSION

In this prospective study of 2,293 colorectal cancer survivors, meeting the public health recommendation of 150 minutes or more of moderate-intensity physical activity per week (ie, 8.75 or more MET hours per week) was associated with lower risk of all-cause and CVD mortality. This study is, to the best of our knowledge, the first to show an association between longer leisure time spent sitting and higher risk of mortality among colorectal cancer survivors. These associations persisted when recreational physical activity and sitting time were assessed before and after colorectal cancer diagnosis, after controlling for several potentially confounding variables, including BMI, smoking, and disease stage, and after performing a series of sensitivity and subgroup analyses. This study adds importantly to the sparse prospective data on the role of physical activity<sup>6-9</sup> and sitting time with mortality for colorectal cancer survivors and provides evidence to support current recommendations for physical activity among cancer survivors.<sup>1,17-19</sup>

Results of other studies on prediagnosis recreational physical activity and survival after colorectal cancer diagnosis are inconsistent. In a prospective study of 526 colorectal cancer survivors that assessed physical activity a median of 5.3 years before cancer diagnosis, the exercise group compared with a nonexercise group, had 23% and 27% lower risks of all-cause and colorectal cancer mortality, respectively, although the former estimate was not statistically significant.<sup>6</sup> In contrast, in studies of 573 women<sup>7</sup> and 661 men,<sup>9</sup> in which physical activity was evaluated approximately 6 months to 2 years before colorectal cancer diagnosis, there were no associations with all-cause or colorectal cancer mortality. When we repeated our prediagnosis analysis by using the last physical activity survey completed before colorectal cancer diagnosis (median, 1.6 years prediagnosis), there was a statistically significant inverse association with all-cause mortality (≥ 8.75 MET hours per week compared with < 3.5 MET hours per

**Table 1.** Characteristics of Patients Diagnosed With Colorectal Cancer by MET Hours of Recreational Physical Activity at Baseline in the Cancer Prevention Study II Nutrition Cohort

MET Hours of Physical Activity Per Week at Baseline							
Characteristic	< 3.5 (n = 255)		3.5-< 8.75 (n = 943)		≥ 8.75 (n = 1,064)		P <sup>a</sup>
	No.	%	No.	%	No.	%	
Age at colorectal cancer diagnosis, years							.24
< 65	39	15.3	123	13.0	123	11.6	
65-< 70	59	23.1	216	22.9	221	20.8	
70-< 75	70	27.5	275	29.2	289	27.2	
75-< 80	60	23.5	221	23.4	279	26.2	
≥80	27	10.6	108	11.5	152	14.3	
							< .001
Sex							
Female	90	35.3	456	48.4	445	41.8	
Male	165	64.7	487	51.6	619	58.2	
							.44
Race <sup>b</sup>							
White	250	98.0	919	97.5	1046	98.3	
Black	2	0.8	16	1.7	9	0.8	
Unknown, other, or not reported	3	1.2	8	0.8	9	0.8	
							< .001
Education level <sup>b,c</sup>							
Less than high school graduate	31	12.2	63	6.7	72	6.8	
High school graduate	90	35.3	269	28.5	261	24.5	
Vocational or technical school or some college or university	69	27.1	295	31.3	314	29.5	
Undergraduate or graduate degree	64	25.1	312	33.1	409	38.4	
							< .001
Cigarette smoking status <sup>d</sup>							
Never	83	32.5	399	42.3	401	37.7	
Current	43	16.9	78	8.3	69	6.5	
Former	126	49.4	462	49.0	582	54.7	
							< .001
Red meat intake, servings per week <sup>d</sup>							
< 1.5	32	12.5	124	13.1	189	17.8	
1.5-< 3	38	14.9	166	17.6	191	18.0	
3-< 5	38	14.9	217	23.0	208	19.5	
5-< 8	50	19.6	187	19.8	193	18.1	
≥ 8	71	27.8	156	16.5	185	17.4	
							.52
Family history of colorectal cancer <sup>b</sup>							
No	238	93.3	881	93.4	1006	94.5	
Yes	17	6.7	62	6.6	58	5.5	
							< .001
Body mass index (kg/m <sup>2</sup> ) <sup>d</sup>							
< 18.5	4	1.6	6	0.6	18	1.7	
18.5-< 25	71	27.8	366	38.8	421	39.6	
25-< 30	116	45.5	389	41.3	457	43.0	
≥ 30	64	25.1	182	19.3	168	15.8	
							.42
Leisure time spent sitting, hours per day <sup>d</sup>							
< 3	96	37.6	393	41.7	457	43.0	
3-< 6	114	44.7	410	43.5	452	42.5	
≥ 6	35	13.7	122	12.9	126	11.8	

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**Table 1.** Characteristics of Patients Diagnosed With Colorectal Cancer by MET Hours of Recreational Physical Activity at Baseline in the Cancer Prevention Study II Nutrition Cohort (continued)

Characteristic	MET Hours of Physical Activity Per Week at Baseline						P <sup>a</sup>
	< 3.5 (n = 255)		3.5-< 8.75 (n = 943)		≥ 8.75 (n = 1,064)		
	No.	%	No.	%	No.	%	
Hypertension <sup>d</sup>							.12
No	156	61.2	539	57.2	655	61.6	
Yes	99	38.8	404	42.8	409	38.4	
Diabetes <sup>d</sup>							.82
No	231	90.6	851	90.2	969	91.1	
Yes	24	9.4	92	9.8	95	8.9	
Colorectal cancer diagnosis site							.87
Colon <sup>e</sup>	186	72.9	699	74.1	779	73.2	
Rectum <sup>f</sup>	69	27.1	244	25.9	285	26.8	
SEER summary stage <sup>g</sup>							.66
Localized	122	47.8	481	51.0	539	50.7	
Regional	133	52.2	462	49.0	525	49.3	
Tumor grade at diagnosis							.31
Well differentiated	22	8.6	111	11.8	147	13.8	
Moderately differentiated	167	65.5	586	62.1	629	59.1	
Poorly differentiated	38	14.9	147	15.6	188	17.7	
Undifferentiated	2	0.8	9	1.0	10	0.9	
Surgery as first-line cancer treatment <sup>h</sup>							.57
No	4	1.6	19	2.0	20	1.9	
Yes	161	63.1	641	68.0	703	66.1	
Chemotherapy as first-line treatment <sup>h</sup>							.48
No	88	34.5	372	39.4	412	38.7	
Yes	77	30.2	288	30.5	311	29.2	
Radiation as first-line treatment <sup>h</sup>							.30
No	144	56.5	600	63.6	647	60.8	
Yes	21	8.2	60	6.4	76	7.1	

NOTE. Some counts do not add to totals because of missing data.

Abbreviations: MET, metabolic equivalent; SEER, Surveillance, Epidemiology, and End Results.

<sup>a</sup>χ<sup>2</sup> test for differences across strata by frequencies.<sup>b</sup>Self-reported on the 1982 questionnaire.<sup>c</sup>Defined as highest completed level of education.<sup>d</sup>Self-reported on the 1992-1993 baseline questionnaire.<sup>e</sup>International Classification of Diseases for Oncology (ICD-O), C18.0, C18.2-C18.9.<sup>f</sup>ICD-O, C19.9, C20.9.<sup>g</sup>Patients diagnosed prior to January 2001 use the SEER Summary Staging Guide, 1977 edition, and those diagnosed January 2001 or after use the SEER Summary Staging Manual 2000.<sup>h</sup>Self-report via questionnaire mailed to participant after initial report of colorectal cancer. A participant could report surgery, chemotherapy, or radiation as first-line cancer treatment, or any combination thereof.

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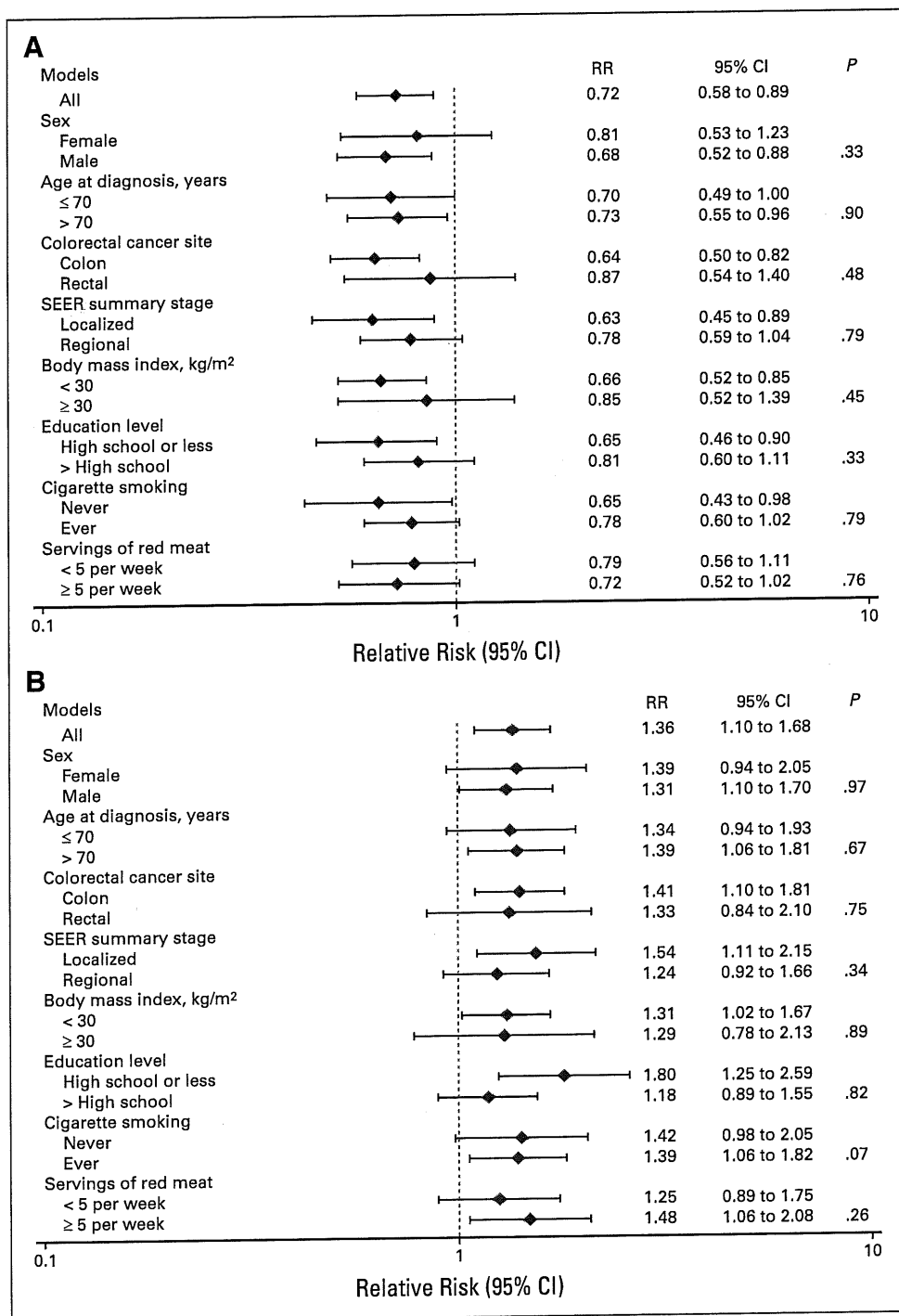
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**Fig 1.** (A) Relative risks (RRs) and 95% CIs for deaths from all causes comparing men and women who reported  $\geq 8.75$  metabolic equivalent hours per week of physical activity to less than 3 metabolic equivalent hours per week at baseline in 1992-1993. *P* values for heterogeneity are drawn from a 2 *df* test; results for the midcategory of physical activity are not shown in the figure. Models are shown for the overall association and are stratified by sex, age, colorectal cancer subsite, SEER summary stage, body mass index, education level, cigarette smoking status, and red meat intake and are adjusted for sex, age at colorectal cancer diagnosis, education, body mass index, smoking, red meat intake, leisure time spent sitting, and tumor stage. (B) RRs and 95% CIs for deaths from all causes comparing men and women who sat for more than 6 hours per day in their leisure time to men and women who sat for less than 3 hours per day at baseline in 1992-1993. *P* values for heterogeneity are drawn from a 2 *df* test; results for the midcategory of sitting time are not shown in the figure. Models are shown for the overall association and are stratified by sex, age, colorectal cancer subsite, SEER summary stage, body mass index, education level, cigarette smoking status, and red meat intake and are adjusted for age at colorectal cancer diagnosis, education, body mass index, smoking, red meat intake, recreational physical activity, and tumor stage.

week; RR, 0.66; 95% CI, 0.54 to 0.79), consistent with our findings from the 1992-1993 baseline and postdiagnosis questionnaires. Previous studies on postdiagnosis recreational physical activity<sup>7-9</sup> are consistent with our findings of lower risk of all-cause mortality among colorectal cancer survivors who are more physically active.

Reasons for an inverse association between recreational physical activity and mortality among patients with colorectal cancer are unclear but might include pathways that involve predisposition to biologically less aggressive colorectal tumors, independent of

disease stage; elements of a training effect whereby physical activity leads to improved functional capacity to tolerate and complete surgery and adjuvant treatment; improvements in systemic biomarkers related to inflammation, oxidative stress, immunity, growth hormones, insulin, and glucose; improvements in cardiovascular health indicators, such as lipoproteins or blood pressure; other mechanisms; some combination of the above; or chance. It should be noted that part of the association between recreational physical activity and lower overall mortality in our study was due to



lower mortality from causes other than colorectal cancer, consistent with studies that show that physical activity is associated with lower mortality from many chronic diseases.<sup>26</sup>

Sitting time is an emerging risk factor for colorectal cancer incidence<sup>10-12</sup> and mortality.<sup>13-16</sup> No study, to the best of our knowledge, has evaluated the association between sitting time and mortality among colorectal cancer survivors specifically, or indeed, among any population of cancer survivors. Thus, these study results of a higher risk of mortality among participants who sat for more of their leisure time are novel but should be replicated in other studies. Given the rarity of data on this topic it may be premature to speculate on a mechanism to explain this association; however, one relevant pathway may involve insulin and glucose.<sup>27,28</sup> Sedentary time, objectively measured by accelerometry, was positively associated with 2-hour plasma glucose in a study of adults without diabetes.<sup>29</sup> A recent meta-analysis identified associations of television viewing time with higher risks of type 2 diabetes and CVD.<sup>15</sup> In this cohort, we previously identified a higher risk of mortality among patients with colorectal cancer with diabetes.<sup>24</sup> Additional mechanisms may include oxidative stress, vitamin D, sex hormones, and lipoprotein lipase activity.<sup>30,31</sup> More studies are needed to confirm an association between sitting time and mortality and to identify the mechanisms that connect sitting time to mortality.

The strengths of this study include its large sample size, prospective design, and inclusion of detailed information on important confounders. An uncommon strength of this study is the ability to examine both pre- and postdiagnosis reports of recreational physical activity and leisure time spent sitting. Limitations to this study include lack of data on cancer recurrence, tumor molecular phenotype,<sup>32-35</sup> and details of treatment. On the basis of the data available, however, there were no differences in treatment by level of baseline physical activity. Because all of the studies on this topic to date are observa-

tional, we cannot rule out the possibility that other factors associated with both physical activity and mortality and not assessed in these studies may be driving these apparent associations. Randomized, controlled trials will be needed to ultimately establish causation.<sup>36</sup>

In conclusion, this study supports public health recommendations for recreational physical activity and the avoidance of sedentary time among colorectal cancer survivors. Clinically, physical activity recommendations should be based on the abilities and overall medical condition of a patient with cancer.<sup>1</sup> Our results add to mounting evidence that physicians should consider counseling colorectal cancer survivors to adopt a physically active lifestyle aiming to achieve 150 minutes per week or more of moderate intensity activity, such as walking, and to avoid prolonged sitting.

#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

#### AUTHOR CONTRIBUTIONS

**Conception and design:** Peter T. Campbell, Alpa V. Patel, Christina C. Newton

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**Administrative support:** Peter T. Campbell, Eric J. Jacobs, Susan M. Gapstur

**Provision of study materials or patients:** Peter T. Campbell, Susan M. Gapstur

**Collection and assembly of data:** Peter T. Campbell, Alpa V. Patel, Eric J. Jacobs, Susan M. Gapstur

**Data analysis and interpretation:** All authors

**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

#### REFERENCES

- Schmitz KH, Courneya KS, Matthews C, et al: American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Med Sci Sports Exerc* 42:1409-1426, 2010
- Speck RM, Courneya KS, Masse LC, et al: An update of controlled physical activity trials in cancer survivors: A systematic review and meta-analysis. *J Cancer Surviv* 4:87-100, 2010
- Lynch BM, Cerin E, Owen N, et al: Prospective relationships of physical activity with quality of life among colorectal cancer survivors. *J Clin Oncol* 26:4480-4487, 2008
- Mosher CE, Sloane R, Morey MC, et al: Associations between lifestyle factors and quality of life among older long-term breast, prostate, and colorectal cancer survivors. *Cancer* 115:4001-4009, 2009
- Demark-Wahnefried W, Morey MC, Sloane R, et al: Reach out to enhance wellness home-based diet-exercise intervention promotes reproducible and sustainable long-term improvements in health behaviors, body weight, and physical functioning in older, overweight/obese cancer survivors. *J Clin Oncol* 30:2354-2361, 2012
- Haydon AM, Macinnis RJ, English DR, et al: Effect of physical activity and body size on survival after diagnosis with colorectal cancer. *Gut* 55:62-67, 2006
- Meyerhardt JA, Giovannucci EL, Holmes MD, et al: Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol* 24:3527-3534, 2006
- Meyerhardt JA, Heseltine D, Niedzwiecki D, et al: Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: Findings from CALGB 89803. *J Clin Oncol* 24:3535-3541, 2006
- Meyerhardt JA, Giovannucci EL, Ogino S, et al: Physical activity and male colorectal cancer survival. *Arch Intern Med* 169:2102-2108, 2009
- Whittemore AS, Wu-Williams AH, Lee M, et al: Diet, physical activity, and colorectal cancer among Chinese in North America and China. *J Natl Cancer Inst* 82:915-926, 1990
- Steindorf K, Tobiasz-Adamczyk B, Popiela T, et al: 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, 2000
- Howard RA, Freedman DM, Park Y, et al: Physical activity, sedentary behavior, and the risk of colon and rectal cancer in the NIH-AARP Diet and Health Study. *Cancer Causes Control* 19:939-953, 2008
- Katzmarzyk PT, Church TS, Craig CL, et al: Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Med Sci Sports Exerc* 41:998-1005, 2009
- Patel AV, Bernstein L, Deka A, et al: Leisure time spent sitting in relation to total mortality in a prospective cohort of US adults. *Am J Epidemiol* 172:419-429, 2010
- Grøntved A, Hu FB: Television viewing and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: A meta-analysis. *JAMA* 305:2448-2455, 2011
- Matthews CE, George SM, Moore SC, et al: Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. *Am J Clin Nutr* 95:437-445, 2012
- World Cancer Research Fund/American Institute for Cancer Research (AICR): Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective. Washington, DC, AICR, 2007
- Physical Activities Guidelines Advisory Committee: Physical Activity Guidelines Advisory Committee Report. US Department of Health and Human Services, Washington, DC, 2008
- Rock CL, Doyle C, Demark-Wahnefried W, et al: Nutrition and physical activity guidelines for cancer survivors. *CA Cancer J Clin* 62:243-274, 2012
- Calle EE, Rodriguez C, Jacobs EJ, et al: The American Cancer Society Cancer Prevention Study II Nutrition Cohort: Rationale, study design, and baseline characteristics. *Cancer* 94:2490-2501, 2002
- Stellman SD, Garfinkel L: Smoking habits and tar levels in a new American Cancer Society prospective study of 1.2 million men and women. *J Natl Cancer Inst* 76:1057-1063, 1986
- Calle EE, Terrell DD: Utility of the National Death Index for ascertainment of mortality among

cancer prevention study II participants. *Am J Epidemiol* 137:235-241, 1993

23. Campbell PT, Newton CC, Dehal AN, et al: Impact of body mass index on survival after colorectal cancer diagnosis: The Cancer Prevention Study-II Nutrition Cohort. *J Clin Oncol* 30:42-52, 2012

24. Dehal AN, Newton CC, Jacobs EJ, et al: Impact of diabetes mellitus and insulin use on survival after colorectal cancer diagnosis: The Cancer Prevention Study-II Nutrition Cohort. *J Clin Oncol* 30:53-59, 2012

25. Chao A, Connell CJ, Jacobs EJ, et al: 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* 13:2187-2195, 2004

26. Warburton DE, Nicol CW, Bredin SS: Health benefits of physical activity: The evidence. *CMAJ* 174:801-809, 2006

27. Giovannucci E: Insulin and colon cancer. *Cancer Causes Control* 6:164-179, 1995

28. Giovannucci E, Harlan DM, Archer MC, et al: Diabetes and cancer: A consensus report. *CA Cancer J Clin* 60:207-221, 2010

29. Healy GN, Dunstan DW, Salmon J, et al: Objectively measured light-intensity physical activity is independently associated with 2-h plasma glucose. *Diabetes Care* 30:1384-1389, 2007

30. Lynch BM: Sedentary behavior and cancer: A systematic review of the literature and proposed biological mechanisms. *Cancer Epidemiol Biomarkers Prev* 19:2691-2709, 2010

31. Bey L, Hamilton MT: Suppression of skeletal muscle lipoprotein lipase activity during physical inactivity: A molecular reason to maintain daily low-intensity activity. *J Physiol* 551:673-682, 2003

32. Ogino S, Chan AT, Fuchs CS, et al: Molecular pathological epidemiology of colorectal neoplasia:

An emerging transdisciplinary and interdisciplinary field. *Gut* 60:397-411, 2011

33. Ogino S, Stampfer M: Lifestyle factors and microsatellite instability in colorectal cancer: The evolving field of molecular pathological epidemiology. *J Natl Cancer Inst* 102:365-367, 2010

34. Meyerhardt JA, Ogino S, Kirkner GJ, et al: Interaction of molecular markers and physical activity on mortality in patients with colon cancer. *Clin Cancer Res* 15:5931-5936, 2009

35. Morikawa T, Kuchiba A, Yamauchi M, et al: Association of CTNNB1 (beta-catenin) alterations, body mass index, and physical activity with survival in patients with colorectal cancer. *JAMA* 305:1685-1694, 2011

36. Courneya KS, Booth CM, Gill S, et al: The Colon Health and Life-Long Exercise Change trial: A randomized trial of the National Cancer Institute of Canada Clinical Trials Group. *Curr Oncol* 15:279-285, 2008

## Art of Oncology Volume 2

*Art of Oncology Volume 2: Honest and Compassionate Responses to the Daily Struggles of People Living With Cancer*, edited by Charles L. Loprinzi, MD, is a collection of 34 brief articles that first appeared in *Journal of Clinical Oncology*. The essays address issues related to end-of-life care, symptom control, ethics, and communication with patients.

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