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Research Article

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# Leisure-Time Spent Sitting and Site-Specific Cancer Incidence in a Large U.S. Cohort

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## Abstract

**Background:** Time spent sitting is distinctly different from accumulating too little physical activity and may have independent deleterious effects. Few studies have examined the association between sitting time and site-specific cancer incidence.

**Methods:** Among 69,260 men and 77,462 women who were cancer-free and enrolled in the American Cancer Society Cancer Prevention Study II Nutrition Cohort, 18,555 men and 12,236 women were diagnosed with cancer between 1992 and 2009. Extended Cox proportional hazards regression was used to estimate multivariable-adjusted relative risks (RR) and 95% confidence intervals (CI) of leisure-time spent sitting with total and site-specific cancer incidence.

**Results:** Longer leisure-time spent sitting, after adjustment for physical activity, BMI, and other factors, was associated with risk of total cancer in women (RR = 1.10; 95% CI, 1.04–1.17 for ≥6 hours vs. <3 hours per day), but not men (RR = 1.00; 95% CI, 0.96–1.05). In women, sitting time was associated with risk of multiple myeloma (RR = 1.65; 95% CI, 1.07–2.54), invasive breast cancer (RR = 1.10; 95% CI, 1.00–1.21), and ovarian cancer (RR = 1.43; 95% CI, 1.10–1.87). There were no associations between sitting time and site-specific cancers in men.

**Conclusion:** Longer leisure-time spent sitting was associated with a higher risk of total cancer risk in women, and specifically with multiple myeloma, breast, and ovarian cancers, but sitting time was not associated with cancer risk in men. Further research is warranted to better understand the differences in associations between men and women.

**Impact:** For women, these findings support American Cancer Society guidelines for cancer prevention to reduce sitting time when possible. *Cancer Epidemiol Biomarkers Prev; 24(9); 1350–9. ©2015 AACR.*

## Introduction

Over the past few decades, time spent sitting has increased due to technological advancements, transportation, and for other reasons. Sitting time is distinctly different from lack of physical activity and has been associated with greater mortality, cardiovascular disease, type II diabetes mellitus, obesity, and some cancers (1). Sitting time has also been associated with markers of chronic disease risk such as weight gain, high cholesterol, high fasting insulin levels, and other biomarkers (2–5). A recent report concluded that average life expectancy in the U.S. would increase by 2 years if excessive sitting time was reduced by 3 hours per day (6).

Although extensive research supports the role of physical activity in cancer prevention (7), few studies have examined associations between sitting time and site-specific cancer incidence. It is, however, biologically plausible that time spent sitting is a risk factor for cancer due to its effects on increasing adiposity and its impact on metabolic dysfunction (8, 9). A recent meta-analysis (10) examined sedentary time in relation to cancer risk, but evidence was limited for most individual cancer sites because of the few studies that considered any single site and because of differences in the types of sitting time (occupational, television, leisure-time, or total) among studies. Overall, the authors reported that evidence was consistent with a positive association between sitting time and colon and endometrial cancer risk.

Individual reductions in sitting time might be easier to promote and implement during leisure-time. However, further research is needed to clarify the relationship between leisure-time spent sitting specifically and site-specific cancer risk. No previous study has systematically examined leisure-time sitting in relation to site-specific cancer risk. Previous publications from the American Cancer Society's Cancer Prevention Study-II Nutrition Cohort (CPS-IINC; ref. 11) found leisure-time sitting to be positively associated with total cancer mortality in women, but not men, and with multiple myeloma in women (12), ovarian cancer (13), and endometrial cancer (14). Therefore, in the present analysis, we conducted a comprehensive and detailed analysis of sitting time in relation to total cancer incidence, and risk of 17 individual cancer sites in women and 15 cancer sites in men, including those previously examined, with follow-up time extended beyond that included in prior studies from this cohort. Because of the strong relationship between sitting time and weight, we examined the relationship between sitting time and cancer risk with and without adjustment for body mass index (BMI). In addition, we also explored whether the association between sitting time and cancer varies by the level of physical activity or BMI.

## Materials and Methods

### Study population

Men and women in this analysis were drawn from the 184,187 participants in the CPS-IINC, a prospective study of

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cancer incidence and mortality initiated by the American Cancer Society in 1992–93 (15). CPS-IINC members resided in 21 states with population-based state cancer registries and were predominantly 50 to 74 years of age at enrollment when they completed a 10-page mailed questionnaire that included questions on demographic, reproductive, medical, and lifestyle factors. Follow-up questionnaires were mailed every 2 years beginning in 1997 to update exposure information and to ascertain newly diagnosed cancers. The response rate among living participants for each of the follow-up questionnaires was at least 88%. Additional details on the recruitment and characteristics of the CPS-IINC are described elsewhere (15). The Emory University Institutional Review Board approves all aspects of the CPS-IINC.

We excluded sequentially from this analysis men and women who were lost to follow-up (i.e., alive at the first follow-up questionnaire in 1997 but did not return the 1997 or any subsequent follow-up questionnaire; $n = 6{,}251$), reported a personal history of cancer at enrollment ($n = 21{,}087$), or had missing data on sitting time ($n = 4{,}305$), physical activity ($n = 3{,}744$), or BMI ($n = 2{,}078$) at baseline. After all exclusions, the analytic cohort consisted of 146,722 individuals (69,260 men and 77,462 women) with a mean age of 63.0 (±6.4 SD) at baseline.

### Case ascertainment

Between enrollment and June 30, 2009, 18,555 men and 12,236 women were diagnosed with cancer. Of these, 25,057 were initially identified by self-report on a follow-up questionnaire and subsequently verified by medical record ($n = 18{,}736$) or through linkage with state cancer registries ($n = 6{,}321$; ref. 16). Linkage further identified 299 cancer diagnoses that were not first self-reported. An additional 5,435 participants were identified as having died from cancer through linkage of the cohort with the National Death Index (17). For these cases, death certificates listed cancer as the primary cause of death between the enrollment date and end of follow-up. Of these deaths, 4,202 were subsequently verified through linkage with state cancer registries. Specific causes of cancer were categorized based on the International Classification of Diseases, Ninth or Tenth Revisions (18, 19).

### Measures of leisure-time sitting and physical activity

Leisure-time sitting was assessed using the question "during the past year, on an average day, (not counting time spent at your job) how many hours per day did you spend sitting (watching TV, reading, etc.)?" Responses included "none, <3, 3–5, 6–8, >8 hours per day." Time spent sitting was categorized as 0–<3, 3–5, or ≥6 hours/day.

Information on exercise activity was collected using the question "during the past year, what was the average time per week you spent at the following kinds of activities: walking, jogging/running, lap swimming, tennis or racquetball, bicycling or stationary biking, aerobics/calisthenics, and dancing?" Summary exercise activity MET-hours/week (20) were calculated for each participant with methods described in detail elsewhere (11). Exercise activity was categorized as none, >0–<8.75, 8.75–<17.5, or ≥17.5 MET-hour/week; for reference, 8.75 MET-hours/week is equivalent to meeting current physical activity recommendations of at least 150 minutes/week of moderate-intensity activity.

Other daily-life activities were assessed using the question "during the past year, what was the average time per week you spent at the following kinds of activities: gardening/mowing/planting, heavy housework/vacuuming, heavy home repair/painting, and shopping?" Summary MET-hours/week were calculated (11) and categorized in sex-specific tertiles. Last, light housekeeping was assessed using the question "during the past year, on an average day, (not counting time spent at your job) how many hours per day did you spend light housekeeping?" and categorized as 0–<3, 3–5, or ≥6 hours/day.

### Statistical analysis

Sitting time and physical activity were modeled as time-dependent variables and extended Cox proportional hazards regression modeling (21) was used to estimate hazard rate ratios (RR), with follow-up time in days as the time-axis. For each participant, end of follow-up was either (i) diagnosis date, (ii) death date, (iv) date of last survey returned (if the participant did not respond to two sequential follow-up survey cycles), or (iv) June 30, 2009, whichever came first. All models were stratified on exact year of age. Associations of sitting time with cancer incidence were assessed in three models: (i) adjusted for age, (ii) adjusted for age and other potential confounders including physical activity (exercise, daily-life, and light housekeeping), and (iii) additionally adjusted for BMI [weight(kg)/height($m^2$)]. Potential confounders assessed at baseline included race (white, black, other/unknown), smoking status (lifelong nonsmoker, current smoker, former smoker, ever smoker with unknown status), duration and frequency of smoking among current smokers (≤35, >35 years; <20, ≥20 cigarettes/day), years since quitting among former smokers (≤5, 6–10, 11–15, 16–20, 21–25, >25), BMI (<18.5, 18.5–<25.0, 25.0–<30.0, ≥30.0 kg/$m^2$), education (≤high school, some college/trade school, college graduate), alcohol consumption (nondrinker, <1 drink/day, ≥1 drink/day), total energy intake (calories/day, sex-specific quartiles), red/processed meat intake (grams/week, sex-specific quartiles), family history of cancer, and prevalent chronic disease (included myocardial infarction, stroke, emphysema, hypertension, and high cholesterol) at baseline. Additional covariates were modeled as time dependent and included diabetes, and in women, menopausal status (pre/peri-, post-, and unknown status) and postmenopausal hormone use (never, current, former use). History of mammography screening and hysterectomy and/or oophorectomy was modeled as time dependent in breast cancer models, endoscopy screening in models of colorectal and pancreatic cancers, and PSA testing in models of prostate cancer. Finally, endometrial and ovarian cancer models were restricted to women with an intact uterus or ovaries, respectively.

We examined the combined effects of sitting time and exercise activity by stratifying sitting time on each level of exercise activity with the most exercise activity/least sitting time defining the referent group. Effect modification was assessed by conducting a −2 log likelihood (LL) test comparing a model with multiplicative interaction terms for the combined variables to a reduced model without the interaction terms. $P$ value for statistical interaction was derived from the $\chi^2$ distribution of the -2LL test statistic. Effect modification by age at enrollment and BMI was also investigated. For all statistical tests, significance was defined as a $P$ value <0.05. Analyses were conducted using SAS version 9. (SAS Institute Inc.).

## Results

This analysis included 69,260 men followed on average of 13.2 years and 77,462 women followed on average for 15.8 years.

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Men were slightly older, leaner, and more likely to have ever smoked cigarettes compared with women at baseline. Men and women who spent the most leisure-time sitting were more likely to be obese, have type II diabetes mellitus or other chronic diseases, have a higher caloric intake, eat more red/processed meat, and have ever smoked (Tables 1 and 2). Leisure-time sitting did not vary substantially by daily-life or exercise activities. The average total (exercise plus daily-life activities) physical activity among study participants was 26.3 MET-hours/week in men and 25.7 in women, and among those who sat 6 or more hours/day was 25.7 in men and 25.3 in women. The majority of MET-hours were contributed by light intensity activities (e.g., gardening and housework), and walking was the most commonly reported exercise activity with 82% of men and 86% of women reporting some walking.

There was statistically significant heterogeneity in associations of sitting time and total cancer incidence between men and women ($P = 0.009$); therefore, all analyses were conducted in men and women separately. In women, leisure-time spent sitting was associated with a statistically significant higher risk of total cancer incidence (RR = 1.10; 95% CI, 1.04–1.17 for ≥6 hours vs. <3 hours/day) after adjustment for physical activity, BMI, and other potential confounders (Table 3). When examining site-specific cancer incidence, higher time spent sitting (≥6 hours vs. <3 hours/day) was associated with higher risks of multiple myeloma (RR = 1.65; 95% CI, 1.07–2.54), invasive breast cancer (RR = 1.10; 95% CI, 1.00–1.21), and ovarian cancer (RR = 1.43; 95% CI, 1.10–1.87). The association with endometrial cancer was statistically significant before adjusting for BMI (RR = 1.34; 95% CI, 1.08–1.67), but was attenuated and no longer statistically significant after BMI adjustment (RR = 1.21; 95% CI, 0.97–1.50). Positive associations with head and neck, esophageal, and gallbladder cancers were suggestive, but were not statistically significant.

In women, sitting 6 or more hours/day was statistically significantly associated with overall cancer among the most active (RR = 1.14; 95% CI, 1.03–1.27), and least active women (RR = 1.13; 95% CI, 1.04–1.23), but not among the moderately active (RR = 1.04; 95% CI, 0.92–1.17) relative to more physically active women reporting <3 hours/day of sitting, although, statistical interaction was not apparent ($P = 0.16$). Exercise activity, BMI, and age did not modify associations of sitting time with total or site-specific cancer risk (data not shown).

In men, leisure-time spent sitting was not associated with total cancer incidence (RR = 1.00; 95% CI, 0.96–1.05 for ≥6 hours vs. <3 hours/day; Table 4). Multivariable-adjusted results were similar with or without adjustment for BMI. There were null associations of leisure-time spent sitting with risk of all site-specific cancers; however, RRs of sitting time with risk of head and neck, gallbladder, and pancreatic cancers were higher than one ($P < 0.1$; Table 4). Although there was evidence that sitting 3 to 5 hours/day was associated with a lower risk of total prostate cancer compared with sitting <3 hours per day, there was no evidence of a dose response, and this association was attenuated when limited to advanced prostate cancer.

The null associations for sitting time and cancer risk for men persisted among all categories of exercise activity and age (data not shown); however, there was some evidence that associations may differ by BMI (interaction $P = 0.04$): sitting time 6 or more hours compared with <3 hours/day was marginally associated with cancer risk in obese men (RR = 1.11; 95% CI, 1.00–1.24) but not in normal weight (RR = 0.97; 95% CI, 0.90–1.05) or overweight (RR = 0.99; 95% CI, 0.93–1.05) men.

In a sensitivity analysis, cases that occurred in the first year of follow-up were excluded due to the potential of reverse causality, and results remained unchanged (data not shown).

## Discussion

The present study is the first to comprehensively examine leisure-time spent sitting in relation to total and site-specific cancer incidence. Women who reported sitting for more than 6 versus less than 3 hours/day during their leisure-time had a 10% higher risk of all cancers combined. Leisure-time sitting was not associated with cancer risk in men with the exception of an 11% higher risk associated with sitting time among obese men. In both men and women, associations were not modified by physical activity or age.

To our knowledge, no previous studies examined associations between leisure-time sitting and total cancer incidence. However, many studies examined leisure-time sitting in relation to cancer mortality (11, 22–27). Of these, three reported statistically significant positive associations, including an earlier analysis from the CPS-IINC. Consistent with the findings reported herein for cancer incidence, in the earlier CPS-II analysis, sitting time was associated with cancer mortality in women only; in contrast, the other two studies reported positive associations in men and women (25, 26).

Sitting time has been studied using various domains such as occupational, leisure, or total time, which has implications for comparing study results. A recent meta-analysis, including 21 prospective cohorts and 22 case–control studies, examined sitting time in relation to site-specific cancer risk (10), but approximately half of those studies examined occupational sitting time, and there were few studies in relation to any individual cancer site. On the basis of the limited evidence available, it was concluded that sitting time was associated with higher colon and endometrial cancer risks. Although we did not observe an association with colon cancer, few previous studies have examined this association, and most previous studies reporting a positive association specifically examined television time (28, 29) or occupational sitting (30–33). While one of these studies (28) also reported an association with total sitting time, risk was greatly attenuated compared to risk associated with television watching.

In this study, leisure-time spent sitting was statistically significantly associated with endometrial cancer prior to adjustment for BMI, but this association was attenuated and no longer statistically significant after including BMI in the model. Similarly, higher risks without adjusting for BMI were previously reported in the CPS-IINC based on 11 years of follow-up (14) and in two other prospective cohorts (34, 35). Collectively, these findings suggest that the association between sitting time and endometrial cancer incidence might be confounded or mediated by BMI.

Sitting time was also associated with higher risks of invasive breast and ovarian cancers and with multiple myeloma in women. Previously published findings from the CPS-IINC (12, 13) showed similar results for ovarian cancer and multiple myeloma, but were based on fewer numbers of incident cancers and shorter follow-up time (9 and years, respectively). In the previous CPS-IINC study of breast cancer based on 15 years of follow-up (36), we showed no association with sitting time, but unlike the present analysis which was restricted to invasive breast cancer, *in situ*

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**Table 1.** Baseline characteristics of CPS-II Nutrition Cohort according to leisure-time spent sitting, women

| | Sitting h/d | | |
|---|---|---|---|
| **Characteristic** | **<3 (*n* = 37,131)** | **3–5 (*n* = 32,756)** | **>5 (*n* = 7,575)** |
| Age | 60.9 | 63.0 | 63.8 |
| Total activity MET-h/wk – mean/median | 26.3/22.0 | 25.1/21.5 | 25.3/20.5 |
| | | Age-adjusted percent[a] | |
| Race | | | |
| White | 97.3 | 97.4 | 96.7 |
| Black | 1.4 | 1.5 | 1.7 |
| Other/unknown | 1.2 | 1.1 | 1.6 |
| Education | | | |
| High school or less | 34.9 | 38.0 | 38.3 |
| Some college or trade school | 31.3 | 31.7 | 31.3 |
| College graduate | 33.1 | 29.6 | 29.6 |
| BMI (kg/m$^2$) | | | |
| <18.5 | 2.1 | 1.6 | 2.0 |
| 18.5–<25.0 | 56.0 | 47.4 | 41.5 |
| 25.0–<30.0 | 30.0 | 33.0 | 32.2 |
| ≥30.0 | 11.9 | 17.9 | 24.4 |
| Alcohol use | | | |
| Nondrinker | 45.5 | 45.1 | 48.9 |
| <1 drink/day | 38.5 | 38.7 | 34.3 |
| ≥ drink/day | 11.9 | 12.8 | 12.7 |
| Smoking status | | | |
| Nonsmoker | 58.6 | 52.4 | 46.4 |
| Current smoker | 33.4 | 36.8 | 39.4 |
| Former smoker | 6.5 | 9.7 | 13.1 |
| Ever smoker, status unknown | 0.3 | 0.3 | 0.4 |
| Diabetes status | | | |
| No | 94.5 | 93.6 | 90.9 |
| Yes | 5.1 | 6.0 | 8.7 |
| Other chronic conditions reported[b] | | | |
| None reported | 44.3 | 38.4 | 35.1 |
| Yes | 55.7 | 61.6 | 64.9 |
| Exercise activity (MET-h/wk) | | | |
| None | 7.9 | 9.4 | 14.5 |
| <8.75 | 44.3 | 46.4 | 43.1 |
| 8.75–<17.5 | 20.5 | 19.9 | 18.2 |
| ≥17.5 | 27.2 | 24.4 | 24.2 |
| Daily-life activity (MET-h/wk) | | | |
| T1: <7.0 | 29.6 | 30.7 | 35.1 |
| T2: 7.0–<15.5 | 34.4 | 33.1 | 28.5 |
| T3: ≥15.5 | 36.0 | 36.2 | 36.3 |
| Light housekeeping (h/d) | | | |
| <3 | 63.0 | 54.8 | 45.5 |
| 3–5 | 27.9 | 34.0 | 29.5 |
| >5 | 7.3 | 9.5 | 22.6 |
| Total energy intake (calories per d) | | | |
| Q1: <1,021 | 24.7 | 21.9 | 19.2 |
| Q2: 1,021–<1,302 | 23.4 | 22.9 | 20.8 |
| Q3: 1,302–<1,633 | 22.4 | 23.5 | 22.5 |
| Q4: ≥1633 | 20.6 | 24.4 | 29.2 |
| Total red meat intake (quartiles-g/wk) | | | |
| Q1: <159.6 | 25.2 | 21.1 | 19.5 |
| Q2: 159.6–<293.9 | 23.4 | 22.9 | 21.0 |
| Q3: 293.9–<470.2 | 22.3 | 23.6 | 23.4 |
| Q4: ≥470.2 | 20.3 | 25.2 | 27.8 |
| Menopausal status | | | |
| Pre/peri-menopausal | 5.7 | 5.3 | 5.3 |
| Postmenopausal | 94.1 | 94.4 | 94.4 |
| Use of postmenopausal hormones | | | |
| Never | 42.4 | 42.7 | 42.6 |
| Current | 28.1 | 27.3 | 25.6 |
| Former | 16.4 | 17.3 | 18.8 |
| Hysterectomy and/or oophorectomy | | | |
| No | 61.7 | 61.3 | 60.3 |
| Yes | 37.4 | 37.9 | 38.5 |

[a]Adjusted to the distribution of the CPS-II Nutrition Cohort women.
[b]Prevalent coronary artery disease, stroke, emphysema, other respiratory disease, hypertension, and high cholesterol.

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**Table 2.** Baseline characteristics of CPS-II Nutrition Cohort according to leisure-time spent sitting, men

| | Sitting h/d | | |
|---|---|---|---|
| **Characteristic** | **<3 (*n* = 28,410)** | **3–5 (*n* = 30,914)** | **>5 (*n* = 9,936)** |
| Age | 62.9 | 64.4 | 65.3 |
| Total activity MET-h/wk – mean/median | 26.8/22.5 | 26.1/22.5 | 25.7/22.0 |
| | | Age-adjusted percent[a] | |
| Race | | | |
| White | 97.4 | 97.5 | 97.7 |
| Black | 1.2 | 1.2 | 1.1 |
| Other/unknown | 1.4 | 1.3 | 1.2 |
| Education | | | |
| High school or less | 26.9 | 27.1 | 26.1 |
| Some college or trade school | 24.4 | 27.5 | 25.6 |
| College graduate | 48.1 | 44.7 | 47.8 |
| BMI (kg/m$^2$) | | | |
| <18.5 | 0.5 | 0.5 | 0.7 |
| 18.5–<25.0 | 39.2 | 33.3 | 32.3 |
| 25.0–<30.0 | 48.7 | 50.5 | 48.6 |
| ≥30.0 | 11.6 | 15.7 | 18.5 |
| Alcohol use | | | |
| Nondrinker | 32.8 | 32.5 | 34.2 |
| <1 drink/d | 38.9 | 38.9 | 36.5 |
| ≥ drink/d | 24.0 | 25.3 | 25.6 |
| Smoking status | | | |
| Nonsmoker | 37.2 | 29.2 | 28.2 |
| Current smoker | 54.8 | 60.3 | 58.1 |
| Former smoker | 7.2 | 9.8 | 13.0 |
| Ever smoker, status unknown | 0.5 | 0.3 | 0.4 |
| Diabetes status | | | |
| No | 92.1 | 90.7 | 88.0 |
| Yes | 7.5 | 9.0 | 11.6 |
| Other chronic conditions reported[b] | | | |
| None reported | 40.8 | 35.7 | 33.4 |
| Yes | 59.2 | 64.3 | 66.6 |
| Exercise (MET-h/wk) | | | |
| None | 11.1 | 12.4 | 15.8 |
| <8.75 | 37.4 | 38.6 | 36.4 |
| 8.75–<17.5 | 20.3 | 19.8 | 17.9 |
| ≥17.5 | 31.2 | 29.3 | 29.8 |
| Daily-life activity (MET-hs/wk) | | | |
| T1: <6.0 | 32.8 | 33.0 | 39.8 |
| T2: 6.0–<15.0 | 32.1 | 32.9 | 27.4 |
| T3: ≥15.0 | 35.1 | 34.0 | 32.8 |
| Light housekeeping (h/d) | | | |
| <3 | 84.9 | 83.2 | 76.0 |
| 3—5 | 3.5 | 5.4 | 8.7 |
| >5 | 0.5 | 0.7 | 4.0 |
| Total energy intake (calories per d) | | | |
| Q1: <1,357 | 25.3 | 22.0 | 18.7 |
| Q2: 1,357–<1,722 | 23.3 | 22.8 | 21.1 |
| Q3: 1,722–<2,163 | 21.6 | 23.5 | 23.4 |
| Q4: ≥2163 | 20.3 | 23.7 | 27.6 |
| Total red meat intake (quartiles-g/wk) | | | |
| Q1: <311.9 | 25.4 | 21.3 | 20.2 |
| Q2: 311.9–<538.7 | 22.9 | 23.0 | 21.2 |
| Q3: 538.7–<835.1 | 21.8 | 23.5 | 23.3 |
| Q4: ≥835.1 | 20.3 | 24.2 | 25.9 |

[a]Adjusted to the distribution of the CPS-II Nutrition Cohort men.
[b]Prevalent coronary artery disease, stroke, emphysema, other respiratory disease, hypertension, and high cholesterol.

breast cancers were included. Only one other prospective study examined invasive breast cancer (31), and showed a borderline higher association, similar in magnitude to this study, with total sitting; thus a higher, albeit modest, risk with leisure-time sitting and invasive breast cancer cannot be ruled out.

The previous CPS-IINC study and one case–control study reported a higher risk between leisure-time sitting and ovarian cancer (37), whereas two studies of occupational (38, 39) and one of total (40) sitting time were null. The only other study of multiple myeloma remains the earlier analysis in the CPS-IINC (12), and results were similar to the present findings. This analysis extends follow-up time for the previously examined cancer sites, and examines 13 additional individual cancer sites and total cancer in women.

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**Table 3.** Relative risks and 95% CIs for sitting time and site-specific cancer incidence in women, 1992–2009

| | | Leisure-time spent sitting (h/d) | | |
|---|---|---|---|---|
| **Cancer site** | | **<3** | **3–5** | **6 or more** |
| Total cancer | Deaths/person-years | 5,865/547,569 | 4,104/363,400 | 1,603/121,924 |
| | Age-adj. Rate[a] | 1,096 | 1,167 | 1,313 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.01 (0.97–1.05) | 1.12 (1.06–1.19) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.01 (0.97–1.05) | 1.10 (1.04–1.17) |
| Head and neck | Deaths/person-years | 47/547,569 | 32/363,400 | 18/121,924 |
| | Age-adj. Rate[a] | 9 | 9 | 15 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.97 (0.61–1.53) | 1.46 (0.84–2.54) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.97 (0.61–1.54) | 1.49 (0.86–2.61) |
| Esophagus | Deaths/person-years | 22/547,569 | 16/363,400 | 7/121,924 |
| | Age-adj. Rate[a] | 4 | 5 | 6 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.05 (0.54–2.04) | 1.14 (0.48–2.74) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.06 (0.54–2.05) | 1.13 (0.47–2.72) |
| Stomach | Deaths/person-years | 45/547,569 | 23/363,400 | 12/121,924 |
| | Age-adj. Rate[a] | 9 | 7 | 10 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.79 (0.47–1.32) | 1.02 (0.54–1.96) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.80 (0.48–1.34) | 1.06 (0.55–2.03) |
| Colon and rectum[d] | Deaths/person-years | 644/547,569 | 404/363,400 | 151/121,924 |
| | Age-adj. Rate[a] | 123 | 118 | 125 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.90 (0.79–1.02) | 0.97 (0.81–1.16) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.89 (0.78–1.01) | 0.95 (0.79–1.14) |
| Liver | Deaths/person-years | 42/547,569 | 28/363,400 | 9/121,924 |
| | Age-adj. Rate[a] | 8 | 8 | 8 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.94 (0.58–1.54) | 0.77 (0.37–1.60) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.92 (0.56–1.51) | 0.73 (0.35–1.53) |
| Gallbladder | Deaths/person-years | 24/547,569 | 24/363,400 | 9/121,924 |
| | Age-adj. Rate[a] | 5 | 7 | 8 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.53 (0.86–2.75) | 1.52 (0.70–3.32) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.49 (0.83–2.68) | 1.43 (0.65–3.14) |
| Pancreas[d] | Deaths/person-years | 182/547,569 | 121/363,400 | 47/121,924 |
| | Age-adj. Rate[a] | 36 | 36 | 39 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.97 (0.77–1.23) | 1.04 (0.75–1.44) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.96 (0.76–1.22) | 1.02 (0.73–1.41) |
| Lung | Deaths/person-years | 552/547,569 | 395/363,400 | 171/121,924 |
| | Age-adj. Rate[a] | 106 | 115 | 142 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.92 (0.81–1.05) | 0.96 (0.80–1.14) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.93 (0.82–1.07) | 0.98 (0.82–1.17) |
| Melanoma | Deaths/person-years | 414/547,569 | 263/363,400 | 92/121,924 |
| | Age-adj. Rate[a] | 77 | 73 | 76 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.98 (0.84–1.14) | 0.99 (0.78–1.24) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.98 (0.84–1.15) | 0.99 (0.79–1.25) |
| Kidney | Deaths/person-years | 101/547,569 | 59/363,400 | 26/121,924 |
| | Age-adj. Rate[a] | 19 | 18 | 21 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.91 (0.66–1.27) | 1.01 (0.65–1.57) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.90 (0.64–1.24) | 0.97 (0.62–1.51) |
| Bladder | Deaths/person-years | 126/547,569 | 109/363,400 | 36/121,924 |
| | Age-adj. Rate[a] | 24 | 32 | 30 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.23 (0.94–1.60) | 1.17 (0.80–1.70) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.23 (0.95–1.60) | 1.17 (0.80–1.70) |
| Non-Hodgkin lymphoma | Deaths/person-years | 384/547,569 | 283/363,400 | 100/121,924 |
| | Age-adj. Rate[a] | 73 | 83 | 82 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.13 (0.96–1.32) | 1.09 (0.87–1.36) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.12 (0.96–1.31) | 1.07 (0.86–1.35) |
| Multiple myeloma | Deaths/person-years | 75/547,569 | 66/363,400 | 30/121,924 |
| | Age-adj. Rate[a] | 15 | 20 | 25 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.31 (0.93–1.84) | 1.64 (1.06–2.53) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.31 (0.93–1.85) | 1.65 (1.07–2.54) |
| Breast[e] | Deaths/person-years | 2,120/547,569 | 1,490/363,400 | 555/121,924 |
| | Age-adj. Rate[a] | 388 | 410 | 451 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.01 (0.95–1.08) | 1.12 (1.02–1.24) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.00 (0.94–1.07) | 1.10 (1.00–1.21) |

*(Continued on the following page)*

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**Table 3.** Relative risks and 95% CIs for sitting time and site-specific cancer incidence in women, 1992–2009 (Cont'd)

| Cancer site | | Leisure-time spent sitting (h/d) | | |
|---|---|---|---|---|
| | | <3 | 3–5 | 6 or more |
| Endometrium[f] | Deaths/person-years | 372/337,664 | 292/227,571 | 112/74,565 |
| | Age-adj. Rate* | 109 | 132 | 146 |
| | MV-adj. RR† (95% CI) | 1.00 | 1.10 (0.94–1.28) | 1.34 (1.08–1.67) |
| | MV-adj. RR‡ (95% CI) | 1.00 | 1.04 (0.89–1.22) | 1.21 (0.97–1.50) |
| Ovary[g] | Deaths/person-years | 231/418,733 | 193/282,043 | 77/92,853 |
| | Age-adj. Rate[a] | 56 | 70 | 85 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.18 (0.97–1.43) | 1.42 (1.09–1.85) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.18 (0.97–1.44) | 1.43 (1.10–1.87) |
| All other sites combined | Deaths/person-years | 613/547,569 | 413/363,400 | 175/121,924 |
| | Age-adj. Rate[a] | 117 | 122 | 146 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.98 (0.87–1.13) | 1.21 (1.02–1.44 |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.98 (0.86–1.11) | 1.15 (0.97–1.37) |

[a]Rate per 100,000 standardized to the age-adjusted distribution of the CPS-II population.
[b]Adjusted for physical activity (exercise, daily-life, and light housekeeping), race, smoking status, duration and frequency of smoking among current smokers, years since quitting among former smokers, education, alcohol consumption, total energy intake, red/processed meat intake, family history of cancer, prevalent chronic disease, diabetes, menopausal status, and postmenopausal hormone use.
[c]Additional adjustment for BMI.
[d]Also adjusted for endoscopy screening.
[e]Also adjusted for history of mammography screening and hysterectomy and/or oophorectomy.
[f]Excluded women without an intact uterus.
[g]Excluded women without ovaries.

The lower risk of prostate cancer among men who sat 3 to 5 hours per day was similar to the inverse association observed in another large prospective cohort (41). However, in both studies, there was no dose–response relationship, and results were attenuated when restricted to advanced prostate cancer only. Thus, based on the limited studies to date, it is unclear whether sitting time is associated with prostate cancer risk. No additional site-specific cancers were associated with leisure-time spent sitting in men or women, although there was a suggestion of an association with head and neck and gallbladder cancer in men and women, esophageal cancer in women, and pancreatic cancer in men.

Several factors could explain a positive association between time sitting and cancer risk. Time spent sitting might be associated with other unhealthy behaviors that are not captured or are incompletely captured through questionnaires. Sitting time may also represent a different behavior than physical inactivity as it has important independent metabolic consequences that may be associated with cancer risk. Laboratory animal and human intervention studies have shown that high sedentary time is associated with higher fasting glucose and other aspects of metabolic dysfunction (reviewed in ref. 8). Sitting time may also displace physical activity which would result in an overall decrease in energy expenditure; for example, many individuals who meet physical activity recommendations spend much of their remaining time sitting in the car, at work, or at home.

In addition, substantial evidence from observational studies and randomized clinical trials shows that reducing time sitting lowers risk of obesity and type II diabetes mellitus, two important risk factors for many cancers (42–46). Residual confounding by excess body weight could contribute to the association between sitting time and cancer risk; however, we also adjusted for BMI using a continuous variable and results were unchanged. High BMI also may be on the causal pathway between longer sitting time and cancer risk (47), but associations at all sites in women except the endometrium were only slightly attenuated by controlling for or stratifying on BMI. Thus, the association between sitting time and cancer risk is unlikely to be explained by BMI alone. In contrast, the positive association with leisure-time sitting in men was limited to obese men. It is plausible that the metabolic alterations due to leisure-time spent sitting are not substantial enough to affect cancer risk in normal weight men or that there remains some residual confounding by obesity, or other factors, in men.

Strengths of our study include its large sample size including over 30,000 incident cancers, prospective design, and ability to control for many cancer risk factors, including physical activity and BMI. The lack of occupational data is a limitation and may lead to some misclassification of total sitting time. However, this is likely to have minimal impact, in particular for women, because the majority (80%) of female participants in CPS-IINC were retired or homemakers at baseline, and among those not retired, very few women worked in jobs that involved any activity (7%). Thus, for women, leisure-time spent sitting likely reflects the majority of their total sitting time. In contrast, the lack of occupational physical activity data may be a broader limitation in men. Although the majority of men were also retired or homemakers (57%), and among those who worked, few had active jobs (21%), reliance on leisure-time sitting and no occupational sitting data may lead to greater misclassification of total sitting time in men than women. Another limitation is the use of self-reported measures of sitting time and physical activity. Although physical activity and sitting time are subject to misreporting and were not directly validated in this study, they are very similar to those used and validated in another prospective study (48) and have also been associated with total mortality (11), weight gain in women (47), and various cancers in this cohort (12–14, 36).

In conclusion, longer leisure-time spent sitting was associated with a modest risk of cancer in women, and specifically with breast and ovarian cancers, and multiple myeloma. Sitting time was also associated with endometrial cancer risk; however, unlike other observed associations, this association appeared to be confounded or perhaps mediated by body weight. In contrast, leisure-time spent sitting was associated with overall cancer risk only among obese men. Given the prevalence of time spent sitting in the

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**Table 4.** Relative risks and 95% confidence intervals for sitting time and site-specific cancer incidence in men, 1992–2009

| | | Leisure-time spent sitting (h/d) | | |
|---|---|---|---|---|
| **Cancer site** | | **<3** | **3–5** | **6 or more** |
| Total cancer | Deaths/person-years | 7,762/366,814 | 6,792/308,731 | 2,959/128,206 |
| | Age-adj. Rate[a] | 2,197 | 2,287 | 2,314 |
| | MV-adj. RR[b] (95% CI) | 1.00 (ref) | 0.99 (0.96–1.03) | 1.00 (0.96–1.05) |
| | MV-adj. RR[c] (95% CI) | 1.00 (ref) | 0.99 (0.96–1.03) | 1.00 (0.96–1.05) |
| Head and neck | Deaths/person-years | 109/366,814 | 107/308,731 | 58/128,206 |
| | Age-adj. Rate[a] | 30 | 36 | 45 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.04 (0.79–1.36) | 1.22 (0.88–1.69) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.04 (0.79–1.37) | 1.22 (0.88–1.69) |
| Esophagus | Deaths/person-years | 119/366,814 | 102/308,731 | 49/128,206 |
| | Age-adj. Rate[a] | 34 | 34 | 38 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.97 (0.74–1.27) | 1.05 (0.75–1.48) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.96 (0.73–1.26) | 1.04 (0.74–1.46) |
| Stomach | Deaths/person-years | 89/366,814 | 101/308,731 | 36/128,206 |
| | Age-adj. Rate[a] | 26 | 36 | 28 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.23 (0.92–1.65) | 1.04 (0.70–1.55) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.23 (0.92–1.65) | 1.05 (0.71–1.55) |
| Colon and rectum[d] | Deaths/person-years | 646/366,814 | 553/308,731 | 248/128/206 |
| | Age-adj. Rate[a] | 182 | 186 | 194 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.96 (0.85–1.07) | 1.03 (0.89–1.19) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.95 (0.84–1.07) | 1.01 (0.87–1.18) |
| Liver | Deaths/person-years | 82/366,814 | 59/308,731 | 30/128,206 |
| | Age-adj. Rate[a] | 24 | 21 | 23 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.76 (0.54–1.07) | 0.84 (0.55–1.29) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.75 (0.53–1.06) | 0.83 (0.54–1.28) |
| Gallbladder | Deaths/person-years | 12/366,816 | 12/308,731 | 9/128,206 |
| | Age-adj. Rate[a] | 3 | 4 | 7 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.21 (0.54–2.74) | 2.14 (0.89–5.16) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.19 (0.53–2.69) | 2.11 (0.87–5.09) |
| Pancreas[d] | Deaths/person-years | 178/366,814 | 165/308,731 | 82/128,206 |
| | Age-adj. Rate[a] | 52 | 59 | 66 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.07 (0.86–1.33) | 1.17 (0.89–1.53) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.06 (0.85–1.31) | 1.14 (0.87–1.49) |
| Lung | Deaths/person-years | 775/366,814 | 772/308,731 | 356/128,206 |
| | Age-adj. Rate[a] | 224 | 260 | 279 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.02 (0.92–1.13) | 1.01 (0.89–1.15) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.03 (0.93–1.14) | 1.01 (0.89–1.15) |
| Melanoma | Deaths/person-years | 494/366,814 | 466/308,731 | 194/128,206 |
| | Age-adj. Rate[a] | 139 | 158 | 153 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.10 (0.96–1.25) | 1.05 (0.89–1.24) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.10 (0.96–1.25) | 1.05 (0.88–1.24) |
| Kidney | Deaths/person-years | 141/366,814 | 179/308,731 | 59/128,206 |
| | Age-adj. Rate[a] | 40 | 61 | 47 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.49 (1.19–1.86) | 1.11 (0.82–1.52) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.47 (1.17–1.84) | 1.09 (0.80–1.48) |
| Bladder | Deaths/person-years | 541/366,814 | 435/308,731 | 211/128,206 |
| | Age-adj. Rate[a] | 160 | 150 | 168 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.94 (0.83–1.08) | 1.01 (0.86–1.19) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.94 (0.83–1.07) | 1.01 (0.86–1.19) |
| Non-Hodgkin lymphoma | Deaths/person-years | 415/366,814 | 389/308,731 | 157/128,206 |
| | Age-adj. Rate[a] | 118 | 135 | 125 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.13 (0.98–1.30) | 1.05 (0.87–1.26) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.12 (0.97–1.29) | 1.04 (0.86–1.25) |
| Multiple myeloma | Deaths/person-years | 104/366,814 | 101/308,731 | 38/128,206 |
| | Age-adj. Rate[a] | 30 | 34 | 32 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.15 (0.87–1.52) | 1.02 (0.70–1.48) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.14 (0.86–1.50) | 1.00 (0.68–1.45) |
| Prostate[e] | Deaths/person-years | 3,782/366,814 | 3,157/308,731 | 1,337/128,206 |
| | Age-adj. Rate[a] | 1,054 | 1,038 | 1,029 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.94 (0.90–0.99) | 0.96 (0.90–1.02) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.94 (0.90–0.99) | 0.97 (0.91–1.03) |

*(Continued on the following page)*

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**Table 4.** Relative risks and 95% confidence intervals for sitting time and site-specific cancer incidence in men, 1992–2009 (Cont'd)

| Cancer site | | Leisure-time spent sitting (h/d) | | |
|---|---|---|---|---|
| | | <3 | 3–5 | 6 or more |
| Advanced prostate[e] | Deaths/person-years | 785/366,814 | 652/308,731 | 268/128,206 |
| | Age-adj. Rate[a] | 218 | 215 | 210 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 0.95 (0.86–1.04) | 0.96 (0.85–1.09) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 0.95 (0.86–1.04) | 0.96 (0.85–1.09) |
| All other sites combined | Deaths/person-years | 640/366,814 | 576/308,731 | 254/128,106 |
| | Age-adj. Rate[a] | 183 | 199 | 202 |
| | MV-adj. RR[b] (95% CI) | 1.00 | 1.03 (0.92–1.15) | 1.03 (0.89–1.20) |
| | MV-adj. RR[c] (95% CI) | 1.00 | 1.03 (0.92–1.15) | 1.03 (0.89–1.19) |

[a]Rate per 100,000 standardized to the age-adjusted distribution of the CPS-II population.
[b]Adjusted for physical activity (exercise, daily-life, and light housekeeping), race, smoking status, duration and frequency of smoking among current smokers, years since quitting among former smokers, education, alcohol consumption, total energy intake, red/processed meat intake, family history of cancer, prevalent chronic disease, and diabetes.
[c]Additional adjustment for BMI.
[d]Also adjusted for endoscopy screening.
[e]Also adjusted for PSA testing.

United States, even a modest positive association can have broad public health implications. However, further research is warranted to better understand the differences in associations between men and women.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

## Authors' Contributions

**Conception and design:** A.V. Patel, P.T. Campbell, S.M. Gapstur
**Development of methodology:** A.V. Patel, P.T. Campbell
**Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.):** A.V. Patel, P.T. Campbell, S.M. Gapstur
**Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis):** A.V. Patel, J.S. Hildebrand, P.T. Campbell, S.M. Gapstur
**Writing, review, and/or revision of the manuscript:** A.V. Patel, J.S. Hildebrand, P.T. Campbell, L.R. Teras, L.L. Craft, M.L. McCullough, S.M. Gapstur
**Other (provided expertise related to physical activity and sedentary behavior constructs in the paper):** L.L. Craft

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