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Physical Activity, Sedentary Behavior, and Endometrial Cancer Risk in the NIH-AARP Diet and Health Study

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Abstract

Consistent with a strong hormonal etiology, endometrial cancer is thought to be influenced by both obesity and physical activity. While obesity has been consistently related to risk, associations with physical activity have been inconclusive. We examined relationships of activity patterns with endometrial cancer incidence in the NIH-AARP Diet and Health Study cohort, which included 109,621 women, ages 50–71, without cancer history, who in 1995–1996 completed a mailed baseline questionnaire capturing daily routine and vigorous (defined as any period of ≥ 20 minutes of activity at work or home causing increases in breathing, heart rate, or sweating) physical activity. A second questionnaire, completed by 70,351 women, in 1996–1997 collected additional physical activity information. State cancer registry linkage identified 1,052 primary incident endometrial cancers from baseline through December 31, 2003. In multivariate proportional hazards models, vigorous activity was inversely associated with endometrial cancer in a dose-response manner (p for trend=0.02) (relative risk (RR) for ≥ 5 times/week vs. never/rarely=0.77, 95% confidence interval (CI): 0.63, 0.95); this association was more pronounced among overweight and obese women (body mass index ≥ 25; RR=0.61, 95% CI: 0.47, 0.79) than among lean women (body mass index <25; RR=0.76, 95% CI: 0.52, 1.10; p for interaction=0.12). While we observed no associations with light/moderate, daily routine or occupational physical activities, risk did increase with number of hours of daily sitting (p for trend=0.02). Associations with vigorous activities, which may interact with body mass index, suggest directions for future

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Novelty and impact of paper: While obesity has been consistently related to endometrial cancer risk, associations with physical activity have been inconclusive, and few studies have examined whether sedentary behaviors are associated with risk. Since physical activity is a modifiable risk factor, our results suggesting a protective effect of vigorous activity and a deleterious role of inactivity on endometrial cancer risk could have important public health implications.

Conflicts of interest: none

research to clarify underlying biologic mechanisms, including those relating to hormonal alterations.

Keywords

Endometrial Neoplasms/epidemiology; Exercise/physiology; Recreation/physiology; Health Behavior; Prospective Studies

Introduction

Endometrial cancer is the most common gynecologic malignancy and the fourth most common cancer among women in the US,1 and excess weight is estimated to account for over half of endometrial cancers.2 Whereas body mass index (BMI) is an established risk factor,3 evidence for an independent role of physical activity in reducing endometrial cancer risk is inconclusive.4 Clarifying the relationship between physical activity, a potentially modifiable risk factor, and endometrial cancer could have important etiologic and public health implications.

To date, ten cohort studies5¯14 and twelve case-control studies15¯26 have examined the association between physical activity and endometrial cancer. Of these, only two cohort studies6, 14 have examined whether sedentary behaviors are associated with endometrial cancer and results were suggestive of an elevated risk with longer durations of TV watching or sitting. Two recent systematic reviews concluded that results suggest an inverse association between physical activity and endometrial cancer but are limited by inconsistent dose-response relationships and may depend on activity type and intensity.27, 28 In addition, because BMI is associated with both physical activity and endometrial cancer, special attention to BMI as a confounding factor is required.27 Additional evidence from prospective cohort studies is needed before specific types and time periods of physical activity might be recommended as a strategy to reduce risk.27, 28 We therefore investigated physical activity and endometrial cancer risk within the large prospective NIH-AARP Diet and Health Study cohort. We considered various types of physical activity during different time periods, evaluated sedentary behaviors, and paid particular attention to potential confounding by BMI.

Materials and Methods

Study Population

The NIH-AARP Diet and Health Study design and methodology have been described in detail.29 The study was initiated in 1995–1996 when a questionnaire was mailed to 3.5 million members of the AARP (formerly known as the American Association of Retired Persons), ages 50–71 years, who resided in one of eight US states (CA, FL, PA, NJ, NC, LA, GA, and MI). This baseline questionnaire captured diet history, demographic characteristics, current weight and height, smoking status, physical activity, medical and reproductive history, menopausal status, menopausal hormone therapy (HT), and personal and familial history of cancer. A total of 617,119 (17.6%) questionnaires were returned, of which 567,169 were satisfactorily completed; of these, 179 duplicate questionnaires were excluded. In 1996–1997, a second questionnaire was sent to the baseline questionnaire respondents to collect additional information on physical activity, menopausal HT use, medical history, and history of cancer. A total of 337,074 men and women completed this questionnaire.

After excluding individuals who died (n=261) or moved out of the cancer registry ascertainment area (n=321) before their baseline questionnaire was received and scanned, proxy respondents to the baseline questionnaire (n=15,760), six individuals who withdrew from the study, and 325,174 men, the baseline study population included 225,468 potentially eligible women. The study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute.

Assessment of Physical Activity

The baseline questionnaire captured several measures of physical activity. Participants were asked to select a response that best described their current daily routine activity, excluding exercise or sports: sit without walking very much; sit but walk fair amount; stand or walk a lot without carrying or lifting things; lift or carry light loads or climb stairs/hills often; or do heavy work or carry heavy loads. Participants were asked to indicate their frequency of vigorous physical activity during a typical month in the past 12 months: never, rarely, 1–3 times per month, 1–2 times per week, 3–4 times per week, or ≥ 5 times per week. Vigorous activity was defined as physical activity at work or home including exercise, sports, and carrying heavy loads that lasted ≥ 20 minutes and caused increases in breathing, heart rate, or sweating. Using the same response categories, participants were also asked to recall their frequency of participation in physical activities or sports during a typical month around the ages of 15–18 years old. We collapsed the never and rarely response categories for analysis.

The second questionnaire asked about several domains of physical activity: occupational, recreational and household, and physical inactivity. History of occupational physical activity was assessed by asking participants if they ever had a job requiring physically demanding work. Those responding affirmatively were asked to report the number of (none, 1–2, 3–5, or ≥ 6 jobs) and total number of years spent (none or <1 year, 1–2, 3–5, 6–9, or ≥ 10 years) in these jobs. The second questionnaire also assessed whether participants ever had a job in which they walked or biked to work for most days of the week and if so, the total number of years they did so (none, <1 year, 1–2, 3–5, 6–9, or ≥ 10 years). We combined the none and <1 year response categories for analysis.

Participants were instructed not to include occupational physical activity when reporting how often they participated in “light” and “moderate and vigorous” recreational and household activities. They could choose from the following options: never, rarely, weekly but <1 hour per week, 1–3 hours per week, 4–7 hours per week, and >7 hours per week. Participants were asked to read lists of examples of “light” and “moderate and vigorous” recreational and household activities and to select the option that best described how often they participated during various ages and time periods: 15–18, 19–29, and 35–39 years old, and in the past 10 years. The never and rarely response categories were collapsed for analysis. Since these physical activity questions captured frequency and dose, we calculated hours exercised per week and metabolic equivalent (MET) hours per week using the Compendium of Physical Activities as a guide.30 First, midpoint values were used for each category of reported frequency/dose of participation in weekly activity: never/rarely was assigned a value of 0 hours; <1 hour per week was assigned a value of 0.5 hours; 1–3 hours per week was assigned a value of 2 hours; 4–7 hours per week was assigned a value of 5.5 hours; and >7 hours per week was assigned a value of 8 hours. MET values were then assigned to each level of activity: light activities, 3.0 MET; and moderate/vigorous activities, 7.0 MET. These MET values were multiplied by the values of activity hours per week and summed across the activity levels to determine MET-hours per week for each of the various ages and time periods.

Information on physical inactivity was based on two questions. Participants were asked about time spent watching TV or videos during a typical 24-hour period over the past 12

months. Time spent watching TV or videos was categorized as none, <1 hour, 1–2, 3–4, 5–6, 7–8, and ≥ 9 hours. In a separate question, participants were also asked to indicate the number of hours spent sitting during a typical 24-hour period over the past 12 months: <3, 3–4, 5–6, 7–8, and ≥ 9 hours. Both measures of inactivity were collapsed as <3, 3–4, 5–6, and ≥ 7 hours per day.

Cohort Follow-up

Cohort members were followed annually for address changes and vital status. Address changes were identified by matching the cohort database to the US Postal Service's National Change of Address database. Vital status was updated through linkage to the US Social Security Administration Death Master File, identifying cohort members who are presumed deceased. Results were verified through a follow-up search of the National Death Index Plus, a central computerized index of death record information compiled annually from state vital statistics offices for research purposes.

Ascertainment of Endometrial Cancer

Incident endometrial cancers were initially identified through probabilistic linkage to eight state cancer registries using first and last name, address, sex, date of birth, and Social Security Number. The cancer registry ascertainment area was recently expanded to include three additional states (TX, AZ, and NV) to capture cancer occurring among participants who moved to those states during follow-up. Histology was defined using International Classification of Diseases for Oncology codes, 3rd edition.31 A previous validation study in this cohort estimated that registry linkage validly identified approximately 90% of all incident cancers.32

Analytic Sample

In our analysis of baseline physical activity data, we excluded 23,911 women who reported a personal cancer history other than non-melanoma skin cancer, 82,132 who reported a prior hysterectomy, and 2,934 women with unknown hysterectomy status. We also excluded women who reported at baseline that their menstrual periods stopped due to surgery (n=1,829) or because of radiation or chemotherapy (n=117), 76 who developed non-epithelial endometrial cancer during follow-up, 8 with no follow-up, 421 (including 4 cases) who were missing baseline information on both daily routine and vigorous activity, and women with missing (n=3,530, including 31 cases) or extreme (defined as > two interquartile ranges from the mean; n=889, including 33 cases) values for baseline BMI (weight in kilograms divided by the square of height in meters). Thus, 109,621 women were included in the baseline physical activity analysis. From baseline through December 31, 2003, 1,052 women developed endometrial cancer, the majority of which were adenocarcinomas (n=978).

To use the physical activity and inactivity data collected in the second questionnaire, we created an analytic subsample restricted to women who responded to the second questionnaire. Of the 109,621 women included in the baseline analysis, 72,046 women (including 701 endometrial cancer cases) responded to the second questionnaire. We further excluded women who died or moved out of the cancer registry ascertainment area before their second questionnaire was received and scanned (n=338), proxy respondents to the second questionnaire (n=565, including 7 prevalent endometrial cancer cases), women with a personal history of cancer at the time of the second questionnaire (n=633, including 44 prevalent endometrial cancer cases), those missing recreational/household activity and physical inactivity information on the second questionnaire (n=82 non-cases), women with extreme values for BMI (n=16 non-cases with BMI > two interquartile ranges from the mean BMI of those responding to the second questionnaire), women with unknown history

of HT use at the time of the second questionnaire (n=58 non-cases), and 3 women with no follow-up, resulting in an analytic subsample of 70,351 women completing both study questionnaires. Of these, 650 women developed endometrial cancer from the time of the second questionnaire through December 31, 2003; adenocarcinoma accounted for 95% of these cancers.

Statistical Analysis

Cox proportional hazards models were used to estimate hazard ratios and 95% confidence intervals (CI) for endometrial cancer associated with physical activity; age was the time scale33 and ties were handled by complete enumeration.34 Follow-up began at the age at which the baseline questionnaire (for the main analyses) or the second questionnaire (for the analytic subsample) was received and scanned and continued through the earliest of the following dates: participant diagnosed with endometrial cancer, moved out of her registry catchment area, died from any cause, or December 31, 2003. To test the proportional hazards assumption, we generated time-dependent covariates by including interactions of physical activity measures with the natural log of age (the time metric); probability values for all time-dependent covariates were >0.05, consistent with proportional hazards.

For the main analyses, we examined the combined effect of baseline vigorous activity and baseline daily routine activity in relation to endometrial cancer by creating a single six-level variable based on the cross-tabulation of vigorous activity (never/rarely, 1 time per month to 2 times per week, or ≥ 3 times per week) and daily routine activity (sit much of day with some walking vs. do more than sit most of day). Multivariate models were used to control for age at entry, race/ethnicity, smoking status, parity, ever use of oral contraceptives, menopausal status (premenopausal, natural menopause at <45, 45–49, 50–54, or ≥ 55 years of age, or unknown age at menopause), and ever use of HT. Since BMI is positively associated with endometrial cancer risk and inversely associated with physical activity, separate multivariate models additionally adjusted for BMI.

In the multivariate models restricted to the analytic subsample of women who completed both questionnaires, we replaced ever use of HT with HT formulation (never used, estrogen only use, estrogen-progestin only use, HT use of other/unknown formulation). In analyses of frequency of light physical activity during a specific time period, we adjusted for frequency of moderate/vigorous physical activity during that same time period, and vice versa. We used a likelihood ratio test, comparing models with and without the interaction terms, to separately examine effect modification by HT formulation and BMI.

Tests for linear trends across the physical activity exposure categories were calculated by treating these categorical variables as ordinal variables. In subsequent models, we adjusted individually for calendar time and several additional factors, including education, age at menarche, self-reported diabetes, self-rated health quality, and alcohol intake; results were essentially the same and are not shown here. In addition, we assessed the internal consistency between physical activity items reported within and between questionnaires by examining pairwise Spearman's rank correlations.

Probability values of <0.05 were considered statistically significant. All tests of statistical significance were two-tailed. Analyses were performed using SAS software release 9.1.3 (SAS Institute Inc., Cary, NC).

Results

Among the 109,621 mostly white, postmenopausal women in this report, current daily routine physical activity (excluding exercise or sports) was most frequently described as

standing or walking a lot without carrying or lifting things (38.8%), followed by sitting during much of the day but walking a fair amount (33.6%). Including exercise and sports, 21.8% of women reported never or rarely engaging in vigorous activity in the past 12 months, while 14.4%, 21.3%, and 42.5% reported engaging in vigorous activity 1–3 times per month, 1–2 times per week, and ≥ 3 times per week, respectively. More than half (55.7%) of the women reported participating in physical activities or sports ≥ 3 times per week between the ages of 15–18 years old.

At baseline, women with the most active current daily routine or most frequent participation in vigorous activity in the past 12 months were leaner than their less-active counterparts (Tables 1a and 1b). Compared with the least active women, women with the most active current daily routine were less likely to be white, to have attended post-secondary education, and to have ever used exogenous hormones, and were more likely to be current smokers. In contrast, women who frequently participated in vigorous activity were more likely to have attended post-secondary education and to have ever used hormone therapy, and were less likely to be current smokers as compared with those who never/rarely engaged in vigorous activity.

The 109,621 women accrued 766,170.7 person-years during an average follow-up of 3.80 years for cases (range: 1 day-8.03 years) and 7.02 years for non-cases (range: 1 day-8.18 years). The mean (SD) ages for entry and exit were 62.6 (5.2) and 66.4 (5.5) years for cases and 61.6 (5.5) and 68.6 (5.6) years for non-cases, respectively. The standardized incidence ratio for endometrial cancer in the full cohort compared with the US National Cancer Institute's Surveillance, Epidemiology and End Results rate (ages 50–79 years) was 0.92 (95% CI: 0.87, 0.97), indicating that the rate in our cohort was slightly lower than that of the US population. As previously described in this cohort,[35, 36] endometrial cancer risk was positively associated with BMI, later age at natural menopause, and use of menopausal HT; reduced endometrial cancer risk was associated with non-white race/ethnicity, smoking, later age at menarche, parity, and oral contraceptive use.

We examined the risk of endometrial cancer according to self-reported physical activity at baseline (Table 2). The risk of endometrial cancer decreased with increasing categories of daily routine activity, excluding exercise or sports (p for trend <0.0001), though this was no longer statistically significant in multivariate analysis further adjusted for BMI (p for trend=0.07). Increasing frequency of vigorous activity, including exercise and sports, was associated with reduced endometrial cancer risk in a dose-response manner before and after adjustment for BMI (p for trend=0.02), such that the relative risk (RR) of endometrial cancer for vigorous activity ≥ 5 times per week compared with never or rarely engaging in vigorous activity was 0.77 (95% CI: 0.63, 0.95). Frequency of participation in physical activities or sports during a typical month between the ages of 15–18 years old was not related to endometrial cancer in age-adjusted or multivariate analyses. Compared with women who reported both never/rarely engaging in vigorous activity and sitting for much of the day, women who participated in vigorous activity ≥ 3 times a week over the past 12 months were at a significant 25% reduced relative risk of endometrial cancer irrespective of their current daily routine activity level (data not shown).

The majority of women who responded to the second questionnaire never had a physically demanding job lasting more than a year (85.1%) and never had a job in which they walked or biked to work most days of the week for a period longer than one year (87.2%) (Table 3). We found no statistically significant associations between any of the measures of prior occupational physical activity and endometrial cancer. In addition, we detected no statistically significant relationships between endometrial cancer and MET-hours per week of recreational and household activities during ages 15–18, 19–29, or 35–39 years, or during

the past 10 years after adjustment for BMI (data not shown). Although time spent watching TV/videos was not associated with endometrial cancer after adjustment for BMI, we observed a positive association between endometrial cancer risk and number of hours spent sitting during a typical 24 hour period in the past 12 months both before and after adjustment for BMI (RRs for 3–4, 5–6 and ≥ 7 vs. <3 hours/day=1.07, 1.31, and 1.26, respectively; p for trend=0.02) (Table 4). To assess whether the association with hours spent sitting was influenced by physical activity, we additionally adjusted for frequency of baseline vigorous activity and observed a slight attenuation in the risk estimates (RRs for sitting 3–4, 5–6 and ≥ 7 vs. <3 hours/day=1.07, 95% CI: 0.84, 1.36; 1.29, 95% CI: 1.02, 1.63; and 1.23, 95% CI: 0.96, 1.57, respectively; p for trend=0.04).

There was no evidence for effect modification of the association between current daily routine activity, vigorous activity, and hours spent sitting during the past 12 months and endometrial cancer by HT formulation (data not shown). In addition, there was no evidence for effect modification of the association between current daily routine activity and hours spent sitting and endometrial cancer by BMI; however, the association with frequency of baseline vigorous activity was more pronounced among overweight and obese women than in lean women (BMI <25), although the interaction was not statistically significant (p for interaction for BMI <25 vs. ≥ 25 = 0.12) (Table 5).

In general, the correlations between activity responses asked on the two questionnaires were statistically significant and offered some suggestion of internal consistency (data not shown). For instance, hours spent sitting per day was positively correlated with hours spent watching TV/videos per day (r=0.21) and inversely associated with baseline activity (r= −0.46 for current daily routine activity at work or home and r= −0.15 for frequency of vigorous activity).

Discussion

In this large prospective study, increased frequency of vigorous physical activity, but not activity of lower intensity, was associated with a 23% reduced RR of endometrial cancer. The association with vigorous activity appeared to be stronger among overweight and obese women (BMI ≥ 25). We did not observe an association with risk for current daily routine or occupational physical activities. Number of hours spent sitting per day, but not watching TV, was related to an increased risk of endometrial cancer, and the association was statistically independent of BMI in this model.

Our findings for vigorous activity are remarkably consistent with a recently reported pooled estimate of the association between endometrial cancer and physical activity from cohort studies published through 2006, also showing a 23% decreased risk of endometrial cancer for the most active compared with the least active women (OR=0.77, 95% CI: 0.70–0.85).27 Few studies have reported relative risk estimates specifically for vigorous activity: our results are similar to those from two case-control studies suggesting reduced risk associated with vigorous activity,20, 23 but are in contrast with those from two cohort studies observing no association.5, 7 Whereas several previous case-control20, 21 and cohort5, 11, 12 studies have demonstrated risk reductions for light and moderate physical activities, we did not observe associations between frequency of light or moderate/vigorous recreational and household activities and endometrial cancer risk during recent years or earlier time periods. We observed no effect modification by HT, and our findings are generally consistent with previous investigations.(reviewed in 7, 27, 28) In the present study, we observed a stronger protective effect associated with vigorous activity among overweight and obese women, although the interaction was not statistically significant. While most cohort and case-control studies have not observed any effect modification by BMI,(reviewed

in 27, 28) our findings are in contrast with one case-control study22 that observed a stronger effect in women with a lower BMI and are consistent with other cohort8, 14 and case-control studies19, 26 that found stronger associations with physical activity among women with a high BMI.

Associations with non-vigorous activity were less clear. Occupational physical activity has been associated with a reduced risk of endometrial cancer in three8, 9, 13 of six6–10, 13 prior cohort studies, which were conducted in Europe and China. We did not observe an association with history of occupational activity; however, we were limited by lack of information on intensity and dose of these activities, as well as by small numbers of women reporting physically demanding jobs, suggesting that occupational activity is unlikely to be an important population-level source of physical activity among similar groups of AARP-eligible women. Our results showing a positive dose-response relation between increased duration of sitting, but not watching TV, and endometrial cancer risk after additional adjustment for BMI are not directly comparable with the findings from the Swedish Mammography and Cancer Prevention Study II Cohorts, which both measured inactivity with a combined question for TV and sitting; one study found elevated risk among those watching TV/sitting ≥ 5 hours per day,6 whereas the other did not observe a statistically significant association for hours per day of TV/sitting after adjustment for BMI.14

There are several plausible biologic mechanisms for the observed associations between vigorous activity, inactivity and endometrial cancer. Endometrial carcinogenesis is thought to be caused, in part, by estrogens that are insufficiently counterbalanced by progesterone.3, 37 Physical activity may reduce endometrial cancer risk directly by decreasing levels of biologically available estrogens, as evidenced by studies reporting lower serum estrogen levels among more active women.38, 39 Physical activity may also indirectly influence endometrial cancer risk through lower body weight,40 since peripheral conversion of androgens to estrogens by aromatase occurs in the adipose tissue.41 Hence, the reduction in bioavailable estrogens associated with increased physical activity may in part explain the stronger associations we observed for vigorous activity among overweight and obese women, who have increased peripheral estrogen synthesis. Although physical activity and BMI are strongly linked, we observed significant dose-response relationships for vigorous activity and inactivity after adjustment for BMI and other potential confounding factors, suggesting that vigorous activity and inactivity independently affect endometrial cancer risk apart from their association with BMI. However, measurement error or residual confounding by BMI could also explain the apparent independence of these correlated factors. Finally, physical activity may influence growth factors and changes in immune function,4 both of which are thought to be related to endometrial cancer risk.2, 42

Although we assessed numerous potential confounding factors, it is possible that the observed associations may be explained by unmeasured lifestyle factors, such as socioeconomic status, which was shown to confound the association between occupational activity and endometrial cancer in a previous study.15 Inclusion of education in multivariate analyses, however, did not materially change results for any of the activity measures. Additional limitations may have affected our findings. Physical activity was self-reported, introducing the possibility of exposure misclassification which would most likely attenuate any true association between physical activity and endometrial cancer if all misclassification were non-differential. Nevertheless, we detected a significant inverse association for frequent vigorous activity of ≥ 20 minutes in duration. Previous studies have demonstrated better recall for vigorous activities than activities of lower intensity,43, 44 which could have contributed to the observed reduced risk with vigorous activity as opposed to null associations for light and moderate/vigorous recreational and household activities in our study. Our physical activity questions were not validated, but the measure of vigorous

activity was structured according to the American College of Sports Medicine's physical activity guidelines, which recommend ≥ 20 minutes of continuous vigorous exercise three times per week as a means of improving cardiorespiratory fitness.45 In addition, most of the pairwise correlations between reported physical activity questionnaire items were weak to modest, indicating both good internal consistency for activity types as well as an ability for the questions to measure different aspects of physical activity without being redundant.

In summary, this study provides evidence for a protective effect of vigorous activity and a deleterious role of inactivity with respect to endometrial cancer risk. Our findings are in support of the accumulating body of evidence from epidemiologic studies, which suggest that physical activity is important in the etiology of endometrial cancer. It will be important to clarify underlying mechanisms, including those relating to hormonal alterations.

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List of abbreviations used

BMI	body mass index
CI	confidence interval
HT	hormone therapy
NIH	National Institutes of Health
RR	relative risk
SD	standard deviation

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Table 1a

Select characteristics of women according to daily routine physical activity level at baseline, NIH-AARP Diet and Health Study

	Current daily routine activity at work or home §									
	Sitting (n=9,293)		Sitting and walking (n=36,032)		Walking and standing (n=41,606)		Climbing stairs or carrying heavy loads (n=18,600)		Heavy work or carrying heavy loads (n=1,737)	
Characteristic	**n**	**%***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age at baseline questionnaire (years)										
<55	2,317	24.9%	6,860	19.0%	5,535	13.3%	2,319	12.5%	317	18.2%
55–59	2,675	28.8%	9,459	26.3%	8,879	21.3%	3,784	20.3%	488	28.1%
60–64	2,286	24.6%	9,459	26.3%	11,628	27.9%	5,250	28.2%	467	26.9%
65–69	1,844	19.8%	9,274	25.7%	14,035	33.7%	6,494	34.9%	424	24.4%
70+	171	1.8%	980	2.7%	1,529	3.7%	753	4.0%	41	2.4%
Body mass index at baseline (kg/m^2)										
<25	3,122	33.6%	15,289	42.4%	21,056	50.6%	9,861	53.0%	829	47.7%
25–29	2,717	29.2%	11,474	31.8%	13,350	32.1%	5,834	31.4%	604	34.8%
30+	3,454	37.2%	9,269	25.7%	7,200	17.3%	2,905	15.6%	304	17.5%
Race/ethnicity										
Caucasian/Non-Hispanic white	8,515	91.6%	32,838	91.1%	37,761	90.8%	17,239	92.7%	1,540	88.7%
Other/Unknown	778	8.4%	3,194	8.9%	3,845	9.2%	1,361	7.3%	197	11.3%
Education										
<High school/high school grad	2,501	27.4%	9,894	28.1%	12,598	31.1%	5,701	31.4%	703	42.6%
Post-high school+	6,614	72.6%	25,293	71.9%	27,928	68.9%	12,472	68.6%	948	57.4%
Smoking										
Never	3,544	39.2%	15,231	43.4%	18,696	46.2%	8,675	48.0%	722	43.4%
Former	4,063	45.0%	14,382	41.0%	16,214	40.1%	6,666	36.8%	573	34.5%
Current	1,425	15.8%	5,475	15.6%	5,569	13.8%	2,750	15.2%	368	22.1%
Age at menarche (years)										
<13	4,727	51.0%	17,603	49.0%	19,155	46.2%	8,634	46.5%	771	44.6%
13–14	3,790	40.9%	15,164	42.2%	18,244	44.0%	8,017	43.2%	724	41.9%
15+	749	8.1%	3,166	8.8%	4,101	9.9%	1,897	10.2%	234	13.5%
Parity										
Nulliparous	1,702	18.6%	6,538	18.4%	6,521	15.9%	2,863	15.5%	282	16.5%

	Current daily routine activity at work or home §									
	Sitting (n=9,293)		Sitting and walking (n=36,032)		Walking and standing (n=41,606)		Climbing stairs or carrying heavy loads (n=18,600)		Heavy work or carrying heavy loads (n=1,737)	
Characteristic	**n**	**%***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
One	1,192	13.0%	4,132	11.6%	4,277	10.4%	1,831	9.9%	190	11.1%
Two	2,479	27.0%	9,746	27.4%	11,097	27.0%	4,624	25.1%	394	23.1%
Three or more	3,802	41.4%	15,152	42.6%	19,215	46.7%	9,104	49.4%	842	49.3%
Ever used oral contraceptives										
No	4,858	52.5%	19,846	55.4%	25,372	61.4%	11,549	62.5%	1,072	62.1%
Yes	4,388	47.5%	15,968	44.6%	15,977	38.6%	6,943	37.5%	655	37.9%
Ever used HT at baseline										
No	5,446	58.6%	21,027	58.4%	24,569	59.1%	11,431	61.5%	1,179	67.9%
Yes	3,847	41.4%	15,005	41.6%	17,037	40.9%	7,169	38.5%	558	32.1%
Age at menopause (years)										
Premenopausal	960	10.3%	2,764	7.7%	2,171	5.2%	891	4.8%	99	5.7%
<45	952	10.2%	3,698	10.3%	4,399	10.6%	1,993	10.7%	216	12.4%
45–49	2,305	24.8%	9,011	25.0%	10,705	25.7%	4,741	25.5%	450	25.9%
50–54	3,983	42.9%	15,794	43.8%	18,585	44.7%	8,329	44.8%	756	43.5%
55+	756	8.1%	3,426	9.5%	4,268	10.3%	1,994	10.7%	145	8.3%
Postmenopausal, age unknown	337	3.6%	1,339	3.7%	1,478	3.6%	652	3.5%	71	4.1%
Frequency of vigorous physical activity during typical month in past 12 months †										
Never/Rarely	3,854	41.7%	8,944	25.0%	7,886	19.1%	2,322	12.6%	152	8.9%
1–3 times/month	1,585	17.2%	6,087	17.0%	5,514	13.4%	2,156	11.7%	98	5.7%
1–2 times/week	1,673	18.1%	7,848	21.9%	8,940	21.7%	4,030	21.8%	228	13.3%
3–4 times/week	1,380	14.9%	8,238	23.0%	11,303	27.4%	5,783	31.3%	477	27.9%
5+ times/week	745	8.1%	4,693	13.1%	7,644	18.5%	4,161	22.6%	757	44.2%

*Missing values were excluded from percentage calculations

†Defined as physical activity that lasted at least 20 mins and caused increases in breathing, heart rate, or sweating

HT, hormone therapy.

Table 1b

Select characteristics of women according to frequency of vigorous physical activity level at baseline, NIH-AARP Diet and Health Study

	Frequency of vigorous physical activity during typical month in past 12 months†									
	Never/rarely (n=23,685)		1–3 times/month (n=15,724)		1–2 times/week (n=23,195)		3–4 times/week (n=27,785)		5+ times/week (n=18,462)	
Characteristic	**n**	**%***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Age at baseline questionnaire (years)										
<55	3,363	14.2%	3,093	19.7%	4,088	17.6%	4,265	15.4%	2,706	14.7%
55–59	5,249	22.2%	4,134	26.3%	5,656	24.4%	6,299	22.7%	4,247	23.0%
60–64	6,529	27.6%	4,175	26.6%	6,243	26.9%	7,652	27.5%	4,931	26.7%
65–69	7,681	32.4%	3,920	24.9%	6,496	28.0%	8,650	31.1%	5,913	32.0%
70+	863	3.6%	402	2.6%	712	3.1%	919	3.3%	665	3.6%
Body mass index at baseline (kg/m^2)										
<25	8,677	36.6%	6,277	39.9%	10,397	44.8%	14,560	52.4%	10,916	59.1%
25–29	7,311	30.9%	5,195	33.0%	7,854	33.9%	8,816	31.7%	5,322	28.8%
30+	7,697	32.5%	4,252	27.0%	4,944	21.3%	4,409	15.9%	2,224	12.0%
Race/ethnicity										
Caucasian/Non-Hispanic white	21,244	89.7%	14,380	91.5%	21,305	91.9%	25,301	91.1%	16,958	91.9%
Other/Unknown	2,441	10.3%	1,344	8.5%	1,890	8.1%	2,484	8.9%	1,504	8.1%
Education										
<High school/high school grad	9,347	40.5%	4,592	29.9%	6,323	27.9%	7,164	26.5%	4,701	26.2%
Post-high school+	13,727	59.5%	10,773	70.1%	16,304	72.1%	19,904	73.5%	13,274	73.8%
Smoking										
Never	9,669	42.0%	6,600	43.0%	10,345	45.8%	12,579	46.6%	8,376	46.8%
Former	8,535	37.1%	5,887	38.4%	8,804	38.9%	11,437	42.4%	7,802	43.6%
Current	4,823	20.9%	2,853	18.6%	3,460	15.3%	2,962	11.0%	1,727	9.6%
Age at menarche (years)										
<13	11,582	49.1%	7,606	48.5%	10,979	47.5%	12,861	46.4%	8,611	46.8%
13–14	9,804	41.5%	6,644	42.3%	9,997	43.2%	12,165	43.9%	7,942	43.1%
15+	2,212	9.4%	1,443	9.2%	2,162	9.3%	2,676	9.7%	1,859	10.1%
Parity										
Nulliparous	4,056	17.3%	2,735	17.6%	3,861	16.8%	4,394	16.0%	3,129	17.2%

	Frequency of vigorous physical activity during typical month in past 12 months†									
	Never/rarely (n=23,685)		1–3 times/month (n=15,724)		1–2 times/week (n=23,195)		3–4 times/week (n=27,785)		5+ times/week (n=18,462)	
Characteristic	**n**	**%***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
One	2,663	11.4%	1,823	11.8%	2,562	11.2%	2,841	10.3%	1,914	10.5%
Two	5,846	25.0%	3,983	25.7%	6,171	26.9%	7,619	27.7%	5,038	27.6%
Three or more	10,826	46.3%	6,965	44.9%	10,347	45.1%	12,613	45.9%	8,148	44.7%
Ever used oral contraceptives										
No	14,755	62.7%	8,859	56.6%	13,255	57.5%	15,886	57.5%	11,004	60.0%
Yes	8,773	37.3%	6,781	43.4%	9,816	42.5%	11,723	42.5%	7,351	40.0%
Ever used HT at baseline										
No	16,019	67.6%	9,239	58.8%	13,607	58.7%	15,331	55.2%	10,572	57.3%
Yes	7,666	32.4%	6,485	41.2%	9,588	41.3%	12,454	44.8%	7,890	42.7%
Age at menopause (years)										
Premenopausal	1,263	5.3%	1,179	7.5%	1,643	7.1%	1,790	6.4%	1,074	5.8%
<45	2,965	12.5%	1,622	10.3%	2,371	10.2%	2,638	9.5%	1,854	10.0%
45–49	6,393	27.0%	4,036	25.7%	5,757	24.8%	6,810	24.5%	4,617	25.0%
50–54	10,049	42.4%	6,923	44.0%	10,307	44.4%	12,560	45.2%	8,267	44.8%
55+	2,199	9.3%	1,412	9.0%	2,351	10.1%	2,928	10.5%	1,897	10.3%
Postmenopausal, age unknown	816	3.4%	552	3.5%	766	3.3%	1,059	3.8%	753	4.1%
Current daily routine activity at work or home										
Sit during day without much walking	3,854	16.6%	1,585	10.3%	1,673	7.4%	1,380	5.1%	745	4.1%
Sit much of day but walk fair amount	8,944	38.6%	6,087	39.4%	7,848	34.5%	8,238	30.3%	4,693	26.1%
Stand/walk a lot during day without carrying/lifting things	7,886	34.1%	5,514	35.7%	8,940	39.4%	11,303	41.6%	7,644	42.5%
Lift/carry light loads or climb stairs/hills often	2,322	10.0%	2,156	14.0%	4,030	17.7%	5,783	21.3%	4,161	23.1%
Heavy work or carry heavy loads	152	0.7%	98	0.6%	228	1.0%	477	1.8%	757	4.2%

*Missing values were excluded from percentage calculations

†Defined as physical activity that lasted at least 20 minutes and caused increases in breathing, heart rate, or sweating

HT, hormone therapy

Table 2

Multivariate adjusted RR and 95% CI for the association between baseline physical activity and endometrial cancer incidence, NIH-AARP Diet and Health Study

Physical activity	No. cancers	Person-years	RR*	95% CI	p for trend	RR §	95% CI	p for trend	RR †	95% CI	p for trend
Current daily routine activity at work or home											
Sit without much walking	104	63,656.5	1.00		<.0001	1.00		<.0001	1.00		0.07
Sit but walk fair amount	389	250,987.7	0.90	(0.73, 1.12)		0.89	(0.72, 1.11)		1.09	(0.87, 1.35)	
Stand/walk a lot without carrying/lifting things	370	292,047.1	0.70	(0.56, 0.87)		0.68	(0.55, 0.85)		0.97	(0.77, 1.21)	
Lift/carry light loads or climb stairs/hills often	150	130,859.8	0.63	(0.49, 0.81)		0.62	(0.48, 0.79)		0.89	(0.69, 1.16)	
Heavy work or carry heavy loads	12	12,284.4	0.57	(0.31, 1.03)		0.59	(0.32, 1.06)		0.81	(0.45, 1.48)	
Vigorous physical activity during typical month in past 12 months											
Never/Rarely	292	162,322.2	1.00		<.0001	1.00		<.0001	1.00		0.02
1–3 times/month	149	110,490.4	0.78	(0.64, 0.95)		0.77	(0.63, 0.93)		0.84	(0.69, 1.02)	
1–2 times/week	221	162,617.4	0.77	(0.65, 0.92)		0.74	(0.62, 0.89)		0.88	(0.73, 1.04)	
3–4 times/week	244	195,345.4	0.70	(0.59, 0.83)		0.66	(0.56, 0.79)		0.85	(0.72, 1.02)	
5+ times/week	139	130,077.2	0.60	(0.49, 0.73)		0.56	(0.46, 0.68)		0.77	(0.63, 0.95)	
Frequency of participation in physical activities or sports during typical month between ages 15–18 years old											
Never/Rarely	169	129,904.3	1.00		0.22	1.00		0.16	1.00		0.22
1–3 times/month	81	71,174.2	0.89	(0.68, 1.16)		0.90	(0.69, 1.18)		0.91	(0.70, 1.19)	
1–2 times/week	197	137,879.0	1.10	(0.90, 1.35)		1.10	(0.90, 1.35)		1.13	(0.92, 1.39)	
3–4 times/week	258	184,622.4	1.06	(0.88, 1.29)		1.09	(0.89, 1.32)		1.10	(0.91, 1.34)	
5+ times/week	340	237,840.6	1.09	(0.90, 1.31)		1.10	(0.92, 1.32)		1.09	(0.91, 1.31)	

*Relative risks adjusted for age (continuous)

§Relative risks adjusted for age (continuous), race (white vs. other/unknown), smoking status (never, former, current, or unknown), parity (nulliparous, one, two, ≥ three births, or unknown), ever use of oral contraceptives (no, yes, unknown), age at menopause (premenopausal, natural menopause at <45, 45–49, 50–54, or ≥ 55 years of age, or unknown age at menopause), and ever use of hormone therapy (no, yes)

†Relative risks additionally adjusted for body mass index (continuous)

Not shown are unknown current daily routine activity (27 cancers and 16,335 person-years), vigorous activity (7 cancers and 5,318 person-years), and activity between the ages of 15–18 years (7 cancers and 4,750 person-years).

CI, confidence interval; RR, relative risk

Table 3

Multivariate adjusted RR and 95% CI for the association between history of occupational physical activity and endometrial cancer incidence among women who completed the second questionnaire, NIH-AARP Diet and Health Study

Occupational physical activity	No. cancers	Person- years	RR*	95% CI	p for trend	RR§	95% CI	p for trend	RR†	95% CI	p for trend
Number of physically demanding jobs											
None	525	370,721.1	1.00		0.78	1.00		0.48	1.00		0.95
1–2	90	63,460.0	1.03	(0.82, 1.29)		1.07	(0.85, 1.33)		0.99	(0.79, 1.23)	
3–5	18	13,188.5	1.01	(0.63, 1.62)		1.09	(0.68, 1.74)		0.98	(0.61, 1.57)	
6+	10	6,898.9	1.07	(0.57, 2.00)		1.14	(0.61, 2.13)		1.03	(0.55, 1.93)	
Number of years with a physically demanding job											
None or less than 1 year	548	387,002.0	1.00		0.59	1.00		0.36	1.00		0.90
1–2	8	9,532.9	0.62	(0.31, 1.25)		0.66	(0.33, 1.32)		0.60	(0.30, 1.20)	
3–5	24	12,877.6	1.38	(0.92, 2.08)		1.47	(0.97, 2.21)		1.34	(0.89, 2.02)	
6–9	9	10,146.5	0.66	(0.34, 1.28)		0.69	(0.36, 1.33)		0.63	(0.33, 1.23)	
10+	54	34,800.6	1.12	(0.84, 1.48)		1.17	(0.88, 1.54)		1.06	(0.80, 1.40)	
Number of years walked or biked to work most days											
None or less than 1 year	560	395,140.9	1.00		0.89	1.00		0.62	1.00		0.68
1–2	31	17,599.2	1.26	(0.88, 1.80)		1.27	(0.88, 1.82)		1.23	(0.86, 1.76)	
3–5	25	19,280.8	0.91	(0.61, 1.36)		0.88	(0.59, 1.32)		0.88	(0.59, 1.31)	
6–9	18	8,009.2	1.55	(0.97, 2.48)		1.50	(0.94, 2.40)		1.54	(0.96, 2.46)	
10+	13	12,625.6	0.70	(0.40, 1.21)		0.65	(0.37, 1.12)		0.66	(0.38, 1.15)	

*Relative risks adjusted for age (continuous)

§Relative risks adjusted for age (continuous), race (white vs. other/unknown), smoking status (never, former, current, or unknown), parity (nulliparous, one, two, ≥ three births, or unknown), ever use of oral contraceptives (no, yes, unknown), age at menopause (premenopausal, natural menopause at <45, 45–49, 50–54, or ≥ 55 years of age, or unknown age at menopause), and hormone therapy formulation (never used, ET use, EPT use, or unknown HT use)

†Relative risks additionally adjusted for body mass index (continuous)

Not shown are unknown number of physically demanding jobs (7 cancers and 3,084 person-years), number of years with a physically demanding job (7 cancers and 2,993 person-years), and number of years walked or biked to work (3 cancers and 4,697 person-years).

CI, confidence interval; RR, relative risk

Table 4

Multivariate adjusted RR and 95% CI for the association between sedentary behaviors and endometrial cancer incidence among women who completed the second questionnaire, NIH-AARP Diet and Health Study

Sedentary Behavior	No. cancers	Person- years	RR*	95% CI	p for trend	RR§	95% CI	p for trend	RR†	95% CI	p for trend
Hours spent watching TV/videos during typical 24 hour period in past 12 months											
<3	198	167,821.7	1.00		0.002	1.00		0.0003	1.00		0.26
3–4	286	192,076.6	1.20	(1.00, 1.44)		1.24	(1.03, 1.49)		1.11	(0.92, 1.33)	
5–6	117	70,739.4	1.30	(1.03, 1.64)		1.36	(1.08, 1.72)		1.08	(0.86, 1.37)	
7+	48	24,935.6	1.53	(1.12, 2.10)		1.66	(1.20, 2.28)		1.21	(0.87, 1.67)	
Hours spent sitting during typical 24 hour period in past 12 months											
<3	111	98,017.6	1.00		<.0001	1.00		<.0001	1.00		0.02
3–4	171	130,998.9	1.14	(0.90, 1.45)		1.15	(0.90, 1.46)		1.07	(0.85, 1.37)	
5–6	203	123,374.0	1.48	(1.17, 1.86)		1.48	(1.18, 1.87)		1.31	(1.04, 1.65)	
7+	164	102,884.6	1.54	(1.21, 1.96)		1.56	(1.22, 1.99)		1.26	(0.99, 1.62)	

*Relative risks adjusted for age (continuous)

§Relative risks adjusted for age (continuous), race (white vs. other/unknown), smoking status (never, former, current, or unknown), parity (nulliparous, one, two, ≥ three births, or unknown), ever use of oral contraceptives (no, yes, unknown), age at menopause (premenopausal, natural menopause at <45, 45–49, 50–54, or ≥ 55 years of age, or unknown age at menopause), and hormone therapy formulation (never used, ET use, EPT use, or unknown HT use)

†Relative risks additionally adjusted for body mass index (continuous)

Not shown are unknown hours spent watching TV/videos (1 cancer and 1,779 person-years) and hours spent sitting (1 cancer and 2,077 person-years).

CI, confidence interval; RR, relative risk

Table 5

Multivariate adjusted RR and 95% CI for the association between baseline vigorous physical activity and endometrial cancer by BMI, NIH-AARP Diet and Health Study

Vigorous physical activity during typical month in past 12 months	No. cancers	Person- years	RR*	95% CI	p for trend	RR §	95% CI	p for trend	p for interaction
BMI <25									
Never/Rarely	53	59,559.7	1.00		0.92	1.00		0.21	0.12
1–3 times/month	37	44,116.1	0.98	(0.65, 1.50)		0.89	(0.59, 1.36)		
1–2 times/week	70	73,250.7	1.10	(0.77, 1.58)		0.97	(0.68, 1.38)		
3–4 times/week	102	102,612.0	1.13	(0.81, 1.58)		0.93	(0.67, 1.31)		
5+ times/week	62	77,168.1	0.91	(0.63, 1.32)		0.76	(0.52, 1.10)		
BMI 25+									
Never/Rarely	239	102,762.5	1.00		<.0001	1.00		<.0001	
1–3 times/month	112	66,374.3	0.76	(0.61, 0.95)		0.76	(0.61, 0.95)		
1–2 times/week	151	89,366.7	0.74	(0.61, 0.91)		0.73	(0.60, 0.90)		
3–4 times/week	142	92,733.5	0.66	(0.53, 0.81)		0.66	(0.53, 0.81)		
5+ times/week	77	52,909.1	0.62	(0.48, 0.80)		0.61	(0.47, 0.79)		

*Relative risks adjusted for age (continuous)

§Relative risks adjusted for age (continuous), race (white vs. other/unknown), smoking status (never, former, current, or unknown), parity (nulliparous, one, two, ≥ three births, or unknown), ever use of oral contraceptives (no, yes, unknown), age at menopause (premenopausal, natural menopause at <45, 45–49, 50–54, or ≥ 55 years of age, or unknown age at menopause), and ever use of hormone therapy (no, yes)

Not shown are unknown vigorous activity among women with BMI <25 (1 cancer and 2,362 person-years) and unknown vigorous activity among women with BMI 25+ (6 cancers and 2,956 person-years).

BMI, body mass index; CI, confidence interval; RR, relative risk