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CLINICAL PERSPECTIVE

The findings from this large, national population–based cohort study indicate that 6-year mortality rates from all causes and from cardiovascular disease causes are significantly higher with increased television viewing time in adults. Each 1-hour increment in television viewing time was found to be associated with an 11% and an 18% increased risk of all-cause and cardiovascular disease mortality, respectively. Furthermore, relative to those watching less television (<2 h/d), there was a 46% increased risk of all-cause and an 80% increased risk of cardiovascular disease mortality in those watching ≥4 hours of television per day, which were independent of traditional risk factors such as smoking, blood pressure, cholesterol, and diet, as well as leisure-time exercise and waist circumference. Although continued emphasis on current public health guidelines on the importance of moderate- to vigorous-intensity exercise should remain, these findings suggest that reducing time spent watching television (and possibly other prolonged sedentary behaviors) may also be of benefit in preventing cardiovascular disease and premature death. Furthermore, these findings suggest that in clinical practice and public health settings, questions about television viewing time (particularly identifying whether individuals watch >4 h/d) may assist in identifying those with elevated mortality risk.

論文名	Television viewing time and mortality: the Australian Diabetes, Obesity and Lifestyle Study (AusDiab)
著　者	Dunstan DW, Barr EL, Healy GN, Salmon J, Shaw JE, Balkau B, Magliano DJ, Cameron AJ, Zimmet PZ, Owen N
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対象の内訳

	ヒト	動物	地　域	欧米	研究の種類	縦断研究
対象	一般健常者	空白		(　　)		コホート研究
性別	男女混合	(　　)		(　　)		(　　)
年齢	50.5歳			(　　)		前向き研究
対象数	5000～10000			(　　)		(　　)

調査の方法	質問紙	(　　)		

アウトカム

予　防	心疾患予防	な し	ガン予防	な し	死亡	(　　)
維持・改善	な し	な し	な し	な し	(　　)	(　　)

図　表

Table 2. Risk of All-Cause, Cardiovascular, Cancer, and Non-Cardiovascular/Noncancer Mortality According to Categories of Television Viewing Time: AusDiab

	Television Viewing Time, h/d		
	<2	≥2 to <4	≥4
Person-y	33 024	20 737	4326
Mortality from any cause			
Deaths, n	105	125	54
Age- and sex-adjusted HR (95% CI)	1 (Reference)	1.20 (0.92–1.56)	1.67 (1.20–2.33)
HR (95% CI) adjusted for age, sex, education, smoking, alcohol, and diet quality	1 (Reference)	1.17 (0.90–1.52)	1.49 (1.06–2.08)
*Multivariate-adjusted HR (95% CI)**	1 (Reference)	1.14 (0.87–1.48)	1.49 (1.06–2.09)
Multivariate- and exercise time–adjusted HR (95% CI)*	1 (Reference)	1.13 (0.87–1.36)	1.46 (1.04–2.05)
Mortality from cardiovascular disease			
Deaths, n	26	39	22
Age- and sex-adjusted HR (95% CI)	1 (Reference)	1.24 (0.75–2.05)	2.12 (1.20–3.77)
HR (95% CI) adjusted for age, sex, education, smoking, alcohol, and diet quality	1 (Reference)	1.22 (0.74–2.03)	1.78 (1.01–3.22)
*Multivariate-adjusted HR (95% CI)**	1 (Reference)	1.20 (0.72–2.00)	1.85 (1.03–3.33)
Multivariate- and exercise time–adjusted HR (95% CI)*	1 (Reference)	1.19 (0.72 – 1.99)	1.80 (1.00–3.25)
Mortality from cancer causes			
Deaths, n	50	53	22
Age- and sex-adjusted HR (95% CI)	1 (Reference)	1.18 (0.80–1.76)	1.68 (1.00–2.80)
HR (95% CI) adjusted for age, sex, education, smoking, alcohol, and diet quality	1 (Reference)	1.15 (0.77–1.69)	1.53 (0.91–2.56)
Multivariate-adjusted HR (95% CI)*	1 (Reference)	1.12 (0.75–1.66)	1.50 (0.89–2.52)
Multivariate- and exercise time–adjusted HR (95% CI)*	1 (Reference)	1.12 (0.75–1.66)	1.48 (0.88–2.49)
Mortality from noncardiovascular and noncancer causes			
Deaths, n	29	33	10
Age- and sex-adjusted HR (95% CI)	1 (Reference)	1.18 (0.71–1.96)	1.18 (0.57–2.45)
HR (95% CI) adjusted for age, sex, education, smoking, alcohol, and diet quality	1 (Reference)	1.15 (0.70–1.91)	1.04 (0.50–2.17)
Multivariate-adjusted HR (95% CI)*	1 (Reference)	1.13 (0.68–1.88)	1.03 (0.49–2.16)
Multivariate- and exercise time–adjusted HR (95% CI)*	1 (Reference)	1.12 (0.67–1.87)	1.03 (0.49–2.15)

*Multivariate models are adjusted for age, sex, smoking (current or ex-smoker), education (≥12 years), total energy intake, alcohol intake, Diet Quality Index, waist circumference, hypertension (blood pressure ≥140/90 mm Hg or antihypertensive medication use), total plasma cholesterol (mmol/L), HDL-C (mmol/L), serum triglycerides (mmol/L, log), lipid-lowering medication use, and glucose tolerance status (impaired fasting glucose, impaired glucose tolerance, undiagnosed diabetes mellitus, known diabetes mellitus according to 1999 World Health Organization criteria[34]).

図表掲載箇所	P388, Table2
概　要 (800字まで)	本研究は、オーストラリアのAustralian Diabetes, Obesity and Lifestyle Study(AusDiab)に参加した8,800名の男女を対象に、平均6.6年間の追跡調査を行い、テレビ視聴時間と総死亡、心血管疾患による死亡、がんによる死亡、その他の死亡との関連を検討したものである。質問紙により過去1週間のテレビ視聴時間を尋ね、2時間/日未満、2-4時間/日、4時間/日以上の3群に分類した。テレビ視聴時間が2時間/日未満の集団と比較すると、4時間/日以上の集団では、総死亡リスク、心血管疾患による死亡リスクがそれぞれ、1.46(95%信頼区間:1.04-2.05)(P=0.03)、1.80(1.00-3.25)(P=0.05)であった。がんによる死亡とその他の死亡については有意な差異はみられなかった。また、テレビ視聴時間が長くなるにつれて、余暇時間の運動時間が短くなることが明らかとなった(P<0.01)。
結　論 (200字まで)	テレビ視聴時間は総死亡および心血管疾患による死亡リスクと関連を持つことが明らかとなった。運動や座位時間を減らすことにより慢性疾患を予防できることが示唆された。
エキスパートによるコメント (200字まで)	身体活動基準の策定に用いられた研究の1つである。近年、身体不活動と死亡や様々な疾患発症との関係が報告されており、本研究においてもテレビ視聴時間と総死亡や心血管疾患による死亡のリスクとの関係が示唆された。余暇時間の過ごし方は国により異なることが考えられるため、日本においても、このような不活動と死亡、疾患発症との関係が検討されることが望まれる。

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Beyond Recreational Physical Activity: Examining Occupational and Household Activity, Transportation Activity, and Sedentary Behavior in Relation to Postmenopausal Breast Cancer Risk

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Objectives. We prospectively examined nonrecreational physical activity and sedentary behavior in relation to breast cancer risk among 97039 postmenopausal women in the National Institutes of Health–AARP Diet and Health Study.

Methods. We identified 2866 invasive and 570 in situ breast cancer cases recorded between 1996 and 2003 and used Cox proportional hazards regression to estimate multivariate relative risks (RRs) and 95% confidence intervals (CIs).

Results. Routine activity during the day at work or at home that included heavy lifting or carrying versus mostly sitting was associated with reduced risk of invasive breast cancer (RR=0.62; 95% CI=0.42, 0.91; P_{trend}=.024).

Conclusions. Routine activity during the day at work or home may be related to reduced invasive breast cancer risk. Domains outside of recreation time may be attractive targets for increasing physical activity and reducing sedentary behavior among postmenopausal women. (*Am J Public Health.* 2010;100: 2288–2295. doi:10.2105/AJPH.2009.180828)

Adult women in the United States aged 50 to 69 years spend on average about 8 waking hours per day being inactive.[1] Recreational physical activity has an established relation to reduced risk of postmenopausal breast cancer[2–4] as well as preventing weight gain, type 2 diabetes, metabolic syndrome, high blood pressure, coronary heart disease, stroke, and early death.[3]

However, the relationship between postmenopausal breast cancer and physical activity outside of recreation time, in the domains of home, occupation, and transportation,[5] has been examined less extensively. Occupational cohort studies[6–8] lack ideal control for potential confounding variables, but they have tended to support an inverse relationship between nonrecreational physical activity and breast cancer. In some prospective cohort studies, women who, on average, engaged in higher levels of household activity each week had lower risk of invasive breast cancer[9,10]; in others, however, no relationship was observed between risk of invasive breast cancer and either nonrecreational[11,12] or occupational physical activity.[9,13,14]

At present, the extent to which sedentary behavior is associated with breast cancer risk has not been examined prospectively. Sedentary behavior is ubiquitous in the daily routines of modern adults[15] and has emerged as a new focus for research on physical activity and health.[16–21] It has been proposed that too much sitting may be distinct from too little moderate–vigorous recreational physical activity.[19] Sedentary behavior may independently reduce overall energy expenditure,[22] leading to adverse effects on insulin sensitivity, fat storage,[23] and estrogen metabolism,[24] pathways that are relevant to breast cancer development.

The study of nonrecreational physical activity and sedentary behavior in relation to breast cancer could prove fruitful because these exposures have been related to risk of other chronic conditions among women and may work through similar pathways. Independent of recreational moderate–vigorous physical activity, standing and walking around the home have been inversely associated with chronic conditions such as obesity and diabetes,[25] and walking and bicycling to work have been inversely associated with all-cause mortality[26–28] and obesity.[29] Sedentary behavior has been positively associated with obesity,[30,31] weight gain,[25] diabetes,[30] all-cause mortality,[32–34] cardiovascular disease mortality,[32–34] cancer mortality,[32] and mortality from other causes.[32] Among women, television watching has been positively associated with increases in obesity and diabetes.[15] Breaks in sedentary behavior have been associated cross-sectionally with beneficial changes in biomarkers of metabolic risk such as waist circumference, adiposity, triglycerides, and 2-hour plasma glucose.[35]

We explored the associations of occupational and household activity, transportation activity (i.e., walking or bicycling to work), and sedentary behavior in relation to breast cancer risk in the National Institutes of Health (NIH)–AARP Diet and Health Study. We hypothesized that (1) occupational and household activity and transportation activity are inversely associated with risk of invasive breast cancer and (2) sedentary behavior is positively associated with risk of invasive breast cancer. We planned a priori to explore these hypotheses for in situ breast cancer as well.

METHODS

The NIH–AARP Diet and Health Study[36] was initiated in 1995 and 1996 with the mailing of a self-administered questionnaire to 3.5 million AARP members aged 50 to 71 years from 6 US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). In 1996 and 1997, a second questionnaire was sent to selected respondents who did not have self-reported breast, prostate, or colorectal cancer at baseline to collect more detailed information on risk factors for cancer (e.g., recreational physical activity, occupational and household activity, transportation activity, sedentary behavior, and reproductive factors).

Among the 566 402 respondents who filled out the baseline survey in satisfactory detail and consented to be in the study, 226 733 were women. Of those women, 138 057 completed the second questionnaire as well, and 129 095 had known postmenopausal status. Of those with known postmenopausal status, we excluded women who indicated they were proxies for the intended respondents on the baseline questionnaire or second questionnaire (n=1505). Because women with prevalent cancer at baseline (or second questionnaire) may have recently altered their physical activity behavior patterns subsequent to cancer diagnosis, we also excluded those with prevalent or self-reported cancer other than nonmelanoma skin cancer at the baseline questionnaire or the second questionnaire (n=8699). We also excluded women whose death record listed cancer as cause of death but who had no confirming cancer registry record (n=721).

We further excluded women who were missing data on nonrecreational physical activity or sedentary behavior (n=4894) or covariate data (n=12 601) (because of possible biased estimation of relative risks [RRs] when correcting for missing values of confounding variables[37,38]), as well as women with extreme values of body mass index (BMI; n=2890) or energy intake (n=656). Extreme values were defined as log-transformed values of 2 or more interquartile ranges below the 25th percentile or above the 75th percentile. After exclusions, our analytic cohort consisted of 97 039 women. Postmenopausal women who were excluded from the study because of missing or outlier data did not differ substantially from those women who were included in terms of probability of invasive (3.0% vs 2.7%) or in situ breast cancer (0.5% vs 0.6%).

Cancer Ascertainment

In 2007, incident breast cancer cases through December 31, 2003, were identified through linkage with 11 state cancer registry databases, certified by the North American Association of Central Cancer Registries as meeting the highest standards for data quality.[36] The case ascertainment method used in the study identified 90% of cancer cases in our cohort.[39]

For each incident breast cancer case, dates of diagnosis and tumor characteristics were obtained from the cancer registries. We considered as incident first primary breast cancer cases those that were invasive or in situ and that were also the first malignancy diagnosed during the follow-up period (though December 31, 2003), if multiple cancers were diagnosed in the same participant.

Assessment of Nonrecreational Physical Activity, Sedentary Behavior, and Covariates

On the baseline questionnaire, participants in our cohort were also asked to select their current level of routine activity during the day at work (or at home, if they did not work) from 5 options: sitting all day; sitting and a little walking; standing or walking, but no lifting; lifting or carrying light loads, or climbing stairs often; and heavy lifting or carrying. On the second questionnaire, participants reported the total number of years they walked or biked to work for most days of the week (0, <1, 1–2, 3–5, 6–9, or ≥10). Participants also were asked to report the number of hours spent sitting while watching television or videos (0, <1, 1–2, 3–4, 5–6, 7–8, or ≥9) and spent sitting overall (<3, 3–4, 5–6, 7–8, or ≥9) in a typical 24-hour period during the last year. Hours spent watching television or videos and hours spent sitting were not mutually exclusive. Because of modest case numbers, we collapsed the "0" and "<1 year" categories for walking or biking to work and the "0," "<1 hour/day," and "1–2 hours/day" categories for television or video watching. These choices of reference categories had little effect on overall trend estimates. For use in subanalyses, we also classified each participant's television watching and overall sitting as a percentage of her waking time, using the following formula: (median hours per day spent watching television or videos)/(24–median hours spent sleeping–median hours spent napping).

We assessed all covariates by self-administered questionnaire. In particular, participants were queried about current height and weight, and BMI was calculated from these data. Participants also reported how often (never, rarely, >0 but <1 h/wk, 1–3 h/wk, 4–7 h/wk, or >7 h/wk) over the past 10 years they typically spent in moderate–vigorous recreational physical activity (e.g., biking, fast walking, aerobics, jogging, running). We collapsed the lowest 3 dose levels of this variable into a category called "<1 h/wk" and the highest 2 dose levels into a category called "≥4 h/wk" because of similarities in the RRs associated with these levels, respectively. Use of these condensed variables as covariates did not result in changes to overall associations.

We did not have direct evidence of the validity or reliability of the questions that we asked regarding nonrecreational activity and sedentary behavior; however, our questions were similar to questions from measures with reasonable validity and reliability that included assessment on occupational and household routine activity,[40–44] television watching,[45] sitting,[46,47] and recreational moderate–vigorous activity.[41–44]

Statistical Analysis

We estimated RRs and 2-sided 95% CIs with Cox proportional hazards models using the SAS PROC PHREG procedure (version 9.1.3; SAS Institute, Cary, NC). We calculated person-years of follow-up time from the date the second questionnaire was received and scanned until the date of a cancer diagnosis, death, or the end of follow-up (December 31, 2003), whichever occurred first. We evaluated the proportional hazards assumption by modeling interaction terms of our exposures and time, and found no significant interactions. We performed the test for linear trend across categories of occupational and household activity, transportation activity, and sedentary behavior by assigning participants the median value of their categories and entering it as a continuous term in a regression model.

Our final multivariate model included covariates with previously established associations with breast cancer risk that also remained statistically significant in our multivariate model: age, family history of breast cancer, recreational moderate–vigorous physical activity, energy intake, alcohol consumption, education, race/ethnicity, smoking, menopausal hormone therapy, number of breast biopsies, and a combined variable for parity and age at birth of first child. Although P_{trend} values became less significant as more adjustment was done, adjusting for covariates (besides age) did not affect the nonrecreational physical activity or sedentary behavior risk estimates we obtained in this analysis. Although not included in the final models, history of mammography screening in the past 3 years also did not act as a confounder. Because it is possible that the potential effects of nonrecreational physical activity or sedentary behavior on breast cancer are mediated in part by BMI, we report on and discuss our models that did not adjust for BMI. Separate multivariate models controlling for BMI are presented for the readers' knowledge.

We planned a priori to test for interactions with recreational moderate–vigorous physical activity level, BMI, education level, estrogen receptor (ER) status and estrogen-progesterone receptor (ER/PR) status of tumors, use of menopausal hormone therapy, and 3-way interactions with moderate–vigorous recreational physical activity and BMI. To determine whether presentation of stratified analyses was necessary, we used the significance of the likelihood ratio tests for interaction variables as well as the difference in model fit by log-likelihood differences of full and nested models. We performed separate analyses restricted to invasive cancers to test for heterogeneity of effects by tumors' ER status (ER– or ER+) and ER/PR status (ER+/PR+, ER+/PR–, ER–/PR+, or ER–/PR–) and compared the test of trend for each outcome using Cochran's Q statistic.[48]

RESULTS

Age-adjusted participant characteristics by lowest and highest categories of routine activity during the day at work or home, years walking and biking to work, hours per day spent watching television or videos, and hours per day spent sitting are provided in Table 1. All comparisons among this large sample were statistically significant at $P<.05$ unless otherwise indicated. Compared with women who routinely spent all day sitting and women who had spent less than 1 year routinely walking or biking to work, women who engaged in heavy lifting or carrying as routine activity during the day and women who had spent 10 or more years routinely walking or biking to work, respectively, were less likely to have ever been smokers or to be physically inactive during recreation. Women who performed heavy lifting or carrying also had lower BMIs on average. Compared with women who spent less than 3 hours a day watching television and women who spent less than 3 hours a day sitting, women watching television or sitting for 9 or more hours per day were more likely to have a BMI greater than 25 kg/m^2, to be physically inactive during recreation, and to have ever smoked. Women with the highest levels of nonrecreational physical activity or sedentary behavior were less likely to currently use menopausal hormone therapy.

Participants' recreational moderate–vigorous physical activity level typical of the past 10 years was positively correlated with higher levels of routine activity during the day at work or home ($\rho=0.24$) and with years spent walking or biking to work ($\rho=0.05$) and negatively correlated with hours spent watching television or videos ($\rho=-0.09$) and hours spent sitting ($\rho=-0.17$; Table 2). Routine activity during the day at work or home was moderately correlated with hours spent sitting ($\rho=-0.47$).

As shown in Table 3, compared with women who sat all day, women who routinely did heavy lifting or carrying during the day had a relative risk (RR) of invasive breast cancer of 0.62 (95% CI=0.42, 0.91). Because routine activity during the day was measured on the baseline questionnaire, we performed subanalyses using person-years since baseline (with prevalent cancer and proxy exclusions relevant only to that questionnaire), and results were similar. Compared with women who walked or biked to work less than 1 year, women who reported walking or biking to work for 10 or more years had a relative risk of invasive breast cancer of 0.86 (95% CI=0.67, 1.11). In a sensitivity analysis, we combined the categories of walking or biking for 6 to 9 years and for 10 or more years, and the relative risk of invasive breast cancer for women who were active commuters for 6 or more years was 0.80 (95% CI=0.65, 0.98; P_{trend}=.06).

Compared with women who watched less than 3 hours of television or videos per day and women who sat for less than 3 hours per day on average, women who watched 9 or more hours of television per day and women who sat for 9 or more hours per day had a relative risk of invasive breast cancer of 1.17 (95% CI=0.93, 1.47) and 1.12 (95% CI=0.95, 1.31), respectively. The results remained null when television watching and sitting variables were classified as a proportion of waking time.

Compared with women who reported sitting all day and women who routinely walked or biked to work for less than 1 year, women who did heavy lifting and carrying during the day and women who walked or biked to work for 10 or more years had a relative risk of in situ breast cancer of 1.21 (95% CI=0.56, 2.61) and 0.92 (95% CI=0.53, 1.60), respectively (Table 4).

Compared with women who watched less than 3 hours of television per day and women who sat for less than 3 hours per day on average, women who watched television for 9 or more hours per day and women who sat for 9 or more hours per day had a relative risk of in situ breast cancer of 1.04 (95% CI=0.58, 1.88) and 1.15 (95% CI=0.80, 1.65), respectively. The results were similar when television watching and sitting variables were classified as percentage of waking time. Combined analyses of in situ and invasive breast cancer yielded results similar to those for invasive breast cancer (data not shown).

Overall, additional adjustment for BMI in models for invasive and in situ breast cancer resulted in modest attenuation of associations (Tables 3 and 4). We found no evidence for effect modification of associations by recreational moderate–vigorous physical activity level, BMI, education level, use of menopausal hormone therapy, or the ER or ER/PR status of tumors (data not shown).

DISCUSSION

Our results suggest that independent of recreational moderate–vigorous physical activity level, increases in routine activity during the day at work or home and, possibly, active commuting may be protective against invasive but not in situ breast cancer. Women who reported engaging in heavy lifting or carrying as routine activity during the day at work or home had a 38% risk reduction for invasive breast cancer compared with those who reported sitting all day. We even observed this benefit (16% risk reduction) among women who reported "sitting, a little walking" (i.e., less sitting). Although the trend did not reach statistical significance, the association we observed for invasive breast cancer and transportation activity (walking or biking to work for 6 or more years compared with less than 1

TABLE 1—Age-Adjusted Characteristics of Postmenopausal Women by Lowest and Highest Categories of Occupational and Household Activity, Transportation Activity, and Sedentary Behavior: National Institutes of Health-AARP Diet and Health Study, 1996–2003

	Routine Activity During Day at Work or at Home		Years Spent Walking or Biking to Work		Television or Video Watching		Sitting	
	Sitting all Day	Heavy Lifting or Carrying	<1 Year	≥10 Years	<3 H/Day	≥9 Hours/Day	<3 Hours/Day	≥9 Hours/Day
No.	7693	1467	85311	2475	33652	2687	20760	7550
Age, y	63	63	63	63	63	63	63	63
Body mass index, kg/m^2	29	26	27	26*	25	29	26	28
Energy intake, kcal/day	1552	1751	1543	1643	1512	1727	1565	1589*
Alcohol intake, g/day	6	7	6	6	6	6*	6	6
Under 1 h of recreational moderate-vigorous physical activity/wk, %	48	11	25	20	21	38	18	42
Ever smoker, %	61	53	54	50	50	64	50	61
College graduate, %	32	21	33	34	46	16	32	34
White, %	94	93	93	91	95	86	91	95
Family history of breast cancer, %	13	14*	13	14*	14	13	13	13*
Nulliparous, %	16	14	14	24	14	14	12	18
Ever had a breast biopsy, %	24	23	24	21	24	24*	24	23*
Current menopausal hormone therapy use, %	43	38*	47	37	51	36	46	44

Note. Age-adjusted means are used for continuous variables and age-adjusted percentages for categorical variables; all are significant at $P<.05$ unless otherwise specified. The total number of participants was 97 039.
*$P>.05$.

year) was in the same direction (14% risk reduction).

Long-term physical activity in the domains of occupation, home, and transportation could lower the risk of postmenopausal breast cancer through the pathways of BMI, estrone, insulin resistance, and C-reactive protein, with BMI and estrone being most convincingly (or probably) associated with both physical activity and risk.[49] Sedentary behavior may affect breast cancer risk through physiological mechanisms different from those that make recreational or nonrecreational physical activity beneficial,[16,32,50,51] such as altered glucose tolerance[52] or lipoprotein lipase activity.[50] We observed that nonrecreational physical activity was related to invasive but not in situ breast cancer in our study. This could suggest that nonrecreational physical activity may be important specifically for preventing breast tumors that are invasive or likely to become invasive. Alternately, the lack of statistical significance for relationships with in situ breast cancer could reflect the lower in situ case numbers. More research is needed to understand the descriptive epidemiology and biology of in situ breast cancer.[53]

The benefit we observed for routine activity during the day at home or work is consistent with the reduced RR of postmenopausal breast cancer observed in the French E3N Cohort[10]

TABLE 2—Spearman Rank Correlations Between Occupational and Household Activity, Transportation Activity, Sedentary Behavior, and Recreational Physical Activity: National Institutes of Health-AARP Diet and Health Study, 1996–2003

	Level of Routine Activity During Day at Work or Home	Years Walked or Biked to Work	Television or Video Watching, Hours/Day	Sitting, Hours/Day
Recreational moderate-vigorous physical activity	0.24	0.05	-0.09	-0.17
Level of routine activity during day at work or home		0.03	-0.06	-0.47
Years walked or biked to work			-0.01	0.003
Television or video watching, h/day				0.23

Note. All correlations are significant at $P<.001$, except between years walked or biked to work and hours per day sitting ($P=.231$). The total number of participants was 97 039.

TABLE 3—Occupational and Household Activity, Transportation Activity, and Sedentary Behavior in Relation to Invasive Breast Cancer Incidence Among Postmenopausal Women: National Institutes of Health-AARP Diet and Health Study, 1996-2003

	No. Person-Years	No. Cases	Age-Adjusted RR (95% CI)	P_{trend}	Multivariate 1 RR (95% CI)[a]	P_{trend}	Multivariate 2 RR (95% CI)[b]	P_{trend}
Occupational and Household Activity								
Routine activity during the day				.003		.024		.092
Sitting all day	49 144	258	1.00		1.00		1.00	
Sitting and a little walking	206 859	933	0.84 (0.73, 0.96)		0.84 (0.73, 0.97)		0.86 (0.75, 0.99)	
Standing or walking, no lifting	251 087	1132	0.81 (0.71, 0.93)		0.83 (0.72, 0.95)		0.86 (0.74, 0.98)	
Lifting or carrying light loads, or climbing stairs often	115 128	514	0.80 (0.69, 0.93)		0.83 (0.71, 0.96)		0.86 (0.74, 1.00)	
Heavy lifting or carrying	9775	29	0.55 (0.38, 0.81)		0.62 (0.42, 0.91)		0.64 (0.43, 0.94)	
Transportation Activity								
Years walked or biked to work				.051		.081		.084
<1	555 972	2540	1.00		1.00		1.00	
1-2	24 197	110	1.00 (0.83, 1.21)		0.99 (0.82, 1.20)		0.99 (0.82, 1.20)	
3-5	25 376	120	1.03 (0.86, 1.23)		1.03 (0.86, 1.24)		1.03 (0.86, 1.24)	
6-9	10 357	33	0.69 (0.49, 0.97)		0.69 (0.49, 0.98)		0.70 (0.50, 0.98)	
≥10	16 090	63	0.84 (0.65, 1.08)		0.86 (0.67, 1.11)		0.86 (0.67, 1.11)	
Sedentary Behavior								
Television or video watching, h/day				.303		.493		.935
<3	220 736	1013	1.00		1.00		1.00	
3-4	272 210	1243	0.97 (0.89, 1.05)		1.02 (0.94, 1.11)		1.00 (0.92, 1.09)	
5-6	103 031	438	0.89 (0.80, 0.99)		0.96 (0.86, 1.08)		0.93 (0.83, 1.05)	
7-8	18 990	90	0.99 (0.80, 1.23)		1.08 (0.87, 1.34)		1.04 (0.84, 1.30)	
≥9	17 025	82	1.03 (0.82, 1.28)		1.17 (0.93, 1.47)		1.12 (0.89, 1.41)	
Sitting, h/day				.006		.101		.243
<3	136 447	564	1.00		1.00		1.00	
3-4	186 096	856	1.11 (0.99, 1.23)		1.08 (0.97, 1.20)		1.07 (0.96, 1.19)	
5-6	171 157	803	1.14 (1.03, 1.27)		1.10 (0.98, 1.22)		1.08 (0.97, 1.20)	
7-8	89 698	419	1.17 (1.03, 1.33)		1.11 (0.97, 1.26)		1.08 (0.95, 1.23)	
≥9	48 594	224	1.19 (1.02, 1.39)		1.12 (0.95, 1.31)		1.08 (0.92, 1.27)	

Note. RR = relative risk; CI = confidence interval. Person-years are rounded to the nearest whole number. The total number of participants was 97 039.

[a]Adjusted for age, energy intake (kilocalories per day), recreational moderate-vigorous physical activity (0, 1-3, or ≥4 h/wk), parity or age at first live birth (never, <20, <25, <30, or ≥30 years), menopausal hormone therapy use (never, current, or former), number of breast biopsies (0, 1, 2, or 3), smoking (ever or never), alcohol intake in grams per day (0, <5, <15, <30, or ≥30), race (White, Black, or other), education (<12 y, high school graduate, some college, or college graduate).

[b]Adjusted for same covariates as in multivariate 1 plus body mass index (continuous).

for high versus low levels of light household activity per week (RR=0.82; 95% CI=0.61, 1.11; P_{trend}<.05), the European Prospective Investigation Into Cancer and Nutrition[9] (RR=0.81; 95% CI=0.70, 0.93; P_{trend}=.001), and various occupational cohort studies,[6–8] but not other prospective cohort studies of nonrecreational physical activity[11,12] or occupational activity.[9,13,14] In our study, the protective effects of routine activity during the day were not confounded by or modified by the education level of the women.

The direction of the relationship between active commuting and invasive breast cancer is consistent with results from a large Finnish cohort study.[54] Although the use of active transportation (i.e., walking or biking) is much less prevalent in the United States than in Europe,[29] currently, 6% of adults in the United States are considered regularly active (≥5 days per week, ≥30 minutes per day) by walking to work.[55] More detailed research with a focus on dose (i.e., duration in minutes and miles, average frequency per week, intensity or pace, and type of route [e.g., hilly, flat]) is needed to understand whether active transportation, including walking to a transit stop,[29] is associated with decreased invasive breast cancer incidence.

As associations of sedentary activities when reported for other chronic disease outcomes have been meaningful,[25,30,32] we cannot rule out the presence of a moderate or weak association between sedentary behavior and invasive breast cancer, which may have been masked by measurement error in the assessment of sedentary behavior. Although the number of hours women spent sitting was not statistically significantly related to invasive breast cancer, the difference between the magnitude of this finding (RR=1.12) and findings for increased levels of routine activity during the day at work or home (which captured a range of activities, including

TABLE 4—Occupational and Household Activity, Transportation Activity, and Sedentary Behavior in Relation to In Situ Breast Cancer Incidence Among Postmenopausal Women: National Institutes of Health-AARP Diet and Health Study, 1996–2003

	No. Person-Years	No. Cases	Age-Adjusted RR (95% CI)	P_{trend}	Multivariate 1 RR (95% CI)[a]	P_{trend}	Multivariate 2 RR (95% CI)[b]	P_{trend}
Occupational and Household Activity								
Routine activity during the day				.333		.644		.79
Sitting all day	49 144	39	1.00		1.00		1.00	
Sitting and a little walking	206 859	209	1.27 (0.90, 1.78)		1.26 (0.89, 1.78)		1.28 (0.91, 1.81)	
Standing or walking, no lifting	251 087	216	1.07 (0.76, 1.51)		1.08 (0.76, 1.53)		1.11 (0.78, 1.58)	
Lifting or carrying light loads, or climbing stairs often	115 128	98	1.06 (0.73, 1.54)		1.11 (0.76, 1.62)		1.15 (0.78, 1.68)	
Heavy lifting or carrying	9775	8	1.03 (0.48, 2.19)		1.21 (0.56, 2.61)		1.25 (0.58, 2.68)	
Transportation Activity								
Years walked or biked to work				.43		.57		.576
<1	555 972	511	1.00		1.00		1.00	
1–2	24 197	17	0.77 (0.47, 1.24)		0.77 (0.47, 1.25)		0.76 (0.47, 1.24)	
3–5	25 376	21	0.90 (0.58, 1.39)		0.92 (0.59, 1.42)		0.92 (0.59, 1.42)	
6–9	10 357	8	0.84 (0.42, 1.69)		0.87 (0.43, 1.75)		0.87 (0.43, 1.76)	
≥10	16 090	13	0.88 (0.51, 1.52)		0.92 (0.53, 1.60)		0.92 (0.53, 1.61)	
Sedentary Behavior								
Television or video watching, h/day				.427		.037		.063
<3	220 736	187	1.00		1.00		1.00	
3–4	272 210	247	1.07 (0.88, 1.29)		1.18 (0.97, 1.43)		1.16 (0.95, 1.41)	
5–6	103 031	103	1.18 (0.92, 1.50)		1.36 (1.06, 1.75)		1.32 (1.03, 1.71)	
7–8	18 990	21	1.30 (0.83, 2.05)		1.54 (0.98, 2.44)		1.50 (0.95, 2.38)	
≥9	17 025	12	0.83 (0.46, 1.49)		1.04 (0.58, 1.88)		1.01 (0.56, 1.83)	
Sitting, h/day				.117		.244		.32
<3	136 447	104	1.00		1.00		1.00	
3–4	186 096	167	1.18 (0.92, 1.50)		1.15 (0.90, 1.47)		1.14 (0.89, 1.46)	
5–6	171 157	170	1.31 (1.02, 1.67)		1.26 (0.99, 1.61)		1.24 (0.97, 1.59)	
7–8	89 698	85	1.25 (0.94, 1.67)		1.19 (0.89, 1.60)		1.17 (0.88, 1.57)	
≥9	48 594	44	1.20 (0.84, 1.72)		1.15 (0.80, 1.65)		1.12 (0.78, 1.61)	

Note. RR = relative risk; CI = confidence interval. Person-years are rounded to the nearest whole number. The total number of participants was 97 039.
[a]Adjusted for age, energy intake (kilocalories per day), recreational moderate-vigorous physical activity (0, 1–3, or ≥4 h/wk), parity or age at first live birth (never, <20, <25, <30, or ≥30 years), menopausal hormone therapy use (never, current, or former), number of breast biopsies (0, 1, 2, or 3), smoking (ever or never), alcohol intake in grams per day (0, <5, <15, <30, or ≥30), race (White, Black, or other), education (<12 y, high school graduate, some college, or college graduate).
[b]Adjusted for same covariates as in multivariate 1 plus body mass index (continuous).

"mostly sitting all day" as the comparison category) is small.

Our study had several strengths, including its large prospective nature and our ability to control for many important confounders. In addition, our question on routine activity captured a range of common daily behaviors that may be important determinants of energy expenditure.

Relative to the US population, participants in our study were more likely to be White and to have had a college education. Our findings may therefore not apply to all US women. The primary limitation of our study is that potential error in the assessment of occupational or household activity, transportation activity, and sedentary behavior could attenuate RRs. In addition to the problem of possible error in recall, we lacked detailed information on intensity, length of bouts, or frequency of routine occupational or household activity and active commuting, which precludes us from determining a true dose for these behaviors that could inform recommendations. We also had no information on the historical time frame of active commuting behavior. However, these limitations in the measurement of our exposures are not unique to our study.[21] To date, measurements of duration and intensity of all domains of physical activity and sedentary behavior have rarely been included in prospective or cross-sectional population studies, possibly because of the time and effort required of survey respondents.[56] Comprehensive questionnaires that capture these characteristics and have known measurement properties are needed to better understand the links between nonrecreational physical activity, sedentary behavior, and disease outcomes.[57]

Our data provide evidence that routine activity during the day at work or home may be related to reduced risk of invasive breast cancer. Given that many postmenopausal women may not be capable of meeting US physical activity guidelines for cancer prevention through recreational moderate–vigorous physical activity alone, domains outside of recreation time may be attractive targets for increasing physical activity and reducing sedentary behavior. ■

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Contributors

S.M. George was the primary author and was responsible for completing all analyses, interpreting data, and drafting and revising the article, in consultation with all authors and most closely with M.F. Leitzmann. All authors provided written comments on drafts of the article, with additional analyses and revisions made as a result of such feedback. A.R. Hollenbeck, A. Schatzkin, and M.F. Leitzmann provided substantial contributions to the cohort study conception and design. All authors gave final approval of the version to be published.

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Human Participant Protection

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

図 表

TABLE 3—Occupational and Household Activity, Transportation Activity, and Sedentary Behavior in Relation to Invasive Breast Cancer Incidence Among Postmenopausal Women: National Institutes of Health-AARP Diet and Health Study, 1996-2003

	No. Person-Years	No. Cases	Age-Adjusted RR (95% CI)	P_{trend}	Multivariate 1 RR (95% CI)[a]	P_{trend}	Multivariate 2 RR (95% CI)[b]	P_{trend}
Occupational and Household Activity								
Routine activity during the day				.003		.024		.092
Sitting all day	49 144	258	1.00		1.00		1.00	
Sitting and a little walking	206 859	933	0.84 (0.73, 0.96)		0.84 (0.73, 0.97)		0.86 (0.75, 0.99)	
Standing or walking, no lifting	251 087	1132	0.81 (0.71, 0.93)		0.83 (0.72, 0.95)		0.86 (0.74, 0.98)	
Lifting or carrying light loads, or climbing stairs often	115 128	514	0.80 (0.69, 0.93)		0.83 (0.71, 0.96)		0.86 (0.74, 1.00)	
Heavy lifting or carrying	9 775	29	0.55 (0.38, 0.81)		0.62 (0.42, 0.91)		0.64 (0.43, 0.94)	
Transportation Activity								
Years walked or biked to work				.051		.061		.084
<1	555 972	2540	1.00		1.00		1.00	
1-2	24 197	110	1.00 (0.83, 1.21)		0.99 (0.82, 1.20)		0.99 (0.82, 1.20)	
3-5	25 376	120	1.03 (0.86, 1.23)		1.03 (0.86, 1.24)		1.03 (0.86, 1.24)	
6-9	10 357	33	0.69 (0.49, 0.97)		0.69 (0.49, 0.98)		0.70 (0.50, 0.98)	
≥10	16 090	63	0.84 (0.65, 1.08)		0.86 (0.67, 1.11)		0.86 (0.67, 1.11)	
Sedentary Behavior								
Television or video watching, h/day				.303		.493		.935
<3	220 736	1013	1.00		1.00		1.00	
3-4	272 210	1243	0.97 (0.89, 1.05)		1.02 (0.94, 1.11)		1.00 (0.92, 1.09)	
5-6	103 031	438	0.89 (0.80, 0.99)		0.96 (0.86, 1.08)		0.93 (0.83, 1.05)	
7-8	18 990	90	0.99 (0.80, 1.23)		1.08 (0.87, 1.34)		1.04 (0.84, 1.30)	
≥9	17 025	82	1.03 (0.82, 1.28)		1.17 (0.93, 1.47)		1.12 (0.89, 1.41)	
Sitting, h/day				.006		.101		.243
<3	136 447	564	1.00		1.00		1.00	
3-4	186 096	866	1.11 (0.99, 1.23)		1.08 (0.97, 1.20)		1.07 (0.96, 1.19)	
5-6	171 157	803	1.14 (1.03, 1.27)		1.10 (0.98, 1.22)		1.08 (0.97, 1.20)	
7-8	89 698	419	1.17 (1.03, 1.33)		1.11 (0.97, 1.26)		1.08 (0.95, 1.23)	
≥9	48 594	224	1.19 (1.02, 1.39)		1.12 (0.95, 1.31)		1.08 (0.92, 1.27)	

Note. RR = relative risk; CI = confidence interval. Person-years are rounded to the nearest whole number. The total number of participants was 97 039.
[a]Adjusted for age, energy intake (kilocalories per day), recreational moderate-vigorous physical activity (0, 1-3, or ≥4 h/wk), parity or age at first live birth (never, <20, <25, <30, or ≥30 years), menopausal hormone therapy use (never, current, or former), number of breast biopsies (0, 1, 2, or 3), smoking (ever or never), alcohol intake in grams per day (0, <5, <15, <30, or ≥30), race (White, Black, or other), education (<12 y, high school graduate, some college, or college graduate).
[b]Adjusted for same covariates as in multivariate 1 plus body mass index (continuous).

図表掲載箇所	P2292, Table3
概 要 (800字まで)	本研究は、The NIH-AARP Diet and Health Studyに参加している女性97,039名を対象に1996年から2003年まで追跡調査を行い、職業や家事に要する身体活動量および余暇時間中の座位時間と閉経期乳がんとの関連を検討したものである。職業や家事に要する身体活動量を5つ(座位中心、座位または少しの歩行、立位または歩行、軽い荷物の運搬・階段を頻繁に利用、力仕事)に分類し、余暇時間の身体活動量は、テレビ視聴時間と座位時間、中高強度活動でそれぞれ1日に費やした時間を質問紙から得た。職業に要する身体活動が座位中心の女性と比較すると、力仕事の女性は浸潤性乳がんの発症リスクが0.62(95%信頼区間:0.42-0.91)と有意に低下した。テレビ視聴の時間が3時間/日未満または、余暇時間中の座位時間が3時間/日未満の女性と、テレビ視聴9時間/日以上または座位9時間/日以上の女性との間には、有意な関連はみられなかった。また、粘膜内乳がんの発症における同様の分析では、いかなる関連もみられなかった。
結 論 (200字まで)	中高年の欧米人女性において、職業や家事に要する身体活動は、余暇時間中の中高強度身体活動量に関わらず、乳がんの発症リスクに量反応的な関連があることが示唆された。しかし、余暇時間中の座位時間と乳がんの発症リスクについては、有意な関連はみられなかった。
エキスパートによるコメント (200字まで)	身体活動基準の策定に用いられた研究の1つである。乳がんについては、これまで身体活動との関連が報告されていたが、さらにその乳がんの種類と身体活動のドメインについても検討した論文である。浸潤性乳がんと粘膜内乳がんとでは、身体活動は浸潤性乳がんに有効であることが示された。がんの種類ごとに関連するリスクファクターを特定したり、さらにそれらリスクファクターを詳細に検討することは、より適切で効率的・効果的ながん予防に有効であると思われる。

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

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Consistent with a strong hormonal etiology, endometrial cancer is thought to be influenced by both obesity and physical activity. Although 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 min 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). Although 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 research to clarify underlying biologic mechanisms, including those relating to hormonal alterations.

Key words: endometrial neoplasms/epidemiology; exercise/physiology; recreation/physiology; health behavior; prospective studies

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, 10 cohort studies[5–14] and twelve case–control studies[15–26] have examined the association between physical activity and endometrial cancer. Of these, only 2 cohort studies[6,14] 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.

Material 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 1 of 8 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), 6 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

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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 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 hr per week, 1–3 hr per week, 4–7 hr per week, and >7 hr 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. Because 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 hr; <1 hr per week was assigned a value of 0.5 hr; 1–3 hr per week was assigned a value of 2 hr; 4–7 hr per week was assigned a value of 5.5 hr; and >7 hr per week was assigned a value of 8 hr. 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 2 questions. Participants were asked about time spent watching TV or videos during a typical 24-hr period over the past 12 months. Time spent watching TV or videos was categorized as none, <1, 1–2, 3–4, 5–6, 7–8 and ≥9 hr. In a separate question, participants were also asked to indicate the number of hours spent sitting during a typical 24-hr period over the past 12 months: <3, 3–4, 5–6, 7–8 and ≥9 hr. Both measures of inactivity were collapsed as <3, 3–4, 5–6 and ≥7 hr 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 8 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 3 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 because of 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 > 2 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 > 2 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 scale[33] 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. Because 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, 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, whereas 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 I and II). 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 III). 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 1 year (87.2%) (Table IV). 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 V). 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 VI).

TABLE I – SELECT CHARACTERISTICS OF WOMEN ACCORDING TO DAILY ROUTINE PHYSICAL ACTIVITY LEVEL AT BASELINE, NIH-AARP DIET AND HEALTH STUDY

Characteristic	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)	
	n	%[1]	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
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[2]										
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

[1]Missing values were excluded from percentage calculations.–[2]Defined as physical activity that lasted at least 20 mins and caused increases in breathing, heart rate, or sweating.
HT, hormone therapy.

In general, the correlations between activity responses asked on the 2 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

TABLE II – SELECT CHARACTERISTICS OF WOMEN ACCORDING TO FREQUENCY OF VIGOROUS PHYSICAL ACTIVITY LEVEL AT BASELINE, NIH-AARP DIET AND HEALTH STUDY

Characteristic	Frequency of vigorous physical activity during typical month in past 12 months[1]									
	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)	
	n	%[2]	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
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

[1]Defined as physical activity that lasted at least 20 mins and caused increases in breathing, heart rate, or sweating.–[2]Missing values were excluded from percentage calculations.
HT, hormone therapy.

activity: our results are similar to those from 2 case–control studies suggesting reduced risk associated with vigorous activity,[20,23] but are in contrast with those from 2 cohort studies observing no association.[5,7] Whereas several previous case–control[20,21] and cohort[5,11,12] 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 as reviewed in Refs. [7,27] and [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. Although most cohort and case–control studies have not observed any effect modification by BMI as reviewed in Refs. 27,28, our findings are in contrast with 1 case–control study[22] that observed a stronger effect in women with a lower BMI and are consistent with other cohort[8,14] and case–control studies[19,26] 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 three[8,9,13] of six[6–10,13] 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

TABLE III – 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[1]	95% CI	*p* for trend	RR[2]	95% CI	*p* for trend	RR[3]	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)	

[1]Relative risks adjusted for age (continuous).–[2]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).–[3]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 IV – 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[1]	95% CI	p for trend	RR[2]	95% CI	p for trend	RR[3]	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 physically demanding jobs											
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–s1.12)		0.66	(0.38–1.15)	

[1]Relative risks adjusted for age (continuous).–[2]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).–[3]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 V – 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[1]	95% CI	p for trend	RR[2]	95% CI	p for trend	RR[3]	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)	

[1]Relative risks adjusted for age (continuous).–[2]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).–[3]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.

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 hr 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

TABLE VI – 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[1]	95% CI	*p* for trend	RR[2]	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)		

[1]Relative risks adjusted for age (continuous).–[2]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.

lower body weight,[40] because 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 min 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 min of continuous vigorous exercise 3 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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