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Physical activity in different periods of life, sedentary behavior and the risk of ovarian cancer in the NIH-AARP Diet and Health Study

Qian Xiao¹, Hannah P. Yang², Nicolas Wentzensen², Albert Hollenbeck³, and Charles E. Matthews¹

¹Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland ²Hormonal and Reproductive Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, Maryland ³AARP, Washington, District of Columbia

Abstract

Background—Physical activity and sedentary behavior may influence ovarian cancer risk, but clear evidence is lacking.

Methods—We prospectively investigated the relations of self-reported physical activity and sedentary behavior to ovarian cancer incidence in a cohort of 148,892 US women aged 50–71 years at baseline (1995–1996), who were followed through 2006. Multivariate Cox proportional hazard models were used to estimate relative risks (RRs) and 95% confidence intervals (CIs). We also performed analysis by hormone use, body-mass index (BMI) and cancer subtype.

Results—We identified 753 incident epithelial ovarian cancers. Overall, neither physical activity nor sedentary behavior at baseline was associated with ovarian cancer risk. Compared with women who never or rarely engaged in vigorous physical activity in the past year, women who reported more than 5 times/week of vigorous physical activity had a RR of 1.05 (95% CI: 0.84, 1.32). Women who sat 7+ hours/day had a RR of 1.05 (95% CI: 0.80, 1.37) compared with those reporting <3 hr of sitting. The associations were not modified by hormone use or BMI, and were similar for both serous and non-serous subtypes.

Conclusions—Physical activity and sedentary behavior in middle and older ages were not associated with ovarian cancer risk.

Impact—We found no clear support for a role of physical activity and sedentary behavior in ovarian cancer risk.

Introduction

Ovarian cancer is the eighth most common cancer, and the most lethal gynecologic cancer among US women (1). Its etiology remains poorly understood and only a few factors have

Correspondence: Qian Xiao, PhD, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 9609 Medical Center Dr, Rockville, Maryland 20850, qian.xiao@nih.gov; phone: 240-276-7207.

Conflict of interest

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been consistently linked to ovarian cancer risk. The most important risk factor is a family history of breast and/or ovarian cancer, while parity and the use of oral contraceptive have protective effects (2).

It has been hypothesized that physical activity may protect against ovarian cancer through its influence on hormonal, inflammatory and immune pathways, or suppression of ovulation (3–5). However epidemiologic studies have reported conflicting results. While most studies found a null or weak inverse association (6–13), two prospective studies reported an elevated risk of ovarian cancer with a high level of vigorous activity (14, 15). Several studies have reported that physical activities at mid-teens or early adulthood (<40 years), are positively associated with ovarian cancer risk (9–11, 16), suggesting that the age period at which women engage in physical activity may be an important factor. Moreover, some studies suggested that the association may also differ by BMI, hormone use and histologic subtypes of the disease (17, 18). In summary, much remains to be understood about the relationship between physical activity and ovarian cancer, and how it is influenced by various factors.

Recent literature suggested that sedentary behavior may play an important role in cancer etiology, independent of moderate to vigorous activity (19). A few studies have examined sedentary behavior in relation to ovarian cancer. One prospective study (11) and two case-control studies (20, 21) have suggested that prolonged sitting may be associated with increased risk of ovarian cancer.

An early study using data from a large prospective cohort, the NIH-AARP Health and Diet Study, found no association between the frequency of moderate or vigorous physical activity participation and ovarian cancer risk (13). Comparing to women reporting no moderate or vigorous activity, women who engaged in both activities had a relative risk of 1.10 (95% CI: 0.82, 1.48) for ovarian cancer. However, the early study only included 309 cases, which limited the study power. Now with three more years in follow-up, the number of cases has more than doubled. Therefore we re-evaluated the relationship between physical activity and ovarian cancer risk in this cohort, extended our analysis to include physical activity in different life periods and sedentary behavior, and examined whether these relationships differ by other risk factors and cancer subtypes.

Materials and Methods

Study population

The NIH-AARP Diet and Health Study was established in 1995–1996. Participants were recruited from AARP members who were 50 to 71 years old and resided in six U.S. states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). Details of the NIH-AARP study were reported previously (22). The baseline questionnaire captured information on physical activity, dietary intake, demographic factors, medical and reproductive history and family history of cancer. Of the 617,119 questionnaires returned, 566,398 were non-duplicate and satisfactorily completed. In 1996–1997, a second questionnaire, the risk factor questionnaire, was mailed to the baseline respondents who did not have self-reported prevalent cancer at baseline or within 6 months from the time of the baseline questionnaire. It collected further information on physical activity, sedentary behavior, and medical history. Of the initial cohort, 337,074 men and women completed the risk factor questionnaire. The study was approved by the National Cancer Institute Special Studies Institutional Review Board.

Assessment of physical activity

In the baseline questionnaire, participants were asked to select a response that best described their daily activity in the past 12 months, beside exercising or playing 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 also asked about how often (never, rarely, 1–3 times per month, 1–2 times per week, 3–4 times per week, or 5 times per week) they engaged in vigorous household, occupational and recreational physical activities during a typical month in the past year. Vigorous activity was defined as physical activities that lasted at least 20 minutes and caused increases in breathing or heart rate, or sweating. We combined the never and rarely response categories in analysis.

In the risk factor questionnaire, participants were given two separate lists of examples of “moderate and vigorous” recreational and household physical activities (MVPA). They were asked to indicate how often (never, rarely, weekly but <1 hour per week, 1–3 hours per week, 4–7 hours per week, and >7 hours per week) they participated these activities 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 combined for analysis. The risk factor questionnaire also collected information on sedentary behaviors. Participants reported the amount of time they spent in a typical day sitting overall (<3, 3–4, 5–6, 7–8, and 9 hours) and watching television or videos (none, <1 hour, 1–2, 3–4, 5–6, 7–8, and 9 hours), during the past year. For analysis, we collapsed the lowest categories for both measures, and they were each coded into 4 categories (<3, 3–4, 5–6, and 7 hours per day).

Ovarian cancer ascertainment

Cohort members were followed annually through the US Postal Service’s National Change of Address database for address changes and through linkage to the US Social Security Administration Death Master File and the National Death Index Plus for vital status. Incident ovarian cancer cases were identified through linkage to eight original and two additional (Arizona and Texas) state cancer registry databases. A previous validation study found that approximately 90% of cancers were identified through registry linkage (23). Cancer registry data included cancer diagnosed, diagnosis date, morphology code, grade, and stage information.

Using the International Classification of Diseases for Oncology, Third Edition (ICD-O-3) (24), we defined cases as first primary epithelial ovarian cancer (ICD-O-3 code: C56.9). Borderline and non-epithelial ovarian cancer cases were excluded in this study. The cases were further classified into the following subtypes: serous (code: 8260, 8441, 8450, 8460, 8461, 8462), endometrioid (code: 8380, 8381, 8560, 8570), mucinous (code: 8470, 8471, 8472, 8480, 8481, 8490), clear cell (code: 8310, 8313), and other epithelial (code: 8010, 8020, 8021, 8050, 8070, 8120, 8140, 8240, 8246, 8255, 8260, 8323, 8440, 8450, 8490, 8562).

Analytic sample

Of those who satisfactorily completed the baseline questionnaire, we excluded individuals who were male (n=339,666), whose questionnaire was completed by proxies of the intended respondent (n=1,265), or who died, requested to be withdrawn or had moved out of the study area before baseline (n=91), leaving a total of 225,376 potentially eligible women.

For analysis of baseline physical activity, we further excluded those who had prevalent cancer except nonmelanoma skin cancer (n=23,876); had a history of oophorectomy or unknown oophorectomy status (n=48,201); and developed non-epithelial or borderline

ovarian cancer during follow-up (n=63). Additionally, we excluded 113 women who were identified through National Death Index with ovarian cancer as the cause of death, but had no information on timing of diagnosis date or cancer histology. The final baseline analytic sample included 153,123 women, of whom 753 developed invasive epithelial ovarian cancer. We additionally removed women who had missing information on daily routine (n=1760, including 16 cases) and vigorous activity (n=4234, including 8 cases) in the respective analysis.

For analysis of physical activity and sedentary behavior reported in the risk factor questionnaire, we restricted to women who responded to this survey. Of the baseline analytic sample, 99,372 women completed the risk factor questionnaire. We excluded women whose questionnaire was completed by proxies (n=835, including 4 cases), who died or moved out of the study area before their risk factor questionnaire was received and scanned (n=14), and who reported to have prevalent cancer in the risk factor questionnaire (n=687, including 5 cases), leaving 96,247 women with 467 cases. We further excluded women with missing information for any of the recreational/household activity and sedentary behavior questions in the respective analysis (overall sitting: n=479, 4 cases; TV watching: n=405, 4 cases; MVPA: n=1495, 7 cases in past 10 years; n=2031, 9 cases at age 35–39; n=2222, 11 cases at age 19 to 29; 2150, 9 cases at age 15 to 18).

Statistical analysis

Relative risks (RR) and 2-sided 95% confidence intervals (CI) were estimated with the Cox proportional hazards model, using the SAS PROC PHREG procedure (SAS 9.2; SAS Institute, Cary, North Carolina). Person-years of follow-up time were calculated from the baseline (for the analysis of baseline physical activity) or from the scan date of the risk factor questionnaire (for the analysis of the MVPA and sedentary behavior in the risk factor questionnaire) until the diagnosis of invasive epithelial ovarian cancer, moved out of the study area, died from any cause, or December 31, 2006, whichever came sooner. We evaluated and confirmed the proportional hazards assumption for the main exposures by including interaction terms with time and using the Wald χ^2 procedure to test if coefficients equaled zero.

We present RRs and 95% CIs from both age adjusted and multivariate models adjusted for risk factors of ovarian cancer that were identified as *a priori* potential confounders, including age at entry (continuous), race/ethnicity (Non-Hispanic White, Non-Hispanic Black and other), education (<12 yrs, high school, some college, college and graduate school), number of live birth (0, 1, 2, 3–4, 5–9, and 10+), age at menarche (<=10 yr, 11–12 yr, 13–14 yr, and 15+ yr), age at menopause (<40 yr, 40–44 yr, 45–49 yr, 50–54 yr, 55+ yr and still menstruating), oral contraceptive use (never, 1–4 yr, 5–9 yr, 10+ yr), any menopause hormone therapy (MHT) use (never, current and former), and smoking (never, current smoker and former smoker). Body mass index (BMI) is a potential mediator of the effect of physical activity or sedentary behavior on ovarian cancer risk. Therefore separate multivariate models with or without BMI were used to assess the associations. In additional models, we further adjusted for sedentary behavior and light activities in the analysis of current MVPA, and current MVPA in the analysis of historical MVPA. We found minimal changes in results after including BMI in the model and therefore excluded BMI in our analysis. In the analysis of MVPA at age 15–18, 19–29 and 35–39, we additionally adjusted for MVPA in the past 10 years in a separate model, to examine the independent effect of MVPA at younger ages. We performed stratified analysis according to BMI and MHT status. Test for interaction were done using the likelihood-ratio test, comparing models with versus models without the product term between BMI and the covariate of interest.

Results

At baseline, most women described their daily routine physical activity (excluding recreational activity) as walking and standing or walking and sitting. 22% of the women reported never or rarely engaging in vigorous activity in the past 12 months, whereas 15%, 21%, 25% and 17% engaged in vigorous activity 1–3 times/month, 1–2 times/week, 3–4 times/week and 5 or more times/week. Compared to women who never or rarely engaged in vigorous physical activities, those who engaged in higher levels of vigorous activities had lower average BMI, were more likely to be college educated, to report excellent health status, and to have ever used MHT, and were less likely to be current smokers (table 1). We also found an inverse correlation between overall sitting and MVPA in the previous 10 years reported in the risk-factor questionnaire (spearman correlation coefficient: -0.19).

No association was observed between either daily activity or vigorous physical activity level and ovarian cancer risk as reported on the baseline questionnaire (table 2). Compared with the reference group (never/rarely engaging in vigorous physical activity), women who reported engaging in vigorous physical activities more than 5 times per week had a relative risk of 1.04 (95% CI, 0.83–1.30) for developing invasive epithelial ovarian cancer. Women who reported doing heavy work or carrying heavy loads as daily routine had a non-significant 50% lower risk of ovarian cancer than did women who reported sitting without much walking. However the number of cases in the former category was extremely small ($n=6$). No reduction in risk was observed among women who climbed stairs or carried light loads routinely. Including BMI in the models had minimal impact on the results. In subgroup analysis stratified by BMI (BMI < 25 and BMI $\geq$ 25), the associations did not differ by strata (data not shown).

We also examined ovarian cancer risk in relation to sedentary behavior and moderate and vigorous physical activity among women who responded to the risk factor questionnaire. The amount of time spent sitting overall was not associated with ovarian cancer risk (RR $7+ \text{ hr vs } <3 \text{ hr}$, 1.06, 95% CI, 0.81–1.39)(table 3). Similarly, no excess risk was observed among women who spent prolonged hours watching TV (RR $7+ \text{ hr vs } <3 \text{ hr}$, 1.02, 95% CI, 0.67–1.55). Further adjusting for recent MVPA or stratifying by BMI or MHT use did not modify these results (data not shown). We also did not detect an interaction between overall sitting and MVPA (p for interaction = 0.66).

MVPA in the 10 years prior to the completion of the risk-factor questionnaire and at age 15–18 was not associated with ovarian cancer risk (table 4). Although there was a suggestion of an increased risk for women who engaged in an intermediate amount of MVPA (<1 hr/wk, 1–3 hr/wk, or 4–7 hr/wk) at early adult life period, the relative risk estimates were not statistically significant and no association was found with higher amount of MVPA (7+ hr/wk) at these life periods. The results remained largely similar when we included overall sitting and MVPA in the 10 years (for analysis of historical MVPA) the model (data not shown). We also found no significant interactions between MVPA at different life periods and BMI or MHT status (data not shown).

We also ran analysis specific to serous versus non-serous type of ovarian cancer, but due to small numbers, we were unable to further examine specific subtypes of non-serous ovarian cancers. Neither physical activity at baseline nor sedentary behavior was related to serous or non-serous ovarian cancer (data not shown). MVPA in the past 10 years was also not associated with either subtype. We observed that among women engaged in intermediate amount of MVPA at earlier age periods, there appeared to be an elevated risk of non-serous ovarian cancer, but not serous subtype, although the increase in risk was only at borderline statistical significance (table 5). For all the aforementioned analysis, we performed

sensitivity analysis by excluding cases diagnosed in the first two years of follow up and it did not alter the results (data not shown).

Discussion

In this population of middle-aged and older US women, we found that ovarian cancer risk was not associated with daily physical activity pattern, time spent on sedentary behaviors, and the amount of MVPA after age 40. However, we cannot rule out the possibility of an increase in risk associated with intermediate levels of MVPA in early adulthood.

The lack of association between physical activity during middle-to-old ages and ovarian cancer risk is largely consistent with results from previous studies, especially prospective studies. A meta-analysis published in 2007 summarized findings from twelve case-control and cohort studies and reported a 20% risk reduction associated with the highest versus lowest levels of recreational physical activity (25). However the summary association did not reach statistical significance when the analysis was restricted to the six cohort studies (RR 0.81, 95% CI 0.57, 1.17), and the three large prospective studies published after the meta-analysis all reported a null association (12, 13)(26).

Three studies to date have looked into the effect of sedentary behavior as a possible risk factor for ovarian cancer. A case-control study conducted in China found that long hours spent sitting at work was associated with increased risk (21). In another case-control study in Turkey, the authors reported no association between sitting time at work and risk of ovarian cancer, but the number of cases was quite small (20). In the only other prospective study of which we are aware, Patel et al. reported that among US women aged 50–74, prolonged sitting in leisure time (6+ vs. < 3 hrs/d) was associated with a significant 55% increase in ovarian cancer risk after adjusting for physical activity (11). In contrast, we did not observe an elevated risk with prolonged sitting overall or television watching, both of which have been associated with all-cause mortality (27) and endometrial cancer (28) in our population.

When we examined the effect of MVPA at earlier ages, we found a statistically nonsignificant increase in risk in women who engaged in intermediate levels of MVPA at age 19–29 and 35–39. The timing at which physical activity might have an effect is intriguing. The etiology and critical period of ovarian cancer development are not well understood, although the protective effects of oral contraceptive use and pregnancy suggest that childbearing ages may be particularly vulnerable to carcinogenic factors. A number of previous studies also evaluated the effects of physical activity at early ages, and the results were mixed (9–11, 15–18, 25, 29–31). Most of these studies reported largely null associations, but there were a few exceptions. Three papers reported reduced risk of ovarian cancer in relation to historical activity levels (18, 30, 31). In an Italian case-control study, occupational physical activity at age 30–39 were inversely associated with ovarian cancer, but no relationship was found for leisure time activity (30). Pan et al. also found decreased risk with increased level of occupational activities, but the results were only significant for the age period of early 50s (18). A third case-control study reported inverse association with leisure time activity at teens and early adulthood (31). In contrast, two studies reported suggestive positive associations between ovarian cancer and physical activity at early life or adulthood (9, 16). Carnide et al. showed 30% to 70% increase in risk with physical activity of <2 times per week, when compared to none/slight activity, in mid-teens and early 30s (16). In the Netherlands Cohort Study, the authors found a history of sports at 1–2 hour/week was associated with doubling the risk of ovarian cancer, although no age period was specified in the paper (9). However the increase in risk in all the studies only achieved borderline significance. Overall, these findings do not support a clear relationship between physical activity at different life periods and ovarian cancer risk.

The association between physical activity and ovarian cancer may be further complicated by the different risk factors associated with different subtypes of ovarian cancer. As elucidated by earlier studies, epithelial ovarian cancer is a group of heterogeneous diseases and each subtype may have a different set of risk factors (26, 32, 33). Although our findings suggested that the modest increase in risk with MVPA in early adulthood was stronger in non-serous types, unfortunately, we were unable to examine the relationship with individual subtypes due to small numbers. Future studies with adequate sample size of non-serous ovarian cancers will be particularly valuable to evaluate the subtype specific effect of physical activity.

It has been postulated that there may be multiple mechanisms through which physical activity may influence ovarian cancer risk. However, the activation of different pathways may lead to different, or even opposite effects on ovarian cancer risk. Physical activity may suppress chronic inflammation, enhance immune function, improve DNA repair mechanism, and decrease circulating levels of endogenous estrogens, all of which may lead to decreased risk of ovarian cancer (3–5). In addition, it is well established that regular strenuous activity disrupts menstrual function and increases the frequency of anovulatory cycles in young women (34, 35), which, according to the “incessant ovulation” hypothesis, may also lead to reduced risk (36). On the other hand, physical activity may plausibly increase ovarian cancer risk. For example, physical activity may stimulate the production of pituitary gonadotropins (37, 38), a high level of which has been proposed as a risk factor for ovarian cancer (2, 39). Additionally, circulating androgen levels tend to increase after exercise (40) and androgenic stimulation of ovarian epithelial cells may lead to tumorigenesis (3). Moreover, exercise may also lower progesterone (41, 42), a potential protective factor against ovarian cancer (3, 39). Given the complexity of the possible physiological and pathological changes involved, the overall effect of physical activity on ovarian cancer risk may be determined by a combination of factors, and as suggested by our study and the works by others, such factors include the timing, dose, and type of activity, woman’s exposure to other risk factors, and the subtypes of the cancer.

There are several limitations of this study. The main limitation is the potential measurement error and misclassification of the self-reported levels of physical activity and sedentary behavior. Our physical activity questions were not validated, although using the same exposure measures, previous studies in this cohort have linked physical activity and sedentary behavior to the risk of postmenopausal breast (43, 44), colorectal (45), and endometrial cancer risk (28), the major cancer sites for which an etiologic connection with physical activity have been consistently established. Additionally, we did not have enough cases of most of the non-serous cancers, making it impossible to examine the association specific to each ovarian cancer subtypes. Lastly, although we tried to control for multiple ovarian cancer risk factors, and adjusting which did not make a big impact on the results, we could not rule out the possibility of residual confounding.

Our study has several strengths. Its prospective nature decreased the likelihood of differential recall bias, a serious limitation of many case-control studies. The large cohort with a fairly long follow-up time has allowed us to not only to test the overall effect of physical activity and ovarian cancer, but also to assess the associations among people with different BMI, MHT use and with serous and non-serous types of ovarian cancer. We have excluded women with a history of any cancer diagnosis, and this reduces the influences of existing malignancies on physical activity. We also conducted a sensitivity analysis, excluding cases diagnosed in the first 2 years, further minimizing the possibility of reverse causation due to undiagnosed ovarian cancer.

In summary, we found no evidence supporting a protective effect of physical activity or an adverse effect of prolonged time in sedentary behavior at middle- to old-ages on ovarian cancer risk. Given the many health benefits of physical activity, including reduced risk for early mortality, heart disease and certain cancers, the current findings should not dissuade women of any age from engaging in physical activity. To better understand the potential positive association between physical activity in early adulthood and ovarian cancer, future studies should be designed to have a better measure of different domains of physical activity and activity at different ages, have adequate power to study specific subtypes of the cancer and to evaluate the influence of other risk factors, and address specific pathways of the complex mechanisms.

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Table 1

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

	Vigorous activity at baseline ^a				
	Never/rarely (n=33,938)	1-3 times/month (n=21,946)	1-2 times/week (n=32,123)	3-4 times/week (n=38,310)	5+ times/week (n=25,049)
Age at baseline, yr ^b	61.8 (5.4)	60.9 (5.4)	61.4 (5.5)	61.9 (5.4)	62.0 (5.4)
BMI, kg ² /m ^b	28.4 (6.9)	27.5 (6.0)	26.7 (5.7)	25.9 (5.2)	25.1 (4.9)
Nulliparous, %	16	16	15	15	16
Age at menarche, <13 yr, % ^c	50	49	48	47	47
Age at menopause, ≥50 yr, % ^c	41	42	44	45	45
White, non-Hispanic, % ^c	90	91	92	91	92
College and post college, % ^c	23	30	33	35	36
Married, % ^c	41	44	44	47	48
Self-reported health, excellent, % ^c	10	14	16	22	30
Current smoker, % ^c	21	18	15	11	10
Former smoker, % ^c	36	37	38	41	42
Ever used OC, % ^c	38	44	43	42	40
Ever used MHT, % ^c	39	47	47	51	48
Family history of any cancer, % ^c	34	35	35	34	35

^aDefined as physical activity that lasted at least 20 minutes and caused increases in breathing, heart rate, or sweating.

^bmean (sd)

^cMissing values were excluded from percentage calculations

Age alone and multivariate adjusted RR and 95% CI for the association between baseline physical activity and ovarian cancer incidence, NIH-AARP Diet and Health Study

Table 2

			Relative risk, 95% CI	
	No. of cases	Person-years	Age adjusted	Multivariate ^a
Daily activity pattern				
Sitting	56	124,280	ref	ref
Sitting and walking	243	486,295	1.06 (0.80, 1.42)	1.05 (0.78, 1.40)
Walking and standing	293	575,539	1.04 (0.78, 1.38)	1.02 (0.76, 1.36)
Climbing stairs or carrying light loads	139	254,518	1.10 (0.81, 1.51)	1.08 (0.79, 1.48)
Heavy work or carrying heavy loads	6	25,928	0.49 (0.21, 1.14)	0.50 (0.21, 1.16)
Vigorous physical activity in the past year				
Never/Rarely	167	325,901	ref	ref
1–3 times/month	104	216,768	0.97 (0.76, 1.24)	0.94 (0.74, 1.21)
1–2 times/week	143	317,864	0.90 (0.72, 1.12)	0.86 (0.68, 1.07)
3–4 times/week	189	381,083	0.97 (0.79, 1.20)	0.92 (0.74, 1.13)
5+ times/week	142	249,232	1.11 (0.89, 1.39)	1.04 (0.83, 1.30)

^a Adjusted for age, no. of live birth, age at menarche, age at menopause, race, education, marital status, oral contraceptive use, MHT use, and smoking.

Association between sedentary behaviors and ovarian cancer incidence among women who completed the second questionnaire, NIH-AARP Diet and Health Study

Table 3

No. of cases		Person-years	Relative risk, 95% CI	
			Age adjusted	Multivariate ^a
Overall sitting (hrs/d)				
<3	109	198,031	ref	ref
3–4	131	259,569	0.91 (0.71, 1.17)	0.90 (0.69, 1.16)
5–6	113	240,401	0.86 (0.66, 1.13)	0.85 (0.65, 1.10)
7+	110	198,673	1.08 (0.83, 1.41)	1.06 (0.81, 1.39)
Watching TV (hrs/d)				
<3	177	323,049	ref	ref
3–4	198	279,440	0.91 (0.74, 1.12)	0.96 (0.78, 1.18)
5–6	61	142,337	0.73 (0.54, 0.98)	0.80 (0.59, 1.07)
7+	27	52,567	0.89 (0.59, 1.33)	1.02 (0.67, 1.55)

^a Adjusted for age, no. of live birth, age at menarche, age at menopause, race, education, marital status, oral contraceptive use, MHT use, and smoking

Association between moderate to vigorous physical activity at different ages and ovarian cancer incidence among women who completed the second questionnaire, NIH-AARP Diet and Health Study

Table 4

		No. of cases	Person-years	Relative risk, 95% CI	
				Age adjusted	Multivariate ^a
Moderate to vigorous physical activity in the past 10 yr					
Never/Rarely	68	123,356		ref	ref
< 1hr/week	50	93,318		0.99 (0.68, 1.42)	0.99 (0.68, 1.42)
1–3 hr/week	109	227,726		0.88 (0.65, 1.19)	0.88 (0.64, 1.18)
4–7 hr/week	134	228,473		1.06 (0.79, 1.42)	1.05 (0.78, 1.41)
7+ hr/week	99	214,357		0.83 (0.61, 1.13)	0.84 (0.61, 1.14)
Moderate to vigorous physical activity, age 35–39					
Never/Rarely	38	83,085		ref	Ref
< 1hr/week	53	80,042		1.46 (0.97, 2.22)	1.46 (0.96, 2.22)
1–3 hr/week	116	204,349		1.26 (0.87, 1.81)	1.26 (0.88, 1.83)
4–7 hr/week	130	237,920		1.20 (0.83, 1.72)	1.23 (0.85, 1.76)
7+ hr/week	121	274,357		0.94 (0.65, 1.36)	1.02 (0.71, 1.47)
Moderate to vigorous physical activity, age 19–29					
Never/Rarely	44	89,238		ref	ref
< 1hr/week	54	76,930		1.44 (0.97, 2.14)	1.44 (0.96, 2.14)
1–3 hr/week	108	197,156		1.12 (0.79, 1.59)	1.14 (0.80, 1.62)
4–7 hr/week	125	227,883		1.11 (0.79, 1.57)	1.17 (0.83, 1.65)
7+ hr/week	125	286,938		0.87 (0.62, 1.22)	0.95 (0.67, 1.35)
Moderate to vigorous physical activity, age 15–18					
Never/Rarely	60	118,609		ref	ref
< 1hr/week	41	77,686		1.05 (0.70, 1.56)	1.06 (0.71, 1.57)
1–3 hr/week	112	192,512		1.15 (0.84, 1.57)	1.18 (0.86, 1.61)
4–7 hr/week	102	199,154		1.01 (0.74, 1.39)	1.04 (0.76, 1.44)
7+ hr/week	142	290,109		0.97 (0.71, 1.31)	1.02 (0.76, 1.39)

^a Adjusted for age, no. of live birth, age at menarche, age at menopause, race, education, marital status, oral contraceptive use, MHT use, and smoking.

Table 5

Association between the history of moderate to vigorous physical activity and ovarian cancer incidence among women who completed the second questionnaire, NIH-AARP Diet and Health Study, by subtypes of ovarian cancer.

		Serous		Non serous	
	No. of cases	RR, 95% CI ^a	No. of cases	RR, 95% CI ^a	
Moderate to vigorous physical activity in the past 10 yr					
Never/Rarely	38	ref	30	ref	
< 1hr/week	25	0.86 (0.52, 1.43)	25	1.15 (0.67, 1.95)	
1–3 hr/week	51	0.71 (0.47, 1.08)	58	1.10 (0.70, 1.71)	
4–7 hr/week	75	1.01 (0.68, 1.51)	59	1.11 (0.71, 1.73)	
7+ hr/week	57	0.83 (0.55, 1.26)	42	0.86 (0.54, 1.39)	
Moderate to vigorous physical activity, age 35–39					
Never/Rarely	22	ref	16	ref	
< 1hr/week	25	1.19 (0.67, 2.11)	28	1.83 (0.99, 3.38)	
1–3 hr/week	60	1.12 (0.69, 1.83)	56	1.46 (0.84, 2.55)	
4–7 hr/week	70	1.13 (0.70, 1.84)	60	1.36 (0.78, 2.37)	
7+ hr/week	68	0.99 (0.61, 1.61)	53	1.06 (0.61, 1.87)	
Moderate to vigorous physical activity, age 19–29					
Never/Rarely	26	ref	18	ref	
< 1hr/week	29	1.29 (0.76, 2.20)	25	1.64 (0.90, 3.02)	
1–3 hr/week	52	0.93 (0.58, 1.50)	56	1.44 (0.85, 2.46)	
4–7 hr/week	69	1.09 (0.70, 1.72)	56	1.27 (0.75, 2.17)	
7+ hr/week	68	0.89 (0.57, 1.41)	57	1.04 (0.61, 1.78)	
Moderate to vigorous physical activity, age 15–18					
Never/Rarely	41	ref	19	ref	
< 1hr/week	18	0.68 (0.39, 1.18)	23	1.87 (1.02, 3.44)	
1–3 hr/week	52	0.81 (0.54, 1.22)	60	1.97 (1.17, 3.30)	
4–7 hr/week	49	0.74 (0.49, 1.13)	53	1.68 (0.99, 2.84)	
7+ hr/week	85	0.92 (0.63, 1.34)	57	1.25 (0.74, 2.11)	

^aAdjusted for age, no. of live birth, age at menarche, age at menopause, race, education, marital status, oral contraceptive use, MHT use, and smoking.