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Recreational physical activity and risk of epithelial ovarian cancer

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Abstract

Background—Physical activity may influence ovarian cancer risk through hormonal, inflammatory, or immune-mediated processes or by suppressing ovulation. In a population-based case-control study of epithelial ovarian cancer, we assessed risk associated with recreational physical activity with a focus on characterizing risk within histologic subtypes.

Methods—Information was collected during in-person interviews with 812 women with ovarian cancer diagnosed in western Washington State from 2002–2005 and 1,313 controls. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs). Exercise was assessed according to the average hours and metabolic equivalent (MET)-hours per week and the number of years in which regular recreational activity occurred.

Results—Relative to women who reported no regular exercise throughout adulthood, the overall risk of invasive, but not borderline, ovarian cancer was reduced among more active women. Reductions in risk of invasive disease were most evident among women with the greatest frequency of high-intensity activity during adulthood. For serous invasive cancer, women in the uppermost category of MET-hours per week of recreational activity in adulthood had 60% the risk of inactive women (95% CI 0.4–0.9), whereas this level of activity was associated with more than a doubling in risk of endometrioid and clear cell invasive tumors.

Conclusions—Our findings are compatible with an overall reduction in risk of invasive epithelial ovarian cancer associated with recreational activity but suggest that this association may differ in women with different histologic types of disease. Inconsistent findings across studies that have considered histologic type indicate that this issue is not yet resolved.

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Keywords

Ovarian cancer; Physical activity; Exercise; Epidemiology

Introduction

Physical activity has been hypothesized to influence risk of ovarian cancer, possibly through its influences on hormonal, inflammatory, or immune-mediated processes or by suppression of ovulation. In a recent meta-analysis, a 20% reduction in risk associated with recreational physical activity was observed in both case-control and cohort studies in analyses that compared the most active to the least active women [1]. However, some heterogeneity in results has been noted; in particular, increases in incidence among women who reported high levels of vigorous activity [2,3] have been observed in two cohort studies. Also, few studies have assessed whether differences in risk exist according to tumor histology. In a large population-based case-control study of epithelial ovarian cancer, we assessed a possible association with recreational physical activity with a focus on characterizing risk within disease subtypes.

Methods

The study population and methods have been described [4,5]. Female residents of a thirteen-county area of western Washington State, 35–74 years of age, diagnosed with a primary invasive or borderline epithelial ovarian tumor from 2002 through 2005 were identified through a population-based registry that is part of the Surveillance, Epidemiology, and End Results program of the US National Cancer Institute. Of 1,058 eligible case women identified, 812 (76.7%) were interviewed; of the interviewed cases, 595 had invasive disease. Tumors were grouped into the following histologic categories: serous (n = 452); mucinous (n = 112); endometrioid (n = 104); clear cell (n = 35); and other epithelial tumors (n = 109; largely adenocarcinomas and carcinomas, not otherwise specified). Controls were selected by random digit dialing [6] using stratified sampling in 5-year age categories, 1-year calendar intervals and two county strata in a 2:1 ratio to women with invasive epithelial ovarian cancer. For 14,561 (82.0%) of the 17,768 telephone numbers belonging to a residence, we determined whether an eligible (i.e., age- and county-eligible and, if so, with at least one ovary and no prior history of ovarian cancer) woman resided there. Of the 1,561 women identified as eligible controls, 1,313 were interviewed (84.1%).

The study was approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center, and all women provided signed informed consent before participating. In-person interviews pertained to the period of time before diagnosis (for cases) or before an assigned, comparable reference date (for controls), and included demographic and lifestyle characteristics, family history of cancer, and reproductive history. To collect information on recreational physical activity, women were asked to recall their “regular” participation (defined as at least 1 h per week, or 4 h per month, for at least 4 months of a year) in exercise or sports activities, including walking or biking to work, from 25 years of age to the reference date. For each reported episode, we recorded the type of activity; beginning and ending dates (month and year) of the activity; months per year and days per week or month of participation in that activity; and usual minutes or hours per day of participation on a typical day when a woman engaged in that activity. Because we expected that walking, jogging, running, and swimming would be frequently reported, and because the intensity of these activities can vary from low to high, we provided participants a card showing the following categories: walking for pleasure or walking the dog; walking for exercise (outdoors or treadmill); walking/jogging in combination; jogging (>12 min per mile); and running (≤12 min per mile). Swimming was

shown as categories of swimming for recreation and swimming laps for exercise or in competition.

Exercise intensity was assigned using a standard source [7] that assigns a metabolic equivalent (MET) score to a wide variety of recreational and other activities. The MET score is defined as the ratio of working metabolic rate to a standard resting metabolic rate, where 1.0 MET is the rate obtained during quiet sitting. For walking and swimming, we assigned scores separately for each category listed above. For other activities (e.g., conditioning exercises) where intensity may vary, we assigned a MET score based on an approximate average of the range of scores provided by Ainsworth et al. [7]. Activities with MET scores of 4 or lower were grouped as low intensity, scores of more than 6 as high intensity, and intermediate scores as moderate intensity. The most commonly reported low-intensity exercises included walking for pleasure (34% of recorded episodes of low-intensity activity for the combined group of cases and controls), yoga (16%), water aerobics (15%) and horseback riding (12%). Commonly reported moderate intensity exercises included walking for exercise (46%), and conditioning exercises, gym workouts using a combination of machines, or weight machine workouts (26%). High-intensity exercise included aerobics (22%), bicycling (20%), jogging or running (17%), lap or competitive swimming (11%), and hiking or backpacking (9%). The types of activities and their relative frequencies were very similar among cases and controls (data not shown).

To reduce the possibility that symptoms of an ovarian cancer which had not yet been diagnosed might have influenced recent physical activity, we truncated our exercise assessment at 1 year before the diagnosis/reference date. Women who reported no regular (as defined above) exercise from age 25 to 1 year before the diagnosis/reference date (23.0% of cases and 20.5% of controls) served as the referent group for all analyses. Within each time period of interest, risk associated with average hours per week of physical activity was examined separately for low, moderate, and high-intensity exercise as well as for all activities combined. We also assessed risk according to MET-hours per week of physical activity (calculated as the average hours per week spent in an activity multiplied by the estimated MET score for that activity) and duration of physical activity in adulthood (calculated as the number of years in which a woman reported an average of 1 h or more per week of activity, from age 25 to 1 year before the diagnosis/reference date).

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using unconditional logistic regression. The analyses shown were adjusted for the frequency-matching variables of age, year of diagnosis/reference date, and county of residence as well as duration of hormonal contraception, number of full-term births, education, and body mass index (BMI) 5 years before the reference date. Eight cases and eight controls were lost from the analysis due to missing information. Other characteristics examined as potentially confounding the associations of interest included race/ethnicity; cigarette smoking; age at menarche; tubal ligation; hysterectomy; history of infertility; use of hormone replacement therapy; family history of breast and/or ovarian cancer; and personal history of breast cancer. None of these latter characteristics changed OR estimates by 10% or more.

We conducted analyses for case groups of women with borderline and invasive epithelial ovarian tumors and in histologic subgroups using polytomous logistic regression. Also, we examined risks separately among women <55 and ≥55 years of age, and within subgroups of BMI (assessed 5 years before the reference date). All analyses were carried out using the STATA statistical package (version 10.0, STATA Corporation, College Station, TX).

Results

Characteristics of cases and controls have previously been described [4,5]. Approximately, 90% of cases and controls were non-Hispanic white women. Consistent with most prior epidemiologic studies of ovarian cancer, cases were less likely than controls to have given birth and reported a lesser extent of exposure to hormonal forms of contraception. Cases were somewhat more likely than controls to be over-weight (BMI 25–<30 kg/m^2) or obese (BMI ≤ 30 kg/m^2) and less likely to have graduated from college.

We observed little evidence that recreational physical activity throughout adulthood (i.e., age 25 years to 1 year before the reference date) was associated with the risk of developing a borderline ovarian tumor (Table 1). Risk of invasive epithelial ovarian cancer tended to be reduced among women who reported physical activity relative to women who reported no activity, although the strength of association was generally modest. Risk reduction was the greatest among women who reported the highest frequency of high-intensity activity (>1.5 h per week, on average: OR = 0.6, 95% CI 0.4–0.9; *p* trend <0.05), although risk reductions were similar in each category of MET-hours per week of combined moderate and high-intensity activity (OR = 0.8, 95% CI 0.6–1.1, relative to inactive women). Similar results were obtained when activity variables were truncated 5 years before the reference date (data not shown).

In analyses that assessed activity in early adulthood or in the more recent past (Table 2 for invasive disease; results not shown for borderline tumors), results were fairly similar to analyses that summarized activity throughout adulthood. Reduced risk was again primarily evident among women who engaged in the greatest extent of high-intensity activity (OR = 0.6, 95% CI 0.3–1.0, among women with >3 h per week of high-intensity activity during either of these time periods).

We observed no association of physical activity with risk of either serous or mucinous borderline epithelial ovarian tumors when these subtypes were assessed separately (data not shown). Because we had little ability to separately examine risk of mucinous invasive ovarian cancer owing to its rarity (*n* = 23), we excluded these tumors when examining histologic subtypes of invasive disease. Relative to inactive women, the risk of serous invasive cancer was reduced among women who reported recreational physical activity, with the strength of associations for this tumor subtype somewhat greater than those observed in analyses of all invasive cancers combined (Table 3). In contrast, the risk of endometrioid/clear cell tumors increased with increasing physical activity, whether assessed as average hours per week or MET-hours per week, in every time or age interval examined. For women in the highest category (upper third) of MET-hours per week, the risk of this histologic subtype was roughly doubled (e.g., OR = 2.2, 95% CI 1.2–4.0, in analyses that considered recreational activity throughout adulthood).

We noted no clear differences in risk associated with physical activity in subgroups of younger (<55 years) and older (≥55 years) women. The association with high-intensity exercise was somewhat stronger in younger women, although any differences between age groups were statistically imprecise (e.g., for invasive disease, ORs and 95% CIs for >1.5 h of recreational physical activity per week during adulthood = 0.5, 0.3–1.0, and 0.7, 0.4–1.2, for younger and older groups, respectively). In analyses stratified by BMI (<25 vs. ≥25), analyses in women with BMI < 25 generally resembled our overall results, with most associations weak or inapparent in overweight and obese women; as for age, differences between women according to BMI were statistically imprecise.

Discussion

Differences in characteristics of cases and controls who did or did not choose to participate in the study may influence the results, as may errors in reporting of physical activity. Physical activity is a complex exposure that may be difficult to recall or summarize over the lifetime. Inadequate or inaccurate reporting occurring to a similar extent among cases and controls could result in nondifferential misclassification of this exposure; this would likely diminish our ability to observe any true associations, if they exist. Also, it is possible that reporting of physical activity, particularly in the more recent past, may have been influenced by the presence of ovarian cancer symptoms in case women. We attempted to reduce the impact of this potential bias by truncating our assessment before the diagnosis/reference date; our results were similar when either physical activity during the 1 year, or 5 years, preceding that date were excluded. Results were also similar when physical activity was summarized throughout adulthood or examined in early or later adulthood.

Studies examining physical activity and ovarian cancer risk have recently been reviewed and summarized [1,8]. Olsen et al. [1] reported similar reductions in risk of 0.79 (95% CI, 0.70–0.85) and 0.81 (95% CI, 0.57–1.19) in meta-analyses of recreational physical activity based upon seven case–control [1,9–14] and six cohort studies [2,3,15–18], respectively, comparing the highest vs. lowest levels of recreational activity. The time period of exposure assessment selected for the meta-analysis was the most recent period presented (for case–control studies) and either baseline or cumulative averages, if available, for cohort studies. Generally, for studies that assessed recreational activity both summarized across intensity categories and separately within one or more categories (e.g., hours per week of vigorous activity), the results for total activity were used in the meta-analysis. All studies adjusted for age and parity and most also adjusted for oral contraceptive use and BMI. No evidence of publication bias was observed based on a funnel plot of effect estimates. Heterogeneity was noted to be absent in the case–control studies and present in cohort studies, due to results of a single study [2], in which women with the highest level of total leisure-time activity at baseline were at increased risk (RR = 1.4, 95% CI 1.0–2.0).

Additional heterogeneity exists among cohort studies. In the Nurses Health Study cohort [3], while overall results (used in the meta-analysis) were consistent with a slight risk reduction associated with recreational physical activity (cumulative average hours per week ≥7: RR = 0.80, 95% CI 0.49–1.32), risk was reported to be increased among women who engaged in frequent vigorous activity. In the Iowa Women's cohort [2], the increased risk noted above was attributable primarily to women who engaged in vigorous physical activity (RR for vigorous activity more than four times per week = 2.38, 95% CI 1.29–4.38). In the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort [19], results were interpreted as null; however, some suggestion of a slight increase in risk associated with increasing MET-hours per week of combined recreational and household activity was observed (RR in upper quartile relative to lowest quartile of exposure = 1.27, 95% CI 0.99–1.61; p trend = 0.096). In a US-based cohort study [8] that, like the EPIC study, was published after the meta-analysis was conducted, no overall association of ovarian cancer risk with physical activity, or vigorous activity, was observed.

An explanation for the heterogeneity in results—with various studies reporting risk reductions, increases, or no association—is not readily apparent. Complexities in the assessment of physical activity and multiple types and sources of error may contribute. Case–control studies may be influenced by selective differences in recalled activity among women who do or do not develop disease. While cohort studies generally do not suffer from such recall bias, cost and practical considerations may limit the extent of information collected in these studies regarding specific types of activities as well as their frequency, duration, and time frame of

occurrence. Also, it is possible that studies focused on recreational physical activity may be impacted in unknown ways by the interrelationships of such activities with performance of occupational and household activities.

Most prior studies of recreational physical activity and ovarian cancer risk have included only women with invasive disease [2,8,10,12–17,19], while others have considered invasive and borderline tumors as a combined case group [3,9,11,18]. In a large study, Olsen [1] analyzed invasive and borderline tumors separately. For the most part, weak inverse associations of risk with physical activity were observed, with similar findings in invasive and borderline tumor subgroups.

While only a few studies have explored differences in risk according to histologic type of disease, results do not appear entirely consistent across these studies or with the findings of the current study. Among the cohort studies, Patel [16] observed similar risk reductions across histologic subtypes. Bertone [3] reported that, if anything, RRs for serous tumors tended to be slightly higher than those for all tumor types combined (e.g., RR for ≥7 h vs. <1 h/week = 1.11, 95% CI 0.61–2.02), with risk for mucinous and endometrioid types similar to the overall results. Leitzmann [8] noted an increased risk of serous cancer (RR = 1.46, 95% CI 0.89–2.40) and a decreased risk of nonserous cancer (RR = 0.77, 95% CI0.45–1.31) among women who engaged in vigorous activity. Among the case–control studies, two studies [13,14] observed point estimates of reduced risk for all histologic types, with wide confidence margins. Pan [12] observed fairly similar risk reductions across histologic types for combined categories of moderate and vigorous activity; however, when vigorous activity was considered separately, risk reductions were observed for serous and endometrioid tumors, with risk increases seen for mucinous and other types. Point estimates of risk were imprecise, and none of these associations exhibited a statistically significant trend in risk across increasing levels of activity. Olsen [1] observed a modest, statistically imprecise, reduced risk of serous and endometrioid invasive cancers among women with a greater extent of recent recreational activity; for clear cell and mucinous invasive tumors, the corresponding point estimates were near the null (1.0 and 1.1 for these tumor types, respectively).

In the current study, relative to women who reported no regular exercise throughout adulthood, the overall risk of invasive—but not borderline—epithelial ovarian cancer was reduced among more active women. Risk of invasive disease was reduced in association with some measures of the degree of recreational activity, most notably with increasing hours per week of high-intensity activity. We observed differences in risk according to histologic subtype of invasive ovarian cancer, such that risk of serous tumors was reduced while risk of endometrioid and clear cell tumors was increased among women with greater levels of activity. These results add further inconsistency to the existing literature regarding differences in risk across histologic subtypes for this exposure. Thus, the question of whether recreational physical activity may influence ovarian cancer risk is not yet resolved.

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Table 1

Risk of borderline and invasive epithelial ovarian cancer in relation to recreational physical activity (age 25 to one year before the diagnosis/reference date)

	Controls	Borderline tumors			Invasive tumors		
Activity level	**(*n*)**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**
Inactive	268	39	1.0	ref	146	1.0	ref
Average hours/week							
<0.5	204	42	1.4	0.8–2.3	79	0.8	0.5–1.1
>0.5–1.5	296	44	1.0	0.6–1.7	136	0.9	0.7–1.3
>1.5–3	253	44	1.1	0.7–1.8	101	0.8	0.6–1.1
>3	284	44	1.1	0.6–1.8	129	0.9	0.7–1.2
Average hours/week, by intensity level of activity							
Low							
<0.5	145	20	1.0	0.5–1.9	63	0.9	0.6–1.3
>0.5–1.5	81	22	1.9	1.0–3.7	49	1.3	0.8–2.0
>1.5	72	13	0.9	0.4–2.0	36	0.9	0.5–1.4
Moderate							
<0.5	257	46	1.2	0.8–2.0	104	0.8	0.6–1.1
>0.5–1.5	292	42	1.0	0.6–1.6	123	0.8	0.6–1.1
>1.5	307	50	1.1	0.7–1.8	141	0.9	0.7–1.2
High							
<0.5	237	40	1.2	0.7–2.0	91	0.8	0.5–1.1
>0.5–1.5	171	27	1.0	0.6–1.8	74	0.8	0.6–1.2
>1.5	174	27	1.1	0.6–1.9	59	0.6	0.4–0.9
Average MET-hours/week (tertiles)							
All intensities							
≤4.8	340	65	1.3	0.8–2.0	147	0.8	0.6–1.1
>4.8–13.2	349	55	1.0	0.6–1.6	145	0.8	0.6–1.1
>13.2	348	54	1.1	0.7–1.7	153	0.9	0.6–1.2
Moderate- or high-intensity activities only							
≤4.5	323	64	1.3	0.9–2.1	141	0.8	0.6–1.1
>4.5–12.8	330	47	1.0	0.6–1.6	133	0.8	0.6–1.1
>12.8	328	51	1.1	0.7–1.7	137	0.8	0.6–1.1

	Controls	Borderline tumors			Invasive tumors		
Activity level	**(*n*)**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**
Duration (years) of activity							
Any intensity							
≤10	408	88	1.2	0.8–1.9	164	0.8	0.6–1.0
>10–20	301	55	1.2	0.7–1.9	147	1.0	0.7–1.3
>20	328	31	0.9	0.5–1.6	134	0.8	0.6–1.1
Moderate or high intensity							
≤10	425	93	1.3	0.8–2.0	182	0.8	0.6–1.1
>10–20	273	41	1.0	0.6–1.6	120	0.9	0.6–1.2
>20	283	28	1.0	0.6–1.7	109	0.8	0.6–1.1

[a]Adjusted for age, calendar year of diagnosis/reference date, county of residence, number of full-term births, duration of hormonal contraception, education, and body mass index 5 years before the reference date

Table 2

Risk of invasive epithelial ovarian cancer in relation to recreational physical activity in early adulthood and in the recent past

	Activity from age 25–35 years				Activity in the 10 years prior to 1 year before diagnosis/reference date			
Activity level	**Controls (*n*)**	**Cases (*n*)**	**OR[a]**	**95% CI**	**Controls (*n*)**	**Cases (*n*)**	**OR[a]**	**95% CI**
Inactive	268	146	1.0	Ref	268	146	1.0	Ref
Average hours/week, by intensity level of activity								
Low								
≤1	72	48	1.4	0.9–2.3	102	48	1.0	0.6–1.5
>1–2	43	17	0.8	0.4–1.6	67	27	0.9	0.5–1.5
>2–3	15	9	1.1	0.4–2.7	19	13	1.4	0.6–3.1
>3	21	14	1.1	0.5–2.3	41	14	0.6	0.3–1.2
Moderate								
≤1	187	74	0.8	0.5–1.1	253	91	0.7	0.5–1.0
>1–2	106	50	0.8	0.5–1.3	153	61	0.8	0.5–1.1
>2–3	74	32	0.9	0.5–1.5	127	56	1.0	0.6–1.4
>3	104	58	1.1	0.7–1.7	193	96	1.0	0.7–1.4
High								
≤1	191	78	0.8	0.5–1.1	172	62	0.7	0.5–1.0
>1–2	81	34	0.8	0.5–1.3	69	26	0.7	0.4–1.2
>2–3	47	24	0.8	0.5–1.5	58	16	0.6	0.3–1.1
>3	85	29	0.6	0.3–1.0	79	26	0.6	0.3–1.0
Average MET-hours/week, tertiles								
All intensities								
1 (Low)	242	95	0.8	0.6–1.2	295	137	0.9	0.7–1.2
2	239	113	1.0	0.7–1.3	296	116	0.8	0.6–1.1
3 (High)	244	115	0.9	0.7–1.3	299	123	0.8	0.6–1.1
Moderate or high intensity only								
1 (Low)	223	79	0.7	0.5–1.0	273	109	0.8	0.6–1.1
2	221	101	0.9	0.6–1.3	276	111	0.8	0.6–1.2
3 (High)	222	106	0.9	0.6–1.3	277	114	0.8	0.6–1.1

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[a] Adjusted for age, calendar year of diagnosis/reference date, county of residence, number of full-term births, duration of hormonal contraception, education, and body mass index 5 years before the reference date

Table 3

Risk of histologic subtypes of invasive epithelial ovarian cancer in relation to recreational physical activity

	Controls	Serous invasive tumors			Endometrioid/clear cell invasive tumors			Other (nonmucinous) invasive tumors		
Activity level	**(*n*)**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**
Inactive	268	95	1.0	Ref	18	1.0	Ref	27	1.0	Ref
Age 25 to 1 year before reference date										
Average hours/week										
<0.5	204	47	0.7	0.5–1.0	12	0.9	0.4–2.0	16	0.9	0.5–1.7
>0.5–1.5	296	77	0.8	0.6–1.1	30	1.8	0.9–3.4	25	1.1	0.6–1.9
>1.5–3	253	53	0.6	0.4–0.9	27	1.6	0.8–3.1	19	0.9	0.5–1.8
>3	284	62	0.7	0.4–1.0	44	2.4	1.3–4.5	16	0.8	0.4–1.5
Average MET-hours/week, tertiles (all intensities)										
≤4.8	340	84	0.7	0.5–1.0	22	1.0	0.5–2.0	35	1.2	0.7–2.1
>4.8–13.2	349	85	0.7	0.5–1.1	42	2.0	1.1–3.7	15	0.5	0.3–1.0
>13.2	348	70	0.6	0.4–0.9	49	2.2	1.2–4.0	26	1.0	0.6–1.9
Average MET-hours/week, tertiles (moderate or high intensity only)										
≤4.5	323	79	0.7	0.5–1.0	22	1.1	0.5–2.1	34	1.2	0.7–2.1
>4.5–12.8	330	76	0.7	0.5–1.0	40	2.0	1.1–3.7	13	0.5	0.2–1.0
>12.8	328	63	0.6	0.4–0.9	44	1.9	1.0–3.5	24	1.0	0.5–1.9
Duration (years) of activity (moderate or high intensity only)										
≤10	425	96	0.7	0.5–1.0	40	1.3	0.7–2.3	37	1.0	0.6–1.7
>10–20	273	64	0.7	0.5–1.1	35	1.8	0.9–3.4	18	0.8	0.4–1.6
>20	283	58	0.6	0.4–0.9	31	2.1	1.1–4.1	16	0.8	0.4–1.6
Age 25 to 35										
Average MET-hours/week, tertiles (all intensities)										
≤6.0	242	53	0.7	0.5–1.0	18	1.4	0.7–2.8	20	1.1	0.6–2.1
>6–16.3	239	55	0.7	0.5–1.1	39	2.4	1.3–4.6	16	0.9	0.5–1.8
>16.3	244	53	0.7	0.4–1.0	38	2.3	1.2–4.4	18	1.1	0.6–2.2
Average MET-hours/week, tertiles (moderate or high intensity only)										
≤5.9	223	43	0.6	0.4–0.9	16	1.2	0.6–2.5	16	1.0	0.5–1.9
>5.9–16.1	221	52	0.8	0.5–1.1	35	1.1	1.1–4.1	13	0.8	0.4–1.6
>16.1	222	46	0.6	0.4–1.0	36	2.1	1.1–4.1	18	1.2	0.6–2.4

	Controls	Serous invasive tumors			Endometrioid/clear cell invasive tumors			Other (nonmucinous) invasive tumors		
Activity level	**(*n*)**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**	**(*n*)**	**OR[a]**	**95% CI**
In the decade before 1 year before reference date										
Average MET-hours/week, tertiles (all intensities)										
≤7.2	295	66	0.7	0.5–1.0	28	1.4	0.8–2.7	38	1.6	0.9–2.7
>7.2–17.5	296	70	0.7	0.5–1.1	32	1.7	0.9–3.2	11	0.5	0.2–1.0
>17.5	299	60	0.6	0.4–0.9	40	2.2	1.1–4.1	17	0.8	0.4–1.6
Average MET-hours/week, tertiles (moderate or high intensity only)										
≤6.6	273	50	0.6	0.4–0.9	23	1.2	0.6–2.3	32	1.3	0.8–2.4
>6.6–17.0	276	68	0.8	0.5–1.1	29	1.7	0.9–3.2	11	0.5	0.2–1.1
>17.0	277	55	0.6	0.4–0.9	38	2.1	1.1–4.0	16	0.8	0.4–1.6

[a]Adjusted for age, calendar year of diagnosis/reference date, county of residence, number of full-term births, duration of hormonal contraception, education, and body mass index 5 years before the reference date