Research Article

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Lifetime Physical Activity and Risk of Endometrial Cancer

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Abstract

Background: The role of moderate physical activity and life patterns of activity in reducing endometrial cancer risk remains uncertain.

Methods: We assessed lifetime histories of activity from recreation, transportation, chores, and occupation and other risk factors in a population-based case-control study of endometrial cancer conducted in the San Francisco Bay area. The analysis was based on 472 newly diagnosed cases ascertained by the regional cancer registry and 443 controls identified by random-digit dialing who completed an in-person interview.

Results: Reduced risks associated with greater lifetime physical activity (highest versus lowest tertile) were found for both total activity [odds ratio (OR), 0.61; 95% confidence interval (95% CI), 0.43-0.87; $P_{trend} = 0.01$] and activity of moderate intensity (OR, 0.44; 95% CI, 0.30-0.64; $P_{trend} < 0.0001$). Compared with women with low lifetime physical activity (below median), those with greater activity throughout life had a higher reduction in risk (OR, 0.62; 95% CI, 0.44-0.88). Inverse associations were stronger in obese and overweight women, but differences were not statistically significantly different from those in normal-weight women.

Conclusion: These findings suggest that physical activity in adulthood, even of moderate intensity, may be effective in lowering the risk of endometrial cancer, particularly among those at highest risk for this disease.

Impact: The results emphasize the importance of evaluating lifetime histories of physical activity from multiple sources, including both recreational and nonrecreational activities of various intensities, to fully understand the relation between physical activity and disease risk. *Cancer Epidemiol Biomarkers Prev; 19(5); 1276–83. ©2010 AACR.*

Introduction

There is increasing epidemiologic evidence that physical activity may reduce the risk of endometrial cancer (1-3), the fourth leading incident cancer in U.S. women (4). Studies of different designs have examined this relation, including linkage (5, 6), prospective cohort (7-16), population-based case-control (17-23), and hospital-based case-control (24-30) studies. Overall, risk is reduced, on average, by 20% to 40% in women with the highest level of physical activity (1-3), although a few studies did not find any evidence of an inverse association (6, 17, 19, 24, 30). According to a recent review of 18 studies (3), seven showed convincing evidence of a protective effect (7, 8, 21, 23, 25, 26, 29), and seven others showed possible evidence of an inverse association (5, 9-11, 18, 20, 22). Few studies, however, measured total physical activity (9, 12, 17, 18, 25); most studies have focused only on selected activities, such as recreational activity (8, 16, 19-22, 26), occupational activity (5-7, 10, 19-21, 24, 25, 27, 28), activity from daily living (9, 12-15, 17, 18, 23, 25, 29), household activities (12, 13, 15, 18, 20, 23, 25), gardening (8, 10, 11), walking or bicycling for transportation (8, 10-12, 18-20, 22, 25), or walking pace (16). Several recent studies assessed sedentary activities (12, 14, 15). Some studies considered intensity of physical activity and examined risk in relation to strenuous, moderate, or light activities (9, 15, 19, 22) or metabolic equivalent of energy expenditure (MET) estimates (13, 14, 16, 23, 29). Most case-control studies examined risk in relation to recent physical activity, with only two studies reporting on lifetime physical activity (20, 23). Thus, studies that examined the full spectrum of lifetime physical activity are lacking (3), and there remain uncertainties about the type, intensity, and timing of physical activities that are most effective in reducing endometrial cancer risk. We report findings from a population-based case-control study of endometrial cancer conducted in the San Francisco Bay area that assessed lifetime histories of sports and exercise, walking and bicycling for transportation, activity from strenuous household and outdoor chores, and occupational activity, thus allowing us to evaluate type, intensity, and timing of physical activity within a single study. We also investigated the joint influence of physical activity and body size because obesity is a major risk factor for endometrial cancer and related to physical inactivity (1, 31).

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Materials and Methods

Study design. Details of the study methods are provided elsewhere (32). Briefly, non-Hispanic white, Hispanic, and African American women ages 35 to 79 years, residing in the San Francisco Bay area (San Francisco, San Mateo, Alameda, Contra Costa, or Santa Clara counties), and newly diagnosed with endometrial cancer were identified through the Greater Bay Area Cancer Registry, which ascertains all incident cancers as part of the Surveillance, Epidemiology and End Results program and the California Cancer Registry. A total of 1,310 cases diagnosed between October 1, 1996 and September 30, 1999 were identified. Of these, 124 (9%) were deceased, and 21 (2%) could not be contacted due to physician-reported contraindications. A brief telephone screening interview that assessed study eligibility and self-identified race/ethnicity was completed by 1,013 (87%) cases. All cases who self-identified as Hispanic or African American and a 60% random sample of cases who self-identified as non-Hispanic white were selected for the study and 500 (77%) cases completed the in-person interview.

Population controls were identified through random-digit dialing, using a modification of the Waksberg method, described elsewhere (33). From the pool of potentially eligible women ages 35 to 79 years, 1,088 controls were randomly selected by frequency matching on race/ethnicity and the expected 5-year age distribution of cases. The telephone screening interview was completed by 940 (86%) women. Of 633 eligible controls without a history of endometrial cancer or hysterectomy, 470 (74%) were interviewed.

Trained professional interviewers administered a structured questionnaire in English or Spanish in the participants' homes. Information was collected on demographic background; lifetime histories of residence, occupation, and physical activity; pregnancies; hormone use; dietary intake; supplement use; body size; and medical history. As described in detail elsewhere (33), the interview assessed lifetime history of regular physical activity from multiple sources, including exercise and sports, walking and bicycling to school or work, strenuous household chores, and strenuous outdoor chores. For each activity, information was recorded on ages when the activity started and ended and the hours per week and months per year when the activity took place. Occupational physical activity was assessed through a lifetime occupational history. For each job held for at least 1 year, information was collected on ages when the job started and ended and the number of hours worked per week. The participants were asked to rate the level of physical activity for each job (i.e., mostly sitting, mostly standing or walking, mostly moderate physical activities, mostly strenuous activities, or hard labor). Sedentary activities were not assessed. Study participants provided written informed consent, and the study was approved by the Institutional Review Board of the Northern California Cancer Center.

For each type of physical activity (i.e., exercise, transportation, chores, and moderate or strenuous jobs), we estimated the average number of hours spent per week between age 10 years and the reference year [defined as the calendar year before diagnosis (cases) or selection into the study (controls)] by summing the hours of activity and dividing by reference age −10. For occupational physical activity, we estimated the average number of hours worked per week in jobs where the woman reported her activity level to be mostly moderately active or mostly strenuous or hard labor. Average lifetime total activity was estimated by summing the average weekly hours for each of the four types of activity. Total physical activity was also estimated for specific life periods, such as ages 10 to 19 years, 20 to 39 years (or age 20 years to reference age if younger than 40 years), 40 years to reference age, and during the 10 years before the reference age. Intensity of physical activity was assessed by assigning to each activity a MET value (34), which is the ratio of the metabolic rate for a specific activity compared with the resting metabolic rate. The MET value for a specific activity was multiplied by the hours per week spent in that activity to estimate MET-hours for each episode of activity, and average MET-hours of total activity was estimated by summing the MET-hours for each type of activity. For specific exercise activities, we assigned standard MET scores (34). For other activities, we assigned MET scores of 3.5 for walking, 6.0 for bicycling, 6.0 for strenuous outdoor chores, 5.0 for strenuous household chores, 4.0 for moderately active jobs, and 6.0 for strenuous jobs. Strenuous activities were defined as exercise ≥6 MET, bicycling to school or work, outdoor chores, and strenuous jobs. Moderate activities included exercise ranging from 3 to 5.9 MET, walking to school or work, household chores, and moderate jobs.

Statistical analysis. We used unconditional logistic regressionmodeling to estimate odds ratios (OR) and 95% confidence intervals (95% CI) associated with physical activity, adjusting for age (continuous), race/ethnicity (non-Hispanic white, Hispanic, African American), education (some high school or less, high school graduation or vocational school, some college, college graduation or higher), family history of endometrial cancer in first-degree relatives (yes, no), age at menarche (<12, 12-13, ≥14 years), full-term pregnancies (0, 1, 2, 3, 4, ≥5), duration of oral contraceptive use (never, <2 years, ≥2 years), duration of hormone therapy use (never, <5 years, ≥5 years), menopausal status (premenopausal or undetermined, postmenopausal), body mass index (BMI; <25, 25-29.9, ≥30), and height (tertiles; <61.9, 61.9-64.5, ≥64.6 inches). Caloric intake was not adjusted for in multivariate analyses, as we observed no association with endometrial cancer risk. BMI as a measure of overall adiposity was calculated as weight (kg) divided by height (m) squared and was based on height measured at interview and self-reported weight in the reference year. When measured height was not available (4% of cases, 3% of controls), self-reported adult height was used; similarly, when self-reported weight in the reference year was not available (2% of cases, 4% of controls), measured weight

Table 1. Characteristics of study population, by case-control status

	Cases (n = 500), n (%)	Controls (n = 470), n (%)	OR (95% CI)*
Age (y)			
<50	54 (11)	71 (15)	
50-59	160 (32)	143 (30)	
60-69	158 (31)	135 (29)	
70-79	128 (26)	121 (26)	
Race/ethnicity			
Non-Hispanic white	391 (78)	332 (71)	
Hispanic	59 (12)	86 (18)	
African American	50 (10)	52 (11)	
Education			
Some high school or less	55 (11)	89 (19)	1.0
High school graduation or vocational school	137 (27)	134 (29)	1.45 (0.92-2.29)
Some college	140 (28)	101 (21)	2.02 (1.26-3.24)
College graduation or higher	168 (34)	146 (31)	1.64 (1.02-2.64)
Family history of endometrial cancer in first-degree relatives			
No	467 (94)	454 (98)	1.0
Yes	28 (6)	10 (2)	2.80 (1.34-5.86)
Age at menarche (y)			
<12	104 (21)	85 (18)	1.0
12-13	287 (58)	254 (54)	0.89 (0.64-1.25)
≥14	105 (21)	129 (28)	0.66 (0.44-0.97)
Full-term pregnancies			
Nulliparous	117 (23)	65 (14)	1.82 (1.29-2.56)
1	50 (10)	60 (13)	1.0
2	144 (29)	135 (29)	1.26 (0.81-1.97)
3	97 (19)	89 (19)	1.25 (0.78-2.02)
4	51 (10)	53 (11)	1.12 (0.65-1.92)
≥5	41 (8)	68 (14)	0.74 (0.42-1.31)
Age at first full-term pregnancy (y)			
<20	75 (20)	96 (24)	1.0
20-24	173 (45)	149 (37)	1.39 (0.94-2.04)
25-29	90 (23)	96 (24)	1.08 (0.69-1.68)
30-34	35 (9)	46 (12)	0.90 (0.53-1.59)
≥35	10 (3)	13 (3)	0.91 (0.38-2.23)
Oral contraceptive use (y)			
Never	245 (50)	184 (40)	1.0
<2	97 (20)	75 (16)	0.97 (0.66-1.42)
2-4.9	50 (10)	64 (14)	0.56 (0.36-0.87)
5-9.9	48 (10)	72 (16)	0.46 (0.30-0.72)
≥10	53 (10)	66 (14)	0.56 (0.36-0.85)
Menopausal hormone therapy use (y)			
Never	223 (45)	244 (53)	1.0
<2	64 (13)	64 (14)	1.08 (0.73-1.59)
2-4.9	29 (6)	49 (10)	0.62 (0.37-1.02)
5-9.9	59 (12)	42 (9)	1.44 (0.92-2.25)
10-14.9	47 (10)	33 (7)	1.49 (0.91-2.44)
≥15	67 (14)	33 (7)	2.14 (1.31-3.49)

(*Continued on the following page*)

Table 1. Characteristics of study population, by case-control status (Cont'd)

	Cases (n = 500), n (%)	Controls (n = 470), n (%)	OR (95% CI)*
Menopausal status			
Postmenopausal	372 (74)	345 (73)	1.0
Premenopausal	100 (20)	104 (22)	1.08 (0.69-1.67)
Cannot be determined	28 (6)	21 (5)	1.31 (0.70-2.47)
BMI			
<25	178 (36)	186 (40)	1.0
25-29.9	135 (27)	164 (35)	0.92 (0.67-1.26)
≥30	184 (37)	117 (25)	1.93 (1.39-2.68)
Height (inches)			
<61.9	108 (22)	157 (33)	1.0
61.9-64.5	182 (36)	154 (33)	1.67 (1.19-2.35)
≥64.6	210 (42)	157 (33)	1.87 (1.32-2.65)

*OR and 95% CI were adjusted for age and race/ethnicity.

was used. Among controls, the correlation between self-report and measurements was high for both height and weight (Pearson correlation coefficient = 0.92; $P < 0.0001$). We considered women postmenopausal if their periods had stopped more than 1 year before diagnosis (cases) or selection into the study (controls), if they had never used hormone therapy, or if they had used hormone therapy only after the cessation of menses. We also considered women postmenopausal if they began using hormone therapy before the cessation of menses but were ages 60 years or older at the time of diagnosis or selection. Menopausal status could not be determined for women who began using hormone therapy before cessation of menses but who were younger than 60 years. All other women were considered premenopausal. Linear trends were assessed across ordinal values of categorical variables. After excluding subjects with missing information on potentially confounding variables, analyses were based on 472 cases and 443 controls.

Results

The characteristics of interviewed cases and controls are shown in Table 1. The majority of cases and controls were non-Hispanic white, ages 50 years and older, and postmenopausal. Compared with controls, higher proportions of cases had a college education, reported a family history of endometrial cancer, started menstruating at a young age, were nulliparous, had short-duration or no oral contraceptive use, had used hormone therapy for 5 years or longer, and were tall or obese (BMI ≥30). Average lifetime total physical activity was lower for cases than for controls (18.8 versus 22.6 h/wk). Of all activities assessed, most were of moderate intensity, and cases had significantly less moderate activity than controls (10.2 versus 13.3 h/wk).

Greater average lifetime physical activity from all sources combined was associated with reduced risk of endometrial cancer (Table 2). Risk decreased with increasing total physical activity (P_{trend} = 0.03), and the highest versus lowest tertile of activity was associated with a 33% lower risk (OR, 0.67; 95% CI, 0.47-0.95). Consideration of intensity slightly strengthened the inverse association (OR, 0.61; 95% CI, 0.43-0.87; P_{trend} = 0.01). For specific types of activities, reduced risks were found for greater occupational moderate or strenuous activity (OR, 0.64; 95% CI, 0.44-0.92 for the highest versus lowest tertile; P_{trend} = 0.01) and greater activity from strenuous household and outdoor chores (OR, 0.67; 95% CI, 0.46-0.96). A strong inverse trend was noted for activities classified as moderate ($P < 0.0001$), with an OR of 0.44 (95% CI, 0.30-0.64) for the highest versus lowest tertile of activity.

Reduced endometrial cancer risk was associated with greater physical activity both in younger and in older adulthood (Table 3). Risk reductions were of similar magnitude for greater physical activity at ages 20 to 39 years (OR, 0.60; 95% CI, 0.43-0.85), age 40 years to reference age (OR, 0.64; 95% CI, 0.45-0.91), and during the 10 years before the reference age (OR, 0.64; 95% CI, 0.45-0.91). There was no evidence of reduced risk for physical activity at ages 10 to 19 years. Considering physical activity patterns during adulthood (data not shown in the table), the risk reduction was greatest for women with higher total activity (≥91.9 versus <91.9 MET-h/wk) both at ages 20 to 39 years and ≥40 years (OR, 0.62; 95% CI, 0.44-0.88) and similar, but slightly lower, for those with higher activity in only one of the two life periods (OR, 0.72; 95% CI, 0.42-1.25 at age 20-39 years; OR, 0.73; 95% CI, 0.45-1.21 at age ≥40 years).

When we stratified the analysis by BMI, there was no evidence of an association with physical activity in normal-weight (BMI <25) women; statistically significant

inverse associations with greater physical activity (above versus below the median) were limited to obese women (OR, 0.50; 95% CI, 0.28-0.91) and overweight women (OR, 0.58; 95% CI, 0.34-0.99; Table 4). Considering the joint effects of body size and physical activity, we found that greater physical activity attenuated the adverse effect of large body size. The increase in risk associated with obesity was much lower in active women (OR, 1.57; 95% CI, 0.94-2.62) than in those with low physical activity (OR, 3.10; 95% CI, 1.91-5.01). The interaction, however, was not statistically significant ($P = 0.43$).

Table 2. Lifetime physical activity and risk of endometrial cancer, by type of activity and intensity

	Cases ($n = 472$), n (%)	Controls ($n = 443$), n (%)	Age-, race-, and BMI-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)*
Total physical activity (h/wk)				
<13.4	204 (43)	149 (33)	1.0	1.0
13.4-27.1	147 (31)	145 (33)	0.78 (0.57-1.07)	0.89 (0.63-1.25)
≥27.2	121 (26)	149 (33)	0.62 (0.45-0.86)	0.67 (0.47-0.95)
			$P_{trend} = 0.004$	$P_{trend} = 0.03$
Total physical activity (MET-h/wk)				
<43.2	207 (44)	151 (34)	1.0	1.0
43.2-91.8	150 (32)	145 (33)	0.78 (0.57-1.06)	0.83 (0.59-1.17)
≥91.9	115 (24)	147 (33)	0.59 (0.43-0.83)	0.61 (0.43-0.87)
			$P_{trend} = 0.002$	$P_{trend} = 0.01$
Occupational activity				
Moderate or strenuous jobs (h/wk)				
0	276 (59)	223 (50)	1.0	1.0
<8.1	111 (24)	108 (24)	0.81 (0.59-1.12)	0.80 (0.56-1.13)
≥8.1	85 (18)	112 (25)	0.61 (0.43-0.86)	0.64 (0.44-0.92)
			$P_{trend} = 0.004$	$P_{trend} = 0.01$
Nonoccupational activity (h/wk)				
<6.3	196 (42)	149 (33)	1.0	1.0
6.3-12.3	147 (31)	149 (33)	0.78 (0.57-1.08)	0.79 (0.57-1.11)
≥12.4	128 (27)	149 (33)	0.70 (0.50-0.97)	0.77 (0.54-1.09)
			$P_{trend} = 0.03$	$P_{trend} = 0.13$
Exercise (h/wk)				
<0.75	150 (32)	146 (33)	1.0	1.0
0.75-2.57	166 (35)	147 (33)	1.09 (0.78-1.50)	1.07 (0.76-1.52)
≥2.58	156 (33)	150 (33)	1.02 (0.73-1.41)	0.93 (0.65-1.33)
			$P_{trend} = 0.93$	$P_{trend} = 0.67$
Walking/bicycling to school or work (h/wk)				
<0.23	174 (37)	147 (33)	1.0	1.0
0.23-0.47	164 (35)	144 (33)	0.92 (0.67-1.27)	0.99 (0.70-1.39)
≥0.48	134 (28)	152 (33)	0.79 (0.57-1.09)	0.80 (0.57-1.13)
			$P_{trend} = 0.16$	$P_{trend} = 0.22$
Strenuous household and outdoor chores (h/wk)				
<3.4	198 (42)	150 (34)	1.0	1.0
3.4-8.1	158 (33)	144 (33)	0.84 (0.62-1.16)	0.88 (0.63-1.24)
≥8.2	116 (25)	149 (33)	0.61 (0.44-0.85)	0.67 (0.46-0.96)
			$P_{trend} = 0.004$	$P_{trend} = 0.03$
Total moderate activity (h/wk)				
<6.9	229 (49)	150 (34)	1.0	1.0
6.9-15.5	151 (32)	148 (33)	0.67 (0.49-0.92)	0.68 (0.49-0.95)
≥15.6	92 (20)	145 (33)	0.41 (0.29-0.58)	0.44 (0.30-0.64)
			$P_{trend} < 0.0001$	$P_{trend} < 0.0001$

*OR and 95% CI were adjusted for age, race/ethnicity, education, family history of endometrial cancer, age at menarche, full-term pregnancies, duration of oral contraceptive use, duration of hormone therapy use, menopausal status, BMI, and height.

Table 3. Lifetime physical activity and endometrial cancer risk, by timing of physical activity

	Cases (*n* = 472), *n* (%)	Controls (*n* = 443), *n* (%)	Age-, race-, and BMI-adjusted OR (95% CI)	Multivariate-adjusted OR (95% CI)*
Physical activity from age 10 to 19 y				
Total physical activity (MET-h/wk)				
<43.2	292 (62)	246 (56)	1.0	1.0
43.2-91.8	110 (23)	142 (32)	0.68 (0.50-0.92)	0.66 (0.47-0.92)
≥91.9	70 (15)	55 (12)	1.07 (0.72-1.60)	1.15 (0.75-1.78)
			P_{trend} = 0.49	P_{trend} = 0.64
Physical activity from age 20 to 30 y				
Total physical activity (MET-h/wk)				
<43.2	203 (43)	146 (33)	1.0	1.0
43.2-91.8	138 (29)	129 (29)	0.77 (0.55-1.06)	0.77 (0.54-1.09)
≥91.9	131 (28)	168 (38)	0.57 (0.42-0.79)	0.60 (0.43-0.85)
			P_{trend} = 0.0006	P_{trend} = 0.004
Physical activity from age 40 y to reference age†				
Total physical activity (MET-h/wk)				
<43.2	218 (47)	158 (37)	1.0	1.0
43.2-91.8	129 (28)	119 (28)	0.82 (0.59-1.14)	0.87 (0.61-1.23)
≥91.9	119 (26)	153 (36)	0.60 (0.44-0.83)	0.64 (0.45-0.91)
			P_{trend} = 0.002	P_{trend} = 0.01
Physical activity during 10 y before reference age				
Total physical activity (MET-h/wk)				
<43.2	261 (55)	202 (46)	1.0	1.0
43.2-91.8	117 (25)	107 (24)	0.92 (0.66-1.27)	0.95 (0.67-1.35)
≥91.9	94 (20)	134 (30)	0.60 (0.43-0.84)	0.64 (0.45-0.91)
			P_{trend} = 0.004	P_{trend} = 0.02

*OR and 95% CI were adjusted for age, race/ethnicity, education, family history of endometrial cancer, age at menarche, full-term pregnancies, duration of oral contraceptive use, duration of hormone therapy use, menopausal status, BMI, and height.
†Excludes 6 cases and 13 controls ages <40 y.

Discussion

The present population-based case-control study is one of only a few studies that assessed endometrial cancer risk in relation to lifetime physical activity from multiple sources. Greater total lifetime physical activity was associated with a 39% risk reduction, which is consistent with an average risk reduction of about 30% found in other studies that assessed total physical activity (1, 3). Our findings further suggest that overweight and obese women may derive the greatest benefit from physical activity, although differences between the subgroups did not reach statistical significance in the present study.

The consideration of all sources of physical activity throughout life likely reduced misclassification bias. For example, non-exercisers may have physical activity from other sources, and thus may not truly be sedentary. As in most other studies, we relied on recall of physical activity and did not measure sedentary activities, which may have introduced some measurement error, particularly because we assessed lifetime history of physical activity. Given that both cohort and case-control studies have reported inverse associations of similar magnitude (average of 23% and 29%, respectively, comparing the most active to the least active women; ref. 2), it is unlikely that the risk reduction observed in this study, as well as in other case-control studies, is solely due to differential recall by cases and controls.

Because few studies assessed lifetime history of physical activity, data are sparse on the effects of physical activity in different life periods. Our findings suggest that physical activity throughout adult life is important, with risk reductions of similar magnitude for physical activity during the reproductive years, older adulthood, and the 10-year period before diagnosis. A recent review concluded that recent activity and lifetime activity may be more important than activity in the distant past (3). We also found no evidence that physical activity at ages 10 to 19 years was associated with endometrial cancer risk, although we cannot exclude the possibility that physical activity in the distant past may be recalled with less accuracy than recent activity.

When we classified reported activities according to intensity, we found a highly significant inverse trend for moderate activities, with a risk reduction of 56% associated with the highest level of activity. Similarly, other

Table 4. Lifetime physical activity and endometrial cancer risk, by BMI

	Average lifetime physical activity (MET-h/wk)					
	<65.1*			>65.1*		
	Cases	Controls	OR (95% CI)†	Cases	Controls	OR (95% CI)†
BMI <25	105	100	1.0	59	74	0.95 (0.57-1.58)
25-29	81	72	1.0	52	84	0.58 (0.34-0.99)
≥30	113	49	1.0	62	64	0.50 (0.28-0.91)
BMI <25	105	100	1.0	59	74	0.90 (0.56-1.43)
25-29	81	72	1.39 (0.88-2.20)	52	84	0.85 (0.52-1.38)
≥30	113	49	3.10 (1.91-5.01)	62	64	1.57 (0.94-2.62)
			P for interaction = 0.43			

*Below and above the median.
†OR and 95% CI were adjusted for age, race/ethnicity, education, family history of endometrial cancer, age at menarche, full-term pregnancies, duration of oral contraceptive use, duration of hormone therapy use, menopausal status, and height.

studies reported inverse associations for light to moderate activities such as household activities (23), regular walking and light gardening (8, 22), and walking for transportation (11, 23). This finding is important because moderate activities, particularly at older ages, are easier to adopt and maintain than strenuous activities.

Given that obesity is a strong risk factor for endometrial cancer and correlated with physical inactivity, we adjusted the analyses for the effect of BMI and, through stratified analyses, we explored whether BMI has a modifying effect on the inverse association with physical activity. Consistent with other studies (2), we found that adjustment for BMI and other risk factors only slightly attenuated the inverse associations, and as some other studies have reported (10, 14-16, 18, 25), we found inverse associations with physical activity to be more pronounced in overweight and obese women. Among obese control women, those who were active (≥65.1 lifetime MET-h/wk) had a lower median BMI (33.8) than those who were inactive (34.7). This finding minimizes the possibility that the inverse association with physical activity observed in obese women was solely due to inaccurate reporting. Given the limited sample size in most studies, including ours, larger studies will be needed to assess the modifying effects of BMI with greater precision before firm conclusions can be drawn.

Endometrial cancer risk is strongly associated with the estrogen/progesterone ratio which is skewed toward elevated estrogen levels; this can result from either an absolute progesterone deficit or an estrogen excess (35). Our findings are consistent with the hypothesis that physical activity may reduce endometrial cancer risk by lowering exposure to estrogen, either directly or through lowering of excess adipose tissue (36). Several cross-sectional studies in postmenopausal women reported lower estrogen levels in physically active women, which was independent of body weight (37-39), and a recent intervention study showed that moderate exercise leading to loss in body fat reduced circulating estrogen levels (40). It has also been suggested that even in the absence of weight loss, physical activity may improve insulin sensitivity and affect bioavailable estrogen (14). Other biological mechanisms may involve effects on inflammation and immune function (3, 36).

In conclusion, the present results add to the growing epidemiologic evidence that physical activity is an important modifiable lifestyle factor affecting the development of endometrial cancer. Given that few risk factors identified to date are potentially modifiable, the findings of this study are of direct public health relevance. Current U.S. guidelines for adults recommend 2.5 h/wk of moderate-intensity physical activity, with additional health benefits conferred by 5 h/wk of moderate activity (41). This level of activity roughly corresponds to the ≥6.9 h/wk of moderate activity that was associated with decreased endometrial cancer risk in the present study. Increases in physical activity are likely to decrease obesity, which has been estimated to account for half of all endometrial cancer cases (42), thereby lowering the incidence of endometrial cancer.

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No potential conflicts of interest were disclosed.

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