Physical Activity and Risk of Endometrial Cancer: A Report from the Shanghai Endometrial Cancer Study

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Abstract

We evaluated the type and amount of physical activity associated with risk of endometrial cancer. In this population-based case-control study, in-person interviews were completed among 832 incident endometrial cancer cases and 846 age-matched controls. Physical activity from exercise, household activities, and transportation was assessed in adolescence and adulthood, as was lifetime occupational activity. Logistic regression was used to estimate adjusted odds ratios (OR) and 95% confidence limits (95% CL). Women reporting exercise participation in both adolescence and adulthood were at nearly a 40% reduced risk (OR, 0.63; 95% CL, 0.42-0.95), compared with women reporting no exercise in either life period. Postmenopausal women who initiated exercise in adulthood were also at reduced risk (OR, 0.76; 95% CL, 0.56-1.02). Reductions in risk were also observed for common lifestyle activities, including household activity (both life periods) and walking for transportation (adulthood). Examination of the independent and combined effect of exercise and lifestyle activities revealed that women with less active lifestyles but who reported exercise were at 35% reduced risk (OR, 0.65; 95% CL, 0.41-1.02), whereas nonexercisers with more active lifestyles were at 40% to 45% reduced risk. These findings suggest that both lifestyle activities of lower intensity (e.g., walking and doing household chores) and intentional exercise can reduce endometrial cancer risk. (Cancer Epidemiol Biomarkers Prev 2005;14(4):779–85)

Introduction

Endometrial cancer accounts for about 5% of all cancers among women in more developed countries of the world (1), and it is the most prevalent gynecologic cancer and fourth most frequently diagnosed cancer among women in the United States (2). In Shanghai, China, the age-adjusted incidence of endometrial cancer increased by 75% between 1972 to 1974 and 1993 to 1994 (3, 4). These striking increases in the incidence of this disease in Shanghai parallel marked weight gain among women in China that has been linked, in part, to physical inactivity (5, 6).

Nongenetic factors have been estimated to account for nearly 80% of endometrial cancer cases (7), and physical inactivity has been found an important and potentially modifiable risk factor for this disease. For example, four (7-10) of seven (57%; refs. 11-13) prospective studies and 9 (14-22) of 10 (90%; ref. 23) case-control studies have suggested that lower levels of physical activity increase risk for endometrial cancer. The average risk reduction in these studies has been roughly 30% to 50%, and only one of these reports has suggested that higher levels of activity increase risk (11). Whereas a number of studies have reported benefit from both occupational (9, 20, 24) and nonoccupational activity (10, 14, 18, 20), our understanding of the amount and intensity of activity that may confer benefit and the influence of changes in activity patterns over the life course remain incomplete.

Accordingly, the purpose of this research was to examine the relationship between newly diagnosed endometrial cancer and a broad range of physical activity behaviors (i.e., household, occupation, walking and cycling for transportation, and exercise). In particular, we considered the type/intensity and duration of activity and the effect of changes in exercise behaviors between adolescence and adulthood on risk.

Materials and Methods

The Shanghai Endometrial Cancer Study was designed to evaluate the genetic and lifestyle factors associated with endometrial cancer risk. Incident cases who were permanent residents of urban Shanghai (age 30-69 years) were identified from the Shanghai Cancer Registry between January 1997 and December 2001. The diagnosis of each case was confirmed by medical chart review and a review of the available pathology slides by senior study pathologists. In-person interviews were completed for 832 of 982 (85%) eligible cases. Among case nonparticipants, 73 (7%) declined participation, 36 (4%) were deceased, 22 (2%) could not be located, 10 (1%) were absent during the study period, and 9 (1%) were excluded for miscellaneous reasons. Controls, frequency matched to cases by age (±5 years), were randomly selected from permanent female residents using the Shanghai Resident Registry. Women who had a hysterectomy were not eligible. Eligible controls (n = 1,165) were identified for possible participation and 846 women (73%) were interviewed for the study. Among control nonparticipants, 277 (24%) declined participation and 42 (4%) were absent during the study period. Trained retired nurses and physicians recruited, consented, and completed structured in-person interviews to gather information about demographic factors, menstrual and reproductive history, hormone use, usual dietary intake, prior disease history, tobacco and alcohol use, family history of cancer, and height and weight history during adolescence and adulthood. Each participant also had a number of anthropometric indices measured using a standard protocol (current weight, height, and waist and hip circumference; ref. 25).

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Physical activity patterns were also assessed during the in-person interview. Regular exercise and sport participation was evaluated for adulthood (past 10 years) and adolescence (13-19 years). Up to five exercise activities were reported in each life period, and quantitative data were obtained for each (i.e., type, duration, years of participation). These data were summarized in terms of intensity [metabolic equivalents (MET)], duration (hours/wk), years of participation, as an average energy expenditure in the period (MET-hours per week per year) using standard methods (26). Women reported each occupation they held for at least 3 years during their lifetime and the calendar year in which they started and ended each job. Occupations were classified into high, medium, or low levels of estimated sitting time and activity level using job codes. For example, occupations categorized into the high sitting time and low-activity categories were clerical workers, government and business clerks, and accountants, whereas occupations categorized into the low sitting time and higher-activity categories were sales clerks, cooks, and machine operators. For each occupation, participants also reported the average time they spent ''standing or walking'' (hours/d) and classified each occupation into one of four activity categories (i.e., heavy, medium, light, or nonphysical work). Multiplying years spent in each occupation by the specific activity variable and summing the result over all occupations calculated summary occupational indices. Time spent in several common nonoccupational (or lifestyle activities) were also evaluated in both adolescence and adulthood [i.e., walking for transportation (minutes/d), cycling for transportation (minutes/d), and housework (hours/d)]. Summary energy expenditure values (MET-hours/d) for lifestyle activities were estimated using the following MET values: housework, 2.0 METs; walking, 3.3 METs; and cycling, 4.0 METs, using relevant compendium values as a reference (26). One MET-hour/d is roughly equivalent to 1 kcal per kg per day or about 15 minutes of participation in a moderate intensity (4 METs) activity for an average adult (27). We have evaluated a similar physical activity assessment instrument among women in Shanghai and found it reasonable measure of physical activity in this population (28).

Statistical Analysis. Unconditional logistic regression models were used to estimate odds ratios (OR) and their 95% confidence limits (95% CL), test for multiplicative interaction, and adjust for confounding (29). Potential confounding factors evaluated included age, education, family income, age at menarche, oral contraceptive use, number of pregnancies, menopausal status, age at menopause, height, body mass index, waist-to-hip ratio, and family history of cancer. Hormone replacement therapy is very uncommon among Chinese women and its use was not related to endometrial cancer risk (i.e., 4.2% for cases and 4.0% for controls). The quantile distributions among controls were used to select cut points to classify continuous exposure variables. Linear trends in the risk estimates for physical activity were tested statistically by entering the categorized ordinal variables for the physical activity exposures in the models. Multiplicative interactions were examined by fitting the two exposure variables and their cross-product terms in the logistic model. Body mass index was evaluated as both a confounder and an effect modifier, and stratified analyses were completed by prediagnosis menopausal status.

Results

The average age of participants was 55.3 years and there were no differences in age by disease status ($P = 0.65$). Women with more education, later age at menopause, family history of cancer, greater height, greater body mass index, and a higher waist-to-hip ratio were at increased risk; whereas women with a later age at menarche, more pregnancies, reporting oral contraceptive use in formulations primarily containing both estrogen and progesterone, and that currently smoked or ever reported alcohol consumption were at reduced risk (Table 1). Family income, a family history of endometrial cancer, and hormone replacement therapy use were not associated with risk. Among the population-based controls, the majority of women (50-60%) reported no exercise in adolescence or adulthood, and fewer than 10% reported exercise in both life periods. The prevalence of exercise in adolescence among premenopausal women was about twice that of postmenopausal women (20.7% versus 8.6%). Whereas exercise participation in adulthood was more prevalent among postmenopausal compared with premenopausal women (32.8% versus 12.3%), about two thirds of women (67.2%) reported no exercise participation in adulthood (Fig. 1).

Exercise participation in both adolescence and adulthood was associated with a 30% to 40% reduction in risk for both premenopausal and postmenopausal women. Among these women, 75% reported at least 6 years of exercise participation and >2 MET-hours per day per year of exercise energy expenditure or about 30 minutes/d of moderate intensity activity (4 METs). Total exercise energy expenditure accumulated in both life periods was inversely associated with endometrial cancer risk (Table 2). Examination of exercise effects using mutually exclusive classifications in each life period (Table 2, *bottom rows*) indicated that postmenopausal women who initiated exercise in adulthood were at about a 25% reduced risk (OR, 0.76; 95% CL, 0.56-1.02) compared with women who reported no exercise participation. Exercise only in adolescence reduced risk by about 20%, although the confidence intervals included the null.

In general, we found no consistent associations between occupational physical activity and endometrial cancer, using either job code information or methodologically stronger self-reports of individual occupational activity exposures (e.g., self-rating and time standing and walking; Table 3). Women with jobs thought to require more sitting time were associated with increased risk among premenopausal women but reduced risk among postmenopausal women (Table 3). These results remained unchanged even after further controlling for exercise participation in adolescence and adulthood (data not shown).

Evaluation of common nonexercise or lifestyle activities, revealed inverse associations between endometrial cancer and household activity (both life periods) and walking for transportation (adulthood). There was no apparent association with cycling for transportation, but only about 20% of women reported this activity in adulthood. Total household activity in both life periods was also inversely associated with risk ($P_{trend} < 0.01$). Inverse relationships were present for total lifestyle activity accumulated in each life period, and maximal reductions in risk of 30% to 40% were evident in comparing the upper to the lower quartiles of activity (Table 4, *bottom row*).

In detailed analyses by menopausal status, there was a suggestion of stronger effects of household and walking activities in adulthood among premenopausal compared with postmenopausal women (roughly 50% versus 30% reduced risk), although this effect was not evident when total lifestyle activity in adulthood was evaluated. Total lifestyle activity reported in adolescence was associated with reduced risk among both postmenopausal and premenopausal women ($OR_{premenopausal}$, 0.83; 95% CL, 0.49-1.40; $OR_{postmenopausal}$, 0.51; 95% CL, 0.35-0.74), although the point estimate did not reach significance for premenopausal women. We found no evidence of striking differences in risk by menopausal status for walking for transportation in adolescence or adulthood. To delineate the independent and combined effects of exercise and lifestyle activity reported in adulthood, we evaluated the joint effect of these exposures using a common referent group (i.e., nonexercisers in the lower quartile of lifestyle activity; Fig. 2). Women with the least active lifestyles (<7.30 MET-hours/d), but that reported exercise participation were at lower risk (OR, 0.65; 95% CL, 0.41-1.02). Similarly, women with more active lifestyles (≥9.85 MET-hours/d) but that did not exercise were at 40% to 45% lower risk ($P < 0.05$).

We also carefully evaluated our main results for effect modification and confounding by body mass index and found no significant multiplicative interactions ($P > 0.05$) or major differences in stratum specific risk estimates for our main results. Similarly, body mass index did not seem a strong confounding factor with the physical activity/endometrial cancer association in these data.

Table 1. Descriptive comparisons between cases (*n* = 832) and controls (*n* = 846) on endometrial cancer risk, the Shanghai Endometrial Cancer Study (1997-2001)

	Case/controls*	OR (95% CI)
Education		
No formal education	75/108	1.00
Elementary	129/126	1.47 (1.01-2.16)
Junior high school	296/286	1.49 (1.07-2.09)
High school	207/227	1.31 (0.93-1.86)
Post-high school/college	125/99	1.82 (1.22-2.70)
Family income (Yuan)		
<10,000	95/89	1.00
10,000-15,000	199/194	0.96 (0.68-1.36)
15,000-20,000	166/155	1.00 (0.70-1.44)
20,000-30,000	197/244	0.76 (0.54-1.07)
>30,000	174/163	1.00 (0.70-1.43)
Reproductive factors		
Age at menarche (y)		
9-12	108/78	1.00
13-14	334/301	0.81 (0.58-1.12)
15	167/178	0.68 (0.48-0.98)
>16	221/287	0.56 (0.40-0.79)
No. pregnancies		
0/1	199/144	1.00
2	199/208	0.69 (0.52-0.93)
3	194/207	0.68 (0.51-0.91)
4	141/157	0.65 (0.48-0.89)
>5	99/130	0.55 (0.39-0.77)
Menopause		
No	327/300	1.00
Yes	505/546	0.85 (0.70-1.03)
Age at menopause (y)		
17-46	69/132	1.00
47-48	90/117	1.45 (0.97-2.16)
49-50	146/155	1.78 (1.23-2.57)
>51	199/142	2.64 (1.84-3.79)
Oral contraceptive use		
Never	685/639	1.00
Ever	147/207	0.66 (0.52-0.84)
Lifestyle factors		
Current smoker		
No	823/816	1.00
Yes	7/25	0.28 (0.12-0.65)
Drink ever		
No	812/804	1.00
Yes	20/42	0.47 (0.27-0.81)
Family history of cancer		
No	535/613	1.00
Yes	289/228	1.45 (1.18-1.79)
Body size		
Height (cm)		
140-152	148/184	1.00
153-156	201/195	1.26 (0.94-1.69)
157-160	246/247	1.22 (0.92-1.61)
160-174	233/218	1.31 (0.99-1.74)
Body mass index (kg/m^2)		
14.5-21.3	120/211	1.00
21.4-23.5	166/198	1.40 (1.04-1.90)
21.6-26.1	214/216	1.66 (1.24-2.21)
26.2-41.9	323/216	2.50 (1.90-3.31)
Waist/hip ratio		
0.60-0.77	99/203	1.00
0.78-0.80	136/190	1.44 (1.04-1.99)
0.81-0.84	237/215	2.22 (1.64-2.99)
0.85-1.21	356/234	3.06 (2.29-4.08)

Abbreviation: 95% CI, 95% confidence interval.

**n* values for cases and controls may be <832/846 due to missing data for some variables.

Discussion

The present findings are consistent with the growing body of literature indicating that high levels of physical activity are associated with reduced risk for endometrial cancer (8, 18, 19, 30). In this research, long-term exercise participation and high levels of common nonexercise or lifestyle activities (e.g., housework and walking for transportation) were associated with 30% to 40% reductions in risk. Our finding that higher levels of household activity and walking support the idea that broad range of lower intensity activities provide important benefit in terms of endometrial cancer risk.

The biological mechanisms through which physical activity influences the natural history of endometrial cancer are believed to be related to hormonal and insulin mediated pathways. Hyperinsulinemia has been linked to reduced sex hormone–binding globulin, which may cause increased estrogen and androgen exposures in endometrial tissue (31). Hyperinsulinemia also increases circulating insulin-like growth factor-I directly, whereas also reducing its binding protein-1 in endometrial tissue, both of which may increase tissue levels of bioavailable insulin-like growth factor-I (31). Higher levels of physical activity are associated with reduced insulin levels (32) and insulin sensitivity (33, 34) and therefore would be predicted to reduce exposure to bioavailable hormones and growth factors. The permissive influence of insulin on hormonal and growth factor exposure is plausible in both premenopausal and postmenopausal women. However, among postmenopausal women, where estrogen exposure is primarily determined by conversion of androgens from adipose tissue (35), physical activity effects on disease risk may be derived through its influence on energy balance and adipose accumulation. Higher physical activity levels have been associated with lower levels of adiposity in Chinese women (6), and reductions in adiposity via increased physical activity levels have been shown to reduce free estradiol levels (36).

There are several strengths and limitations to this research that should be considered when interpreting our results. First, like other case-control studies, recall bias is a concern. However, the consistency of our findings with a number of prospective studies (7-10) suggests that recall bias did not seem a major concern. Selection bias is also possible. Whereas this population-based study with true community controls had reasonably high response rates for both cases (85%) and controls (73%), the modest differences in these rates between comparison groups indicates some potential for the introduction of bias. However, if selection bias were present, we believe that it would be expressed most acutely in the exercise exposure data because participants in research studies are often more health conscious than nonparticipants. Our finding of a protective association in both exercise and nonexercise activity commonly done by most participants argues against a selection bias in our results. The validity of self-reported physical activity is also a concern. Our validation work with a nearly identical version of the physical activity assessment used in this research supports the ability of this instrument to stratify women into high and low activity levels for the physical activity domains we examined in this research, even light to moderate intensity

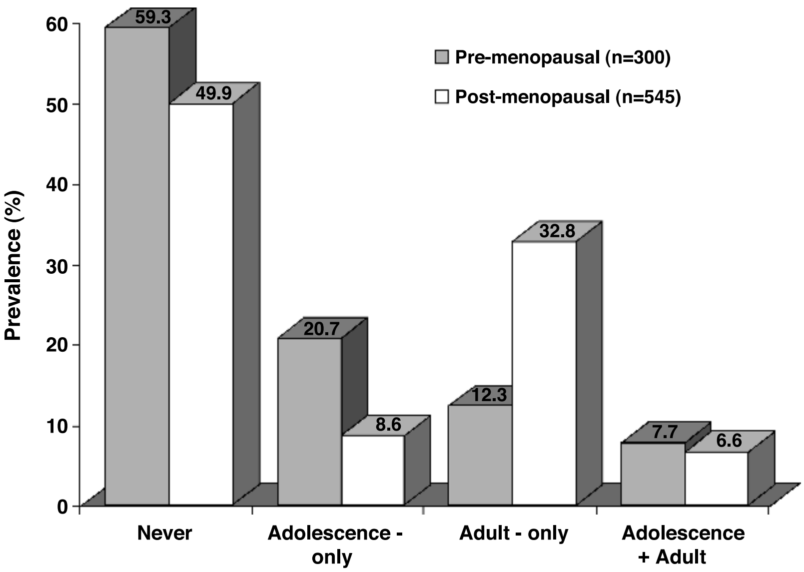

Figure 1. Prevalence of exercise participation among control women by life period and menopausal status.

household activity (28). A notable strength of this instrument was that it examined a broad range of physical activities and particularly household activities. Household activity is an important source of energy expenditure among women (37).

It is not immediately clear why we did not observe an inverse association between occupational physical activity and endometrial cancer, as have a number of previous studies (9, 20). It may be that the measures of occupational activity we used in this research were not sufficiently precise to identify the association. Indeed, our finding of apparent modification of the occupational sitting time variable by menopausal status was unexpected and may be due to the inherent limitations in using job codes to estimate physical activity levels. It is also possible that occupational activity levels in this study were relatively homogenous and that the major differences in their overall activity patterns were determined by nonoccupational activity. We also observed a possible differential effect on the type of adolescent physical activity by menopausal status. That is, the effect of exercise in adolescence seemed to reduce risk for premenopausal but not postmenopausal women (Table 2, *top*), and the effect for total lifestyle activity reported in adolescence seemed stronger among postmenopausal compared with premenopausal women (see Results). There are several possible explanations for these findings. It may be that domain-specific activity levels differed by life period and age in these women. For example, 20.7% of premenopausal women

Table 2. Exercise in adolescence, adulthood, and in mutually exclusive life periods in relation to endometrial cancer risk, the Shanghai Endometrial Cancer Study (1997-2001)

	Cases/controls*	All women, OR† (95% CI)	Premenopausal, OR† (95% CI)	Postmenopausal, OR† (95% CI)
Adolescence (MET-h/d/y)				
None	679/666	1.00	1.00	1.00
0.1-0.9	57/46	1.17 (0.76-1.80)	1.24 (0.67-2.31)	1.00 (0.53-1.89)
1.0-1.7	20/46	0.39 (0.22-0.68)	0.50 (0.20-1.24)	0.35 (0.17-0.74)
1.8-3.5	43/41	0.89 (0.56-1.44)	0.91 (0.46-1.82)	0.85 (0.43-1.69)
3.6-17.6	33/47	0.63 (0.39-1.04)	0.37 (0.17-0.77)	1.17 (0.57-2.38)
P_{trend}		0.02	0.02	0.42
Adult (MET-h/d/y)				
None	579/559	1.00	1.00	1.00
0.1-0.5	59/83	0.67 (0.46-0.97)	0.75 (0.36-1.54)	0.62 (0.40-0.98)
0.6-1.2	73/67	0.93 (0.64-1.36)	1.32 (0.58-2.96)	0.85 (0.55-1.31)
1.3-2.6	67/69	0.86 (0.58-1.26)	0.81 (0.35-1.85)	0.86 (0.56-1.34)
2.7-11.3	54/69	0.76 (0.50-1.13)	0.75 (0.32-1.75)	0.77 (0.48-1.22)
P_{trend}		0.12	0.54	0.19
Total (MET-h/d/y)				
None	479/450	1.00	1.00	1.00
0.1-0.7	100/105	0.84 (0.60-1.16)	1.22 (0.68-2.19)	0.67 (0.45-1.00)
0.8-1.8	101/101	0.89 (0.64-1.24)	0.98 (0.55-1.78)	0.83 (0.56-1.24)
1.9-3.4	84/94	0.74 (0.53-1.05)	0.78 (0.43-1.40)	0.73 (0.48-1.13)
3.5-19.1	68/96	0.60 (0.42-0.86)	0.45 (0.25-0.83)	0.69 (0.44-1.10)
P_{trend}		<0.01	0.02	0.06
Mutually exclusive life periods				
Never	479/450	1.00	1.00	1.00
Adolescent-only	100/109	0.79 (0.57-1.10)	0.81 (0.52-1.27)	0.76 (0.45-1.27)
Adult-only	200/216	0.81 (0.63-1.05)	0.99 (0.59-1.68)	0.76 (0.56-1.02)
Adolescent + adult	53/70	0.63 (0.42-0.95)	0.57 (0.28-1.17)	0.69 (0.41-1.14)
P_{trend}		0.01	0.23	0.03

Abbreviation: 95% CI, 95% confidence interval.

**n* values for all cases and controls.

†Adjusted for age, age at menarche, menopausal status and age, number of pregnancies, oral contraceptive use, current smoking, ever drinking, family history of cancer, education, height, and body mass index.

Table 3. Occupational physical activity and endometrial cancer risk, the Shanghai Endometrial Cancer Study (1997-2001)

Job code indices	Cases/controls*	All women, OR† (95% CI)	Premenopausal, OR† (95% CI)	Postmenopausal, OR† (95% CI)
Sitting				
Q1 (less)	190/206	1.00	1.00	1.00
Q2	205/210	0.98 (0.73-1.33)	1.32 (0.81-2.14)	0.81 (0.55-1.19)
Q3	214/213	0.96 (0.71-1.31)	1.34 (0.83-2.18)	0.75 (0.50-1.14)
Q4 (more)	223/216	0.93 (0.67-1.30)	1.90 (1.04-3.49)	0.64 (0.42-0.99)
P_{trend}		0.67	0.05	0.05
Activity energy expenditure				
Q1 (less)	213/212	1.00	1.00	1.00
Q2	209/213	0.80 (0.60-1.08)	0.67 (0.42-1.07)	0.96 (0.65-1.43)
Q3	221/203	1.05 (0.78-1.42)	0.95 (0.60-1.50)	1.15 (0.76-1.72)
Q4 (more)	189/203	0.86 (0.63-1.18)	0.75 (0.41-1.38)	0.89 (0.60-1.32)
P_{trend}		0.70	0.57	0.68
Self-rating of exertion				
Q1 (less)	208/204	1.00	1.00	1.00
Q2	221/221	0.99 (0.74-1.32)	1.00 (0.63-1.57)	1.08 (0.73-1.61)
Q3	203/205	0.97 (0.72-1.32)	0.79 (0.49-1.26)	1.15 (0.77-1.74)
Q4 (more)	199/215	0.87 (0.64-1.20)	0.79 (0.46-1.37)	0.96 (0.64-1.44)
P_{trend}		0.42	0.28	0.82
Standing and walking (h/d)				
0-1.6	339/332	1.00	1.00	1.00
1.7-3.3	218/212	0.96 (0.74-1.25)	0.92 (0.59-1.41)	0.96 (0.68-1.33)
3.4-5.5	144/177	0.81 (0.61-1.07)	0.85 (0.54-1.34)	0.78 (0.54-1.14)
5.6-13.3	131/123	1.09 (0.79-1.50)	1.20 (0.67-2.14)	1.03 (0.70-1.53)
P_{trend}		0.78	0.93	0.70

Abbreviation: 95% CI, 95% confidence interval.
**n* values for all cases and controls.
†Adjusted for age, age at menarche, menopausal status and age, number of pregnancies, oral contraceptive use, current smoking, ever drinking, family history of cancer, education, height, and body mass index.

reported exercise in adolescence but only 8.6% of postmenopausal women did so. In terms of the possible differential effect of adolescent lifestyle activities by menopausal status ($OR_{premenopausal}$, 0.83; 95% CL, 0.49-1.40; $OR_{postmenopausal}$, 0.51; 95% CL, 0.35-0.74), in detailed analyses, older women (postmenopausal) reported engaging in more lifestyle activity in adolescence than younger women (i.e., 7.0 versus 6.6 hours/d), although these differences were not significant ($P = 0.10$). Another plausible interpretation of these data is that the nonsignificant reduction in risk among premenopausal women is in fact a weaker effect. However, reduced sample size in stratified analyses, particularly for the smaller group of premenopausal women, limits our ability to make precise inference for stratified effects.

Table 4. Lifestyle physical activity and endometrial cancer risk, the Shanghai Endometrial Cancer Study (1997-2001)

	Adolescence			Adulthood	
	Cases/controls*	OR† (95% CI)		Cases/controls	OR† (95% CI)
Household activity (h/d)					
0	242/200	1.00	0-2	331/274	1.00
1	210/213	0.78 (0.59-1.05)	3	219/226	0.81 (0.62-1.05)
2	177/184	0.74 (0.55-1.00)	4	154/183	0.69 (0.51-0.92)
>3	199/247	0.67 (0.50-0.90)	>5	128/162	0.62 (0.46-0.85)
P_{trend}		0.01			<0.01
Walking for transportation (min/d)					
0-25	140/151	1.00	0-26	210/182	1.00
26-52	238/242	1.00 (0.73-1.38)	27-55	236/223	0.87 (0.65-1.17)
53-65	245/240	0.97 (0.71-1.33)	56-60	223/242	0.68 (0.51-0.91)
>66	207/211	0.98 (0.71-1.35)	>61	163/199	0.64 (0.47-0.87)
P_{trend}		0.84			<0.01
Cycling for transportation (min/d)					
No	805/814	1.00	0	648/667	1.00
Yes	25/31	0.77 (0.43-1.37)	2-29	40/27	1.82 (1.07-3.11)
			30-50	67/74	0.88 (0.60-1.29)
			>51	76/75	1.24 (0.86-1.81)
P_{trend}		—			0.44
Total lifestyle activity (MET-h/d)					
0-3.63	229/184	1.00	0-7.29	217/189	1.00
3.64-6.20	240/245	0.71 (0.54-0.95)	7.30-9.83	286/232	0.98 (0.74-1.30)
6.21-8.80	166/172	0.72 (0.53-0.99)	9.84-12.75	145/213	0.57 (0.42-0.78)
>8.81	197/245	0.63 (0.46-0.84)	>12.76	184/212	0.71 (0.52-0.96)
P_{trend}		<0.01			<0.01

Abbreviation: 95% CI, 95% confidence interval.
**n* values for all cases and controls.
†Adjusted for age, age at menarche, menopausal status and age, number of pregnancies, oral contraceptive use, current smoking, ever drinking, family history of cancer, education, height, and body mass index.

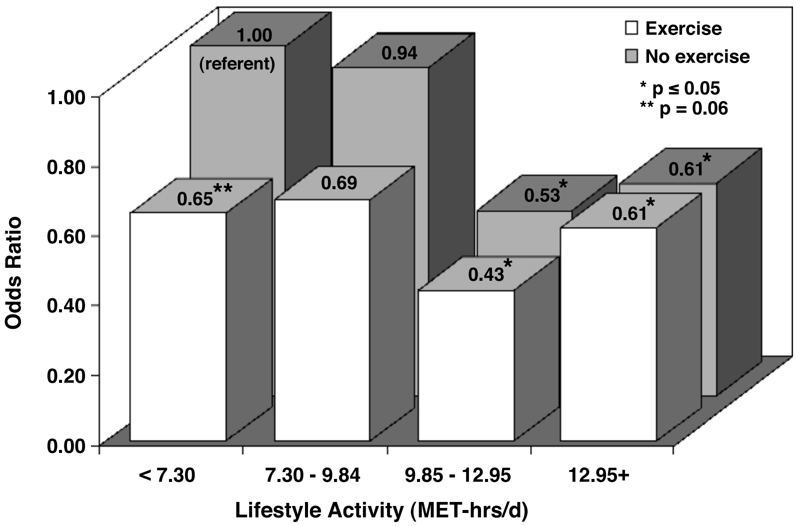

Figure 2. Lifestyle activity and endometrial cancer risk by exercise participation in adulthood. Odds ratio was adjusted for age, age at menarche, menopausal status and age, number of pregnancies, oral contraceptive use, current smoking, ever drinking, family history of cancer, education, height, and body mass index.

Terry et al. (7) estimated that nongenetic factors, including physical activity, were responsible for nearly 80% of endometrial cancer cases in the Swedish Twins cohort study. Physical activity done at work, home, and for transportation has been associated with reductions in risk by about 30% to 40% in most (8, 9, 14, 15, 18, 20) but not all studies (11, 12, 23). A limitation of much of this literature has been the lack of detailed analyses focusing on the type and amount of wide variety of activities on risk. Quantitative estimates of the type and duration activity associated with reduced risk is needed to translate epidemiologic findings into meaningful information for public health officials to use in making evidence-based recommendations for cancer risk reduction (38).

For household activity and walking for transportation in adulthood, we observed graded inverse relationships between these activities and endometrial cancer risk, suggesting that benefit may be derived from modest amounts of activity. Women that reported >26 minutes/d of walking for transportation or >2 hours/d of household activity were at reduced risk. Importantly, we found that women with the lowest levels of household and transportation related activity but that participated in regular exercise were at about 35% lower risk. Similarly, nonexercisers with more active lifestyles were also at reduced risk.

Our finding that participation in exercise and sport activities reduce risk significantly was consistent with a number of other studies (7, 17, 18). The clear benefit from consistent participation across the life course in this research supports the idea that young women should be encouraged to participate in sport and exercise activities in youth and maintain this pattern of activity into middle and older ages. Our finding that fewer than 10% of women in this population reported this pattern of exercise over their lifetime (Fig. 1) suggests that the population-attributable risk for never exercisers would be substantial. We are aware of only one other study that has examined the effect of increasing physical activity over time on subsequent endometrial cancer risk. Moradi et al. (9), examining patterns of change in occupational activity, reported that women who moved from sedentary to highly active occupations were at similar risk as women who remained consistently in highly active occupations. Our finding that postmenopausal women who initiated exercise in adulthood were at a 25% lower risk of endometrial cancer (OR, 0.76; 95% CL, 0.56-1.02) than women who never exercised, suggests that it is possible that women can make changes in their physical activity patterns that will result in risk reduction. However, given the width of the confidence interval in this risk estimate, our results should be interpreted with some caution. We and others have reported that changes in activity levels in later life can reduce breast cancer risk (39-41). Additional research that carefully evaluates changes in activity patterns over the life course is needed to extend our understanding of the potential for physical activity to be recognized as a truly *modifiable* risk factor for cancer.

In conclusion, these findings are consistent with the growing body of literature indicating that high levels of physical activity are associated with reduced risk for endometrial cancer. In this research, long-term exercise participation and high levels of common nonexercise activities were associated with 30% to 40% reductions in risk. Our findings for household activity and walking for transportation support the idea that a broad range of lower intensity activities may provide important benefit. Given the low-level exercise participation among middle-aged and older women in this and other populations (42, 43), this research has important public health consequences in highlighting the potential for both exercise and lifestyle activities to reduce endometrial cancer risk.

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