

Prospective Cohort Study of Pre- and Postdiagnosis Physical Activity and Endometrial Cancer Survival

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PURPOSE The aim of this study was to evaluate associations between pre- and postdiagnosis physical activity and survival in survivors of endometrial cancer by physical activity domain, intensity, dose (metabolic-equivalent task [MET]-hours/week/year), and change from pre- to postdiagnosis.

METHODS We conducted a prospective cohort study in Alberta, Canada, of 425 women who were diagnosed with histologically confirmed invasive endometrial cancer between 2002 and 2006 and observed to 2019. The interviewer-administered Lifetime Total Physical Activity Questionnaire recorded prediagnosis (assessed at a median of 4.4 months after diagnosis) and postdiagnosis physical activity (assessed at a median of 3.4 years after diagnosis). Associations between physical activity and overall and disease-free survival were assessed using Cox proportional hazards models adjusted for age, stage, grade, treatments, body mass index, menopausal status, hormone therapy use, family history of cancer, and comorbidities.

RESULTS After a median follow-up of 14.5 years, there were 60 deaths, including 18 endometrial cancer deaths, and 80 disease-free survival events. Higher prediagnosis recreational physical activity was statistically significantly associated with improved disease-free survival ($> 14 \text{ v } \leq 8$ MET-hours/week/year; hazard ratio [HR], 0.54; 95% CI, 0.30 to 0.96; $P_{\text{trend}} = .04$), but not overall survival (HR, 0.56; 95% CI, 0.29 to 1.07; $P_{\text{trend}} = .06$). Higher postdiagnosis recreational physical activity ($> 13 \text{ v } \leq 5$ MET-hours/week/year) was strongly associated with both improved disease-free survival (HR, 0.33; 95% CI, 0.17 to 0.64; $P_{\text{trend}} = .001$) and overall survival (HR, 0.33; 95% CI, 0.15 to 0.75; $P_{\text{trend}} = .007$). Participants who maintained high recreational physical activity levels from pre- to postdiagnosis also had improved disease-free survival (HR, 0.35; 95% CI, 0.18 to 0.69) and overall survival (HR, 0.43; 95% CI, 0.20 to 0.94) compared with those who maintained low physical activity levels.

CONCLUSION Recreational physical activity, especially postdiagnosis, is associated with improved survival in survivors of endometrial cancer.

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INTRODUCTION

Globally, endometrial cancer is the sixth most common cancer among women.¹ In 2018, endometrial cancer was diagnosed in an estimated 380,000 women and resulted in approximately 90,000 deaths.¹ In Canada, the 5-year survival rate for endometrial cancer is 83%, but mortality rates have worsened by 2% since 1984, making it one of few cancers for which mortality rates are rising.² Obesity and diabetes are strong risk factors for endometrial cancer and survivors are thus also at increased risk of dying from these conditions and related diseases, such as cardiovascular disease^{3,4}; therefore, interventions in this population that improve survival are needed.^{5,6} Whereas physical inactivity is an established risk factor for endometrial cancer incidence, independent of obesity, few studies have examined the associations between physical activity

and endometrial cancer survival.⁷⁻¹⁰ To date, results are inconclusive and limited in scope. Specifically, no studies have examined associations between physical activity and endometrial cancer survival by domain or intensity of activity, nor by change from pre- to postdiagnosis physical activity levels.

The primary objective of this study was to assess the strength of the associations between pre- and postdiagnosis physical activity by domain (total, recreational, household, and occupational), dose, frequency, intensity and duration for overall and disease-free survival. Our secondary objective was to assess the strength of the association between changes from pre- to postdiagnosis physical activity with survival outcomes. We hypothesized that women who accumulated greater amounts of pre- and postdiagnosis physical activity would have better survival outcomes after an endometrial cancer diagnosis.

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Limited research exists on whether physical activity is associated with survival after an endometrial cancer diagnosis. To our knowledge, this study was the first to examine how different domains and intensities of pre- and postdiagnosis physical activity, as well as changes in physical activity from pre- to postdiagnosis, are associated with survival outcomes.

Knowledge Generated

Higher recreational physical activity, especially when done postdiagnosis, was strongly associated with improved overall and disease-free survival after endometrial cancer. The strongest associations with survival were experienced by women who maintained high levels of recreational physical activity throughout their prediagnosis lifetime and into their endometrial cancer survivorship.

Relevance

Staying physically active or becoming physically active after an endometrial cancer diagnosis may improve survival outcomes. Clinicians should recommend physical activity to patients with newly diagnosed endometrial cancer and survivors to improve health-related fitness, quality of life, and possibly even survival.

METHODS

Setting and Participants

Participants were 425 women residing in Alberta, Canada, with histologically confirmed invasive endometrial cancer who participated in a previous case-control study.¹¹ Cases were diagnosed from 2002 to 2006, identified through the Alberta Cancer Registry (ACR), and then observed for survival outcomes. Eligibility criteria were age 30 to 80 years, English speaking, able to complete an in-person interview, and no previous cancer diagnosis, with the exception of non-melanoma skin cancer. Of the 549 patients in the case-control study, eight were ineligible because of misclassification ($n = 1$) or missing data ($n = 7$), 51 died before follow-up data collection, 30 declined participation, and 35 were lost to follow-up, leaving 425 who participated in the follow-up assessments (77%) and who were analyzed in this study¹¹ (Appendix Fig A1, online only). Ethics approval for follow-up and medical record review were received from the ethics boards of the former Alberta Cancer Board, the University of Calgary, and the University of Alberta. All participants provided written informed consent for the cohort study.

Data Collection

Physical activity assessment. We measured prediagnosis physical activity participation using the Lifetime Total Physical Activity Questionnaire, previously tested for reliability.¹² Trained interviewers used cognitive interviewing methods and a recall calendar to assess the frequency, duration, and intensity of occupational, household, and recreational physical activities from childhood until diagnosis.¹³ Baseline assessment occurred at a median of 4.4 months (interquartile range, 3.4-5.7 months) after diagnosis. During in-person follow-up interviews conducted between 2006 and 2011, postdiagnosis physical activity levels were measured for each participant using a modified Lifetime Total Physical Activity Questionnaire that captured

their physical activity since diagnosis. These follow-up assessments occurred at a median of 3.4 years (interquartile range, 3.4-5.7 years) after diagnosis.

Covariates. At baseline assessment, participants reported their demographic characteristics (age at diagnosis, highest education, marital status, race), comorbidities (summarized as a baseline comorbidity score of none, 1, or ≥ 2), menstrual and reproductive history (age at menarche, number of pregnancies ≥ 20 weeks, age at menopause, menopausal status), hormone use history, and first degree family history of uterine or colorectal cancer. Alcohol intake (gram/day/year), smoking habits, diet, and participant height, weight, and waist and hip circumferences were captured at baseline and follow-up. Total caloric intake (kcal/day) was measured using the self-administered Canadian Diet History Questionnaire.¹⁴ Anthropometric measurements were taken in triplicate and averaged using standardized methods and calibrated scales. Postdiagnosis comorbid conditions were determined using the Charlson Comorbidity Index.¹⁵

Chart abstractions and vital status. Between 2006 and 2019, data on staging, treatment, vital status, new primary cancers, and recurrences or progressions were abstracted from medical charts via ACR and Vital Statistics Alberta by health record technicians with no access to the physical activity data. Staging followed the American Joint Committee on Cancer guidelines.¹⁶ Cancer grade was previously determined from tissue samples obtained at hysterectomy and classified by a study pathologist.¹⁷ Participants were observed from cancer diagnosis until death or until the final vital status check on March 20, 2019, whichever occurred first. Cause of death for all cases was ascertained by ACR through linkages with Statistics Canada.

Statistical analyses. We used the Compendium of Physical Activities to assign metabolic equivalent task (MET) values to each self-reported physical activity.¹⁸ One MET is defined

as 1 kcal/kg per hour and is roughly equivalent to the energy cost of sitting quietly. For each individual, total physical activity was estimated as the sum of nonsedentary occupational, household, and recreational activity. Intensities of activity were categorized as light (nonsedentary time < 3 METs), moderate (3-5.9 METs) and vigorous (\geq 6 METs). Sedentary behavior was defined as occupational activity with assigned METs \leq 1.5.

Cox proportional hazards models were used to compute hazard ratios (HRs) for the primary outcomes of (1) disease-free survival, defined as the time to first endometrial cancer recurrence/progression or any death, and (2) overall survival, defined as the time to death from any cause. Sample size was predetermined on the basis of the availability of cases from our previous case-control study of endometrial cancer risk.¹¹ Missing values for covariates, such as smoking, alcohol, and body mass index (BMI; < 3% missing) were replaced by the majority reference group for categorical variables and mean value imputation for continuous variables. We evaluated the proportional hazards assumption by including an interaction term between each physical activity variable and follow-up time. Wald tests were used to select variables for inclusion in Cox proportional hazards models, except for known prognostic variables (age at diagnosis, cancer stage, cancer grade, and primary treatment) which were forced into the model. Women with unknown or nonapplicable cancer grade were grouped as a separate category for adjustment. For postdiagnosis physical activity, we adjusted for time to first new primary cancer as a time-dependent covariate in the analysis of disease-free survival and time to first endometrial cancer recurrence, progression, or new primary cancer in the analysis of overall survival.

We conducted the analysis on pre- and postdiagnosis physical activity based on the overall MET-hour/week/year spent in each of the physical activity domains (total, recreational, occupational, and household) and intensities (nonsedentary total, light, and moderate-to-vigorous physical activity), as well as occupational sedentary behavior. We also assessed interactions between physical activity and age and BMI (at diagnosis and postdiagnosis) as continuous variables by entering their cross-products into multivariable Cox proportional hazards models. The effect of physical activity change pattern from pre- to postdiagnosis on survival outcomes was evaluated by dividing the study population into four subgroups on the basis of participation in low or high amounts of physical activity pre- and postdiagnosis. We used a common median split point for both physical activity assessments, which for recreational physical activity was 10 MET-hours/week/year. Sensitivity analyses excluded women with incomplete cancer stage or assigned a cancer stage category. All tests for statistical significance were based on two-sided Wald tests. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.6.¹⁹

RESULTS

At baseline, participants' median age was 58 years, BMI was 31.0 kg/m², and > 75% were married, White, postmenopausal, and nonsmokers or ex-smokers. Most participants were diagnosed with stage I endometrial cancer (\geq 80%) and had undergone a hysterectomy (97%), with 31% also receiving radiation therapy (Table 1). Compared with participants, nonparticipants were older, had more comorbidities, higher stages and grades of endometrial cancer at baseline, received more chemotherapy treatment, and experienced worse survival outcomes (Appendix Table A1, online only). During the median follow-up of 14.5 years, there were 60 deaths (endometrial cancer-specific deaths [n = 18]; other deaths [n = 42]). A total of 80 unique disease-free survival events occurred (endometrial cancer recurrences [n = 20], disease progression recurrence/disease progression followed by death [n = 22], and deaths [n = 38]).

Prediagnosis Physical Activity and Survival

There was no dose-response relationship between increasing total prediagnosis (ie, lifetime physical activity) and survival outcomes; Table 2. Physical activity performed at higher levels (> 127 MET-hour/week/year) was not associated with disease-free survival or overall survival compared with the lowest tertile of physical activity (\leq 104 MET-hour/week/year). However, compared with women in the lowest tertile, those in the middle tertile for lifetime total physical activity (> 104 to \leq 127 MET-hour/week/year) had an HR of 0.41 (95% CI, 0.20 to 0.85) for overall survival.

When examining survival outcomes by domains of prediagnosis physical activity, we observed a statistically significant improvement (HR, 0.44; 95% CI, 0.22 to 0.90) in overall survival in the middle tertile (> 8 to \leq 14 MET-hour/week/year) versus the lowest tertile (\leq 8 MET-hour/week/year) for recreational physical activity, but not for occupational and household physical activity. Moreover, prediagnosis recreational physical activity was the only domain associated with improved disease-free survival, for which a statistically significant dose-response relationship was also noted (HR, 0.54; 95% CI, 0.30 to 0.96; $P_{\text{trend}} = .04$). Stratification by BMI modified the association for prediagnosis recreational physical activity with overall survival ($P_{\text{interaction}} = .04$). Specifically, participants with a BMI of 30 kg/m² or greater at baseline had improved overall survival with increasing amounts of recreational physical activity ($P_{\text{trend}} = .013$). HR for the highest versus lowest tertile was 0.30 (95% CI, 0.11 to 0.81), whereas participants with a BMI less than 30 kg/m² had an HR of 1.28 (95% CI, 0.45 to 3.64; Appendix Tables A2 and A3, online only). No statistically significant interactions between prediagnosis physical activity with baseline age were noted (results not shown).

TABLE 1. Baseline Descriptive Characteristics of the Alberta Endometrial Cancer Cohort Study Population by Vital Status, 2002-2019 (N = 425)

Characteristic	All (N = 425)	Alive (n = 365)	DFS Events (n = 80)	Overall Deaths (n = 60)
Median age at diagnosis, years (IQR)	58 (54-65)	58 (53-64)	63 (56-71)	65 (58-73)
Highest education				
High school diploma	132 (32.0)	108 (30.5)	31 (40.3)	24 (40.7)
Nonuniversity certificate	189 (45.8)	161 (45.5)	36 (46.8)	28 (47.5)
University degree	92 (22.3)	85 (24.0)	10 (13.0)	7 (11.9)
Married or common in-law	396 (93.2)	339 (92.9)	75 (93.8)	57 (95.0)
White	407 (96.7)	347 (96.1)	76 (95.0)	60 (100.0)
Median age at menarche, years (IQR)	12 (11-13)	12 (11-13)	12 (11-13)	12 (11-14)
No. of pregnancies ≥ 20 weeks gestation				
0	75 (18.2)	67 (18.9)	14 (18.2)	8 (13.6)
1-2	179 (43.3)	159 (44.9)	26 (33.8)	20 (33.9)
> 2	159 (38.5)	128 (36.2)	37 (48.1)	31 (52.5)
Median age at menopause, years (IQR)	51 (49-54)	51 (49-54)	50 (47-53)	50 (47-53)
Menopausal status				
Pre- and perimenopausal	100 (24.3)	94 (26.4)	13 (16.9)	6 (6.2)
Postmenopausal	312 (75.7)	259 (73.4)	64 (83.1)	53 (89.8)
Overall AJCC stage				
I	340 (80.0)	301 (82.5)	46 (57.5)	39 (65.0)
II	55 (12.9)	44 (12.1)	16 (20.0)	11 (18.3)
III	20 (4.7)	13 (3.6)	9 (11.3)	7 (11.7)
IV	4 (0.9)	3 (0.8)	3 (3.8)	1 (1.7)
Incomplete	6 (1.4)	4 (1.1)	6 (7.5)	2 (3.3)
FIGO grade, %				
< 6	238 (56.0)	211 (57.8)	36 (45.0)	27 (45.0)
6-50	102 (24.0)	90 (24.7)	16 (20.0)	12 (20.0)
> 50	50 (11.8)	36 (9.9)	18 (22.5)	14 (23.3)
Other	35 (8.2)	28 (7.7)	10 (12.5)	7 (11.7)
Primary treatment ^a				
Surgery	416 (97.9)	359 (98.4)	72 (90.0)	57 (95.0)
Chemotherapy	28 (6.6)	22 (6.0)	7 (8.8)	6 (10.0)
Hormone therapy	4 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)
Radiation therapy	131 (30.8)	110 (30.1)	28 (35.0)	21 (35.0)
First-degree family history of uterine or colorectal cancer	65 (15.8)	51 (14.5)	17 (21.5)	14 (23.3)
Ever had hormone therapy	141 (34.3)	130 (36.8)	15 (19.7)	11 (19.0)
Ever had myocardial infarction ^b	7 (1.7)	5 (1.4)	2 (2.5)	2 (3.3)
Ever had type II diabetes ^b	50 (11.8)	38 (10.4)	14 (17.5)	12 (20.0)
Ever had angina pectoris ^b	17 (4.0)	12 (3.3)	5 (6.3)	5 (8.3)
Ever had hypertension ^b	129 (31.2)	100 (28.3)	31 (40.3)	29 (49.2)
Ever had pulmonary embolism ^b	7 (1.7)	4 (1.1)	3 (3.8)	3 (5.1)
Ever had thrombosis ^b	25 (5.9)	18 (4.9)	8 (10.0)	7 (11.7)
Ever had a stroke ^b	3 (0.7)	2 (0.6)	1 (1.3)	1 (1.7)
Ever had high cholesterol or triglycerides ^b	134 (31.5)	108 (29.6)	34 (42.5)	26 (43.3)

(continued on following page)

TABLE 1. Baseline Descriptive Characteristics of the Alberta Endometrial Cancer Cohort Study Population by Vital Status, 2002-2019 (N = 425) (continued)

Characteristic	All (N = 425)	Alive (n = 365)	DFS Events (n = 80)	Overall Deaths (n = 60)
Type of smoker				
Nonsmoker	208 (50.4)	178 (50.3)	40 (52.0)	30 (50.9)
Current smoker	56 (13.6)	44 (12.4)	13 (16.9)	12 (20.3)
Ex-smoker	131 (31.7)	115 (32.5)	23 (29.9)	16 (27.1)
Occasional smoker	18 (4.4)	17 (4.8)	1 (1.3)	1 (1.7)
BMI, kg/m ² (IQR)	31.0 (26.0-36.9)	30.9 (25.9-36.1)	31.1 (27.2-37.3)	31.4 (27.2-37.9)
Waist circumference, cm (IQR)	95.5 (83.6-109.0)	95.0 (82.9-107.8)	98.9 (87.0-116.9)	100.0 (85.0-116.9)
Total caloric intake, kcal/day (IQR)	1,481 (1,158-1,876)	1,491 (1,188-1,868)	1,347 (1,059-1,916)	1,333 (1,032-1,982)
Alcohol intake, gram/day/year (IQR)	1.0 (0.3-2.8)	1.1 (0.3-2.9)	0.8 (0.0-2.1)	0.6 (0.0-2.1)
Prediagnosis physical activity, MET-hour/week/year (IQR)				
Total physical activity	116.2 (97.9-138.5)	116.9 (98.6-138.5)	111.1 (93.8-141.2)	107.1 (92.1-139.7)
Recreational physical activity	10.6 (6.7-16.8)	10.9 (7.2-16.8)	8.7 (6.1-15.0)	7.7 (5.6-15.0)
Occupational physical activity	43.2 (31.3-59.0)	43.9 (32.6-60.5)	41.0 (24.3-55.8)	39.4 (23.4-50.0)
Household physical activity	56.1 (40.5-73.1)	55.1 (40.2-72.4)	56.8 (40.9-79.7)	58.2 (44.0-79.4)
Postdiagnosis physical activity, MET-hour/week/year (IQR)				
Total physical activity	85.2 (54.4-116.9)	90.4 (57.4-120.6)	61.6 (37.3-97.4)	60.8 (39.4-92.3)
Recreational physical activity	8.3 (3.0-16.7)	8.8 (3.5-17.4)	4.7 (2.1-10.6)	4.6 (2.3-10.6)
Occupational physical activity	10.2 (0.0-38.2)	11.6 (0.0-41.9)	2.3 (0.0-25.6)	0.1 (0.0-23.3)
Household physical activity	45.3 (30.3-67.2)	46.5 (31.1-68.4)	35.1 (25.2-57.2)	35.2 (26.0-57.2)
Postdiagnosis BMI (IQR)	31.3 (26.6-37.3)	31.3 (26.7-37.0)	31.6 (27.1-38.5)	31.1 (26.2-38.9)
Postdiagnosis Charlson Comorbidity Score (IQR)	1.0 (0.5-2.0)	1.0 (0.5-2.0)	1.5 (0.5-2.5)	1.8 (1.0-3.0)

NOTE. Data presented as No. (%) unless otherwise indicated.

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, body mass index; DFS, disease-free survival; FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile range.

^aThe frequencies for treatment are not mutually exclusive as participants could have multiple treatments.

^bPrediagnosis medical conditions: diabetes, angina pectoris, high cholesterol, pulmonary embolism, myocardial infarction, hypertension, stroke, and thrombosis were summarized to a baseline comorbidity score: none, 1 or ≥ 2 .

Postdiagnosis Physical Activity and Survival

Participants in the highest tertile for total physical activity (> 105 MET-hour/week/year) had a nonstatistically significant improved overall survival (HR, 0.45; 95% CI, 0.20 to 1.01) and statistically significantly improved disease-free survival (HR, 0.36; 95% CI, 0.18 to 0.70) compared with those in the lowest physical activity level tertile (≤ 64 MET-hour/week/year; Table 3). In addition, there was a statistically significant dose-response with increasing tertiles of total physical activity and improved overall and disease-free survival for multivariable-adjusted models ($P_{\text{trend}} = .05$ and $.002$, respectively).

The highest (> 13 MET-hour/week/year) versus lowest (≤ 5 MET-hour/week/year) tertile of postdiagnosis recreational physical activity participation was strongly associated with disease-free and overall survival in multivariable-adjusted models (HR, 0.33; 95% CI, 0.17 to 0.64; and HR, 0.33; 95% CI, 0.15 to 0.75, respectively). Results from Kaplan-Meier analyses also support statistically significant improvements in disease-free survival (Fig 1A; $P < .001$) and

overall survival (Fig 1B; $P < .001$) for women who participated in the highest amounts of recreational physical activity. In addition, improved disease-free survival was noted for participants in the middle versus lowest tertile for occupational physical activity (HR, 0.52; 95% CI, 0.29 to 0.92), as well as the highest tertiles compared with the lowest tertiles for household physical activity participation (HR, 0.44; 95% CI, 0.24 to 0.83). In multivariable-adjusted models, there was a dose-response for increasing recreational physical activity with improved overall survival ($P_{\text{trend}} = .007$), but not for occupational ($P_{\text{trend}} = .17$) or household ($P_{\text{trend}} = .12$) physical activity.

No statistically significant interactions were found between postdiagnosis physical activity with postdiagnosis BMI or age (results not shown). A statistically significant dose-response relationship indicated increased disease-free survival for hours/week spent participating in moderate-to-vigorous intensity recreational physical activity ($P_{\text{trend}} = .05$; Appendix Table A4, online only). All other analyses of survival outcomes with occupational sedentary behavior and pre- or

TABLE 2. Disease-Free Survival and Overall Survival in Relation to Lifetime (prediagnosis) Physical Activity, Alberta Endometrial Cancer Cohort Study, 2002-2019 (N = 425)

Teriles of Physical Activity Level	Disease-Free Survival			Overall Survival		
	No. of Events/ No. of Cases	Age-Adjusted HR (95% CI)	Multivariable- Adjusted HR (95% CI)	No. of Deaths/ No. of Cases	Age-Adjusted HR (95% CI)	Multivariable-Adjusted HR (95% CI)
Total physical activity, MET-hours/week/year						
≤ 104	33/141	1.0	1.0	27/141	1.0	1.0
> 104 to ≤ 127	19/139	0.59 (0.33 to 1.05)	0.57 (0.31 to 1.06)	13/139	0.50 (0.25 to 0.99)	0.41 (0.20 to 0.85)
> 127	28/145	0.80 (0.48 to 1.34)	1.06 (0.61 to 1.85)	20/145	0.70 (0.39 to 1.26)	0.81 (0.43 to 1.50)
<i>P</i> for trend		.40	.84		.23	.45
Recreational physical activity, MET-hours/week/year						
≤ 8	36/141	1.0	1.0	30/141	1.0	1.0
> 8 to ≤ 14	21/139	0.61 (0.36 to 1.06)	0.69 (0.38 to 1.24)	12/139	0.43 (0.22 to 0.84)	0.44 (0.22 to 0.90)
> 14	23/145	0.63 (0.37 to 1.08)	0.54 (0.30 to 0.96)	18/145	0.67 (0.37 to 1.21)	0.56 (0.29 to 1.07)
<i>P</i> for trend		.08	.04		.13	.06
Occupational physical activity, MET-hours/week/year						
≤ 36	34/141	1.0	1.0	28/141	1.0	1.0
> 36 to ≤ 52	24/139	0.92 (0.53 to 1.59)	0.85 (0.47 to 1.56)	18/139	0.90 (0.48 to 1.70)	0.91 (0.46 to 1.77)
> 52	22/145	0.84 (0.47 to 1.49)	1.08 (0.59 to 1.96)	14/145	0.75 (0.38 to 1.50)	0.83 (0.40 to 1.72)
<i>P</i> for trend		.55	.84		.43	.62
Household physical activity, MET-hours/week/year						
≤ 45	25/140	1.0	1.0	16/140	1.0	1.0
> 45 to ≤ 67	21/141	0.68 (0.37 to 1.25)	0.39 (0.20 to 0.77)	18/141	0.85 (0.42 to 1.73)	0.50 (0.23 to 1.07)
> 67	34/144	1.00 (0.56 to 1.79)	0.75 (0.40 to 1.41)	26/144	1.04 (0.52 to 2.08)	0.88 (0.43 to 1.81)
<i>P</i> for trend		.82	.76		.81	.92

NOTE. Where disease-free survival and overall survival models were adjusted for age, age × age, overall cancer stage (I and incomplete/II/III and IV), cancer grade (≤ 50%/other/>50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), baseline body mass index, baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, lifetime (prediagnosis) comorbidity score, and lifetime (prediagnosis) smoking. Models of each subtype of activities were further adjusted for the other types of activities.

Abbreviations: HR, hazard ratio; MET, metabolic-equivalent task.

postdiagnosis physical activity according to intensity were nonstatistically significant (results not shown). We conducted sensitivity analyses to determine the effect of including individuals for whom cancer stage was incomplete (*n* = 6) and found that the results were unchanged.

Change From Pre- to Postdiagnosis Physical Activity and Survival

Associations between changes in pre- to postdiagnosis physical activity with overall and disease-free survival are

reported in Table 4, and the sample size of each of the four change pattern subgroups are reported in Appendix Table A5 (online only). Compared with women who participated in low levels of recreational physical activity (< 10 MET-hour/week/year) before and after diagnosis (unchanged-low), women who maintained high levels of recreational physical activity (> 10 MET-hour/week/year) from pre- to postdiagnosis (unchanged-high) had longer disease-free survival (HR, 0.35; 95% CI, 0.18 to 0.69) and overall survival (HR, 0.43; 95% CI,

TABLE 3. Disease-Free Survival and Overall Survival in Relation to Postdiagnosis Physical Activity, Alberta Endometrial Cancer Cohort Study, 2002-2019 (N = 425)

Teriles of Physical Activity Level	Disease-Free Survival			Overall Survival		
	No. of Events/No. of Cases	Age-Adjusted HR (95% CI)	Multivariable-Adjusted HR (95% CI)	No. of Deaths/No. of Cases	Age-Adjusted HR (95% CI)	Multivariable-Adjusted HR (95% CI)
Total physical activity, MET-hours/week/year						
≤ 64	42/140	1.0	1.0	33/140	1.0	1.0
> 64 to ≤ 105	22/141	0.48 (0.29 to 0.80)	0.58 (0.33 to 1.01)	17/141	0.48 (0.27 to 0.86)	0.73 (0.39 to 1.39)
> 105	16/144	0.38 (0.21 to 0.68)	0.36 (0.18 to 0.70)	10/144	0.34 (0.16 to 0.70)	0.45 (0.20 to 1.01)
<i>P</i> for trend		< .001	.002		.001	.05
Recreational physical activity, MET- hours/week/year						
≤ 5	40/141	1.0	1.0	30/141	1.0	1.0
> 5 to ≤ 13	26/139	0.58 (0.35 to 0.96)	0.55 (0.32 to 0.94)	21/139	0.64 (0.36 to 1.14)	0.65 (0.35 to 1.21)
> 13	14/145	0.30 (0.16 to 0.56)	0.33 (0.17 to 0.64)	9/145	0.27 (0.13 to 0.57)	0.33 (0.15 to 0.75)
<i>P</i> for trend		< .001	.001		< .001	.007
Occupational physical activity, MET- hours/week/year						
≤ 1	37/141	1.0	1.0	31/141	1.0	1.0
> 1 to ≤ 25	22/140	0.65 (0.38 to 1.11)	0.52 (0.29 to 0.92)	16/140	0.55 (0.30 to 1.02)	0.53 (0.28 to 1.03)
> 25	21/144	0.74 (0.41 to 1.34)	0.55 (0.29 to 1.03)	13/144	0.66 (0.32 to 1.35)	0.67 (0.31 to 1.42)
<i>P</i> for trend		.23	.04		.13	.17
Household physical activity, MET-hours/week/year						
≤ 35	39/140	1.0	1.0	28/140	1.0	1.0
> 35 to ≤ 56	20/140	0.48 (0.28 to 0.83)	0.46 (0.25 to 0.82)	16/140	0.54 (0.29 to 1.01)	0.45 (0.23 to 0.89)
> 56	21/145	0.44 (0.26 to 0.76)	0.44 (0.24 to 0.83)	16/145	0.46 (0.24 to 0.86)	0.62 (0.29 to 1.32)
<i>P</i> for trend		.002	.006		.013	.12

NOTE. The disease free survival model was adjusted for age, age × age, overall cancer stage (I and incomplete/II/III and IV), cancer grade (≤ 50%/other/> 50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), postdiagnosis body mass index, baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, postdiagnosis Charlson Comorbidity score, time to first new primary cancer, and prediagnosis total physical activity. The overall survival model was adjusted for age, age × age, overall cancer stage (I and missing/II/III and IV), cancer grade (≤ 50%/other/> 50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), postdiagnosis body mass index, baseline menopausal status, baseline hormone replacement therapy use, first-degree family history of cancer, postdiagnosis Charlson Comorbidity score, time to first any of endometrial cancer recurrence/progression or new primary cancer, and prediagnosis total physical activity. Models of each subtype of activities were further adjusted for the other types of activities.

Abbreviations: HR, hazard ratio; MET, metabolic-equivalent task.

0.20 to 0.94). Kaplan-Meier curves further support these findings for unadjusted disease-free survival (Fig 2A; *P* = .005) and overall survival (Fig 2B; *P* = .03). Similar patterns of association were also noted for total physical activity, but not presented herein because of the small number of events noted in each physical activity level change category.

DISCUSSION

Women who were diagnosed with endometrial cancer and reported participating in higher amounts of recreational physical activity prediagnosis had a 46% lower risk of cancer recurrence or death. Postdiagnosis total physical

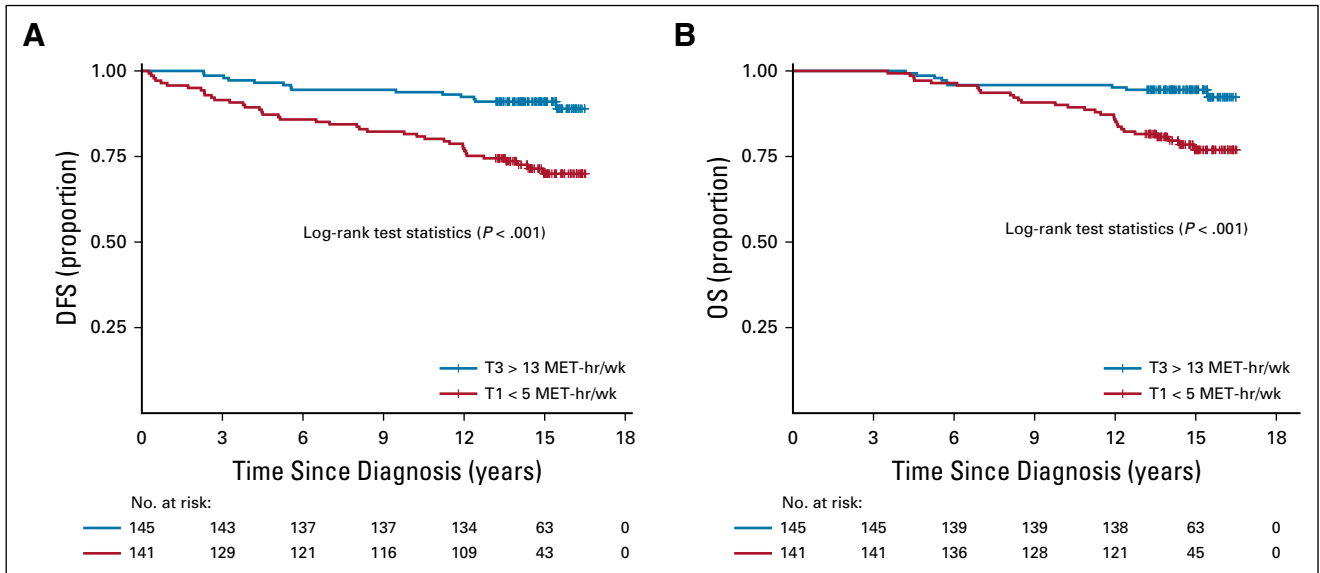


FIG 1. Kaplan-Meier curves for (A) disease-free survival (DFS) and (B) overall survival (OS) among survivors of endometrial cancer based on tertile of postdiagnosis recreational physical activity (metabolic-equivalent task-hours/week/years).

activity was associated with a 64% improvement in disease-free survival, and recreational physical activity was associated with 67% improvement in both overall and disease-free survival. Finally, women who sustained high versus low levels of recreational physical activity from pre- to postdiagnosis had a 57% increase in overall survival and a 65% increase in disease-free survival. Our findings suggest a substantial benefit for survivors of endometrial cancer who are physically

active throughout their lifespan and recreationally active postdiagnosis.

Relatively few studies have investigated the relationship between physical activity and endometrial cancer survival, and findings have been inconsistent.⁷⁻¹⁰ Using data from 983 women in the Women’s Health Initiative, Arem and colleagues⁷ found no survival benefit with higher levels of prediagnosis physical activity after a median follow-up of

TABLE 4. Physical Activity Change From Prediagnosis to Postdiagnosis on the Basis of Recreational Physical Activity, Alberta Endometrial Cancer Cohort Study, 2002-2019 (N = 425)

Types of Physical Activity Change ^a	No. of Events/No. of Cases	Person-Years	Event Rate per 100 Person-Years	Multivariable-Adjusted HR (95% CI) ^b
Disease-free survival				
Unchanged low physical activity	37/139	1,749.2	2.1	1.0
Decreased from high to low	20/95	1,243.0	1.6	0.56 (0.30 to 1.05)
Increased from low to high	8/52	704.9	1.1	0.68 (0.30 to 1.55)
Unchanged high physical activity	15/139	1,970.4	0.8	0.35 (0.18 to 0.69)
<i>P</i> for trend				.004
Overall survival				
Unchanged low physical activity	28/139	1,903.6	1.5	1.0
Decreased from high to low	14/95	1,331.0	1.1	0.65 (0.31 to 1.36)
Increased from low to high	7/52	725.3	1.0	0.73 (0.30 to 1.78)
Unchanged high physical activity	11/139	1,995.4	0.6	0.43 (0.20 to 0.94)
<i>P</i> for trend				.04

Abbreviation: HR, hazard ratio.

^aThe high and low physical activity levels were defined as same median split point at 10 metabolic-equivalent tasks-hours/weeks/years for both prediagnosis and postdiagnosis. Covariates adjusted were all previous corresponding variables, further adjusted for baseline total physical activity and postdiagnosis occupational and household physical activity.

^bCovariates adjusted were all previously corresponding variables, further adjusted for baseline total physical activity and post-diagnosis occupational and household physical activity.

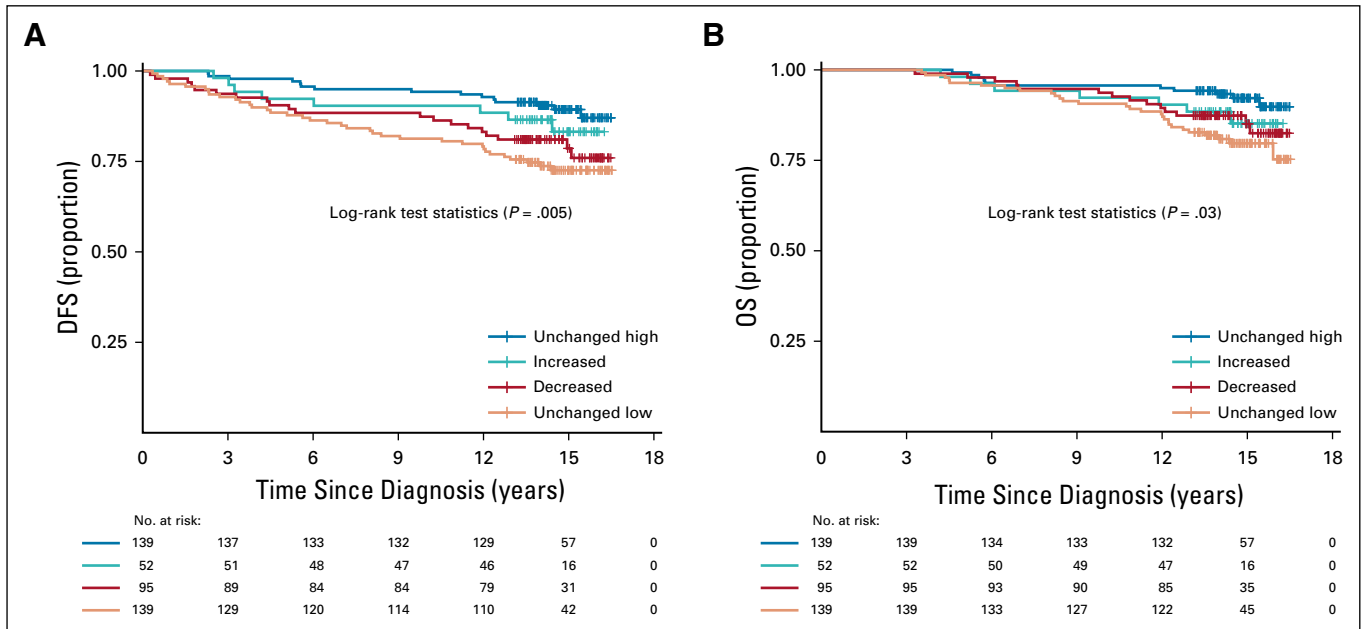


FIG 2. Kaplan-Meier curves for (A) disease-free survival (DFS) and (B) overall survival (OS) among survivors of endometrial cancer based on change in recreational physical activity from pre- to postdiagnosis. The high and low physical activity levels were defined as the same median split point at 10 metabolic-equivalent tasks-hours/week/years for both prediagnosis and postdiagnosis.

5.2 years and 163 all-cause deaths. Among 875 women in the National Institutes of Health's AARP (NIH-AARP) Diet and Health Study, > 7 hours/week of prediagnosis, recreational, moderate-to-vigorous intensity physical activity was associated with a statistically significant 43% decrease in 5-year all-cause mortality, but this association was attenuated after adjusting for BMI.⁸ Results from our analyses suggest that BMI may be an important modifier in the association between prediagnosis recreational activity and endometrial cancer outcomes as only participants with a BMI ≥ 30 kg/m² at baseline had improved overall survival with higher amounts of recreational physical activity.

Overall and disease-free survival were higher among women who participated in more total and recreational physical activity postdiagnosis. Our findings are supported by those of a recent observational study that used National Health Interview Survey-linked mortality files with follow-up.¹⁰ The study found that among 1,038 survivors of endometrial cancer, women who participated in at least 150 minutes/week of moderate-intensity physical activity or 75 minutes/week of vigorous-intensity aerobic physical activity after diagnosis experienced reductions in all-cause mortality compared with survivors who engaged in neither.¹⁰ Conversely, in participants from the NIH-AARP endometrial cancer cohort, postdiagnosis recreational physical activity performed at moderate-to-vigorous intensity was not statistically significantly associated with all-cause mortality at any level of MET expenditure.⁹

To our knowledge, our study is the first to examine how changes in pre- to postdiagnosis physical activity levels

relate to endometrial cancer survival. Research involving survivors of breast cancer has shown that maintaining an inactive lifestyle or decreasing recreational physical activity from pre- to postdiagnosis may increase all-cause mortality.²⁰⁻²² Furthermore, increasing recreational physical activity may decrease all-cause mortality.²³ In female survivors of colorectal cancer, increasing recreational physical activity after diagnosis also yielded reductions in cancer-specific and overall mortality.²⁴ Our findings revealed that the greatest survival benefits were experienced by women who sustained high levels of recreational physical activity from pre- to postdiagnosis and highlight the importance of promoting physical activity throughout the lifespan as a modifiable risk factor to reduce the incidence and mortality from endometrial cancer. We observed survival benefits with > 5 to ≤ 13 MET-hours/week/year of recreational activity (equivalent to 100-300 minutes/week of moderate-intensity [3-4.5 MET] activity), a level that is achievable by most populations and comparable to those observed in our population controls.¹¹

The mechanisms whereby physical activity alters endometrial cancer risk and prognosis are not fully understood. Many hypothesized biologic pathways suggest that physical activity attenuates the risk of dying through its impact on obesity,²⁵ although our analyses adjusted for BMI suggests physical activity has an association with survival independently of obesity. Physical activity may contribute to reducing the risk of dying from endometrial cancer by reducing adiposity levels, inflammation, adipokines, insulin resistance, and endogenous sex hormones.²⁶⁻²⁸

Cardiorespiratory fitness, an important predictor of all-cause mortality and survival in patients with cancer, is reduced in women with gynecologic cancers compared with healthy controls.^{29,30} Therefore, postdiagnosis physical activity participation may be particularly important for improving cardiorespiratory fitness, decreasing obesity and inflammation, and improving insulin resistance, and through these mechanisms, enhancing survival outcomes in survivors of endometrial cancer.

Despite the increasing evidence that physical activity improves cancer outcomes,³¹ more than one half of survivors of cancer are physically inactive.³²⁻³⁴ Consequently, numerous agencies are raising awareness regarding physical activity benefits for cancer survival.^{27,35-38} For example, the Moving Through Cancer exercise prescription developed by the American College of Sports Medicine helps health care professionals design and deliver physical activity programs for patients with cancer and survivors, with the ultimate goal of improving patient-reported outcomes and survival.³⁸ Our study provides needed data on the domain, dose, and timing of physical activity that may maximize survival outcomes for survivors of endometrial cancer.

The strengths of our study include the population-based sampling from across Alberta, detailed physical activity data, comprehensive assessment of covariates, direct anthropometry measures, comprehensive outcome assessments captured by specialized professionals, and

a long follow-up period to observe endometrial cancer outcomes, which has a high survival rate (83%). Limitations include a small cohort with modest number of events, which decreased statistical power to detect dose-response associations, a lack of objective measures of physical activity or fitness, a single measure of physical activity at one time point pre- and postdiagnosis, lack of specific cause of death other than for endometrial cancer, a relatively homogeneous White population, and possible Type I error because of multiple comparisons.

In conclusion, the findings from our study support emerging evidence that lifetime physical activity, as well as postdiagnosis recreational physical activity, are associated with improved survival outcomes among survivors of endometrial cancer. Although maintaining high levels of physical activity from pre- to postdiagnosis is most beneficial for improving survival, physical activity after an endometrial cancer diagnosis is more strongly associated with improved survival than prediagnosis physical activity. Future observational research investigating the relationship between physical activity and endometrial cancer survival should use objective measures of physical activity and examine the effects of health-related fitness on survival. Clinical trials involving an exercise intervention with long-term follow-up for survival outcomes are also warranted; however, such trials would be challenging given the high survival rate in this group.

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Provision of study material or patients: Christine M. Friedenreich

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Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Prospective Cohort Study of Pre- and Postdiagnosis Physical Activity and Endometrial Cancer Survival

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APPENDIX

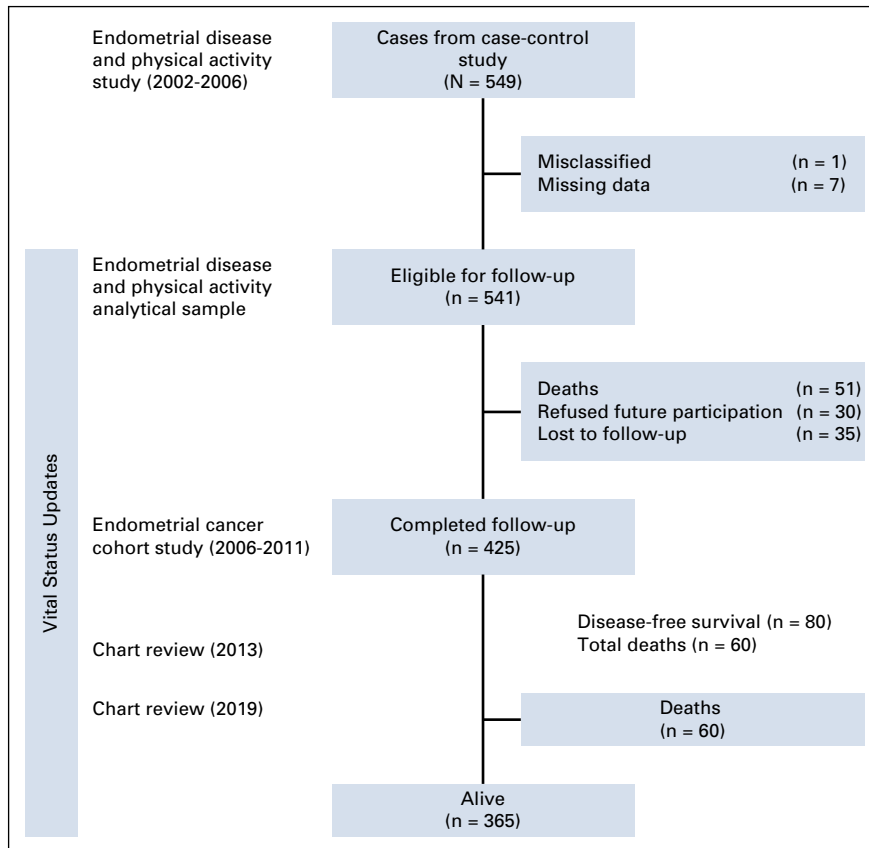


FIG A1. Flowchart of study participants in the Alberta Endometrial Cancer Cohort Study, 2002-2019.

TABLE A1. Characteristics of Participants (N = 425) and Nonparticipants (n = 116) in the Alberta Endometrial Cancer Cohort Study

Characteristic	Participants (N = 425)	Nonparticipants (n = 116)
Death ^a	60 (14.1)	51 (44.0)
Recurrence/progression ^a	42 (9.9)	31 (26.7)
Median age at diagnosis, years (IQR)	58 (54-65)	61 (53-67)
Highest education		
High school diploma	132 (32.0)	39 (36.1)
Nonuniversity certificate	189 (45.8)	49 (45.4)
University degree	92 (22.3)	20 (18.5)
Married or common in-law	396 (93.2)	104 (90.0)
White ^a	407 (96.7)	101 (88.6)
Median age at menarche, years (IQR) ^a	12 (11-13)	13 (12-14)
No. of pregnancies ≥ 20 weeks gestation		
0	75 (18.2)	19 (17.6)
1-2	179 (43.3)	43 (39.8)
> 2	159 (38.5)	46 (42.6)
Median age at menopause, years (IQR)	51 (49-54)	50 (47-53)
Menopausal status		
Pre- and perimenopausal	100 (24.3)	21 (19.4)
Postmenopausal	312 (75.7)	87 (81.6)
Overall AJCC stage ^a		
I	340 (80.0)	81 (70.0)
II	55 (12.9)	14 (12.1)
III	20 (4.7)	14 (12.1)
IV	4 (0.9)	5 (4.3)
Missing	6 (1.4)	2 (1.7)
FIGO grade ^a , %		
< 6	238 (56.0)	49 (42.2)
6-50	102 (24.0)	23 (19.8)
> 50	50 (11.8)	24 (20.7)
Other	35 (8.2)	20 (17.2)
Primary treatment		
Surgery	416 (97.9)	112 (96.6)
Chemotherapy ^a	28 (6.6)	15 (12.9)
Hormone therapy	4 (0.9)	0 (0.0)
Radiation therapy	131 (30.8)	35 (30.2)
First-degree family history of uterus or colorectal cancer	65 (15.8)	23 (19.8)
Ever hormone therapy use	141 (34.3)	38 (35.2)
Comorbidity ^b		
None	252 (61.0)	54 (50.0)
1	139 (33.7)	45 (41.7)
≥ 2	22 (5.3)	9 (8.3)

(continued on following page)

TABLE A1. Characteristics of Participants (N = 425) and Nonparticipants (n = 116) in the Alberta Endometrial Cancer Cohort Study (continued)

Characteristic	Participants (N = 425)	Nonparticipants (n = 116)
Type of smoker		
Nonsmoker	208 (50.4)	57 (52.8)
Current smoker	56 (13.6)	13 (12.0)
Ex-smoker	131 (31.7)	34 (31.5)
Occasional smoker	18 (4.4)	4 (3.7)
BMI, kg/m ² (IQR)	31.0 (26.0-36.9)	31.1 (27.3-37.5)
Waist circumference, cm (IQR)	95.5 (83.6-109.0)	95.9 (88.0-110.0)
Total caloric intake, kcal/day (IQR)	1,481 (1,158-1,876)	1,487 (1,108-1,906)
Daily alcohol intake, gram/day (IQR)	1.0 (0.3-2.8)	0.8 (0.0-3.1)
Prediagnosis physical activity, MET-hour/week (IQR)		
Total physical activity	116.2 (97.9-138.5)	116.5 (93.0-134.9)
Recreational physical activity	10.6 (6.7-16.8)	10.8 (7.4-16.9)
Occupational physical activity	43.2 (31.3-59.0)	42.9 (23.8-63.6)
Household physical activity	56.1 (40.5-73.1)	56.6 (40.7-79.3)

NOTE. Data presented as No. (%) unless otherwise indicated.

Abbreviations: AJCC, American Joint Committee on Cancer; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; IQR, interquartile range.

^aSignificantly different at $P = .05$.

^bPrediagnosis medical conditions: diabetes, angina pectoris, high cholesterol, pulmonary embolism, myocardial infarction, hypertension, stroke, and thrombosis were summarized to a baseline comorbidity score: none, 1 or ≥ 2 .

TABLE A2. Disease-Free Survival in Relation to Lifetime (prediagnosis) Physical Activity Stratified by Baseline BMI, Alberta Endometrial Cancer Cohort Study, 2002-2019 (N = 425)

< 30 BMI			≥ 30 BMI			<i>P</i> for Interaction
Tertiles of Physical Activity Level	No. of Events/No. of Cases	Multivariable-Adjusted HR (95% CI)	Tertiles of Physical Activity Level	No. of Events/No. of Cases	Multivariable-Adjusted HR (95% CI)	
Total physical activity, MET-hours/week/year			Total physical activity, MET-hours/week/year			
≤ 106	14/63	1.0	≤ 102	18/76	1.0	.56
> 106 to ≤ 127	7/64	0.41 (0.13 to 1.27)	> 102 to ≤ 127	13/77	0.70 (0.32 to 1.52)	
> 127	10/65	1.03 (0.37 to 2.91)	> 127	18/80	1.18 (0.57 to 2.44)	
<i>P</i> for trend		.94			.65	
Recreational physical activity, MET-hours/week/year			Recreational physical activity, MET-hours/week/year			
≤ 9	10/64	1.0	≤ 7	24/77	1.0	.86
> 9 to ≤ 16	8/62	0.69 (0.22 to 2.11)	> 7 to ≤ 13	13/77	0.58 (0.27 to 1.24)	
> 16	13/66	1.02 (0.39 to 2.69)	> 13	12/79	0.46 (0.21 to 1.02)	
<i>P</i> for trend		.91			.05	
Occupational physical activity, MET-hours/week/year			Occupational physical activity, MET-hours/week/year			
≤ 33	14/63	1.0	≤ 38	19/77	1.0	.53
> 33 to ≤ 51	10/63	5.41 (1.35 to 21.7)	> 38 to ≤ 55	15/77	0.67 (0.31 to 1.47)	
> 51	7/66	2.46 (0.67 to 9.01)	> 55	15/79	1.09 (0.51 to 2.30)	
<i>P</i> for trend		.21			.87	
Household physical activity, MET-hours/week/year			Household physical activity, MET-hours/week/year			
≤ 46	11/63	1.0	≤ 44	13/76	1.0	.36
> 46 to ≤ 68	7/63	0.40 (0.12 to 1.29)	> 44 to ≤ 66	15/78	0.61 (0.25 to 1.48)	
> 68	13/66	0.49 (0.16 to 1.50)	> 66	21/79	1.00 (0.43 to 2.31)	
<i>P</i> for trend		.28			.69	

NOTE. Where disease-free survival and overall survival models were adjusted for age, age × age, overall cancer stage (I and incomplete/II/III and IV), cancer grade (≤ 50%/other/> 50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, lifetime (prediagnosis) comorbidity score, and lifetime (prediagnosis) smoking. Models of each subtype of activities were further adjusted for the other types of activities.

Abbreviations: BMI, body mass index; HR, hazard ratio; MET, metabolic-equivalent task.

TABLE A3. Overall Survival in Relation to Lifetime (prediagnosis) Physical Activity Stratified by Baseline BMI, Alberta Endometrial Cancer Cohort Study, 2002-2019 (N = 425)

< 30 BMI			≥ 30 BMI			<i>P</i> for Interaction
Tertiles of Physical Activity Level	No. of Events/No. of Cases	Multivariable-Adjusted HR (95% CI)	Tertiles of Physical Activity Level	No. of Events/No. of Cases	Multivariable-Adjusted HR (95% CI)	
Total physical activity, MET-hours/week/year			Total physical activity, MET-hours/week/year			
≤ 106	10/63	1.0	≤ 102	16/76	1.0	.44
> 106 to ≤ 127	5/64	0.35 (0.09 to 1.36)	> 102 to ≤ 127	9/77	0.45 (0.19 to 1.07)	
> 127	7/65	0.94 (0.29 to 3.00)	> 127	13/80	0.72 (0.33 to 1.57)	
<i>P</i> for trend		.92			.40	
Recreational physical activity, MET-hours/week/year			Recreational physical activity, MET-hours/week/year			
≤ 9	8/64	1.0	≤ 7	20/77	1.0	.04
> 9 to ≤ 16	4/62	0.42 (0.11 to 1.54)	> 7 to ≤ 13	10/77	0.56 (0.24 to 1.30)	
> 16	10/66	1.28 (0.45 to 3.64)	> 13	8/79	0.30 (0.11 to 0.81)	
<i>P</i> for trend		.67			.013	
Occupational physical activity, MET-hours/week/year			Occupational physical activity, MET-hours/week/year			
≤ 33	11/63	1.0	≤ 38	16/77	1.0	.78
> 33 to ≤ 51	7/63	4.49 (0.92 to 21.9)	> 38 to ≤ 55	12/77	0.78 (0.34 to 1.80)	
> 51	4/66	2.12 (0.47 to 9.64)	> 55	10/79	0.83 (0.35 to 1.98)	
<i>P</i> for trend		.35			.64	
Household physical activity, MET-hours/week/year			Household physical activity, MET-hours/week/year			
≤ 46	6/63	1.0	≤ 44	9/76	1.0	.74
> 46 to ≤ 68	6/63	0.36 (0.10 to 1.37)	> 44 to ≤ 66	13/78	0.67 (0.24 to 1.83)	
> 68	10/66	0.53 (0.15 to 1.91)	> 66	16/79	1.08 (0.42 to 2.81)	
<i>P</i> for trend		0.40			.61	

NOTE. Where disease-free survival and overall survival models were adjusted for age, age × age, overall cancer stage (I and incomplete/II/III and IV), cancer grade (≤ 50%/other/>50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, lifetime (prediagnosis) comorbidity score, and lifetime (prediagnosis) smoking. Models of each subtype of activities were further adjusted for the other types of activities.

Abbreviations: BMI, body mass index; HR, hazard ratio; MET, metabolic-equivalent task.

TABLE A4. Disease-Free Survival and Overall Survival in Relation to Postdiagnosis Occupational Sedentary Behavior and Physical Activity by Different Intensities, Alberta Endometrial Cancer Cohort Study (N = 425)

Tertiles of Physical Activity Level	No. of DFS Events/No. of Cases	Multivariable-Adjusted HR (95% CI)	No. of Overall Deaths/No. of Cases	Multivariable-Adjusted HR (95% CI)
Total physical activity, hour/week/year				
≤ 22	41/140	1.0	32/140	1.0
> 22 to ≤ 34	22/141	0.80 (0.39 to 1.67)	18/141	1.21 (0.51 to 2.89)
> 34	17/144	0.76 (0.22 to 2.63)	10/144	1.60 (0.35 to 7.26)
<i>P</i> for trend		.62		.55
Occupational sedentary behavior, hour/week/year				
≤ 1	38/141	1.0	30/141	1.0
> 1 to ≤ 12	22/139	0.61 (0.35 to 1.05)	18/139	0.73 (0.39 to 1.37)
> 12	20/145	0.59 (0.29 to 1.22)	12/145	0.65 (0.28 to 1.54)
<i>P</i> for trend		.07		.24
Total light physical activity: MET < 3.0, hour/week/year				
≤ 14	33/140	1.0	25/140	1.0
> 14 to ≤ 21	27/141	0.65 (0.37 to 1.16)	22/141	0.62 (0.32 to 1.20)
> 21	20/144	0.68 (0.33 to 1.41)	13/144	0.58 (0.24 to 1.40)
<i>P</i> for trend		.23		.18
Total MVPA physical activity: MET ≥ 3.0, hour/week/year				
≤ 3	44/141	1.0	34/141	1.0
> 3 to ≤ 12	18/140	0.57 (0.31 to 1.06)	14/140	0.64 (0.31 to 1.31)
> 12	18/144	0.70 (0.32 to 1.54)	12/144	1.22 (0.47 to 3.19)
<i>P</i> for trend		.21		.95
Recreational MVPA physical activity: MET ≥ 3.0, hour/week/year				
≤ 1	40/140	1.0	32/140	1.0
> 1 to ≤ 3	23/141	0.63 (0.35 to 1.11)	17/141	0.71 (0.37 to 1.37)
> 3	17/144	0.54 (0.28 to 1.04)	12/144	0.47 (0.21 to 1.06)
<i>P</i> for trend		.05		.06

NOTE. Where disease free survival model was adjusted for age, age × age, overall cancer stage (I and incomplete/II/III and IV), cancer grade (≤ 50%/other/>50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), postdiagnosis body mass index, baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, postdiagnosis Charlson Comorbidity score, time to first new primary cancer, prediagnosis total physical activity, and postdiagnosis total physical activity in MET-hours/week/year. Overall survival model was adjusted for age, age × age, overall cancer stage (I and missing/II/III and IV), cancer grade (≤ 50%/other/> 50% International Federation of Gynecology and Obstetrics score), cancer treatments (surgery, chemotherapy, or radiation therapy), postdiagnosis body mass index, baseline menopausal status, baseline hormone therapy use, first-degree family history of cancer, postdiagnosis Charlson Comorbidity score, time to first of endometrial cancer recurrence/progression or new primary cancer, prediagnosis total physical activity, and postdiagnosis total physical activity in MET-hours/week/year.

Abbreviations: DFS, disease-free survival; HR, hazard ratio; MET, metabolic-equivalent task; MVPA, moderate-to-vigorous physical activity.

TABLE A5. Sample Size for Patterns of Recreational Physical Activity Change From Pre- to Postdiagnosis (N = 425)

Prediagnosis Recreational Activity (MET-hour/week/year)	Postdiagnosis Recreational Activity (MET-hour/week/year)		
	< 10	≥ 10	Total
< 10	139 ^a	52 ^c	191
≥ 10	95 ^b	139 ^d	234
Total	234 ^a	191 ^a	425

NOTE. Values represent the number of survivors of endometrial cancer in each pattern of pre- and postdiagnosis physical activity.

^aSubgroup of women who were unchanged low.

^bSubgroup of women who decreased.

^cSubgroup of women who increased.

^dSubgroup of women unchanged high.