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Article

Accelerometer-measured physical activity, sedentary behavior, and mortality among cancer survivors: the Women's Health Accelerometry Collaboration

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Abstract

Background: Data on prospective associations of accelerometer-measured physical activity, sedentary behavior, and mortality among cancer survivors are lacking. Our study examined accelerometer-measured daily physical activity (including light, moderate to vigorous, total, and steps), sedentary behavior (sitting time and mean bout duration), and mortality among cancer survivors in the Women's Health Accelerometry Collaboration.

Methods: Postmenopausal women in the Collaboration who reported a cancer diagnosis at least 1 year prior to wearing an ActiGraph GT3X+ device on the hip for at least 4 of 7 days from 2011 to 2015 were included. Outcomes included all-cause, cancer-related, and cardiovascular disease (CVD)–related mortality. Covariate-adjusted Cox regression estimated hazard ratios (HRs) and 95% CIs for each physical activity and sedentary behavior measure in association with mortality.

Results: Overall, 2479 cancer survivors (mean [SD] age, 74.2 [6.7] years) were followed up for 8.3 years. For all-cause mortality ($n = 594$ cases), every 78.1 minutes per day in light physical activity, 96.5 minutes per day in total physical activity, 102.2 minutes per day in sitting time, and 4.8 minutes in a sitting bout duration had hazard ratios of 0.92 (95% CI = 0.84 to 1.01), 0.89 (95% CI = 0.80 to 0.98), 1.12 (95% CI = 1.02 to 1.24), and 1.04 (95% CI = 0.96 to 1.12), respectively. Linear associations for cancer mortality ($n = 168$) and CVD mortality ($n = 109$) were not statistically significant, except for steps (hazard ratio per 2469 steps/d = 0.66, 95% CI = 0.45 to 0.96) and sitting time (hazard ratio = 1.30, 95% CI = 1.02 to 1.67) for CVD mortality. Nonlinear associations showed benefits of moderate to vigorous physical activity (for all-cause and CVD mortality) and steps (all-cause mortality only) maximized at approximately 60 minutes per day and 5000–6000 steps per day, respectively.

Conclusions: Among postmenopausal cancer survivors, higher physical activity and lower sedentary behavior was associated with reduced hazards of all-cause and CVD mortality.

Introduction

The number of persons with a history of cancer ("cancer survivors") in the United States was estimated at 18.1 million in 2022[1] and is projected to reach 22.1 million by 2030.[2] Cardiovascular disease (CVD) mortality is a major competing cause of death among older adults (individuals aged ≥65 years) living with cancer, notwithstanding improvements in survival and prognoses overall.[3,4] Therefore, there is a growing need for cardiovascular mortality prevention strategies among cancer survivors. Evidence demonstrates numerous benefits of physical

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activity for cancer survivors, including improved cardiorespiratory fitness, physical function, psychosocial health, and survival.[5-9] Conversely, limited epidemiological data link sedentary behavior and cancer survival, with possible increased risk of cancer mortality as sedentary time increases.[10] Most evidence of physical activity or sedentary behavior associations with cancer survivorship is from self-reported measures.[6,7,9] Although cost-effective and relatively easily to administer, these measures are prone to recall and social desirability biases.[11,12] Furthermore, self-reported measures inaccurately capture light-intensity physical activity and cannot capture daily step counts, which are important to consider given that current guidelines recommend that cancer survivors avoid inactivity if unable to meet physical activity guidelines.[13] Accelerometry in part mitigates bias but was only recently available in cohort studies with long enough follow-up time to assess prospective physical activity and sedentary behavior associations with health outcomes.[14,15]

The present study examined associations of accelerometer-derived measures of physical activity (light physical activity, moderate to vigorous physical activity, total physical activity, daily steps) and sedentary behavior (sitting time, sitting bout duration) with all-cause, cancer-related, and CVD-related mortality among cancer survivors in the Women's Health Accelerometry Collaboration (WHAC), a combined cohort of postmenopausal US women who participated in either the Women's Health Study (WHS) or the Women's Health Initiative (WHI) Objective Physical Activity and Cardiovascular Health (OPACH) study.

Methods

Study design and participants

The WHAC was created through the harmonization of accelerometry, covariate, cancer incidence, and mortality data from WHS and OPACH, detailed previously.[16] Briefly, the WHS was a randomized trial testing aspirin, β-carotene, and vitamin E for prevention of CVD and cancer among 39 876 US women aged 45 years or older, subsequently followed up observationally.[17-19] From 2011 to 2014, 18 289 WHS women participated in an ancillary study that collected accelerometry data, and 17 062 returned devices with usable data.[20] The OPACH study, ancillary to the WHI Long Life Study,[21] is a prospective study of accelerometry with chronic disease and aging outcomes.[22] Among the 9252 women who provided consent to participate in the WHI Long Life Study, 7048 participated in OPACH and 6489 returned accelerometers with usable data. Combining these with the 17 062 WHS women resulted in 23 551 WHAC women with accelerometer data. All women provided written informed consent; institutional review boards at the Brigham and Women's Hospital and Fred Hutchinson Cancer Research Center approved these studies.

Accelerometer measures

Participants in both cohorts wore ActiGraph GT3X+ triaxial accelerometers for 7 consecutive days, returning them by mail.[16,20,22] In WHS, women wore accelerometers over the right hip, removing them only during sleep or when in water.[20] In OPACH, women were asked to wear accelerometers over the right hip, including during sleep but not when in water[22]; subsequently, time spent sleeping was removed for all analyses based on daily diary recorded times in and out of bed. Accelerometers recorded 3-dimensional raw acceleration signals at 30 Hz; ActiLife, version 6, software (ActiGraph, LLC) aggregated signals to counts per 15-second epochs; and accelerometer nonwear time was removed using the validated Choi algorithm.[23,24] Accelerometer wear adherence was defined as 10 or more hours on 4 or more days of device wear, consistent with other protocols.[25-27] Awake wear time was accounted for using the residuals method.[28]

Physical activity metrics were derived from the raw acceleration signals based on the Accelerometer Activity Index.[29] Average intensity per day was summarized as average Accelerometer Activity Index/15 seconds. Using OPACH calibration study–derived accelerometry cutpoints,[30,31] daily average time in intensity-specific categories measured from Accelerometer Activity Index/15-second cut points were defined as light physical activity (101-586 Accelerometer Activity Index/15 seconds), moderate to vigorous physical activity (≥587 Accelerometer Activity Index/15 seconds), and total physical activity (≥101 Accelerometer Activity Index/15 seconds). Steps per day were determined using ActiLife, version 6, software. Sedentary behavior metrics (total sitting time and mean sitting bout duration) were classified by the Convolutional Neural Network Hip Accelerometer Posture (CHAP) algorithm, developed among 709 older adults (mean [SD] age = 77 [6.5] years; 59% women) who concurrently wore a GT3X+ device over the right hip and a thigh-worn activPAL device (PAL Technologies, Ltd).[32] The CHAP has strong agreement with activPAL classification of minute-level sitting compared with nonsitting and is more accurate than traditional cut point methods.[32]

Cancer diagnosis

Medical records were obtained for women self-reporting a diagnosis of any cancer (except nonmelanoma skin cancer) on an annual mailed questionnaire.[33] Women with a cancer diagnosis 1 year or more before accelerometer data collection were considered cancer survivors. Physician adjudicators coded cancers using *International Classification of Diseases for Oncology*; cancer survivors were classified by cancer subtype. For women with a history of more than 1 cancer diagnosis at least 1 year prior to accelerometry, the most recent diagnosed site was selected as their cancer diagnosis.

Mortality outcomes

For both cohorts, deaths were reported by family members and postal authorities and were confirmed with medical records, interviews with next of kin, death certificates, and linkage with the National Death Index.[34] The cause of death was based on death certificates, medical records, or other records using the *International Statistical Classification of Diseases, Tenth Revision*.[16] Definitions for CVD mortality data between cohorts varied slightly. In WHS, CVD mortality was death due to ischemic heart disease, acute myocardial infarction, cerebrovascular disease, sudden death, or other cardiovascular cause. For OPACH, cardiovascular death was due to definite or possible coronary heart disease, cerebrovascular disease, and other/unknown cardiovascular cause.

Primary endpoints of interest were mortality from (1) all causes, (2) cancer, and (3) CVD. Follow-up time was computed from the first day of accelerometry to date of death through December 31, 2022 (WHS) or February 19, 2023 (OPACH). For analyses of cancer and CVD mortality, participants who died from noncancer and non-CVD causes were right-censored.

Covariates

Covariates were selected a priori based on their suspected or established confounding of associations between physical activity and mortality in cancer survivors. In both cohorts, age, race and ethnicity, and education were self-reported at enrollment

Table 1. Cancer survivor characteristics, overall and by quartiles of total physical activity in the Women's Health Accelerometry Collaboration.

		Quartile of total physical activity (min/d)			
Characteristic	**Total**	**<291.9**	**291.9-354.3**	**354.4-418.6**	**>418.6**
No.	2479	620	620	620	619
Cohort, No. (%)					
WHS	1865 (75.2)	360 (58.1)	467 (75.3)	492 (79.4)	546 (88.2)
OPACH	614 (24.8)	260 (41.9)	153 (24.7)	128 (20.6)	73 (11.8)
Age group, No. (%)					
<70 y	718 (29.0)	102 (16.5)	171 (27.6)	193 (31.1)	252 (40.7)
70-79 y	1198 (48.3)	284 (45.8)	301 (48.5)	314 (50.6)	299 (48.3)
≥80 y	563 (22.7)	234 (37.7)	148 (23.9)	113 (18.2)	68 (11.0)
Age, mean (SD), y	74.2 (6.7)	77.0 (7.1)	74.5 (6.5)	73.6 (6.2)	71.8 (5.7)
Race and ethnicity, No. (%)					
Non-Hispanic White	2134 (86.1)	502 (81.0)	531 (85.6)	541 (87.3)	560 (90.5)
Non-Hispanic Black	208 (8.4)	84 (13.5)	56 (9.0)	42 (6.8)	26 (4.2)
Hispanic	100 (4.0)	28 (4.5)	23 (3.7)	29 (4.7)	20 (3.2)
AAPI, AIAN, or other/unknown	37 (1.5)	6 (1.0)	10 (1.6)	8 (1.3)	13 (2.1)
Highest education level, No. (%)					
High school diploma/GED or less	121 (4.9)	50 (8.1)	32 (5.2)	25 (4.0)	14 (2.3)
Some college	1137 (45.9)	278 (44.8)	285 (46.0)	284 (45.8)	290 (46.8)
College graduate	1200 (48.4)	289 (46.6)	297 (47.9)	301 (48.5)	313 (50.6)
Missing	21 (0.8)	3 (0.5)	6 (1.0)	10 (1.6)	2 (0.3)
Smoking status, No. (%)					
Current	71 (2.9)	23 (3.7)	26 (4.2)	13 (2.1)	9 (1.5)
Former	1195 (48.2)	302 (48.7)	309 (49.8)	290 (46.8)	294 (47.5)
Never	1212 (48.9)	294 (47.4)	285 (46.0)	317 (51.1)	316 (51.1)
Missing	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Alcohol use, No. (%)					
Never or rarely	948 (38.2)	280 (45.2)	248 (40.0)	224 (36.1)	196 (31.7)
Monthly	406 (16.4)	125 (20.2)	105 (16.9)	98 (15.8)	78 (12.6)
Weekly	775 (31.3)	147 (23.7)	182 (29.4)	214 (34.5)	232 (37.5)
Daily	350 (14.1)	68 (11.0)	85 (13.7)	84 (13.5)	113 (18.3)
Body mass index, No. (%)					
<18.5	50 (2.0)	9 (1.5)	7 (1.1)	14 (2.3)	20 (3.2)
18.5-24.9	1008 (40.7)	140 (22.6)	211 (34.0)	309 (49.8)	348 (56.2)
25.0-29.9	862 (34.8)	213 (34.4)	246 (39.7)	217 (35.0)	186 (30.0)
≥30.0	559 (22.5)	258 (41.6)	156 (25.2)	80 (12.9)	65 (10.5)
Body mass index, mean (SD)	26.7 (5.3)	29.5 (5.9)	27.2 (5.0)	25.4 (4.4)	24.6 (4.1)
Self-rated general health, No. (%)					
Excellent	365 (14.7)	42 (6.8)	86 (13.9)	106 (17.1)	131 (21.2)
Very good	1114 (44.9)	243 (39.2)	262 (42.3)	289 (46.6)	320 (51.7)
Good	832 (33.6)	257 (41.5)	232 (37.4)	203 (32.7)	140 (22.6)
Fair or poor	166 (6.7)	78 (12.6)	39 (6.3)	21 (3.4)	28 (4.5)
Missing	2 (0.1)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)
RAND-36 physical functioning score					
Mean (SD)	73.5 (24.1)	61.0 (25.9)	73.4 (23.2)	78.1 (20.3)	81.3 (21.6)
Missing, No. (%)	198 (8.0)	52 (8.4)	52 (8.4)	39 (6.3)	55 (8.9)
Current hormone therapy use, No. (%)	98 (4.0)	21 (3.4)	19 (3.1)	25 (4.0)	33 (5.3)
History of CVD, No. (%)	150 (6.1)	59 (9.5)	42 (6.8)	32 (5.2)	17 (2.7)
History of diabetes, No. (%)	348 (14.0)	138 (22.3)	101 (16.3)	75 (12.1)	34 (5.5)
Years between cancer diagnosis and WHAC baseline, mean (SD)	8.7 (5.0)	8.6 (4.9)	8.5 (4.9)	8.7 (5.1)	8.9 (5.1)
Accelerometer measures, mean (SD)					
Light physical activity, min/d	301.6 (78.1)	206.8 (39.2)	277.7 (25.4)	325.9 (27.4)	396.3 (48.6)
Moderate to vigorous physical activity, min/d	53.9 (32.9)	27.9 (17.3)	45.6 (21.9)	58.3 (23.9)	83.8 (36.2)
Steps/d	4635 (2469)	2524 (1255)	4066 (1644)	5064 (1778)	6888 (2634)
Sitting time, min/d	575.6 (102.2)	677.1 (71.4)	598.3 (65.0)	552.8 (67.0)	474.0 (79.5)
Sitting bout duration, min/bout	13.3 (4.8)	17.6 (5.8)	13.6 (3.4)	11.8 (2.7)	10.1 (2.6)
Device wear time, min/d	888.0 (73.1)	893.1 (78.6)	882.2 (70.6)	884.5 (71.8)	892.2 (70.7)

Abbreviations: AAPI = Asian American or Pacific Islander; AIAN = American Indian or Alaskan Native; CVD = cardiovascular disease; OPACH = Objective Physical Activity and Cardiovascular Health Study; WHAC = Women's Health Accelerometry Collaboration; WHS = Women's Health Study.

into the original study. Data on health history and health behaviors were ascertained annually or biannually, and responses from the measure closest in time to accelerometer measurement were used. Self-rated general health was assessed by the question, "In general, would you say your health is excellent, very good, good, fair or poor?" Women also reported on smoking status, frequency of alcohol use, postmenopausal hormone therapy use, history of diabetes (self-reported), CVD (adjudicated), and time between cancer diagnosis and accelerometer measurement (years). Height and weight were self-reported in WHS and measured by study personnel in OPACH near in time to accelerometer measurement. Body mass index (BMI) was calculated and categorized as underweight (<18.5), healthy weight (18.5–24.9), overweight (25.0–29.9), or obese (≥30.0). Physical function was based

Table 2. Associations between accelerometer measures and all-cause mortality among cancer survivors in the Women's Health Accelerometry Collaboration.

	Quartile of exposure				
Accelerometer variable	**1 (Low) Referent**	**2 HR (95% CI)**	**3 HR (95% CI)**	**4 (High) HR (95% CI)**	**Per SD[a] HR (95% CI)**
Light physical activity					
Range, min/d	<247.8	247.8 to 300.3	300.4 to 352.7	>352.7	—
No. cases (incidence rate)[b]	207 (42.0)	146 (28.7)	140 (27.2)	101 (19.0)	—
Model 1[c]	1.00	0.88 (0.71 to 1.09)	0.84 (0.68 to 1.05)	0.63 (0.49 to 0.81)	0.84 (0.77 to 0.91)
Model 2[d]	1.00	0.98 (0.78 to 1.22)	0.97 (0.77 to 1.23)	0.80 (0.61 to 1.04)	0.92 (0.84 to 1.01)
Moderate to vigorous physical activity					
Range, min/d	<30.0	30.0-49.4	49.5-71.6	>71.6	—
No. cases (incidence rate)[b]	277 (60.4)	167 (32.8)	81 (15.2)	69 (12.7)	—
Model 1[c]	1.00	0.80 (0.66 to 0.98)	0.44 (0.34 to 0.58)	0.52 (0.39 to 0.71)	0.70 (0.62 to 0.79)
Model 2[d]	1.00	0.95 (0.77 to 1.18)	0.59 (0.44 to 0.78)	0.71 (0.51 to 0.99)	0.83 (0.73 to 0.95)
Total physical activity					
Range, min/d	<291.9	291.9-354.3	354.4-418.6	>418.6	—
No. cases (incidence rate)[b]	234 (48.9)	153 (30.0)	121 (23.3)	86 (16.0)	—
Model 1[c]	1.00	0.83 (0.67 to 1.02)	0.70 (0.56 to 0.88)	0.58 (0.45 to 0.75)	0.79 (0.72 to 0.87)
Model 2[d]	1.00	0.94 (0.75 to 1.17)	0.86 (0.66 to 1.10)	0.74 (0.56 to 0.99)	0.89 (0.80 to 0.98)
Steps					
Range, steps/day	<2893	2893-4223	4224-5925	>5926	—
No. cases (incidence rate)[b]	279 (60.6)	165 (32.5)	85 (16.0)	65 (11.9)	—
Model 1[c]	1.00	0.73 (0.60 to 0.90)	0.46 (0.35 to 0.59)	0.46 (0.34 to 0.63)	0.66 (0.58 to 0.75)
Model 2[d]	1.00	0.88 (0.71 to 1.09)	0.60 (0.45 to 0.80)	0.64 (0.46 to 0.91)	0.79 (0.69 to 0.91)
Sitting time					
Range, min/day	<514.1	514.1-577.2	577.3-643.4	>643.4	—
No. cases (incidence rate)[b]	99 (18.5)	124 (24.1)	144 (27.9)	227 (47.4)	—
Model 1[c]	1.00	1.19 (0.91 to 1.55)	1.19 (0.92 to 1.55)	1.61 (1.26 to 2.06)	1.23 (1.12 to 1.34)
Model 2[d]	1.00	1.10 (0.84 to 1.45)	1.08 (0.82 to 1.41)	1.29 (0.98 to 1.70)	1.12 (1.02 to 1.24)
Sitting bout duration					
Range, min/bout	<10.3	10.3-12.4	12.5-15.3	>15.3	—
No. cases (incidence rate)[b]	120 (22.7)	136 (26.4)	155 (30.6)	183 (36.9)	—
Model 1[c]	1.00	1.14 (0.89 to 1.46)	1.37 (1.08 to 1.74)	1.34 (1.06 to 1.69)	1.14 (1.06 to 1.22)
Model 2[d]	1.00	1.13 (0.88 to 1.46)	1.19 (0.93 to 1.52)	1.08 (0.84 to 1.39)	1.04 (0.96 to 1.12)

Abbreviations: HR = hazard ratio; Q = quartile.

[a] SD (exposure variable): 78.1 min/d (light physical activity), 32.9 min/d (moderate to vigorous physical activity), 96.5 min/d (total physical activity), 2469 steps/d (steps), 102.2 min/d (sitting time), 4.8 min/bout (sitting bouts).

[b] Incidence rate per 1000 person-years.

[c] Model 1 was adjusted for age (years) and race and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, other or unknown).

[d] Model 2 was adjusted for age, race and ethnicity, education level (high school/GED or less, some college, college graduate), smoking status (current, former, never), alcohol use (never or rarely, monthly, weekly, daily), general health (excellent, very good, good, fair, or poor), postmenopausal hormone use (yes or no), history of diabetes, history of cardiovascular disease, body mass index, physical function (RAND-36 score), cancer type, and number of years since cancer diagnosis at Women's Health Accelerometry Collaboration baseline (years).

on responses to the RAND-36 questionnaire (scored 0-100; higher scores reflect better function).[35]

Analytic sample

From the 23 551 WHAC participants with accelerometer data, we included 2651 cancer survivors. We excluded 19 WHS women who had had cancer before the start of the original WHS randomized trial. Then, we excluded 62 WHAC women with nonadherent accelerometer wear, 51 women with accelerometer data on which the CHAP algorithm could not be applied, and 40 women who had died within the first year of accelerometer wear to minimize confounding by health status.[36] The analytic sample comprised 2479 cancer survivors, more than half of whom were breast cancer survivors (Table S1). Covariate data were missing for physical function ($n = 198$), education ($n = 21$), self-rated general health ($n = 2$), and smoking status ($n = 1$).

Statistical analysis

Multivariable cohort-stratified Cox proportional hazards models[37] estimated hazard ratios (HRs) and 95% CIs for each mortality outcome in association with each accelerometer-derived exposure. Each physical activity and sedentary behavior variable was modeled categorically and continuously (in 1-SD increments). Cohort-stratified proportional hazards models allowed for baseline hazards to differ by cohort.[37] The proportional hazards assumption was inspected using Schoenfeld residual plots, finding no violations. We present results adjusted for age as well as race and ethnicity (model 1) as well as an adjusted model (model 2) that includes education, smoking status, alcohol use, general health, postmenopausal hormone use, diabetes history, CVD history, BMI, physical function, cancer type, and years since cancer diagnosis at WHAC baseline. Associations for physical activity and sedentary behavior with mortality outcomes were plotted graphically using restricted cubic splines with knots at the 10th, 50th, and 90th percentiles and a Wald test for spline components.

For all-cause mortality, multiplicative interactions were evaluated using likelihood ratio tests comparing model 2 with interaction terms for continuous accelerometer variables with the model without the interaction terms. Strata of interest explored for multiplicative interaction included age (62-74 vs 75-94 years), BMI (<30 vs ≥30), physical function score (<75 vs ≥75), years between cancer diagnosis and accelerometer measurement (<5 vs ≥5 years), moderate to vigorous physical activity (<50 vs ≥50 min/d), and sitting time (<575 vs ≥575 min/d). Finally, we tested associations in breast cancer survivors only to examine whether estimates differed meaningfully from the primary results. For all primary

Table 3. Associations between accelerometer measures and cancer mortality among cancer survivors in the Women's Health Accelerometry Collaboration.

Accelerometer variable	Tertile of exposure 1 (Low) Referent	2 HR (95% CI)	3 (High) HR (95% CI)	Per SD[a] HR (95% CI)
Light physical activity				
Range, min/d	<267.2	267.2-333.6	>333.6	—
No. cases (incidence rate)[b]	64 (9.7)	66 (9.7)	38 (5.4)	—
Model 1[c]	1.00	1.29 (0.91 to 1.84)	0.76 (0.50 to 1.15)	0.88 (0.75 to 1.03)
Model 2[d]	1.00	1.48 (1.02 to 2.16)	0.90 (0.58 to 1.41)	0.93 (0.78 to 1.11)
Moderate to vigorous physical activity				
Range, min/d	<36.1	36.1-63.6	>63.6	—
No. cases (incidence rate)[b]	86 (13.7)	48 (6.9)	34 (4.7)	—
Model 1[c]	1.00	0.78 (0.54 to 1.14)	0.74 (0.47 to 1.18)	0.85 (0.69 to 1.04)
Model 2[d]	1.00	0.92 (0.61 to 1.38)	0.85 (0.51 to 1.43)	0.91 (0.73 to 1.15)
Total physical activity				
Range, min/d	<313.4	313.4-393.0	>393.0	—
No. cases (incidence rate)[b]	75 (11.6)	56 (8.2)	37 (5.2)	—
Model 1[c]	1.00	0.91 (0.64 to 1.3)	0.75 (0.49 to 1.14)	0.86 (0.73 to 1.02)
Model 2[d]	1.00	1.01 (0.69 to 1.49)	0.87 (0.54 to 1.37)	0.92 (0.76 to 1.11)
Steps				
Range, steps/d	<3314	3314-5255	>5255	—
No. cases (incidence rate)[b]	89 (14.2)	45 (6.5)	34 (4.7)	—
Model 1[c]	1.00	0.69 (0.47 to 1.00)	0.72 (0.46 to 1.14)	0.82 (0.66 to 1.01)
Model 2[d]	1.00	0.77 (0.51 to 1.17)	0.79 (0.47 to 1.34)	0.90 (0.71 to 1.14)
Sitting time				
Range, min/d	<535.7	535.7-619.3	>619.3	—
No. cases (incidence rate)[b]	37 (5.2)	59 (8.6)	72 (11.1)	—
Model 1[c]	1.00	1.35 (0.89 to 2.06)	1.32 (0.87 to 2.01)	1.16 (0.99 to 1.37)
Model 2[d]	1.00	1.33 (0.86 to 2.04)	1.15 (0.72 to 1.83)	1.08 (0.90 to 1.29)
Sitting bout duration				
Range, min/bout	<11.0	11.0-14.2	>14.2	—
No. cases (incidence rate)[b]	47 (6.6)	60 (8.9)	61 (9.2)	—
Model 1[c]	1.00	1.54 (1.05 to 2.27)	1.38 (0.94 to 2.04)	1.12 (0.98 to 1.27)
Model 2[d]	1.00	1.44 (0.97 to 2.14)	1.13 (0.75 to 1.71)	1.04 (0.90 to 1.20)

Abbreviations: HR = hazard ratio; T = tertile.
[a] SD (exposure variable): 78.1 min/d (light physical activity), 32.9 min/d (moderate to vigorous physical activity), 96.5 min/d (total physical activity), 2469 steps/d (steps), 102.2 min/d (sitting time), 4.8 min/bout (sitting bouts).
[b] Incidence rate per 1000 person-years.
[c] Model 1 was adjusted for age and race and ethnicity.
[d] Model 2 was adjusted for age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, body mass index, physical function, cancer type, and number of years since cancer diagnosis at Women's Health Accelerometry Collaboration baseline.

analyses, including assessment of the multiplicative interaction terms, multiple imputation was applied using chained equations with predictive mean matching for 20 iterations and 25 imputations to address missing covariate data.[38]

Sensitivity analyses included (1) repeating analyses but excluding women who had died within the first 2 years of follow-up to further evaluate the potential of confounding by health status[36]; (2) complete case analyses; (3) Cox regression analyses for WHS and OPACH separately for the outcome of CVD mortality due to differences in outcome definitions; and (4) competing risk analyses (Fine-Gray method),[39] where competing events for cancer and CVD mortality were noncancer deaths and non-CVD deaths, respectively. All analyses were conducted in R, version 4.0.2, statistical software (R Foundation for Statistical Computing).

Results

There were 594 all-cause mortality events (168 cancer events; 109 CVD events) during an average (SD) of 8.3 (2.1) years (range = 1.0-11.4) of follow-up. Overall, participants were on average (SD) aged 74.2 (6.7) years, and the majority identified as non-Hispanic White (86.1%) (Table 1). Average (SD) participant BMI was 26.7 (5.3). Average (SD) years lived between cancer diagnosis and accelerometer measurement was 8.7 (5.0) (range = 1.0-20.9). Women in the highest total physical activity quartile vs the lowest were younger and less likely to have CVD or diabetes and more likely to have lower a BMI, higher frequency of alcohol use, better self-rated general health, and better physical function.

In model 2, the hazard ratio for each 1-SD increment in accelerometer measure for all-cause mortality was 0.92 (95% CI = 0.84 to 1.01) for light physical activity (SD = 78.1 min/d), 0.89 (95% CI = 0.80 to 0.98) for total physical activity (SD = 96.5 min/d), 1.12 (95% CI = 1.02 to 1.24) for sitting time (SD = 102.2 min/d), and 1.04 (95% CI = 0.96 to 1.12) for sitting bouts (SD = 4.8 min/bout) (Table 2). Point estimates for cancer mortality were attenuated, and all 95% CIs included the null (Table 3). For CVD mortality, statistically significant linear associations were present for steps

Table 4. Associations between accelerometer measures and cardiovascular disease mortality among cancer survivors in the Women's Health Accelerometry Collaboration.

	Tertile of exposure			
Accelerometer variable	1 (Low) Referent	2 HR (95% CI)	3 (High) HR (95% CI)	Per SD[a] HR (95% CI)
Light physical activity				
Range, min/d	<267.2	267.2-333.6	>333.6	—
No. cases (incidence rate)[b]	57 (8.6)	29 (4.3)	23 (3.3)	—
Model 1[c]	1.00	0.76 (0.48 to 1.20)	0.64 (0.39 to 1.06)	0.85 (0.70 to 1.04)
Model 2[d]	1.00	0.90 (0.55 to 1.47)	0.79 (0.45 to 1.37)	0.97 (0.78 to 1.23)
Moderate to vigorous physical activity				
Range, min/d	<36.1	36.1-63.6	>63.6	—
No. cases (incidence rate)[b]	76 (12.1)	25 (3.6)	8 (1.1)	—
Model 1[c]	1.00	0.55 (0.34 to 0.90)	0.29 (0.13 to 0.65)	0.51 (0.36 to 0.71)
Model 2[d]	1.00	0.72 (0.43 to 1.20)	0.39 (0.17 to 0.90)	0.61 (0.42 to 0.89)
Total physical activity				
Range, min/d	<313.4	313.4-393.0	>393.0	—
No. cases (incidence rate)[b]	60 (9.3)	34 (5.0)	15 (2.1)	—
Model 1[c]	1.00	0.82 (0.53 to 1.27)	0.52 (0.29 to 0.95)	0.76 (0.61 to 0.95)
Model 2[d]	1.00	1.00 (0.62 to 1.62)	0.72 (0.37 to 1.39)	0.89 (0.69 to 1.15)
Steps				
Range, steps/d	<3314	3314-5255	>5255	—
No. cases (incidence rate)[b]	70 (11.2)	30 (4.3)	9 (1.2)	—
Model 1[c]	1.00	0.72 (0.45 to 1.13)	0.38 (0.18 to 0.81)	0.52 (0.37 to 0.73)
Model 2[d]	1.00	0.92 (0.56 to 1.52)	0.53 (0.23 to 1.20)	0.66 (0.45 to 0.96)
Sitting time				
Range, min/d	<535.7	535.7-619.3	>619.3	—
No. cases (incidence rate)[b]	15 (2.1)	27 (3.9)	67 (10.3)	—
Model 1[c]	1.00	1.33 (0.70 to 2.55)	2.50 (1.39 to 4.52)	1.45 (1.16 to 1.80)
Model 2[d]	1.00	1.27 (0.65 to 2.47)	2.28 (1.20 to 4.34)	1.30 (1.02 to 1.67)
Sitting bout duration				
Range, min/bout	<11.0	11.0-14.2	>14.2	—
No. cases (incidence rate)[b]	31 (4.4)	27 (4.0)	51 (7.7)	—
Model 1[c]	1.00	1.01 (0.60 to 1.70)	1.46 (0.92 to 2.30)	1.18 (1.01 to 1.37)
Model 2[d]	1.00	0.94 (0.55 to 1.62)	1.21 (0.72 to 2.01)	1.09 (0.91 to 1.30)

Abbreviations: HR = hazard ratio; T = tertile.

[a] SD (exposure variable): 78.1 min/d (light physical activity), 32.9 min/d (moderate to vigorous physical activity), 96.5 min/d (total physical activity), 2469 steps/d (steps), 102.2 min/d (sitting time), 4.8 min/bout (sitting bouts).

[b] Incidence rate per 1000 person-years.

[c] Model 1 was adjusted for age and race and ethnicity.

[d] Model 2 was adjusted for age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, body mass index, physical function, cancer type, and number of years since cancer diagnosis at Women's Health Accelerometry Collaboration baseline.

(SD = 2469 steps/d; HR = 0.66, 95% CI = 0.45 to 0.96) and sitting time (HR = 1.30, 95% CI = 1.02 to 1.67) (Table 4).

Statistically significant nonlinear associations for all-cause mortality were observed with moderate to vigorous physical activity ($P_{NONLINEAR} = .003$) and steps ($P_{NONLINEAR} = .024$) only (Figure 1). For steps, the dose-response curve shows hazard ratios begin to decline at approximately 2500 steps per day, and the rate of hazard ratio decline begins leveling off at approximately 5000-6000 steps per day. A similar dose-response pattern was evident for moderate to vigorous physical activity, with the maximal mortality benefit occurring at approximately 60 minutes per day before leveling off. No statistically significant nonlinear associations were observed for cancer mortality (Figure S1). For CVD mortality (Figure S2), the dose-response association with moderate to vigorous physical activity ($P_{NONLINEAR} = .025$) had a pattern similar to all-cause mortality, where maximal mortality benefit was present at approximately 60 minutes per day.

Associations for accelerometer measures with all-cause mortality were generally consistent when stratified on cohort subgroups (Table 5). Multiplicative interaction analyses were statistically significant by age group (<75 vs ≥75 years) for moderate to vigorous physical activity (HR = 1.01, 95% CI = 0.84 to 1.21, vs 0.72, 95% CI = 0.59 to 0.87; $P_{INTERACTION} = .04$) and by years between diagnosis and accelerometry (<5 vs ≥5 years) for sitting time (HR = 1.04, 95% CI = 0.87 to 1.24, vs 1.22, 95% CI = 1.08 to 1.38; $P_{INTERACTION} = .05$). Analyses limited to breast cancer survivors were similar to the primary analysis.

Findings from sensitivity analyses, excluding deaths within the first 2 years of follow-up (Tables S2-S4), and complete case analyses (Tables S5-S7) were similar to the primary results. Some associations with CVD mortality differed qualitatively by cohort (Table S8), though estimates were in the same direction and analyses were imprecise due to fewer cases and smaller sample sizes. The subdistribution hazard ratios for cancer and CVD mortality that account for noncancer and non-CVD deaths, respectively, were in the same direction as the primary analysis hazard ratios (Table S9).

Discussion

To our knowledge, this is the largest comprehensive analysis of associations between accelerometer-measured physical activity, sedentary behavior, and mortality in cancer survivors and the first such study exclusively in postmenopausal women. Greater moderate to vigorous physical activity, total physical activity, and steps were associated with reduced hazard of all-cause mortality, while greater sitting time was associated with a higher

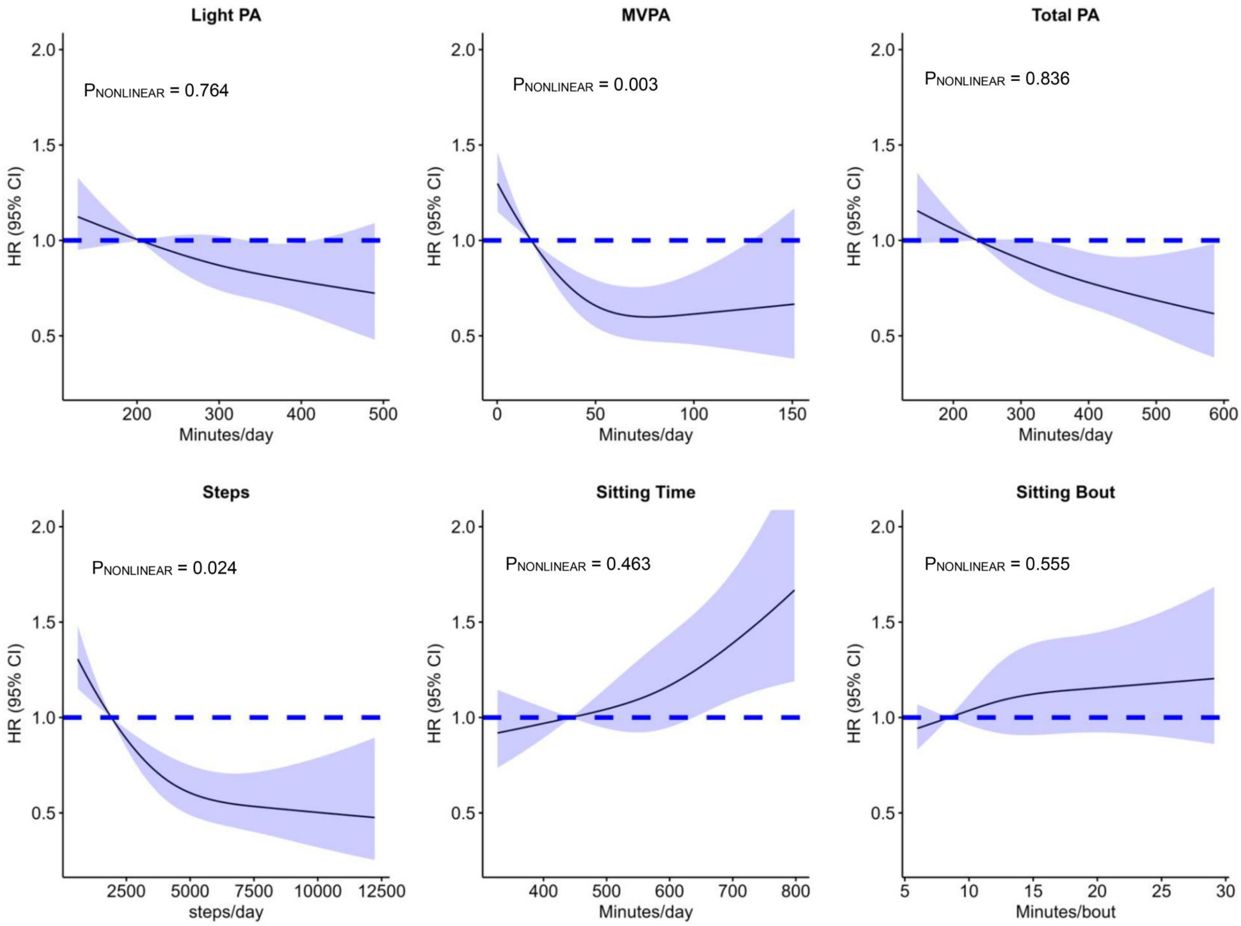

Figure 1. Restricted cubic splines for the hazard of all-cause mortality, by accelerometer measures, in the Women's Health Accelerometry Collaboration. Abbreviation: HR = hazard ratio.

Knots were at the 10th (referent), 50th, and 90th percentiles. *P* values are for Wald tests at spline components for nonlinear associations. Shaded area is the bounds of the 95% CIs. Models were adjusted for age, race and ethnicity, education level, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, body mass index, physical function, cancer type, and years since cancer diagnosis at Women's Health Accelerometry Collaboration baseline.

hazard. These associations were also statistically significant for CVD mortality, except total physical activity. All estimates for cancer mortality were attenuated to null. Sensitivity and stratification analyses for all-cause mortality further support engaging in physical activity and limiting sedentary behavior among cancer survivors to promote longevity.

The observed benefits of physical activity parallel findings from self-reported physical activity,[7,8,40] including WHI studies,[41,42] and with studies using National Health and Nutrition Examination Survey (NHANES) accelerometer data from cancer survivors.[43,44] For an approximate 1.5 hour per day increment in total physical activity, we observed an 11% reduced hazard for all-cause mortality, which is lower than the estimate from both the NHANES studies by Loprinzi and Nooe (15% per 1 h/d)[44] and by Salerno et al. (32% per 1 h/d).[43] These NHANES studies differed from each other in several ways, including participant inclusion criteria, adherent accelerometer wear definition, and follow-up time, which may have contributed to different estimates.[43,44] Compared with our study, Salerno et al.[43] also observed stronger all-cause mortality associations with light physical activity and moderate to vigorous physical activity; these could be due to different adherent accelerometer wear criteria, ActiGraph models, cut point processing methods, demographic characteristics, or the higher proportion of deaths in their sample.[43] Nevertheless, our findings confirm the beneficial associations of physical activity with long-term survivorship after cancer diagnosis for postmenopausal women.

Daily steps is an intuitive metric for total physical activity accumulation, and identifying a target range for optimal health benefits has garnered interest for future public health recommendations.[8] Ours is the first study to quantify the association between steps and mortality outcomes among cancer survivors. The dose-response curve indicated most of the all-cause mortality risk benefit is achieved at approximately 5000 to 6000 steps per day, with minimal additional benefits gained beyond this amount (Figure 1). This number is slightly lower than the 7000 steps per day target suggested from a previous analysis of steps and all-cause mortality among 16 741 WHS women (mean [SD] = 72.0 [5.7] years) who were mostly (88%) without a history of cancer at baseline.[45] Although acknowledging that women in our study were slightly older and the benefit was predominantly in women aged 75 years or older, most mortality benefit was identified at a lower step count threshold than previously found among mostly cancer-free women.[45] These findings may suggest that older female cancer survivors require fewer steps per day than cancer-free women to achieve maximal health benefit, although additional research is warranted.

Table 5. Associations between accelerometer measures and all-cause mortality among cancer survivors in the Women's Health Accelerometry Collaboration, stratified by cohort subgroup.

Cohort group	Events, No. (%)	Light physical activity[a] HR (95% CI)[b]	Moderate to vigorous physical activity[a] HR (95% CI)[b]	Total physical activity[a] HR (95% CI)[b]	Daily steps[a] HR (95% CI)[b]	Sitting time[a] HR (95% CI)[b]	Sitting bout[a] HR (95% CI)[b]
Overall (*n* = 2479)	594 (24.0)	0.92 (0.84 to 1.01)	0.83 (0.73 to 0.95)	0.89 (0.80 to 0.98)	0.79 (0.69 to 0.91)	1.12 (1.02 to 1.24)	1.04 (0.96 to 1.12)
Age, y							
<75 (*n* = 1406)	165 (11.7)	0.89 (0.74 to 1.07)	1.01 (0.84 to 1.21)	0.91 (0.76 to 1.09)	0.93 (0.77 to 1.13)	1.02 (0.87 to 1.20)	0.93 (0.78 to 1.11)
≥75 (*n* = 1073)	429 (40.0)	0.93 (0.83 to 1.04)	0.72 (0.59 to 0.87)	0.88 (0.77 to 1.00)	0.70 (0.57 to 0.86)	1.16 (1.03 to 1.31)	1.07 (0.98 to 1.17)
P[c]		.39	.04	.77	.11	.84	.66
BMI							
<30 (*n* = 1924)	446 (23.2)	1.14 (0.93 to 1.40)	0.80 (0.56 to 1.15)	1.10 (0.88 to 1.38)	0.97 (0.68 to 1.36)	0.96 (0.78 to 1.18)	1.01 (0.89 to 1.15)
≥30 (*n* = 555)	148 (26.7)	0.87 (0.78 to 0.97)	0.82 (0.71 to 0.95)	0.83 (0.74 to 0.94)	0.75 (0.64 to 0.87)	1.18 (1.05 to 1.32)	1.06 (0.95 to 1.18)
P[c]		.39	.12	.65	.57	.80	.94
Physical function,[d] score							
<75 (*n* = 878)	331 (37.7)	0.97 (0.85 to 1.09)	0.82 (0.67 to 1.00)	0.93 (0.81 to 1.07)	0.83 (0.67 to 1.04)	1.08 (0.94 to 1.24)	1.01 (0.91 to 1.11)
≥75 (*n* = 1403)	196 (14.0)	0.87 (0.74 to 1.03)	0.93 (0.76 to 1.13)	0.86 (0.72 to 1.03)	0.85 (0.70 to 1.04)	1.14 (0.97 to 1.35)	1.16 (0.99 to 1.35)
P[c]		.20	.29	.13	.08	.39	.03
Years between diagnosis and accelerometry, y							
<5 (*n* = 736)	198 (26.9)	0.98 (0.84 to 1.15)	0.77 (0.62 to 0.97)	0.93 (0.78 to 1.10)	0.77 (0.61 to 0.98)	1.04 (0.87 to 1.24)	1.03 (0.90 to 1.18)
≥5 (*n* = 1743)	396 (22.7)	0.85 (0.76 to 0.95)	0.83 (0.70 to 0.98)	0.82 (0.72 to 0.93)	0.75 (0.63 to 0.90)	1.22 (1.08 to 1.38)	1.11 (1.01 to 1.23)
P[c]		.06	.44	.07	.16	.05	.06
Moderate to vigorous physical activity, min/d[e]							
<50 (*n* = 1265)	452 (35.7)	0.96 (0.86 to 1.08)	—	—	0.80 (0.61 to 1.04)	1.09 (0.97 to 1.22)	1.03 (0.94 to 1.12)
≥50 (*n* = 1214)	142 (11.7)	0.85 (0.70 to 1.04)	—	—	0.96 (0.76 to 1.21)	1.10 (0.88 to 1.37)	0.95 (0.72 to 1.25)
P[c]		.56			.26	.82	.51
Sitting time, min/d[e]							
<575 (*n* = 1245)	224 (18.0)	0.98 (0.82 to 1.17)	0.86 (0.72 to 1.04)	0.92 (0.76 to 1.12)	0.77 (0.62 to 0.94)	—	—
≥575 (*n* = 1234)	370 (30.0)	0.89 (0.77 to 1.02)	0.76 (0.61 to 0.95)	0.84 (0.72 to 0.98)	0.76 (0.60 to 0.96)	—	—
P[c]		.42	.26	.43	.62		
Breast cancer only (*n* = 1288)	258 (20.0)	0.93 (0.80 to 1.07)	0.87 (0.72 to 1.06)	0.90 (0.77 to 1.05)	0.80 (0.65 to 0.98)	1.07 (0.92 to 1.24)	1.04 (0.91 to 1.18)

Abbreviations: BMI = body mass index; HR = hazard ratio.

[a] SD (exposure variable): 78.1 min/d (light physical activity), 32.9 min/d (moderate to vigorous physical activity), 96.5 min/d (total physical activity), 2469 steps/d (steps), 102.2 min/d (sitting time), 4.8 min/bout (sitting bouts).

[b] Model is adjusted for age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, BMI, physical function, cancer type, and years since cancer diagnosis at Women's Health Accelerometry Collaboration baseline. Variables were not included in the model when stratifying by the variable.

[c] *P* value for multiplicative interaction from likelihood ratio tests.

[d] 198 participants (67 deaths) were excluded for missing physical function data.

[e] Estimates not shown for accelerometer measures that consist of the stratifying variable (eg, moderate to vigorous physical activity is a component of total physical activity).

Greater sedentary behavior was strongly associated with increased hazard for all-cause and CVD mortality in our study. This finding contrasts with the findings of Salerno et al. (HR per 1 h/d of sedentary behavior = 1.08, 95% CI = 0.94 to 1.23),[43] which may be partly due to the imprecision of the cut point methods used to determine sedentary behavior in that study. We used the CHAP algorithm, which is superior to cut point methods for measuring both sitting time and posture.[32,46] Although our associations between sitting time and mortality were linear, the spline curves (Figure 1) show that sitting for more than approximately 11 hours per day was associated with increased risk of mortality. Given that cancer survivors have a higher prevalence of accelerometer-measured sedentary behavior than individuals without cancer,[47] our finding that sitting time was associated with increased mortality hazard supports current public health recommendations for cancer survivors to move more and sit less.[13]

Unlike findings from self-reported measures,[8-10] our accelerometer-measured physical activity and sedentary behaviors were not strongly associated with cancer mortality. However, all hazard ratios were in the same direction as those for all-cause mortality, suggesting that lowered precision due to fewer events may partially explain nonsignificant findings. Future studies in larger cancer cohorts with more cancer mortality cases may help clarify these associations.

The role of physical activity and sedentary behavior in risk of all-cause and CVD mortality is well established.[8] However, the mechanisms through which increasing physical activity and limiting sedentary behaviors may potentially reduce cancer mortality are still emerging, with evidence suggesting reduced recurrence and improved survival through mechanisms similar to those affecting cancer incidence.[7] These mechanisms include reducing adiposity; correcting metabolic dysregulation; and lowering chronic inflammation, oxidative stress, and impaired immune function.[48] Increasing physical activity may also enhance tumor vasculature and cytotoxic immune response, impeding metastasis. More research is needed to distinguish the multiple biological mechanisms that could explain the relationship between physical activity and sedentary behavior on cancer mortality.

Study strengths include harmonization of accelerometry, covariate, cancer, and mortality data from WHS and OPACH to create one of the largest samples of postmenopausal women cancer survivors with hip-worn accelerometry data. We also addressed confounding by health status through restricting sensitivity analyses to deaths occurring 2 or more years after accelerometry measurement. Limitations include the lack of data regarding stage at cancer diagnosis, cancer treatments, and other cancer-specific characteristics. Our analysis was limited to 1 postdiagnosis accelerometer measurement. Cancer survivors often change their physical activity behaviors following diagnosis, during treatment, and after treatment is complete.[47,49-51] However, postdiagnosis behaviors may be more susceptible to intervention than those before diagnosis.[52] The necessary requirement of survival from date of cancer diagnosis until accelerometry measurement introduces potential survival bias. The subdistribution hazard ratios from the cause-specific mortality analyses using the Fine and Gray method (Table S9) should be interpreted with caution because the method assumes that deaths from other causes are independent censoring events.[39] Our findings are not generalizable to populations beyond older women with cancer and should be replicated in younger and more diverse cohorts.

Among nearly 2500 postmenopausal female cancer survivors in the United States, accelerometer-assessed physical activity was associated with reduced hazard for all-cause and CVD-specific mortality, while greater sedentary behaviors were associated with higher hazard. Associations were attenuated and less precise for cancer-specific mortality. Encouraging cancer survivors to sit less and engage in physical activity of all intensities may help promote long-term survival.

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Author contributions

Eric Hyde, PhD (Conceptualization, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing—original draft, Writing—review & editing), Kelly R. Evenson, PhD (Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Writing—review & editing), Gretchen E. Bandoli, PhD (Conceptualization, Formal analysis, Methodology, Supervision, Writing—review & editing), Jinging Zou, PhD (Conceptualization, Methodology, Supervision, Writing—review & editing), Noe C. Crespo, PhD (Conceptualization, Supervision, Writing—review & editing), Humberto Parada Jr, PhD (Conceptualization, Formal analysis, Methodology, Supervision, Writing—review & editing), Michael J. Lamonte, PhD (Methodology, Writing—review & editing), Annie Green Howard, PhD (Data curation, Methodology, Writing—review & editing), Steve Nguyen, PhD (Formal analysis, Software, Visualization, Writing—review & editing), Meghan B. Skiba, PhD (Writing—review & editing), Tracey E. Crane, PhD (Writing—review & editing), Marcia L. Stefanick, PhD (Writing—review & editing), I-Min Lee, ScD (Data curation, Formal analysis, Methodology, Project administration, Supervision, Writing—review & editing), Andrea Z. LaCroix, PhD (Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Resources, Supervision, Writing—review & editing).

Supplementary material

Supplementary material is available at *JNCI Cancer Spectrum* online.

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Conflicts of interest

The authors declare they have no conflict of interest.

Data availability

Access to the WHAC data used in this manuscript would require collaboration with the senior authors, approval by the WHS and WHI studies, completion of data use agreements, and institutional review board approval from the participating institutions.

References

1. Tonorezos E, Devasia T, Mariotto AB, et al. Prevalence of cancer survivors in the United States. *JNCI J Natl Cancer Inst*. 2024. https://doi.org/10.1093/jnci/djae135
2. American Cancer Society. Cancer facts and figures 2023. Accessed November 1, 2023. https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html
3. Curigliano G, Cardinale D, Dent S, et al. Cardiotoxicity of anticancer treatments: epidemiology, detection, and management. *CA Cancer J Clin*. 2016;66:309-325. https://doi.org/10.3322/caac.21341
4. Scott JM, Nilsen TS, Gupta D, Jones LW. Exercise therapy and cardiovascular toxicity in cancer. *Circulation*. 2018;137:1176-1191. https://doi.org/10.1161/circulationaha.117.024671
5. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev*. 2012;2012:CD008465. https://doi.org/10.1002/14651858.CD008465.pub2
6. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: consensus statement from International Multidisciplinary Roundtable. *Med Sci Sports Exerc*. 2019;51:2375-2390. https://doi.org/10.1249/mss.0000000000002116
7. Patel AV, Friedenreich CM, Moore SC, et al. American College of Sports Medicine Roundtable report on physical activity, sedentary behavior, and cancer prevention and control. *Med Sci Sports Exerc*. 2019;51:2391-2402. https://doi.org/10.1249/mss.0000000000002117
8. 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee scientific report. 2018.
9. Friedenreich CM, Stone CR, Cheung WY, Hayes SC. Physical activity and mortality in cancer survivors: a systematic review and meta-analysis. *JNCI Cancer Spectr*. 2020;4:pkz080. https://doi.org/10.1093/jncics/pkz080
10. Biswas A, Oh PI, Faulkner GE, et al. Sedentary time and its association with risk for disease incidence, mortality, and hospitalization in adults: a systematic review and meta-analysis. *Ann Intern Med*. 2015;162:123-132. https://doi.org/10.7326/m14-1651
11. Biskup M, Macek P, Terek-Derszniak M, et al. Agreement between accelerometer-assessed and self-reported physical activity and sedentary behavior in female breast cancer survivors. *Diagnostics (Basel)*. 2023;13:3447. https://doi.org/10.3390/diagnostics13223447
12. Boyle T, Lynch BM, Courneya KS, Vallance JK. Agreement between accelerometer-assessed and self-reported physical activity and sedentary time in colon cancer survivors. *Support Care Cancer*. 2015;23:1121-1126. https://doi.org/10.1007/s00520-014-2453-3
13. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans*, 2nd ed. U.S. Department of Health and Human Services; 2018.
14. Lee IM, Shiroma EJ. Using accelerometers to measure physical activity in large-scale epidemiological studies: issues and challenges. *Br J Sports Med*. 2014;48:197-201. https://doi.org/10.1136/bjsports-2013-093154
15. Wijndaele K, Westgate K, Stephens SK, et al. Utilization and harmonization of adult accelerometry data: review and expert consensus. *Med Sci Sports Exerc*. 2015;47:2129-2139. https://doi.org/10.1249/mss.0000000000000661
16. Evenson KR, Bellettiere J, Cuthbertson CC, et al. Cohort profile: the Women's Health Accelerometry Collaboration. *BMJ Open*. 2021;11:e052038. https://doi.org/10.1136/bmjopen-2021-052038
17. Cook NR, Lee IM, Gaziano JM, et al. Low-dose aspirin in the primary prevention of cancer: the Women's Health Study: a randomized controlled trial. *JAMA*. 2005;294:47-55. https://doi.org/10.1001/jama.294.1.47
18. Lee IM, Cook NR, Gaziano JM, et al. Vitamin E in the primary prevention of cardiovascular disease and cancer: the Women's Health Study: a randomized controlled trial. *JAMA*. 2005;294:56-65. https://doi.org/10.1001/jama.294.1.56
19. Ridker PM, Cook NR, Lee IM, et al. A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. *N Engl J Med*. 2005;352:1293-1304. https://doi.org/10.1056/NEJMoa050613
20. Lee IM, Shiroma EJ, Evenson KR, Kamada M, LaCroix AZ, Buring JE. Using devices to assess physical activity and sedentary behavior in a large cohort study, the Women's Health Study. *J Meas Phys Behav*. 2018;1:60-69. https://doi.org/10.1123/jmpb.2018-0005
21. Women's Health Initiative. Long life study (W64). Accessed December 1, 2024. https://www.whi.org/study/W64
22. LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective Physical Activity and Cardiovascular Disease Health in Older Women (OPACH) study. *BMC Public Health*. 2017;17:192. https://doi.org/10.1186/s12889-017-4065-6
23. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. *Med Sci Sports Exerc*. 2012;44:2009-2016. https://doi.org/10.1249/MSS.0b013e318258cb36
24. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc*. 2011;43:357-364. https://doi.org/10.1249/MSS.0b013e3181ed61a3
25. Migueles JH, Cadenas-Sanchez C, Ekelund U, et al. Accelerometer data collection and processing criteria to assess

physical activity and other outcomes: a systematic review and practical considerations. *Sports Med*. 2017;47:1821-1845. https://doi.org/10.1007/s40279-017-0716-0
26. Evenson KR, Scherer E, Peter KM, Cuthbertson CC, Eckman S. Historical development of accelerometry measures and methods for physical activity and sedentary behavior research worldwide: a scoping review of observational studies of adults. *PLoS One*. 2022;17:e0276890. https://doi.org/10.1371/journal.pone.0276890
27. Crane TE, Skiba MB, Miller A, Garcia DO, Thomson CA. Development and evaluation of an accelerometer-based protocol for measuring physical activity levels in cancer survivors: development and usability study. *JMIR Mhealth Uhealth*. 2020;8:e18491. https://doi.org/10.2196/18491
28. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol*. 1986;124:17-27. https://doi.org/10.1093/oxfordjournals.aje.a114366
29. Bai J, Di C, Xiao L, et al. An activity index for raw accelerometry data and its comparison with other activity metrics. *PLoS One*. 2016;11:e0160644. https://doi.org/10.1371/journal.pone.0160644
30. Wang G, Wu S, Evenson KR, et al. Calibration of an accelerometer activity index among older women and its association with cardiometabolic risk factors. *J Meas Phys Behav*. 2022;5:145-155. https://doi.org/10.1123/jmpb.2021-0031
31. Evenson KR, Wen F, Herring AH, et al. Calibrating physical activity intensity for hip-worn accelerometry in women age 60 to 91 years: the Women's Health Initiative OPACH calibration study. *Prev Med Rep*. 2015;2:750-756. https://doi.org/10.1016/j.pmedr.2015.08.021
32. Greenwood-Hickman MA, Nakandala S, Jankowska MM, et al. The CNN Hip Accelerometer Posture (CHAP) method for classifying sitting patterns from hip accelerometers: a validation study. *Med Sci Sports Exerc*. 2021;53:2445-2454. https://doi.org/10.1249/mss.0000000000002705
33. Curb JD, McTiernan A, Heckbert SR, et al. WHI Morbidity and Mortality Committee. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. *Ann Epidemiol*. 2003;13:S122-128. https://doi.org/10.1016/s1047-2797(03)00048-6
34. Centers for Disease Control and Prevention. National Death Index. Accessed May 7, 2024. https://www.cdc.gov/nchs/ndi/index.htm
35. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item health survey 1.0. *Health Econ*. 1993;2:217-227. https://doi.org/10.1002/hec.4730020305
36. Matthews CE, Troiano RP, Salerno EA, et al. Exploration of confounding due to poor health in an accelerometer-mortality study. *Med Sci Sports Exerc*. 2020;52:2546-2553. https://doi.org/10.1249/mss.0000000000002405
37. de Jong VMT, Moons KGM, Riley RD, et al. Individual participant data meta-analysis of intervention studies with time-to-event outcomes: a review of the methodology and an applied example. *Res Synth Methods*. 2020;11:148-168. https://doi.org/10.1002/jrsm.1384
38. White IR, Royston P. Imputing missing covariate values for the Cox model. *Stat Med*. 2009;28:1982-1998. https://doi.org/10.1002/sim.3618
39. Austin PC, Fine JP. Practical recommendations for reporting Fine-Gray model analyses for competing risk data. *Stat Med*. 2017;36:4391-4400. https://doi.org/10.1002/sim.7501
40. Cao C, Friedenreich CM, Yang L. Association of daily sitting time and leisure-time physical activity with survival among US cancer survivors. *JAMA Oncol*. 2022;8:395-403. https://doi.org/10.1001/jamaoncol.2021.6590
41. Dieli-Conwright CM, Nelson RA, Simon MS, et al. Cardiometabolic risk factors, physical activity, and postmenopausal breast cancer mortality: results from the Women's Health Initiative. *BMC Womens Health*. 2022;22:32. https://doi.org/10.1186/s12905-022-01614-3
42. Irwin ML, McTiernan A, Manson JE, et al. Physical activity and survival in postmenopausal women with breast cancer: results from the Women's Health Initiative. *Cancer Prev Res (Phila)*. 2011;4:522-529. https://doi.org/10.1158/1940-6207.Capr-10-0295
43. Salerno EA, Saint-Maurice PF, Wan F, et al. Prospective associations between accelerometry-derived physical activity and sedentary behaviors and mortality among cancer survivors. *JNCI Cancer Spectr*. 2023;7:pkad007. https://doi.org/10.1093/jncics/pkad007
44. Loprinzi PD, Nooe A. Objectively measured physical activity and all-cause mortality among cancer survivors: national prospective cohort study. *South Med J*. 2019;112:234-237. https://doi.org/10.14423/smj.0000000000000956
45. Lee I-M, Shiroma EJ, Kamada M, Bassett DR, Matthews CE, Buring JE. Association of step volume and intensity with all-cause mortality in older women. *JAMA Intern Med*. 2019;179:1105-1112. https://doi.org/10.1001/jamainternmed.2019.0899
46. Bellettiere J, Nakandala S, Tuz-Zahra F, et al. CHAP-adult: a reliable and valid algorithm to classify sitting and measure sitting patterns using data from hip-worn accelerometers in adults aged 35. *J Meas Phys Behav*. 2022;5:215-223. https://doi.org/10.1123/jmpb.2021-0062
47. Thraen-Borowski KM, Gennuso KP, Cadmus-Bertram L. Accelerometer-derived physical activity and sedentary time by cancer type in the United States. *PLoS One*. 2017;12:e0182554. https://doi.org/10.1371/journal.pone.0182554
48. Friedenreich CM, Shaw E, Neilson HK, Brenner DR. Epidemiology and biology of physical activity and cancer recurrence. *J Mol Med (Berl)*. 2017;95:1029-1041. https://doi.org/10.1007/s00109-017-1558-9
49. Kenkhuis MF, Van Roekel EH, Breedveld-Peters JJL, et al. Longitudinal associations of sedentary behavior and physical activity with quality of life in colorectal cancer survivors. *Med Sci Sports Exerc*. 2021;53:2298-2308. https://doi.org/10.1249/mss.0000000000002703
50. Eng L, Pringle D, Su J, et al. Patterns, perceptions, and perceived barriers to physical activity in adult cancer survivors. *Support Care Cancer*. 2018;26:3755-3763. https://doi.org/10.1007/s00520-018-4239-5
51. Huy C, Schmidt ME, Vrieling A, Chang-Claude J, Steindorf K. Physical activity in a German breast cancer patient cohort: one-year trends and characteristics associated with change in activity level. *Eur J Cancer*. 2012;48:297-304. https://doi.org/10.1016/j.ejca.2011.08.005
52. Albers FEM, Moreno-Betancur M, Milne RL, English DR, Lynch BM, Dashti SG. Pre-diagnostic exposures and cancer survival: can a meaningful causal estimand be specified? *Epidemiology*. 2025;36:408-412. https://doi.org/10.1097/EDE.0000000000001844

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https://doi.org/10.1093/jncics/pkaf034
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