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Accelerometer-Measured Physical Activity, Sedentary Behavior, and Healthy Longevity in Older Women

A Dissertation submitted in partial satisfaction of the requirements
for the degree Doctor of Philosophy

in

Public Health (Epidemiology)

by

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2024

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The Dissertation of Eric Taylor Hyde is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

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ABSTRACT OF THE DISSERTATION

Accelerometer-Measured Physical Activity, Sedentary Behavior, and Healthy Longevity in Older Women

by

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Background: As the US population of older women continues to increase, promoting healthy longevity has become a public health priority. Increasing physical activity (PA) and limiting sedentary behavior (SB) can be an effective strategy for facilitating healthy longevity, as it is known to reduce the risk of developing many chronic conditions, manage the progression of current conditions, and helps maintain independence and mobility. However, evidence on the associations between accelerometer-measured PA (i.e., light, moderate-to-vigorous, total, daily steps), SB (i.e., sitting time, mean sitting bout duration), and healthy longevity among older women is lacking.

Methods: Aim 1 and Aim 2 use data from the Women's Health Accelerometry Collaboration (WHAC). Aim 1 quantified the prospective associations between accelerometer-measured PA, SB, and survival to age 90 with intact mobility among women ages 78–89 years at baseline in WHAC. Aim 2 examined the prospective associations

between accelerometer-measured PA, SB and all-cause, cancer, and cardiovascular disease mortality among cancer survivors in WHAC. In Aim 3, we characterized the longitudinal changes in accelerometer-measured PA among older women in the Women's Health Initiative Strong and Healthy (WHISH) trial.

Results: In Aim 1, increasing PA of any intensity, taking more steps, and reducing prolonged sitting were associated with increased odds of survival to age 90 with and without intact mobility. Among over 2,500 US cancer survivors examined in Aim 2, accelerometer-assessed PA and daily steps were associated with reduced risk of all cause and cardiovascular disease mortality, while higher levels of SB were associated with increased risks. In Aim 3, we showed that PA measures decreased over time. However, sociodemographic and health status factors were associated with different trajectories of PA over time.

Conclusion: These data provide further evidence that more PA of any intensity and shortened prolonged sitting are associated with reducing mortality risk after cancer and healthy longevity among older women. Furthermore, we highlight the variability in PA trajectories over time related to demographic and health-related factors, which could support targeted screening and intervention efforts.

Chapter 1 Introduction

Older Women in the United States

In the United States, the share of older adults (adults ages ≥ 65 years) will grow from about 15% in 2016 to nearly 25% of the population in 2060.[1] It is also projected that women will comprise the majority of the nearly 95 million older adults in 2060.[1] As women are known to have higher life expectancies than men[2], the economic and societal burdens associated with a higher proportion of American women suffering from chronic conditions and other aging-related afflictions are substantial.[3,4] As such, strategies for the promotion of healthy longevity for older women in general and also for those with chronic conditions is a crucial public health priority.

Healthy Aging and Longevity Definitions

While the terms "healthy aging" and "healthy longevity" are often used interchangeably and there is significant overlap in their definitions, they carry slightly different emphasis and meaning in research. The World Health Organization defines healthy aging as "the process of developing and maintaining the functional ability that enables wellbeing in older age"[5], though many other definitions also exist.[6] While there are slight variations in the specific definitions of healthy aging used in research, most generally include the following key components: (1) the absence of disease and disability or effective management of conditions to maintain a good quality of life; (2) maintaining physical function and independence in activities of daily living; (3) preservation of cognitive function, emotional well-being, and mental health; (4) social connectedness, presence of meaningful relationships, and engaging in social activities; and (5) longevity.[6,7] Despite developments in healthy aging research, these concepts are challenging to capture in epidemiologic studies due to the multifaceted dimensions of healthy aging. Healthy longevity, on the other hand, focuses primarily promoting health span, particularly the extension of the life span free from major diseases and disabilities.[8] In cohort studies, both healthy aging and healthy longevity are often operationalized as survival to a given age, disease status, and/or functional ability.[9]

Physical Activity, Sedentary Behavior and Health in Older Adults

Increasing physical activity (PA) and limiting sedentary behavior (SB) is known to reduce the risk of developing many chronic conditions and managing the progression of current conditions.[10] In their review of systematic reviews, observational studies, and randomized controlled trials of physical activity and health outcomes, the 2018 Physical Activity Guidelines Advisory Committee concluded that strong evidence suggests older adults

who meet PA guidelines are less likely to die prematurely and have a reduced risk of heart disease, stroke, cancer at multiple sites, type 2 diabetes, obesity, hypertension, osteoporosis, dementia, and many other chronic health conditions.[10,11] In addition to disease prevention and management, being physically active and avoiding SB makes it easier to perform activities of daily living, including eating, bathing, toileting, dressing, getting into or out of a bed or chair, and moving around the house or neighborhood. Physically active older adults are less likely to experience falls, and if they do fall, they are less likely to be seriously injured.[10,11] PA can also preserve physical function and mobility, which may help maintain independence longer and delay the onset of major disability. Promoting PA and reducing SB for health aging and longevity is especially important because older adults are the least physically active of any age group and spend over 60% of their awake time adults in sedentary behaviors.[12-14] As US older adults continue to age, PA levels are lowest and SB are highest among the oldest old.[12,15]

Considerations for Cancer Survivors

Over two-thirds of cancer survivors are 65 years or older.[16] As the number of US older adults with cancer grows and expected survival time increases, the improved prognosis has created a growing need to address the unique health issues facing cancer survivors that result from the disease, its treatment, and related comorbid conditions. For example, over a quarter of cancer survivors experience fatigue many years after treatment has ended.[17] The risk of developing of heart disease is elevated by some cancer treatments[18] and cardiovascular mortality is emerging as a major competing cause of death in cancer survivors.[18,19] As such, health behaviors such as PA among cancer survivors has become an important focus for healthy aging. Strong evidence has demonstrated the numerous benefits of PA for cancer survivors, including improved physical function, cardiorespiratory fitness, psychosocial health, and survival after cancer.[20-22] Conversely, limited epidemiological data linking sedentary time and cancer survival exist, though there is some suggestion of increased risk for cancer mortality.[23]

Classification of Physical Activity and Sedentary Behavior

According to the Physical Activity Guidelines for Americans, 2nd edition, PA is defined as "any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level".[10] PA volume is the total amount of activity accumulated over a specific time period.[24] Absolute rates of energy expenditure during PA are commonly described as light, moderate, or vigorous intensity. Energy expenditure is expressed by multiples of the metabolic equivalent of task (MET), where 1.0 MET is the rate of energy expenditure while sitting at rest. Sedentary behavior is separate from PA and is defined as "any waking behavior characterized

by a low level of energy expenditure (less than or equal to 1.5 METs) ***and*** in a sitting, reclining, or lying position".[10] Light-intensity activity is non-sedentary waking behavior that requires 1.5 to less than 3.0 METs; examples include walking at a slow or leisurely pace (2 mph or less), cooking activities, or light household chores. Moderate-intensity activity requires 3.0 to less than 6.0 METs; examples include walking briskly (2.5 to 4 mph), playing doubles tennis, or raking the yard. Vigorous-intensity activity requires 6.0 or more METs; examples include jogging, running, carrying heavy groceries or other loads upstairs, shoveling snow, or participating in a strenuous fitness class. Activities that are of vigorous or moderate-intensity are frequently aggregated into a category called moderate-to-vigorous intensity physical activities (MVPA). Another type of total PA volume measure is daily step counts ("daily steps"), which can be taken at any intensity level.

Measurement of Physical Activity

The gold standard for measuring energy expenditure from PA is doubly labeled water, a technique that quantifies total daily energy expenditure in free-living conditions.[25] However, this method is rarely used in large-scale epidemiologic studies due to its technical and expensive procedures. Therefore, measurement of PA and SB in cohort studies has been traditionally performed using self-reported questionnaires. While questionnaires are low cost and can provide context such as type, location, and purpose of physical activities[26], they suffer from recall and social desirability biases, variability in intensity perceptions, and challenges with quantifying time spent in light-intensity activities.[27,28] Due to these limitations and the fact that accelerometers are more accurate than self-report, the use of these devices in cohorts studies has become increasingly more common. In addition, accelerometers address several limitations of self-reported questionnaires that are prevalent among older adults, such as capturing physical activity among those with cognitive impairment, assessment of light-intensity physical activity, daily step counts, and measuring shorter bouts or breaks in physical activity.[26,28]

Advancements in Accelerometer-Measured Physical Activity and Sedentary Behavior

While many different brands of research-grade accelerometers exist, the brand most commonly used in cohort studies is the AcitGraph triaxial accelerometer.[29] The triaxial accelerometer is small (4.6x3.3x1.5 cm) and light weight (19 grams), with a dynamic range of +/-6 G. These accelerometers are generally placed on the right hip and are worn for up to 7 days. While directions for wear time vary by study design, participants are typically instructed to always wear the device except for when in water. These accelerometers collect acceleration data at a given pre-specified frequency, which is most commonly 30 Hz.[29] The raw acceleration signals are then processed by

the ActiGraph's proprietary software to calculate "counts" per epoch, which is an aggregated measure of the raw acceleration signal over a given time epoch.[30] The proprietary nature of counts makes comparisons between studies that use different devices difficult because counts could have different definitions across manufacturers.[31] To overcome limitations of counts, efforts have been made to establish summary metrics from the raw data with transparent formulas. One such metric is the accelerometer activity index (AAI).[32] The AAI is a measure of the variability of the raw acceleration signal, relative to the signal variability when the device is not perceived to be moving. It is calculated as the standard deviation of the raw accelerometer signal during activity, divided by the standard deviation of the signal at rest.[32] Thus, the AAI has a similar interpretation across devices. In a recent calibration study that compared AAI versus counts per 15s epoch, AAI predicted activity intensity (i.e. MET values) better than did counts among older women (R^2 = 0.74 versus 0.54).[33] In addition to counts, the ActiGraph GT3X+ device measures daily step counts using a proprietary algorithm.

Relatedly, hip worn ActiGraph devices do not detect sedentary postures well using the counts summary metric[34,35] even though it has been commonly used in previous studies of sedentary behavior. Emerging algorithms can leverage raw acceleration data instead of the counts summary metrics to better identify postural transitions (i.e., sit-to-stand). One such algorithm is the Convolutional Neural Network Hip Accelerometer Posture (CHAP) classification method, which was developed using a deep neural network to classify sitting versus non-sitting postures using raw acceleration data from hip worn ActiGraph devices. The CHAP was found to more accurate for classifying sit-to-stand transitions and sitting patterns from free-living hip-worn accelerometer data in older adults than the ActiGraph counts summary metric.[36] Both the AAI and CHAP algorithm are emerging tools that have only recently been implemented in epidemiological studies of physical activity and sedentary behavior in lieu of count-based metrics.[37]

Review of Epidemiologic Studies on Physical Activity and Healthy Aging Outcomes

Few published studies have examined PA and healthy longevity as an outcome explicitly. However, several have examined the association between PA and healthy aging, though there has been wide range of outcome definitions used which makes comparisons across studies difficult. **Table 1** highlights this issue and summarizes the components of healthy aging definitions identified in a recent systematic review and meta-analysis of PA and healthy aging.[38] Most included studies (*n* = 19/23; 82.6%) included physical performance to define healthy aging and more than half (*n* = 13/23; 56.5%) included information regarding disease status and mental health. Less than

half (*n* = 10/23; 43.5%) included survival to a specific age in the definition of healthy aging, whereas health status and subjective measurements were less frequently included. PA was measured via self-reported questionnaire in all included studies. Most studies (*n* = 17/23; 73.9%) reported a statistically significant positive association between PA and healthy aging while the remaining studies reported a non-significant association. As an example, one study examined 13,535 Nurses' Health Study participants who were free of major chronic diseases at baseline in 1986 and had survived to age 70 years or older at the end of follow-up.[39] The authors defined healthy aging as no history of 10 major chronic diseases and no cognitive impairment, physical impairment, or mental health limitations. The study found higher PA levels at midlife, as measured by METs from self-reported questionnaires, were significantly associated with better odds of healthy aging.[39]

Gaps in the Literature

In the systematic review, it should be noted that none of the included studies used accelerometer-measured PA and only included one measurement period, which may fail to fully capture changes in PA behaviors and the effect on healthy longevity outcomes. Studies of accelerometer-measured PA and SB with healthy longevity are still emerging. However, investigations into the associations of accelerometry with specific components of healthy longevity, such as mortality, are abundant. There is strong consensus that higher levels of accelerometer-measured PA, at any intensity, and less time spent sedentary are associated with substantially reduced risk for premature mortality in older adults.[40,41] Most of this evidence is among general older adult populations, and few studies have tested the associations between accelerometer-measured PA and SB with survival specifically among older adults with chronic conditions such as cancer. In addition, higher PA and lower SB levels measured by accelerometers are also both prospectively associated with the ability to complete activities of daily living in older adults.[42] However, the associations between accelerometer-measured PA and SB with survival to late age with intact physical function has not been explored previously. Clarifying the potential roles SB, daily steps and light-intensity PA have in promoting healthy longevity among older adults is particularly important given that older adults spend the highest proportion of their day sedentary than any other age group[13] and most of their PA time is light-intensity.[43-45] While a single accelerometer measurement can provide valuable insights into behaviors of older adults, few studies have examined patterns of repeated measures of PA using accelerometers. Measuring PA trajectories over time can help illustrate how PA behaviors change into later older adulthood and can help screen for adults who may benefit most from PA promotional strategies.

Table 1. Components of healthy aging definitions used in prospective studies of physical activity and health aging taken from Daskalopoulou et al.

Authors	Survival	Health Status	Physical Performance	Diseases	Mental Health	Subjective Measurements	Others*
Almeida et al., 2013	x	x	x		x		
Andrews et al., 2002			x		x		
Bell et al., 2014	x		x	x	x		
Britton et al., 2008		x	x	x	x		
Burke et al., 2001				x			
Ford et al., 2000							x
Gu et al., 2009	x		x				
Gureje et al., 2014			x	x		x	
Hamer et al., 2013			x	x	x		
Hodge, English et al., 2013	x		x	x	x		
Hodge, O'Dea et al., 2013	x		x	x	x		
Kaplan et al., 2008		x	x				
LaCroix et al., 2016	x		x	x			
Li et al., 2001			x		x	x	
Newman et al., 2003			x	x	x		
Palmore, 1979	x		x			x	
Pruchno & Wilson-Genderson, 2014			x	x		x	
Sabia et al., 2012			x	x	x		
Shields & Martel, 2006		x	x		x		
Sun et al., 2010	x		x	x	x		
Tampubolon, 2016							x
Terry et al., 2005	x			x	x		
Vaillant & Mukamal, 2001	x		x			x	x

Specific Aims

In this dissertation, I aimed to clarify the nuances and precision in estimates of PA and SB and healthy aging and longevity among older women in general, whether these behaviors prolong lifespan among cancer survivors, and describe how PA trajectories in older women changer over time. The following aims are addressed:

Aim 1: Quantify the associations between accelerometer-measured PA, SB and healthy longevity in the Women's Health Accelerometry Collaboration (WHAC). We hypothesized that higher levels of PA and lower levels of SB were associated with higher odds of surviving to age 90 years with intact mobility compared to dying before age 90 years.

Aim 2: Quantify the associations of accelerometer-measured PA and SB with total, cardiovascular disease, and cancer mortality among cancer survivors in WHAC. We hypothesized that higher levels of PA and lower levels of SB were associated with reduced hazard for all-cause, cardiovascular disease, cancer mortality among cancer survivors. In addition, we hypothesized that high amounts of PA could mitigate the harmful effects of SB on mortality.

Aim 3: Characterize the longitudinal changes in accelerometer-measured PA among older women in the Women's Health Initiative Strong and Healthy (WHISH) pragmatic trial. Specifically, (1) describe changes in PA measures over approximately 7 years of follow-up in aging women and (2) identify characteristics that are associated with different trajectories of PA change over time. We hypothesized that baseline PA, health status, health behaviors, and psychosocial factors would be associated with PA behavior trends over time.

Chapter 2 Accelerometer-measured physical activity, sedentary behavior, and healthy longevity: the Women's Health Accelerometry Collaboration

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Abstract

Background: While physical activity (PA) and sedentary behavior (SB) have consistently been shown to influence mortality risk, less is known about their associations with survival to late age with intact mobility. We examined associations between accelerometer-measured daily PA and SB and odds of survival to age 90 with and without mobility disability.

Methods: Postmenopausal women in Women's Health Accelerometry Collaboration (WHAC) were categorized into three groups based on their mobility status at age 90 years: (1) survived to age 90 with intact mobility ("intact mobility"); (2) survived to age 90 with mobility disability ("mobility disability"); and (2) died before age 90. Eligible participants wore an ActiGraph GT3X+ on the hip for ≥4 of 7 days from 2011–2015. Covariate-adjusted multinomial logistic regression models estimated odds ratios (ORs) of PA (light, moderate-to-vigorous [MVPA], total, steps) and SB (sitting time, mean bout duration) with intact mobility and mobility disability relative to dying before age 90. Isotemporal substitution models were used to evaluate the theoretical impact on healthy aging of replacing 30 min/day of sitting time with light or MVPA.

Results: Among the 3,809 women included (mean [SD] age, 83.3 [2.6] years), 1,741 (45.7%) had intact mobility, 1,355 (35.6%) had mobility disability, and 713 (18.7%) died before age 90. Compared to dying before age 90, the OR (95% confidence intervals [CI]) for every 1-SD increment in predictor variables and survival with intact mobility were 1.45 (1.31, 1.61) for light PA, 1.92 (1.71, 2.16) for MVPA, 1.65 (1.48, 1.83) for total PA, 2.04 (1.81, 2.31) for steps, 0.66 (0.59, 0.73) for sitting time, and 0.73 (0.66, 0.81) for sitting bouts. Estimates for mobility disability were similar, though attenuated. Replacing 30 min/day of sitting with light (OR=1.09, 95% CI: 1.05, 1.14) or MVPA (OR=2.04, 95% CI: 1.75, 2.38) was associated with increased odds of intact mobility.

Conclusions: Increased PA and reduced SB was associated with survival to age 90 both with and without mobility disability. These findings corroborate the potential role "moving more and sitting less" has in promoting healthy longevity.

Introduction

In the United States, the population of older adults (ages ≥65 years) will grow from about 15% in 2016 to nearly 25% of the population in 2060, of which more than half will be women.[46] As women have longer life expectancies than men,[2] the economic, healthcare, and societal burdens experienced by older women due to chronic conditions and other age-related afflictions are substantial.[3,4] As such, strategies for the promotion of healthy longevity among older women is a public health priority.[8] While definitions of healthy longevity vary, it is often operationalized in cohort studies as survival to a given age, disease status, or functional ability.[9] Increasing physical activity (PA) and limiting sedentary behaviors (SB) can be an effective strategy for facilitating healthy longevity because it reduces the risk of premature mortality, the development of many chronic conditions, and can help preserve physical function.[10]

Previous studies have consistently reported positive associations between PA and various aspects of healthy longevity in women,[38,39,47-49] however most evidence has relied on self-reported PA which is less accurate compared to accelerometry, and can lead to incomplete understanding of the role of PA in maintaining good health.[50] In addition, light-intensity PA, daily steps, and sitting bout lengths are poorly captured using self-reported questionnaires.[50,51] Accelerometers can produce reliable estimate of these behaviors and can therefore provide an opportunity to address limitations in previous research.[28] Given that there is a finite amount of time in a day, it is prudent to consider how time spent in one behavior could displace time spent on another and the subsequent estimated effects on health outcomes. While some studies have used isotemporal substitution modeling (ISM)[52,53] to show that replacing SB with PA could theoretically reduce mortality risk,[54] few studies have examined how displacing sitting time with PA may impact associations with healthy longevity.[47]

Using prospective data from the Women's Health Accelerometry Collaboration (WHAC), we examined the associations of accelerometer-measured PA and SB at age 78–89 years, with survival to age 90 with and without mobility disability. In addition, we examined the theoretical and statistical impact of substituting sitting time with light PA and MVPA on healthy longevity.

Methods

Study Population

The WHAC was created through the harmonization of accelerometry, covariate, and mortality data from the Women's Health Study (WHS) and the WHI Objective Physical Activity and Cardiovascular Health Study

(OPACH), which has been described in detail elsewhere.[37] In WHAC, 25,337 women were sent an accelerometer, with 18,289 contributing from WHS and 7,048 from OPACH. After excluding those that did not return the accelerometer, did not wear the accelerometer, or experienced accelerometer malfunction, 22,976 women contributed at least four adherent days of accelerometry wear defined as wearing the device for at least 10 hours during a day while awake.

Measures

Accelerometry

Women in both WHS and OPACH wore the ActiGraph GT3X+ triaxial accelerometer (ActiGraph LLC, Pensacola, FL) for up to seven consecutive days in 2011–2015.[37,55,56] In WHS, women were asked to wear the accelerometer over the right hip, removing it only during sleep or when in water.[55] In OPACH, women were asked to wear the accelerometer over the right hip including during sleep but not when in water;[56] subsequently, the time spent sleeping was removed for all analyses based on times in and out of bed recorded in daily diaries. The accelerometer recorded three-dimensional raw acceleration signals at 30 Hz, which were aggregated using ActiLife software (V.6) to counts per 15s epochs with the normal filter setting. Accelerometer non-wear time was removed using the validated Choi algorithm.[57,58] Besides daily steps, all PA metrics were derived from the raw acceleration signals based on the Accelerometer Activity Index (AAI).[32] Average intensity per day was summarized as average AAI/15s. Using OPACH calibration-study derived accelerometry cutpoints,[33,59] daily average time spent in intensity-specific categories measured from AAI/15-second cutpoints were defined as follows: light low 101-269, light high 270-586, and MVPA ≥587. Light low and light high PA were combined for light PA (101-586 AAI/15-seconds) and all variables were combined for total PA (≥101 AAI/15-seconds). Steps per day were determined using the ActiGraph GT3X+ manufacturer's step algorithm. Sitting time and bout duration were classified by the Convolutional Neural Network Hip Accelerometer Posture (CHAP) algorithm, which is intended for application on hip-worn ActiGraph GT3X+ data.[36] The CHAP algorithm classifies each 10 second nonoverlapping window of continuous data as either "sitting" or "non-sitting" postures.[36] From this output, total daily sitting time (minutes/day) and mean sitting bout duration (min/bout) were derived. Accelerometer awake wear time was accounted for using the residuals method.[60]

Healthy Longevity

Mobility disability was determined from the RAND-36 physical function score.[61] The RAND-36 assesses an individual's ability to perform everyday physical activities, such as walking, climbing stairs, bending, and lifting. It consists of multiple items related to physical functioning, and responses are scored and aggregated to generate a composite score (range 0–100) representing overall physical function. Scores of ≤50 indicate severe impairment in physical function[62] and represented mobility disability in our study. The RAND-36 was administered every year in OPACH and sporadically in WHS after accelerometry baseline, and the response closest in time to reaching age 90 years was used to distinguish healthy longevity from mobility disability at that time (**Table 2**). For both cohorts, deaths were reported by family members or postal authorities, with medical records, interviews with next of kin, and death certificates obtained to confirm the event. The National Death Index[63] was searched periodically for cohort members. From these data, women were classified into three mutually exclusive categories: (1) lived to age 90 with intact mobility ("intact mobility"); (2) lived to age 90 with mobility disability ("mobility disability"); or (3) died before their 90th birthday ("died").

Covariates

Sociodemographic variables, including age, race and ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, Other), and education (high school or less, some college, college or more) were collected at study enrollment. Participants from both cohorts regularly completed mailed questionnaires regarding their medical history and health behaviors and the administration closest to the time of accelerometer wear was used. Women self-reported general health (excellent, very good, good, fair, poor), smoking status (current, former, never), and alcohol intake (never, rarely, monthly, weekly, daily). They also reported on postmenopausal hormone use and history of diabetes. Cardiovascular disease (including history of myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, or stroke) and cancer were self-reported and then physician adjudicated using medical records. Height and weight were self-reported in WHS and measured by study personnel in OPACH. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and defined as underweight (<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), or obese (>=30.0).

Analytic Sample

Inclusion criteria for this analysis consisted of WHAC women who were: (1) born prior to December 31, 1942, and therefore eligible to reach age 90 at the time outcomes were adjudicated in December, 31 2022 (n=18,181

excluded), (2) ≤89 years at accelerometry baseline (n=242) and (3) survived at least one year post accelerometry measurement (n=67). These criteria resulted in an initial sample of 4,486 women with adherent accelerometer data. Women were further excluded if they were missing physical function data (n=401), if they were lost-to-follow-up prior to their age 90 birth year (n=228), or if they were missing covariate data (n=48). The resulting final analytic sample was 3,809 women. Compared to women who were excluded, women in the analytic sample were younger, had a higher proportion of non-Hispanic White and college graduates, and had slightly higher BMI **(Table 3)**. In addition, included women spent more time in MVPA, sitting, and took more steps/day than excluded women.

Statistical Analysis

Sociodemographic and health characteristics of women were examined across the three outcomes. The associations of continuous (per 1-standard deviation [SD] increments) and categorical (quartiles) measures of the accelerometer-derived measures with the healthy longevity outcomes were assessed using multinomial logistic regression models, using women who died as the referent group. Odds ratios (OR) and 95% confidence intervals (CI) were estimated to approximate the odds of survival to age 90 with or without mobility disability relative to death before age 90 across the exposure measures. The models were adjusted for cohort, age, race and ethnicity, education, BMI, self-reported general health, smoking status, alcohol intake, postmenopausal hormone use, history of diabetes, cardiovascular disease, and cancer. Trend tests across PA and SB exposure categories were calculated by replacing the exposure quartile variable in the model with the continuous variable. We fitted ISMs to quantify the associations of replacing 30 min/day of sitting time for light PA or MVPA with healthy longevity while keeping total amount of time of all 3 behaviors constant. Daily steps and sitting bouts were not included in these analyses. Briefly, the ISM is originally expressed as the following model (adapted from Shi et al.[47]):

$$\text{Healthy longevity outcomes} = \beta_0 \text{sitting time} + \beta_1 \text{light PA} + \beta_2 \text{MVPA} + \beta_3 \text{total awake time (i.e., sitting + light PA + MVPA)} + \beta_4 \text{covariates.}$$

When eliminating sitting time from the model, β_1 represents the effect of substituting 30 min/day of light PA for 30 min/day of sitting, while holding total awake time constant, and β_2 represents the effect of substituting 30 min/day of MVPA for 30 min/day of sitting while holding total awake time constant. Similar interpretations for the remaining substitution models apply when light or MVPA are omitted from the model. For comparison purposes, we included

a partition model which included the same variables except for total awake time. The interpretation for this model is that each coefficient for a certain behavior represents the effect of adding, rather than substituting, that behavior.

Since survival to old age and activity patterns could vary by age at baseline, BMI and chronic disease status, additional analyses tested for multiplicative interaction by age group (78–81, 82–84, and 85–89 years), obesity (BMI <30 vs. ≥30 kg/m^2) and chronic disease (history of diabetes, cancer, and/or cardiovascular disease at baseline vs. none) status variables using a product term for each in separate multinomial logistic regression models. In addition, a sensitivity analysis was conducted excluding women with mobility disability at baseline or missing physical function data at baseline, which limits the analysis to only women with intact mobility at baseline. Given that both healthy longevity outcomes are common in our sample, the odds ratio overestimates the risk ratio.[64] Therefore, we conducted a sensitivity analysis by running two separate generalized linear models with a log-link and binomial distribution (intact mobility vs death and mobility disability vs death) to estimate adjusted risk ratios to compare to the primary analysis. All analyses were conducted in R v4.0.2 (R Foundation for Statistical Computing; Vienna, Austria.

Results

Sample Characteristics

The sample included 3,809 WHAC (2,361 OPACH and 1,448 WHS) women **(Table 4)**. Mean (SD) age at baseline was 83.3 (2.6) years. Compared to women in the lowest quartile of total PA, women in the highest quartile were younger, had higher alcohol intake, lower BMI, better self-rated health, and lower chronic disease prevalence. The mean (SD) of each accelerometer measure were: 285.9 (80.1) min/day for light PA, 35.6 (24.4) min/day for MVPA, 321.5 (92.0) for total PA, 3,332 (1,855) steps/day for steps, 602.2 (104.2) min/day for sitting time, and 13.6 (5.1) min/bout for sedentary bouts (**Table 4)**. Distributions for the 3 outcomes were: 1,741 (45.7%) intact mobility, 1,355 (35.6%) mobility disability, and 713 (18.7%) died before age 90.

Healthy Longevity

Compared to the odds of dying, all accelerometer measures had statistically significant dose-response associations with odds of intact mobility or mobility disability (all $p<0.05$; **Table 5**). Per one-SD increment at baseline, the adjusted ORs (95% CI) of intact mobility compared to dying were 1.45 (1.31, 1.61) for light PA, 1.92 (1.71, 2.16) for MVPA, 1.65 (1.48, 1.83) for total PA, 2.04 (1.81, 2.31) for steps, 0.66 (0.59, 0.73) for sitting time, and 0.73 (0.66, 0.81) for sitting bout duration. Compared to women in the lowest quartile of PA measures, the ORs

(95% CI) for intact mobility for women in the highest quartile ranged from 2.42 (1.83, 3.20) for light PA to 6.86 (5.09, 9.24) for steps. Similar strong, though inverse, associations were seen comparing the highest quartile of sitting time (OR=0.34, 0.26, 0.46) and bouts (OR=0.55; 0.42, 0.73) compared to the lowest quartiles. The adjusted ORs (95% CI) of mobility disability compared to dying were 1.23 (1.11, 1.36) for light PA, 1.25 (1.11, 1.42) for MVPA, 1.27 (1.14, 1.41) for total PA, 1.28 (1.13, 1.46) for steps, 0.82 (0.73, 0.92) for sitting time, and 0.83 (0.75, 0.91) for sitting bout duration. Quartile-based analyses displayed similar patterns for all PA and SB measures.

The theoretical/statistical replacement of sitting time with either light or MVPA was associated with increased odds of both intact mobility and mobility disability **(Table 6).** For example, replacing 30 min/day of sitting with MVPA was associated with 2.0 times the odds of intact mobility (OR=2.04, 95% CI: 1.75, 2.38) and 1.2 times the odds of mobility disability (OR=1.22, 95% CI: 1.04, 1.44). Statistically significant associations were also present for replacing sitting with light PA (intact mobility: OR=1.09, 95% CI: 1.05, 1.14; mobility disability: OR=1.06, 95% CI: 1.02, 1.11).

Except for steps, associations between PA and SB with odds of intact mobility and mobility disability did not differ across age groups **(Table 7)**. The association between greater daily steps and higher odds of intact mobility was strongest among women ages 85–89 years at baseline, though associations were significant for other age groups as well. Regardless of obesity status, higher PA (and lower SB) levels were associated with increased odds intact mobility and mobility disability **(Table 7)**. For all PA measures, estimates were of higher magnitude among women with BMI ≥30 kg/m^2 compared to those with <30 kg/m^2 for mobility disability ($P_{INTERACTION}$<0.05). Estimates did not differ by chronic disease status for light or total PA **(Table 7)**. However, for both survival outcomes, ORs for MVPA and steps were of higher magnitude among women with ≥1 chronic condition compared to those with none. In addition, higher SB levels were associated with statistically significantly reduced odds of mobility disability (per 1-SD sitting time OR=0.70, 95% CI: 0.58, 0.84; sitting bouts OR=0.71, 95% CI: 0.61, 0.83) among those with ≥1 chronic condition, whereas these behaviors were not significantly associated with mobility disability among those with no chronic conditions. Sensitivity analysis limited to women with intact mobility at baseline were generally consistent in direction and magnitude with the primary analysis (**Table 8**). As expected, the estimated relative risk ratios from log-binomial logistic regression models were attenuated compared to the ORs from the primary analysis particularly for SB measures **(Table 9)**, however all risk ratios remained statistically significant.

Discussion

In our study of postmenopausal women ages 78–89 years, higher levels of accelerometer-measured PA were associated with improved odds of survival to age 90 with or without mobility disability, while SB was associated with lower odds. The theoretical and statistical replacement of sitting time with light or MVPA was associated with increased odds of both survival outcomes. The benefits of PA and harms of SBs on the odds of healthy aging were more pronounced among women with obesity or at least one chronic disease. Altogether, these findings suggest that reducing sitting time and increasing PA may be associated with stronger odds of survival to late age with intact physical function.

Our finding of independent associations between accelerometer-measured PA with healthy longevity in older women is consistent with previous studies using self-reported PA,[39,47] including two previous analyses using WHI data,[48,49] though effect size magnitudes differed likely due to multiple reasons. In addition to the use of accelerometer-derived PA/SB measures, our study differed from previous studies in the definition of healthy longevity in the following two ways: (1) we assessed survival to age 90, which is a later age than previous studies (range=70–85 years), and (2) we did not include absence of chronic disease status as part of the criterion. The decision to focus solely on survival to late age and intact mobility was made in part due to the high prevalence of disease at baseline (33% with cardiovascular disease, diabetes, and/or cancer; **Table 4**), which is likely due in part to the older age at baseline (mean age=83.3 years), and the likelihood of very few women in our sample being free of chronic disease at age 90. In addition, the inclusion of intact mobility was informed in part by the recognized relationships between mobility in older adults and functional independence, health-related qualify of life, psychosocial health, and mortality.[65]

Approximately 1 in 4 US older adults (ages ≥65 years) report having a mobility disability,[66] and the prevalence of mobility disability increases sharply with older adult age groups.[67,68] This pervasive public health problem was reflected in our study where, among the 3,096 women who survived to age 90 in our study, close to half (43.8%) reported having a mobility disability. Substantial evidence demonstrates an inverse dose-response relationship between PA and risk of physical functional limitations among older adults.[11,69] While higher PA levels increased the odds of both survival with and without mobility disability, the magnitude of the associations with mobility disability were consistently lower than for intact mobility. Among oldest old adults, there are several

factors (e.g., fatigue, lower back pain, joint stiffness) that are associated with both PA/SB and limited mobility in later life. These conditions are likely not life threatening, thus allowing older women to experience the survival benefits associated with higher levels PA and lower levels of SB, but not the freedom from mobility disability.

Three previous studies have examined self-reported total PA only and reported similar dose-response patterns with odds of survival to late age with no chronic diseases or mobility disability.[39,48,49] Shi et al. examined light PA and MVPA separately and, similar to our study, reported stronger associations for MVPA than for light PA.[47] While the benefits of MVPA on odds of healthy longevity are well established,[38] far less is known about the role of light PA which is poorly assessed by most questionnaires. Most PA performed by older adults is light intensity,[45,70] which is estimated to contribute to daily PA energy expenditure at a similar amount as MVPA.[45] In addition, light PA measured on either the absolute (i.e., determined by accelerometer cutpoints) or relative (i.e., percentage of maximal possible effort) scales are both associated with all-cause mortality in older women.[71] Our finding of an independent association of light PA with healthy longevity in older women extends those of previous research and warrants further consideration for future potential behavioral interventions.

We observed strong associations between daily steps, which can be taken at any intensity, with healthy longevity outcomes that were similar in magnitude to those from accelerometer-derived MVPA. For every 1,855 steps/day taken (approximated to <1 mile[72]) in our study, women had over 2 fold higher odds of healthy survival. Acknowledging that this may be a difficult target for some older adults to achieve, the strong linear association found in our study suggests that taking lower than 1,855 steps/day can still confer higher benefits for healthy longevity. In addition, our findings suggest that the benefits of higher steps counts are stronger among women with chronic conditions than among healthy older women. While previous studies did not measure daily step counts, two studies asked about frequency and duration of walking outside the home and found similar beneficial associations with survival to late age with no chronic diseases or mobility disability.[39,48] Daily steps are an intuitive metric for total PA and, in light of our findings, clinical and public health practitioners may consider daily step targets as a tool for PA and healthy longevity promotion among older women, particularly those suffering from chronic conditions.

SB was inversely associated with odds of survival to age 90 with and without mobility disability, which extends the findings of previous studies in older women[47,48] and ours is, to our knowledge, the first to include a measure of sitting bout duration. Shi et al. found that replacing 1 hour/day of sitting time with either light or MVPA

increased the odds of survival to age 70 with no physical, memory, or mental health disabilities.[47] Similarly, we observed that replacing 30 min/day of sitting time with either light or MVPA could increase the odds of survival to age 90 with or without mobility disability. These findings underscore that while engaging in SB can be harmful, replacing this time with lower intensity PA may confer health benefits and be more feasible for older adult populations. Given the significant inverse associations between SB and healthy aging in our study, public health promotion campaigns targeting older adults should consider not only increasing PA but also decreasing total and prolonged SB.

All women experienced higher odds of survival to age 90 with and without mobility disability with higher PA and lower SB levels independent of obesity status. Obesity is strongly associated with risk of both mobility disability[73] and mortality.[74] While engaging in higher intensity activities can be particularly difficult for women with obesity, our findings suggest that engaging in more accessible behaviors such as more time in light PA, taking more daily steps, and breaking up prolonged sitting time throughout the day may be effective in promoting healthy survival among this population.

Strengths and Limitations

Our study has several strengths. To our knowledge, this is the first study to assess healthy longevity among older women with accelerometer-measured PA and SB. These are more accurate measures than self-reported PA/SB,[50] which are prone to recall and social desirability biases.[75] In addition, the use of accelerometry provided an opportunity to examine light PA, steps, and sitting bout lengths which are poorly captured in self-report. This study leveraged the strength of the WHAC cohort, which is the product of harmonized activity, covariate, health status, and mortality data from WHS and OPACH and thus created a large sample of US women ages 78–89 years with hip-worn accelerometry data. There are some limitations to our findings. We were unable to control for known confounders such as diet, medication, and other chronic diseases, which may have resulted in overestimation of effect sizes. We excluded 228 women with usable accelerometer data who were eligible to reach age 90 but were lost-to-follow-up. Excluded women had slightly lower levels of PA compared to our analytic sample **(Table 3)**, which may have biased our estimates away from the null. We estimated ORs, which overestimate the risk when the outcome is common; however, in sensitivity analyses we estimated risk ratios and while the risk ratio estimate magnitudes were smaller, they were in the same direction as ORs and were statistically significant (**Table 9)**. In

addition, the generalizability of our findings is restricted to older women and similar studies should be conducted in younger, male, and more diverse cohorts.

Conclusions

In this large cohort of older US women with hip-worn accelerometer data, engaging in more PA of any intensity level, taking more steps, and limiting total and prolonged SB were associated with higher odds of survival to age 90 with or without mobility disability. The theoretical replacement of 30 min/day of sitting time with either light or MVPA increased the odds of healthy longevity by 9% and 104%, respectively. Our findings extend those of previous studies of PA, SB, and healthy aging among older women, and provide further justification for the recommendation to move more and sit less to age well into tenth decade of life.

Table 2. Timing of RAND-36 physical function measures in WHS and OPACH

Time	WHS (accelerometry measured 2011-2015)	OPACH (accelerometry measured 2012-2014)
Baseline	-	2012-2014
Time 1	2015-2017	2015-2016
Time 2	-	2016-2017
Time 3	-	2017-2018
Time 4	2018	2018-2019
Time 5	2019	2019-2020
Time 6	-	2020-2021

OPACH, Objective Physical Activity and Cardiovascular Health Study; WHS, Women's Health Study

Table 3. Comparison of included and excluded participants who were eligible to reach age 90 by December 31, 2022

Baseline characteristics	Eligible to reach age 90	Included	Excluded	P-value[a]
N	4,486	3,809	677	
Cohort, *n (%)*				
WHS	1,710 (38.1)	1,448 (38.0)	262 (38.7)	0.768
OPACH	2,776 (61.9)	2,361 (62.0)	415 (61.3)	
Age (years), *mean (SD)*	83.3 (2.8)	83.3 (2.6)	83.6 (3.4)	0.002
Race and ethnicity, *n (%)*				
Non-Hispanic White	3,688 (82.2)	3,155 (82.8)	533 (78.7)	0.029
Non-Hispanic Black	503 (11.2)	407 (10.7)	96 (14.2)	
Hispanic	265 (5.9)	224 (5.9)	41 (6.1)	
Other or unknown	30 (0.7)	23 (0.6)	7 (1.0)	
Highest education level, *n (%)*				
High school/GED or less	600 (13.5)	494 (13.0)	106 (16.6)	0.011
Some college	2,049 (46.1)	1,746 (45.8)	303 (47.3)	
College graduate	1,800 (40.5)	1,569 (41.2)	231 (36.1)	
Smoking status, *n (%)*				
Current	85 (1.9)	70 (1.8)	15 (2.3)	0.699
Former	1,918 (42.9)	1,639 (43.0)	279 (42.0)	
Never	2,471 (55.2)	2,100 (55.1)	371 (55.8)	
Alcohol use, *n (%)*				
Never or rarely	1,782 (39.8)	1,490 (39.1)	292 (43.3)	0.129
Monthly	1,075 (24.0)	913 (24.0)	162 (24.0)	
Weekly	1,191 (26.6)	1,033 (27.1)	158 (23.4)	
Daily	435 (9.7)	373 (9.8)	62 (9.2)	
Body mass index (kg/m^2), *n (%)*				
<18.5	129 (2.9)	112 (2.9)	17 (2.5)	0.127
18.5-24.9	1,953 (43.5)	1,645 (43.2)	308 (45.5)	
25.0-29.9	1,555 (34.7)	1,310 (34.4)	245 (36.2)	
≥30.0	849 (18.9)	742 (19.5)	107 (15.8)	
Mean (SD)	26.1 (5.0)	26.2 (5.0)	25.7 (4.6)	0.025
Self-rated general health, *n (%)*				
Excellent	501 (11.2)	430 (11.3)	71 (10.5)	0.063
Very good	1,962 (43.8)	1,688 (44.3)	274 (40.7)	
Good	1,699 (37.9)	1,433 (37.6)	266 (39.5)	
Fair or poor	320 (7.1)	258 (6.8)	62 (9.2)	
Current HRT use, *n (%)*	141 (3.1)	125 (3.3)	16 (2.4)	0.256
History of cardiovascular disease, *n (%)*	507 (11.3)	425 (11.2)	82 (12.1)	0.511
History of diabetes, *n (%)*	656 (14.6)	550 (14.4)	106 (15.7)	0.443
History of cancer, *n (%)*	593 (13.2)	507 (13.3)	86 (12.7)	0.713
≥1 chronic disease[b], *n (%)*	1,486 (33.1)	1,258 (33.0)	228 (33.7)	0.774
RAND-36 physical function score, *mean (SD)*	64.7 (24.9)	65.0 (24.8)	62.9 (25.8)	0.072

Table 3. (cont'd) Comparison of included and excluded participants who were eligible to reach age 90 by December 31, 2022

Baseline characteristics	Eligible to reach age 90	Included	Excluded	P-value[a]
N	4,486	3,809	677	
Accelerometer measures, *mean (SD)*				
Light PA, min/day	285.2 (80.1)	285.9 (80.1)	284.5 (80.7)	0.798
MVPA, min/day	35.0 (24.3)	35.6 (24.4)	32.2 (23.6)	0.001
Total PA, min/day	320.1 (92.0)	321.5 (92.0)	316.6 (91.7)	0.280
Steps per day	3,285 (1,840)	3,332 (1,855)	3,082 (1,738)	0.002
Sitting time, min/day	602.5 (104.8)	602.2 (104.2)	610.2 (108.3)	0.039
Sitting bout duration, min	13.6 (5.2)	13.6 (5.1)	13.7 (5.6)	0.444
Device awake wear, min/day	887.0 (77.2)	888.8 (76.1)	877.1 (82.5)	<0.001

Abbreviations: HRT, hormone replacement therapy; GED, General Educational Development; MVPA, moderate-to-vigorous physical activity; OPACH, Objective Physical Activity and Cardiovascular Health Study; SD, standard deviation; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study.

[a]P-value from a t-test (continuous variables) or Chi Square test (categorical variables) comparing included and excluded participants

[b]History of cardiovascular disease, diabetes, and/or cancer at accelerometer measurement

Table 4. Baseline characteristics overall and by quartiles of total physical activity in the Women's Health Accelerometry Collaboration

Characteristic	Total	Quartile of Total PA			
		Q1	Q2	Q3	Q4
N	3,809	954	950	952	953
Cohort, *n (%)*					
WHS	1,448 (38.0)	281 (29.5)	355 (37.4)	385 (40.4)	427 (44.8)
OPACH	2,361 (62.0)	673 (70.5)	595 (62.6)	567 (59.6)	526 (55.2)
Age (years), *mean (SD)*	83.3 (2.6)	83.7 (2.7)	83.4 (2.6)	83.3 (2.6)	82.7 (2.4)
Race and ethnicity, *n (%)*					
Non-Hispanic White	3,155 (82.8)	803 (84.2)	800 (84.2)	774 (81.3)	778 (81.6)
Non-Hispanic Black	407 (10.7)	104 (10.9)	97 (10.2)	109 (11.4)	97 (10.2)
Hispanic	224 (5.9)	45 (4.7)	50 (5.3)	60 (6.3)	69 (7.2)
Other or unknown	23 (0.6)	2 (0.2)	3 (0.3)	9 (0.9)	9 (0.9)
Highest education level, *n (%)*					
High school/GED or less	494 (13.0)	118 (12.4)	132 (13.9)	118 (12.4)	126 (13.2)
Some college	1,746 (45.8)	432 (45.3)	454 (47.8)	421 (44.2)	439 (46.1)
College graduate	1,569 (41.2)	404 (42.3)	364 (38.3)	413 (43.4)	388 (40.7)
Smoking status, *n (%)*					
Current	70 (1.8)	21 (2.2)	21 (2.2)	15 (1.6)	13 (1.4)
Former	1,639 (43.0)	430 (45.1)	401 (42.2)	413 (43.4)	395 (41.4)
Never	2,100 (55.1)	503 (52.7)	528 (55.6)	524 (55.0)	545 (57.2)
Alcohol use, *n (%)*					
Never or rarely	1,490 (39.1)	406 (42.6)	373 (39.3)	351 (36.9)	360 (37.8)
Monthly	913 (24.0)	258 (27.0)	231 (24.3)	225 (23.6)	199 (20.9)
Weekly	1,033 (27.1)	212 (22.2)	266 (28.0)	264 (27.7)	291 (30.5)
Daily	373 (9.8)	78 (8.2)	80 (8.4)	112 (11.8)	103 (10.8)
Body mass index (kg/m^2), *n (%)*					
<18.5	112 (2.9)	14 (1.5)	20 (2.1)	34 (3.6)	44 (4.6)
18.5-24.9	1,645 (43.2)	245 (25.7)	360 (37.9)	460 (48.3)	580 (60.9)
25.0-29.9	1,310 (34.4)	364 (38.2)	365 (38.4)	314 (33.0)	267 (28.0)
≥30.0	742 (19.5)	331 (34.7)	205 (21.6)	144 (15.1)	62 (6.5)
Mean (SD)	26.2 (5.0)	28.5 (5.4)	26.8 (5.1)	25.4 (4.5)	24.0 (3.9)
Self-rated general health, *n (%)*					
Excellent	430 (11.3)	68 (7.1)	99 (10.4)	118 (12.4)	145 (15.2)
Very good	1,688 (44.3)	362 (37.9)	413 (43.5)	441 (46.3)	472 (49.5)
Good	1,433 (37.6)	417 (43.7)	369 (38.8)	353 (37.1)	294 (30.8)
Fair or poor	258 (6.8)	107 (11.2)	69 (7.3)	40 (4.2)	42 (4.4)
Current HRT use, *n (%)*	125 (3.3)	19 (2.0)	26 (2.7)	34 (3.6)	46 (4.8)
History of cardiovascular disease, *n (%)*	425 (11.2)	135 (14.2)	122 (12.8)	106 (11.1)	62 (6.5)
History of diabetes, *n (%)*	550 (14.4)	194 (20.3)	143 (15.1)	125 (13.1)	88 (9.2)
History of cancer, *n (%)*	507 (13.3)	132 (13.8)	128 (13.5)	126 (13.2)	121 (12.7)
≥1 chronic disease[a], *n (%)*	1,258 (33.0)	379 (39.7)	333 (35.1)	300 (31.5)	246 (25.8)

Table 4. (cont'd) Baseline characteristics overall and by quartiles of total physical activity in the Women's Health Accelerometry Collaboration

Characteristic	Total	Quartile of Total PA			
		Q1	Q2	Q3	Q4
N	3,809	954	950	952	953
Accelerometer measures, *mean (SD)*					
Light PA, min/day	285.9 (80.1)	188.8 (37.2)	259.1 (22.8)	310.6 (24.5)	385.2 (49.8)
MVPA, min/day	35.6 (24.4)	18.7 (12.9)	30.6 (17.1)	37.7 (20.1)	55.3 (28.7)
Total PA, min/day	321.5 (92.0)	207.4 (40.0)	289.7 (17.8)	348.4 (17.0)	440.5 (52.0)
Steps per day	3,332 (1,855)	1901 (951)	2941 (1234)	3545 (1440)	4941 (2105)
Sitting time, min/day	602.2 (104.2)	698.2 (75.8)	621.9 (75.5)	577.3 (73.1)	511.5 (90.3)
Sitting bout duration, min	13.6 (5.1)	18.4 (5.8)	14.1 (3.6)	11.9 (2.9)	9.9 (3.1)
Device awake wear, min/day	888.8 (76.1)	891.4 (82.6)	883.5 (74.5)	887.8 (74.4)	892.5 (72.2)

Abbreviations: HRT, hormone replacement therapy; GED, General Educational Development; MVPA, moderate-to-vigorous physical activity; OPACH, Objective Physical Activity and Cardiovascular Health Study; SD, standard deviation; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study.

[a]History of cardiovascular disease, diabetes, and/or cancer at accelerometer measurement

Table 5. Associations of physical activity and sedentary behavior on healthy aging outcomes

Accelerometer Variable	Lived to Age 90 with Intact Mobility (n=1,741)	Lived to Age 90 with Mobility Disability (n=1,355)
	OR (95% CI)[a]	OR (95% CI)[a]
Light PA (range or SD, min/day)		
Continuous form (per 80.1)	1.45 (1.31, 1.61)	1.23 (1.11, 1.36)
Quartile 1 (<229.5)	1.00 (REF)	1.00 (REF)
Quartile 2 (229.5–283.5)	1.49 (1.14, 1.93)	1.29 (0.99, 1.68)
Quartile 3 (283.6–337.8)	1.82 (1.39, 2.38)	1.48 (1.13, 1.95)
Quartile 4 (>337.8)	2.42 (1.83, 3.20)	1.65 (1.23, 2.20)
MVPA (range or SD, min/day)		
Continuous form (per 24.4)	1.92 (1.71, 2.16)	1.25 (1.11, 1.42)
Quartile 1 (<18.1)	1.00 (REF)	1.00 (REF)
Quartile 2 (18.1–30.5)	1.95 (1.50, 2.55)	1.04 (0.82, 1.35)
Quartile 3 (30.6–48.4)	3.77 (2.84, 5.00)	1.70 (1.29, 2.25)
Quartile 4 (>48.4)	5.39 (4.03, 7.20)	1.56 (1.16, 2.11)
Total PA (range or SD, min/day)		
Continuous form (per 92.0)	1.65 (1.48, 1.83)	1.27 (1.14, 1.41)
Quartile 1 (<256.5)	1.00 (REF)	1.00 (REF)
Quartile 2 (256.5–319.1)	1.69 (1.30, 2.20)	1.36 (1.05, 1.77)
Quartile 3 (319.2–380.0)	2.10 (1.60, 2.75)	1.46 (1.11, 1.92)
Quartile 4 (>380.0)	3.27 (2.47, 4.34)	1.72 (1.28, 2.30)
Steps (range or SD, steps/day)		
Continuous form (per 1,855)	2.04 (1.81, 2.31)	1.28 (1.13, 1.46)
Quartile 1 (<2,052)	1.00 (REF)	1.00 (REF)
Quartile 2 (2,052–2,991)	2.46 (1.88, 3.22)	1.27 (0.98, 1.64)
Quartile 3 (2,992–4,258)	3.50 (2.66, 4.62)	1.63 (1.25, 2.13)
Quartile 4 (>4,259)	6.86 (5.09, 9.24)	1.67 (1.23, 2.28)
Sitting time (range or SD, min/day)		
Continuous form (per 104.2)	0.66 (0.59, 0.73)	0.82 (0.73, 0.92)
Quartile 1 (<536.7)	1.00 (REF)	1.00 (REF)
Quartile 2 (536.7–605.4)	0.84 (0.64, 1.10)	1.02 (0.75, 1.37)
Quartile 3 (605.5–676.6)	0.59 (0.45, 0.78)	0.81 (0.60, 1.08)
Quartile 4 (>676.6)	0.34 (0.26, 0.46)	0.75 (0.56, 1.01)
Sitting bout (range or SD, min/bout)		
Continuous form (per 5.1)	0.73 (0.66, 0.81)	0.83 (0.75, 0.91)
Quartile 1 (<10.2)	1.00 (REF)	1.00 (REF)
Quartile 2 (10.2–12.7)	1.10 (0.84, 1.44)	1.27 (0.95, 1.70)
Quartile 3 (12.7–15.9)	0.71 (0.54, 0.93)	1.02 (0.77, 1.35)
Quartile 4 (>15.9)	0.55 (0.42, 0.73)	0.76 (0.57, 1.00)

Abbreviations: CI, confidence interval; PA, physical activity; OR, adjusted odds ratio; SD, standard deviation

[a]Models are adjusted for cohort, age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, history of cancer, and body mass index. Referent group: died before age 90 (n=713)

All p-values for a linear trend across quartiles were <0.001 except for sitting time (p=0.021) and bouts (p=0.016) for survival with mobility disability.

Table 6. Odds of healthy aging outcomes according to isotemporal substitution of 30 min/day of 3 activities.

Models	Lived to Age 90 with Intact Mobility			Lived to Age 90 with Mobility Disability		
	Sitting Time	Light PA	MVPA	Sitting Time	Light PA	MVPA
	OR (95% CI)[a]	OR (95% CI)[a]	OR (95% CI)[a]	OR (95% CI)[a]	OR (95% CI)[a]	OR (95% CI)[a]
Substitution Model						
Sitting time	Replaced	1.09 (1.05, 1.14)	2.04 (1.75, 2.38)	Replaced	1.06 (1.02, 1.11)	1.22 (1.04, 1.44)
Light PA	0.91 (0.88, 0.95)	Replaced	1.87 (1.57, 2.22)	0.94 (0.90, 0.98)	Replaced	1.15 (0.96, 1.38)
MVPA	0.49 (0.42, 0.57)	0.54 (0.45, 0.64)	Replaced	0.82 (0.69, 0.96)	0.87 (0.72, 1.04)	Replaced
Partition Model[b]	0.96 (0.92, 1.00)	1.05 (1.00, 1.10)	1.96 (1.68, 2.29)	0.99 (0.95, 1.03)	1.05 (1.00, 1.10)	1.21 (1.02, 1.43)

Abbreviations: CI, confidence interval; PA, physical activity; OR, adjusted odds ratio

[a]Total awake time is the sum of time spent sitting, in light PA, and in MVPA. Models include a term for total awake time and are additionally adjusted for the following covariates: cohort, age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, history of cancer, and body mass index. Outcome referent group: died before age 90 birth year.

[b]Presented for comparison purposes. Model includes sitting time, light PA, MVPA, and covariates but not total awake time. ORs represent a comparison of a given healthy aging outcome for every 30 min/day increment in the exposure variable but not restricting total time.

Table 7. Associations of physical activity and sedentary behavior on healthy aging outcomes by age group, obesity status, and chronic disease status.

Accelerometer Variable	Lived to Age 90 with Intact Mobility	Lived to Age 90 with Mobility Disability
	OR (95% CI)[a]	OR (95% CI)[a]
Ages 78–81 years (n=1,098)		
Light PA	1.38 (1.17, 1.62)	1.19 (0.98, 1.43)
MVPA	1.69 (1.42, 2.01)	1.19 (0.97, 1.47)
Total PA	1.53 (1.30, 1.80)	1.21 (1.00, 1.46)
Steps	1.73 (1.45, 2.07)	1.19 (0.96, 1.48)
Sitting time	0.71 (0.60, 0.85)	0.96 (0.79, 1.18)
Sitting bouts	0.87 (0.72, 1.04)	1.03 (0.84, 1.25)
Ages 82–84 years (n=1,512)		
Light PA	1.45 (1.24, 1.70)	1.15 (0.99, 1.35)
MVPA	1.87 (1.54, 2.26)	1.24 (1.01, 1.52)
Total PA	1.63 (1.38, 1.92)	1.19 (1.01, 1.40)
Steps	1.99 (1.62, 2.43)	1.28 (1.04, 1.58)
Sitting time	0.67 (0.57, 0.79)	0.84 (0.71, 0.99)
Sitting bouts	0.70 (0.59, 0.82)	0.82 (0.71, 0.95)
Ages 85–89 years (n=1,199)		
Light PA	1.52 (1.15, 2.02)	1.32 (1.00, 1.74)
MVPA	2.57 (1.74, 3.80)	1.43 (0.97, 2.11)
Total PA	1.82 (1.35, 2.45)	1.39 (1.03, 1.86)
Steps	3.21 (2.12, 4.87)[b]	1.61 (1.07, 2.43)
Sitting time	0.56 (0.42, 0.75)	0.70 (0.53, 0.92)
BMI <30 kg/m^2 (n=3,107)		
Light PA	1.44 (1.29, 1.62)	1.20 (1.07, 1.36)
MVPA	1.90 (1.68, 2.16)	1.22 (1.07, 1.41)
Total PA	1.66 (1.48, 1.86)	1.24 (1.10, 1.40)
Steps	2.03 (1.78, 2.32)	1.25 (1.09, 1.45)
Sitting time	0.65 (0.58, 0.74)	0.84 (0.74, 0.95)
Sitting bouts	0.70 (0.62, 0.80)	0.84 (0.74, 0.96)
BMI ≥30 kg/m^2 (n=750)		
Light PA	1.63 (1.27, 2.08)	1.48 (1.18, 1.87)[b]
MVPA	2.25 (1.60, 3.17)	1.61 (1.16, 2.25)[b]
Total PA	1.80 (1.39, 2.32)	1.55 (1.22, 1.96)[b]
Steps	2.62 (1.80, 3.81)	1.80 (1.26, 2.56)[b]
Sitting time	0.63 (0.49, 0.81)	0.72 (0.56, 0.91)
Sitting bouts	0.81 (0.69, 0.96)	0.80 (0.69, 0.94)

Table 7. (cont'd) Associations of physical activity and sedentary behavior on healthy aging outcomes by age group, obesity status, and chronic disease status.

Accelerometer Variable	Lived to Age 90 with Intact Mobility	Lived to Age 90 with Mobility Disability
	OR (95% CI)[a]	OR (95% CI)[a]
No chronic conditions (n=2,584)		
Light PA	1.40 (1.23, 1.59)	1.19 (1.04, 1.36)
MVPA	1.74 (1.52, 2.00)	1.11 (0.96, 1.30)
Total PA	1.58 (1.39, 1.79)	1.20 (1.05, 1.38)
Steps	1.83 (1.59, 2.12)	1.11 (0.95, 1.31)
Sitting time	0.70 (0.61, 0.80)	0.90 (0.78, 1.04)
Sitting bouts	0.81 (0.70, 0.93)	0.96 (0.84, 1.11)
≥1 chronic condition (n=1,274)		
Light PA	1.54 (1.29, 1.85)	1.30 (1.09, 1.55)
MVPA	2.39 (1.90, 3.01)[b]	1.60 (1.27, 2.02)[b]
Total PA	1.78 (1.48, 2.15)	1.38 (1.15, 1.66)
Steps	2.63 (2.05, 3.36)[b]	1.73 (1.36, 2.21)[b]
Sitting time	0.59 (0.49, 0.72)	0.70 (0.58, 0.84)[b]
Sitting bouts	0.69 (0.59, 0.81)	0.71 (0.61, 0.83)[b]

CI, confidence interval; PA, physical activity; OR, adjusted odds ratio

Outcome referent group: died before age 90 birth year

[a]Estimates are per 1-standard deviation increment in exposure. Models are adjusted for cohort, age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, history of cancer, and body mass index.

[b]P-value for multiplicative interaction <0.05 relative to ages 78–81 and 82–84

[c]P-value for multiplicative interaction <0.05 relative to BMI <30 kg/m^2 or no chronic conditions

Table 8. Associations of physical activity and sedentary behavior on healthy aging outcomes after excluding women with mobility disability at baseline or missing physical function data at baseline (n=2,665)

Accelerometer Variable	Lived to Age 90 with Intact Mobility (n=1,559)	Lived to Age 90 with Mobility Disability (n=708)
	OR (95% CI)	OR (95% CI)
Light PA		
Continuous form (per 77.4 min/day)	1.37 (1.21, 1.56)	1.20 (1.04, 1.39)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	1.62 (1.15, 2.27)	1.47 (1.01, 2.13)
Quartile 3	1.67 (1.20, 2.34)	1.55 (1.07, 2.23)
Quartile 4	2.37 (1.68, 3.35)	1.74 (1.18, 2.56)
P_{TREND}	<0.001	0.006
MVPA		
Continuous form (per 25.0 min/day)	1.68 (1.46, 1.93)	1.25 (1.07, 1.46)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	1.49 (1.05, 2.11)	0.97 (0.67, 1.40)
Quartile 3	3.04 (2.11, 4.38)	1.74 (1.18, 2.55)
Quartile 4	3.92 (2.72, 5.64)	1.65 (1.11, 2.44)
P_{TREND}	<0.001	<0.001
Total PA		
Continuous form (per 88.6 min/day)	1.53 (1.34, 1.74)	1.25 (1.08, 1.44)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	1.53 (1.09, 2.15)	1.43 (0.99, 2.06)
Quartile 3	1.94 (1.38, 2.72)	1.54 (1.06, 2.24)
Quartile 4	2.92 (2.06, 4.14)	1.92 (1.30, 2.84)
P_{TREND}	<0.001	0.001
Steps		
Continuous form (per 1,901 steps/day)	1.77 (1.53, 2.04)	1.27 (1.08, 1.49)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	2.00 (1.41, 2.83)	1.18 (0.82, 1.70)
Quartile 3	3.01 (2.11, 4.28)	1.72 (1.19, 2.49)
Quartile 4	5.41 (3.75, 7.80)	1.76 (1.19, 2.63)
P_{TREND}	<0.001	<0.001

Table 8. (cont'd) Associations of physical activity and sedentary behavior on healthy aging outcomes after excluding women with mobility disability at baseline or missing physical function data at baseline (n=2,665)

Accelerometer Variable	Lived to Age 90 with Intact Mobility (n=1,559)	Lived to Age 90 with Mobility Disability (n=708)
	OR (95% CI)	OR (95% CI)
Sitting time		
Continuous form (per 101.1 min/day)	0.67 (0.59, 0.77)	0.78 (0.67, 0.91)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	0.71 (0.51, 0.98)	0.88 (0.61, 1.27)
Quartile 3	0.51 (0.37, 0.71)	0.65 (0.45, 0.95)
Quartile 4	0.39 (0.27, 0.55)	0.70 (0.47, 1.03)
P_{TREND}	<0.001	0.027
Sitting bout		
Continuous form (per 4.6 min/bout)	0.82 (0.71, 0.93)	0.82 (0.71, 0.95)
Quartile 1	1.00 (REF)	1.00 (REF)
Quartile 2	1.37 (0.99, 1.90)	1.39 (0.96, 2.00)
Quartile 3	0.78 (0.57, 1.07)	0.96 (0.67, 1.36)
Quartile 4	0.72 (0.51, 1.01)	0.65 (0.44, 0.96)
P_{TREND}	0.009	0.018

Abbreviations: CI, confidence interval; PA, physical activity; OR, adjusted odds ratio; SD, standard deviation

[a]Models are adjusted for cohort, age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, history of cancer, and body mass index. Referent group: died before age 90 (n=398).

Table 9. Relative risk ratios estimated from logistic regression models compared to the primary analysis

Logistic Regression Model	**Intact Mobility**	**Mobility Disability**
No./Total (%)	1,741/2,454 (70.9%)	1,355/2,068 (65.5%)
	RR (95% CI)[a]	**RR (95% CI)[b]**
Light PA	1.32 (1.13, 1.54)	1.20 (1.06, 1.38)
MVPA	1.60 (1.28, 2.01)	1.24 (1.06, 1.45)
Total PA	1.49 (1.24, 1.81)	1.25 (1.08, 1.45)
Steps	1.75 (1.34, 2.29)	1.28 (1.08, 1.50)
Sitting time	0.95 (0.93, 0.98)	0.87 (0.81, 0.93)
Sitting bout duration	0.90 (0.86, 0.94)	0.83 (0.77, 0.90)
Multinomial Regression Models	**Intact Mobility**	**Mobility Disability**
No./Total (%)	1,741/3,809 (45.7%)	1,355/3,809 (35.6%)
	OR (95% CI)	**OR (95% CI)**
Light PA	1.45 (1.31, 1.61)	1.23 (1.11, 1.36)
MVPA	1.92 (1.71, 2.16)	1.25 (1.11, 1.42)
Total PA	1.65 (1.48, 1.83)	1.27 (1.14, 1.41)
Steps	2.04 (1.81, 2.31)	1.28 (1.13, 1.46)
Sitting time	0.66 (0.59, 0.73)	0.82 (0.73, 0.92)
Sitting bout duration	0.73 (0.66, 0.81)	0.83 (0.75, 0.91)

CI, confidence interval; OR, adjusted odds ratio; PA, physical activity; RR, adjusted risk ratio; SD, standard deviation

Estimates are per 1-standard deviation increment in exposure. Models are adjusted for cohort, age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, history of diabetes, history of cardiovascular disease, history of cancer, and body mass index.

[a]Log-binomial logistic regression model comparing intact mobility to death before age 90

[b]Log-binomial logistic regression model comparing mobility disability to death before age 90

Chapter 2, in part, is currently being prepared for submission for publication of the material. Hyde, Eric T.; Bandoli, Gretchen E.; Crespo, Noe C.; Parada Jr., Humberto; Zou, Jingjing; LaCroix, Andrea Z. The dissertation author was the primary investigator and author of this paper.

Chapter 3 Accelerometer-measured physical activity, sedentary behavior, and mortality among cancer survivors: the Women's Health Accelerometry Collaboration

Eric T. Hyde, Gretchen E. Bandoli, Jingjing Zou, Noe C. Crespo, Humberto Parada Jr., and Andrea Z. LaCroix

Abstract

Background: Our study examined the associations between accelerometer-measured daily physical activity (PA) (including light, moderate-to-vigorous PA [MVPA] total PA, and steps) and sedentary behavior (SB) (including sitting time and mean bout duration) with all-cause, cancer, and cardiovascular disease mortality among cancer survivors in the Women's Health Accelerometry Collaboration (WHAC).

Methods: Postmenopausal women in WHAC who reported a cancer diagnosis ≥1 year prior to wearing an ActiGraph GT3X+ on the hip for ≥4 of 7 days from 2011–2015 were included. Outcomes included all-cause, cancer, and cardiovascular disease mortality. Multivariable Cox regression estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for each PA and SB measure in association with mortality outcomes.

Results: 2,616 cancer survivors were included (mean [SD] age, 74.3 [6.7] years) and followed for 8.2 average years. For all-cause mortality (n=646), every 1-SD increment in light PA, MVPA, total PA, and step counts had HRs (95% CIs) of 0.92 (0.84, 1.00), 0.84 (0.74, 0.96), 0.89 (0.80, 0.98), and 0.82 (0.71, 0.94). Sitting time and bout duration had HRs (95% CI) of 1.12 (1.02, 1.23) and 1.05 (0.97, 1.13), respectively. Associations for cancer mortality (n=184) and cardiovascular disease (n=119) were similar in magnitude but not statistically significant except for MVPA (HR=0.59, 95% CI:0.41, 0.84) and steps (HR=0.64, 95% CI:0.45, 0.93) for cardiovascular disease mortality.

Conclusion: Greater levels of PA of any intensity level and reducing SB were associated with reduced risk of all-cause, cancer, and cardiovascular disease mortality among postmenopausal cancer survivors.

Introduction

In 2022, the number of individuals with a history of cancer ("cancer survivors") in the United States was estimated to be 18.1 million.[76] This number is projected to reach 26.0 million by 2040.[77] As the number of US older adults living with cancer grows and expected survival time increases, the improved prognosis has created a growing need to address the health issues faced by cancer survivors that result from the disease, its treatment, related comorbid conditions, and aging. For example, cardiovascular mortality is a major competing cause of death in cancer survivors.[18,19] As such, health behaviors such as physical activity (PA) and sedentary behavior (SB) may be an important focus for improving cancer survivorship and quality of life. Strong evidence has demonstrated the numerous benefits of PA for cancer survivors, including improved physical function, cardiorespiratory fitness, psychosocial health, and survival after cancer.[11,20-22,78] Conversely, limited epidemiological data linking sedentary time and cancer survival exist, though there is some suggestion of increased risk for cancer mortality with increasing time spent sedentary.[23] Additionally, the majority of evidence on the associations between PA and SB with cancer survivorship is based on self-reported measures. While cost effective and relatively easy to administer, particularly in large epidemiological studies, self-reported assessments of PA and sitting time in cancer survivors are prone to recall and social desirability biases.[79,80] Furthermore, self-reported assessments do not accurately capture light-intensity PA or daily step counts, which are important behaviors given that current guidelines recommend that cancer survivors should avoid inactivity if they are unable to meet the MVPA guideline.[10] These issues can be mitigated to some extent by the using accelerometry to assess PA and sedentary behaviors.[28,81]

To help address these limitations in the existing literature, the primary aim of this study was to examine the associations of accelerometer-derived measures of PA (light PA, MVPA, total PA, and daily steps) and SB (sitting time and mean sedentary bout duration) with all-cause, cancer, and cardiovascular disease mortality among 2,616 cancer survivors in the Women's Health Accelerometry Collaboration (WHAC), a combined prospective cohort of postmenopausal US women who participated in either the Women's Health Study (WHS) or the Women's Health Initiative Objective Physical Activity and Cardiovascular Health (OPACH) Study.

Methods

Study Population

The WHAC was created through the harmonization of accelerometry, covariate, cancer incidence and mortality data from WHS and OPACH, which has been described in detail elsewhere.[37] Briefly, the WHS is a

completed randomized trial that tested aspirin, beta-carotene, and vitamin E for the prevention of cardiovascular disease and cancer among 39,876 US women aged ≥45 years (1992–2004), who were subsequently followed observationally.[82-84] From 2011–2014, 18,289 WHS women participated in an ancillary study that collected accelerometry data; 17,466 (96%) women returned devices with usable data.[55] The OPACH study is an ancillary to the WHI Long Life Study,[85] and is a prospective study of accelerometry with chronic disease and aging outcomes.[56] Among the 9,252 women consented to the WHI Long Life Study, 7,048 participated in OPACH; 6,489 (92%) women returned accelerometers with usable data. WHAC accelerometry data was collected from 2011–2015 and mortality outcomes were ascertained through 2022. In both cohorts, women reported if they had been diagnosed with a cancer prior to the accelerometer data collection, including type of cancer and time since diagnosis. All women provided written informed consent and the studies were approved by the Institutional Review Boards at the University of North Carolina – Chapel Hill, Brigham and Women's Hospital, and the Fred Hutchinson Cancer Research Center.

Measures

Accelerometry

Both cohorts requested participants wear the ActiGraph GT3X+ triaxial accelerometer (ActiGraph LLC, Pensacola, FL) for up to seven consecutive days and return it by mail.[37,55,56] In WHS, women were asked to wear the accelerometer over the right hip, removing it only during sleep or when in water.[55] In OPACH, women were asked to wear the accelerometer over the right hip including during sleep but not when in water;[56] subsequently, the time spent sleeping was removed for all analyses based on times in and out of bed recorded in daily diaries. The accelerometer recorded three-dimensional raw acceleration signals at 30 Hz, which were aggregated using ActiLife software (V.6) to counts per 15s epochs with the normal filter setting. Accelerometer non-wear time was removed using the validated Choi algorithm.[57,58] Accelerometer wear adherence was defined as wearing time of ≥10 hours on ≥4 days of device wear, consistent with other protocols.[29,86] Awake wear time was accounted for using the residuals method.[60]

PA metrics were derived from the raw acceleration signals based on the Accelerometer Activity Index (AAI).[32] Average intensity per day was summarized as average AAI/15-seconds. Using OPACH calibration-study derived accelerometry cutpoints,[33,59] daily average time spent in intensity-specific categories measured from AAI/15-second cutpoints were defined as follows: light low 101-269, light high 270-586, and MVPA ≥587. Light low and light high were also combined for light (101-586 AAI/15-seconds) and all PA variables were combined for

total activity (≥101 AAI/15-seconds). Steps per day were determined using the ActiLife proprietary software. SB metrics (total daily sitting time and mean sitting bout duration) were classified by the Convolutional Neural Network Hip Accelerometer Posture (CHAP) algorithm, which is intended for application on hip-worn ActiGraph GT3X+ data and has strong agreement with criterion inclinometer classification of minute-level sitting vs nonsitting (sensitivity 97%, specificity 89%, balanced accuracy 93%).[36]

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[63]. The cause of death was based on death certificates, medical records, or other records using the ICD 10th edition.[37] While cancer mortality data and definitions were mirrored between cohorts, cardiovascular disease mortality data could not be harmonized and therefore definitions varied slightly. In WHS, cardiovascular disease mortality was defined as death due to ischemic heart disease, acute myocardial infarction, cerebrovascular disease, sudden death, and other cardiovascular cause. The definition for cardiovascular disease mortality in OPACH was death due to definite or possible coronary heart disease, cerebrovascular disease, and other/unknown cardiovascular cause.

The primary endpoints of interest for this study were: (1) all-cause, (2) cancer, and (3) cardiovascular disease mortality. Time-to-event was computed from the first day of accelerometry to the date of death through December 31, 2022 for WHS or February 19, 2023 for OPACH. For analyses of cancer and cardiovascular disease mortality, participants who died from non-cancer and non-cardiovascular disease causes were right-censored, respectively.

Covariates

In both cohorts, age, race and ethnicity, and education level were self-reported at enrollment into the original study. Data on health history and health behaviors were ascertained annually, and responses from the measure closest in time to accelerometer baseline were used. Self-rated general health was assessed with 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 and cardiovascular disease, and time between cancer diagnosis and accelerometer measurement (in years). Height and weight were self-reported in WHS and measured by study personnel in OPACH. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m^2) and categorized as underweight (<18.5), healthy weight (18.5–24.9), overweight (25.0–29.9), or obese (≥30.0 kg/m^2). Physical function was based on responses to the

RAND-36 (scores range from 0 to 100; higher scores reflect better function).[61] Missingness was present for physical function (n=208), education (n=24), self-rated general health (n=2), and smoking status (n=1). Multiple imputation was performed using chained equations with predictive mean matching for 20 iterations and 25 imputations.[87]

Analytic Sample

From the 23,955 WHAC participants with accelerometer data, we included 2,799 (11.6%) who reported being cancer survivors. We also excluded 105 women with non-adherent accelerometer wear, 52 women with accelerometer data on which AAI and/or CHAP algorithms could not be applied, and 45 women who died within the first year of accelerometer wear. Thus, the analytic sample comprised of 2,616 cancer survivors, over half of which were breast cancer survivors (**Table 10**).

Statistical Analysis

Multivariable cohort-stratified Cox proportional hazards models[88] estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for each mortality outcome in association with each accelerometer-derived exposure. Each PA and SB variable were modeled categorically by quartiles (for all-cause) or tertiles (cancer and cardiovascular disease), and continuously (per 1-SD increment; all outcomes). Cohort-stratified proportional hazards models, whereby a strata term for cohort was included in each model, were used to allow for baseline hazards of the two cohorts to differ.[88] The proportional hazards assumption was inspected using plots of the Schoenfeld residuals and no violations were evident. We present results adjusted for age and race and ethnicity (Model 1), and a fully adjusted model (Model 2) which included adjustment for age, race and ethnicity, education, smoking status, alcohol use, general health, postmenopausal hormone use, diabetes history, cardiovascular disease history, BMI, physical function, cancer type, and years since cancer diagnosis at WHAC baseline. Associations for PA and SB 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 cross-product terms for continuous accelerometer variables with the reduced model without the interaction terms. Strata of interest explored for multiplicative interaction included age (<75 vs. ≥75 years), race and ethnicity (non-Hispanic White vs. other), BMI (<30 vs. ≥30 kg/m^2), physical function score (<75 vs. ≥75), years between cancer diagnosis and accelerometer measurement (<2 vs. ≥2 years), and cancer type (breast cancer vs. other). Due to the high correlation between PA and sitting time (Spearman ρ = -0.78) that precluded mutual adjustment for each exposure the same model, we additionally explored whether associations varied by the sample median MVPA (<50 vs. ≥50 min/day) and sitting time (<575 vs. ≥575 min/day). Sensitivity

analyses included (1) repeating the analyses but excluding women who died within the first 2 years of follow-up to further evaluate the potential of confounding by health status[89]; (2) a complete case analysis to compare with primary results using imputation; (3) independent Cox regression analyses for OPACH and WHS separately for the outcome of cardiovascular disease mortality due to differences in outcome definitions; and (4) competing risk analyses (Fine-Gray method)[90] where competing events for cancer and cardiovascular disease mortality were non-cancer deaths and non-cardiovascular disease deaths, respectively. All analyses were conducted in R v4.0.2 (R Foundation for Statistical Computing; Vienna, Austria).

Results

Sample Characteristics

There were 636 all-cause mortality events (184 cancer; 119 cardiovascular disease) identified through a mean (SD) of 8.2 (2.1) years (range=1.0–11.4) of follow-up. Participant baseline characteristics stratified by quartiles of total PA are presented in **Table 11.** Overall, participants had a mean (SD) age of 74.3 (6.7) years, were mostly non-Hispanic White (86%), and overweight (BMI=26.7 kg/m^2, SD=5.2). The average years lived between cancer diagnosis and accelerometer measurement was 8.3 (SD=5.2). Women with higher versus lower levels of PA were younger, had lower BMI, and higher frequency of alcohol use, better self-rated general health, better physical function, and were less likely to have a history of cardiovascular disease or diabetes. The mean (SD) of each accelerometer measure were: 302.0 (78.3) min/day for light PA, 53.9 (32.9) min/day for MVPA, 355.9 (96.7) for total PA, 4,637 (2,470) steps/day for steps, 575.7 (102.4) min/day for sitting time, and 13.2 (4.7) min/bout for sedentary bouts (**Table 11**).

Mortality

In Model 2, all PA measures had inverse associations (per 1-SD increment) with all-cause mortality (light PA, HR=0.92, 95% CI:0.84, 1.00; MVPA, HR=0.84, 95% CI:0.74, 0.96; total PA, HR=0.89, 95% CI:0.80, 0.98; steps, HR=0.82, 95% CI:0.71, 0.94) and both sedentary behavior measures had harmful associations (sitting time, HR=1.12, 95% CI:1.02, 1.23; sitting bout, HR=1.05, 95% CI:0.97, 1.13) **(Table 12)**. Point estimates were similar for cancer mortality across all accelerometer measures **(Table 13)**, however all 95% confidence intervals included the null. For cardiovascular disease mortality, significant associations indicating reductions in risk were present for MVPA (HR=0.59, 95% CI:0.41, 0.84) and steps (HR=0.64, 95% CI:0.45, 0.93) (**Table 14)**.

The restricted cubic splines for accelerometer measures and all-cause mortality are plotted on **Figure 1.** All measures displayed significant linear associations ($P_{LINEAR}<0.01$) except for sitting bouts. In addition, significant

nonlinear associations were observed for MVPA ($P_{NONLINEAR}<0.001$) and steps ($P_{NONLINEAR}=0.002$). For steps, the dose-response curve shows HRs begin declining at approximately 2,500 steps/day and the optimal mortality risk benefit occurs approximately 5,000–6,000 steps/day before leveling off. A similar dose-response pattern is evident for MVPA with the HRs leveling off at approximately 50–75 min/day.

Sub-Group Analyses

In general, associations for accelerometer measures with all-cause mortality were consistent when stratified on cohort subgroups **(Table 15)**. Multiplicative interaction analyses were nonsignificant except for age (<75 vs ≥75 years; MVPA: HR=1.02; 95% CI:0.86, 1.22 vs HR=0.70; 95% CI:0.58, 0.86; $P_{INTERACTION} = 0.05$; steps: HR=0.97; 95% CI:0.81, 1.17 vs HR=0.68; 95% CI:0.56, 0.83; $P_{INTERACTION}= 0.03$), physical function (<75 vs ≥75 score; total PA: HR=0.95; 95% CI:0.83, 1.08 vs HR=0.86; 95% CI:0.72, 1.03; $P_{INTERACTION} = 0.04$; steps: HR=0.91; 95% CI:0.74, 1.11 vs HR=0.85; 95% CI:0.70, 1.04; $P_{INTERACTION}= 0.02$; sitting bouts: HR=1.03; 95% CI:0.93, 1.13 vs HR=1.13; 95% CI:0.97, 1.31; $P_{INTERACTION}= 0.05$) and years between diagnosis and accelerometry measurement (<2 vs ≥2 years; steps: HR, 0.85; 95% CI:0.66, 1.15 vs 0.77; 95% CI:0.66, 0.90; $P_{INTERACTION} = 0.04$). Most differences in subgroup-specific estimates were small-to-modest, except for MVPA and steps for age group.

Sensitivity Analyses

Sensitivity analyses excluding deaths within the first two years of follow-up (**Tables 16–18**) and complete case analyses (**Tables 19–21**) were similar to the primary results. Some associations with cardiovascular disease mortality differed qualitatively by cohort (**Table 22)**, though estimates were in the same direction and analyses were imprecise due to fewer cases and smaller sample sizes. Competing risk analysis (Fine-Gray method) producing subdistribution HRs for cancer and cardiovascular disease mortality that were slightly attenuated compared to the primary results (**Table 23)**.

Discussion

To our knowledge, this is the largest comprehensive analysis exploring the associations between accelerometer-measured PA, sedentary behavior, and mortality outcomes in cancer survivors, and the first such study exclusively in older women cancer survivors—an understudied population. Higher amounts of all PA measures were associated with reduced risk of all-cause mortality, while more sedentary behavior was associated with increased risk. Lower risk of cardiovascular mortality was observed with greater amounts of MVPA and steps. Similar patterns were observed for cancer mortality, though estimates did not reach statistical significance. Sensitivity analyses and stratification by cohort subgroups affirmed our primary findings, which emphasize the

importance of engaging in PA and limiting sedentary behaviors among cancer survivors to promote healthy longevity.

The benefits of PA observed in our study are consistent with the findings from self-reported PA and sedentary behavior,[11,22,91] including WHI studies,[92,93] and with two previous studies using NHANES accelerometer data from cancer survivors.[94,95] For an approximate 1.5 hour/day increment in total PA, we observed a 14% reduced hazard for all-cause mortality which was similar to the estimate from the NHANES study by Loprinzi & Nooe (15% per 1 hour/day)[95] but differed from the analysis of NHANES data by Salerno et al. (32% per 1 hour/day)[94]. Unsurprisingly, Salerno et al. also observed stronger all-cause mortality associations with light PA (49% reduced hazard per 1 hour/day) and MVPA (37%) than those found in the present study. The stronger PA-mortality associations in their study may be due to longer average time between diagnosis and accelerometer measurement, different demographic and health status characteristics of the sample, or a higher proportion of deaths (45% of sample).[94] Nevertheless, our findings confirm the positive associations of PA of all intensities for long-term survivorship after cancer diagnosis for older women.

Daily steps is an intuitive metric for total PA accumulation and identifying a target range for optimal health benefits has garnered interest for future public health recommendations.[11] Ours is the first study to quantify the association with mortality outcomes among cancer survivors. Approximately each 2,500 steps/day increment (roughly equivalent to one mile[72]) was associated with lower risk of 18% and 36% for all-cause and cardiovascular disease mortality, respectively. The dose-response curve indicated optimal mortality risk benefit occurs at approximately 5,000–6,000 steps/day, which is lower than the 7,000 steps/day target suggested from previous WHS analysis of 16,741 women who were mostly (88%) without a history of cancer at baseline.[96] In other words, increases in daily step counts to a threshold lower than one found among mostly cancer-free women should be further investigated as an intervention to prolong cancer survivorship.

Engaging in more sedentary behaviors was associated with increased risks for all-cause mortality in our study. This contrasts with the findings of Salerno et al.,[94] which may be due in part to the imprecision of cutpoint methods that was used for determining sedentary behavior in their study. We used the CHAP algorithm, which is superior to cutpoint methods for measuring both sitting time and posture.[36,97] While associations with mortality were only linear in our study, the shape of the spline curves (**Figure 1)** show that sitting for more than approximately 10 hours/day was associated with increased risk of mortality. Given that cancer survivors have a higher prevalence of

accelerometer-measured sedentary time than non-cancer survivors,[98] our finding that both sitting time and bout length were associated with increased mortality risk supports current public health recommendations for cancer survivors to move more and sit less.[10]

Unlike findings from self-reported measures,[11,23,78] accelerometer-measured PA and sedentary behavior was not significantly associated with cancer mortality in our study. However, all point estimates for PA and sedentary behavior measures were similar between all-cause and cancer mortality, indicating that lowered precision due to few case counts (646 vs 174) may be responsible for the non-significant findings. Future studies in larger cancer cohorts may help clarify these associations.

The role of PA and sedentary behavior in risk of all-cause and cardiovascular disease mortality is well established.[11] However, the mechanisms through which increasing PA and limiting sedentary behaviors may potentially reduce cancer mortality are still emerging, with evidence suggesting they may reduce recurrence and improve survival through mechanisms similar to those affecting cancer incidence.[22] These mechanisms include reducing adiposity, correcting metabolic dysregulation, and lowering chronic inflammation, oxidative stress, and impaired immune function.[99] Increasing PA may also enhance tumor vasculature and cytotoxic immune response, impeding metastasis. Overall, multiple biological mechanisms could explain the relationship between PA and sedentary behavior on cause-specific mortality and more research is needed to clarify these associations.

Strengths and Limitations

Study strengths include the harmonization of accelerometry, covariate, cancer, and mortality data from WHS and OPACH to create one of the largest samples of older US women cancer survivors with usable hip-worn accelerometry data. Another strength was the ability to address reverse causation through sensitivity analyses restricting deaths to ≥2 after accelerometry measurement. Limitations include the lack of data regarding stage at cancer diagnosis, cancer treatment modalities, and other cancer-specific characteristics, and it is possible that survivors with late-stage diagnoses or more rigorous treatment procedures have different PA behaviors and thus differential associations with survival. In addition, our analysis was limited to one post-diagnosis accelerometer measurement. Cancer survivors often change their PA behaviors after diagnosis, during treatment and coping therapies, and after treatment is completed, and having only one post-diagnosis accelerometer assessment prevented us from disentangling theses effects on survival. Cancer survivors were more 8 years postdiagnosis on average and

thus had survived long enough to be included in our analysis. Generalizability is restricted to older women and our findings should be replicated in younger, male, and more diverse cohorts.

Conclusions

Among over 2,500 postmenopausal US female cancer survivors, accelerometer-assessed PA and daily steps were associated with reduced hazard of all cause and cardiovascular disease mortality, while higher amounts of sedentary behaviors were associated with increased hazards. Associations were weaker and not statistically significant for cancer mortality. Encouraging cancer survivors to sit less and engage in PA of all intensities may help promote long term survival.

Table 10. Distribution of cancer types among WHAC cancer survivors

Cancer type	Overall (n=2,616)	WHS (n=1,959)	OPACH (n=657)
	n (Col %)	n (Col %)	n (Col %)
Breast	1,342 (51.3)	1,050 (53.6)	292 (44.4)
Endometrial	223 (8.5)	187 (9.5)	36 (5.5)
Malignant melanoma	188 (7.2)	143 (7.3)	45 (6.8)
Colon	172 (6.6)	98 (5.0)	74 (11.3)
Lung	85 (3.2)	56 (2.9)	29 (4.4)
Ovarian	57 (2.2)	40 (2.0)	17 (2.6)
Bladder	56 (2.1)	36 (1.8)	20 (3.0)
Rectal	53 (2.0)	38 (1.9)	15 (2.3)
Kidney	44 (1.7)	28 (1.4)	16 (2.4)
Head and neck	21 (0.8)	14 (0.7)	7 (1.1)
Myeloma	21 (0.8)	14 (0.7)	7 (1.1)
Other (n<20 per type in WHAC)	354 (13.5)	255 (13.0)	99 (15.1)

Abbreviations: OPACH, Objective Physical Activity and Cardiovascular Health Study; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study

Table 11. WHAC cancer survivor characteristics overall and by quartiles of total PA.

Characteristic	Total	Quartiles of total PA (min/day)			
		<292.1	**292.1–354.3**	**354.4–418.6**	**>418.6**
N	2,616	654	654	654	654
Cohort, *n (%)*					
WHS	1,959 (74.9)	277 (42.4)	163 (24.9)	138 (21.1)	79 (12.1)
OPACH	657 (25.1)	377 (57.6)	491 (75.1)	516 (78.9)	575 (87.9)
Age (years), *n (%)*					
<70	754 (28.8)	104 (15.9)	183 (28.0)	201 (30.7)	266 (40.7)
70-79	1,263 (48.3)	299 (45.7)	314 (48.0)	333 (50.9)	317 (48.5)
≥80	599 (22.9)	251 (38.4)	157 (24.0)	120 (18.3)	71 (10.9)
Mean (SD)	74.3 (6.7)	77.1 (7.1)	74.5 (6.6)	73.6 (6.1)	71.8 (5.7)
Race and ethnicity, *n (%)*					
Non-Hispanic White	2,251 (86.0)	528 (80.7)	563 (86.1)	570 (87.2)	590 (90.2)
Non-Hispanic Black	218 (8.3)	89 (13.6)	55 (8.4)	46 (7.0)	28 (4.3)
Hispanic	108 (4.1)	31 (4.7)	25 (3.8)	29 (4.4)	23 (3.5)
Other or unknown	39 (1.5)	6 (0.9)	11 (1.7)	9 (1.4)	13 (2.0)
Highest education level, *n (%)*					
High school/GED or less	130 (5.0)	53 (8.1)	34 (5.2)	28 (4.3)	15 (2.3)
Some college	1,195 (45.7)	294 (45.0)	296 (45.3)	301 (46.0)	304 (46.5)
College graduate	1,267 (48.4)	304 (46.5)	318 (48.6)	313 (47.9)	332 (50.8)
Missing	24 (0.9)	3 (0.5)	6 (0.9)	12 (1.8)	3 (0.5)
Smoking status, *n (%)*					
Current	74 (2.8)	24 (3.7)	26 (4.0)	14 (2.1)	10 (1.5)
Former	1,260 (48.2)	319 (48.8)	321 (49.1)	306 (46.8)	314 (48.0)
Never	1,281 (49.0)	310 (47.4)	307 (46.9)	334 (51.1)	330 (50.5)
Missing	1 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Alcohol use, *n (%)*					
Never or rarely	1,003 (38.3)	290 (44.3)	266 (40.7)	238 (36.4)	209 (32.0)
Monthly	431 (16.5)	136 (20.8)	110 (16.8)	105 (16.1)	80 (12.2)
Weekly	816 (31.2)	156 (23.9)	191 (29.2)	224 (34.3)	245 (37.5)
Daily	366 (14.0)	72 (11.0)	87 (13.3)	87 (13.3)	120 (18.3)
Body mass index (kg/m^2), *n (%)*					
<18.5	54 (2.1)	10 (1.5)	10 (1.5)	14 (2.1)	20 (3.1)
18.5-24.9	1,056 (40.4)	151 (23.1)	221 (33.8)	318 (48.6)	366 (56.0)
25.0-29.9	919 (35.1)	223 (34.1)	262 (40.1)	238 (36.4)	196 (30.0)
≥30.0	587 (22.4)	270 (41.3)	161 (24.6)	84 (12.8)	72 (11.0)
Mean (SD)	26.7 (5.2)	29.4 (6.0)	27.1 (5.0)	25.5 (4.3)	24.7 (4.1)
Self-rated general health, *n (%)*					
Excellent	384 (14.7)	42 (6.4)	92 (14.1)	112 (17.1)	138 (21.1)
Very good	1,180 (45.1)	257 (39.3)	282 (43.1)	306 (46.8)	335 (51.2)
Good	871 (33.3)	271 (41.4)	240 (36.7)	211 (32.3)	149 (22.8)
Fair or poor	179 (6.8)	84 (12.8)	39 (6.0)	24 (3.7)	32 (4.9)
Missing	2 (0.1)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)

Table 11. (cont'd) WHAC cancer survivor characteristics overall and by quartiles of total PA.

Characteristic	Total	Quartiles of total PA (min/day)			
		<292.1	**292.1–354.3**	**354.4–418.6**	**>418.6**
N	2,616	654	654	654	654
RAND-36 physical functioning score					
Mean (SD)	73.2 (24.2)	60.5 (25.9)	73.9 (22.9)	77.7 (20.7)	80.8 (21.9)
Missing (%)	208 (8.0)	53 (8.1)	57 (8.7)	39 (6.0)	59 (9.0)
Current HRT use, *n (%)*	109 (4.2)	20 (3.1)	22 (3.4)	26 (4.0)	41 (6.3)
History of cardiovascular disease, *n (%)*	160 (6.1)	64 (9.8)	45 (6.9)	32 (4.9)	19 (2.9)
History of diabetes, *n (%)*	362 (13.8)	144 (22.0)	106 (16.2)	77 (11.8)	35 (5.4)
Years between diagnosis and WHAC baseline, *mean (SD)*	8.3 (5.2)	8.2 (5.0)	8.1 (5.1)	8.3 (5.3)	8.5 (5.3)
Accelerometer measures, *mean (SD)*					
Light PA, min/day	302.0 (78.3)	207.4 (40.2)	278.1 (25.7)	326.0 (27.7)	396.5 (49.7)
MVPA, min/day	53.9 (32.9)	27.7 (17.3)	45.6 (21.6)	58.2 (23.8)	84.2 (36.1)
Total PA, min/day	355.9 (96.7)	235.1 (45.0)	323.7 (17.4)	384.1 (18.4)	480.7 (52.6)
Steps per day	4637 (2470)	2522 (1257)	4056 (1622)	5056 (1750)	6913 (2642)
Sitting time, min/day	575.7 (102.4)	676.6 (71.6)	598.9 (64.9)	552.9 (67.2)	474.6 (81.4)
Sitting bout duration, min/bout	13.2 (4.7)	17.6 (5.7)	13.6 (3.4)	11.8 (2.6)	10.1 (2.7)
Device awake wear, min/day	888.1 (73.7)	891.9 (80.9)	883.4 (70.8)	884.2 (72.3)	892.9 (70.1)

Abbreviations: GED, General Educational Development; SD, standard deviation; WHAC, Women's Health Accelerometry Collaboration; OPACH, Objective Physical Activity and Cardiovascular Health Study; MVPA, moderate-to-vigorous physical activity; PA, physical activity; WHS, Women's Health Study.

Table 12. Associations between accelerometer measures and all-cause mortality among cancer survivors in WHAC

Accelerometer variable	Quartiles of exposure				Per 1-SD[a]
	Q1 (Low)	Q2	Q3	Q4 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA					
Range (min/day)	<248.9	248.9–300.7	300.8–352.9	>352.9	—
Cases (rate)[b]	217 (41.8)	160 (30.0)	149 (22.8)	110 (19.6)	—
Model 1[c]	1.00	0.92 (0.75, 1.13)	0.86 (0.69, 1.06)	0.66 (0.52, 0.84)	0.85 (0.79, 0.92)
Model 2[d]	1.00	1.05 (0.84, 1.30)	0.97 (0.77, 1.21)	0.81 (0.63, 1.04)	0.92 (0.84, 1.00)
MVPA					
Range (min/day)	<29.9	29.9–49.5	49.6–71.7	>71.7	—
Cases (rate)[b]	295 (61.3)	179 (33.5)	85 (15.1)	77 (13.4)	—
Model 1[c]	1.00	0.81 (0.67, 0.98)	0.44 (0.34, 0.57)	0.55 (0.41, 0.74)	0.72 (0.64, 0.81)
Model 2[d]	1.00	0.95 (0.77, 1.17)	0.57 (0.43, 0.76)	0.72 (0.52, 0.99)	0.84 (0.74, 0.96)
Total PA					
Range (min/day)	<292.1	292.1–354.3	354.4–418.6	>418.6	—
Cases (rate)[b]	251 (49.9)	165 (30.8)	126 (23.0)	94 (16.6)	—
Model 1[c]	1.00	0.84 (0.69, 1.03)	0.68 (0.55, 0.85)	0.60 (0.47, 0.77)	0.81 (0.74, 0.88)
Model 2[d]	1.00	0.93 (0.75, 1.15)	0.80 (0.62, 1.02)	0.72 (0.55, 0.95)	0.89 (0.80, 0.98)

Table 12. (**cont'd**) Associations between accelerometer measures and all-cause mortality among cancer survivors in WHAC

Accelerometer variable	Quartiles of exposure				Per 1-SD[a]
	Q1 (Low)	Q2	Q3	Q4 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Steps					
Range (steps/day)	<2889	2889–4215	4216–5959	>5959	—
Cases (rate)[b]	298 (61.6)	178 (33.4)	86 (15.3)	74 (12.9)	—
Model 1[c]	1.00	0.75 (0.62, 0.91)	0.44 (0.34, 0.56)	0.50 (0.37, 0.66)	0.69 (0.61, 0.77)
Model 2[d]	1.00	0.89 (0.72, 1.10)	0.57 (0.43, 0.76)	0.66 (0.47, 0.91)	0.82 (0.71, 0.94)
Sitting time					
Range (min/day)	<514.0	514.0–577.6	577.7–643.4	>643.4	—
Cases (rate)[b]	108 (19.2)	130 (23.9)	158 (29.1)	240 (47.6)	—
Model 1[c]	1.00	1.16 (0.89, 1.49)	1.21 (0.94, 1.55)	1.57 (1.24, 1.99)	1.21 (1.11, 1.32)
Model 2[d]	1.00	1.10 (0.85, 1.43)	1.12 (0.87, 1.45)	1.31 (1.00, 1.70)	1.12 (1.02, 1.23)
Sitting bout duration					
Range or SD (min/bout)	<10.3	10.3–12.4	12.4–15.3	>15.3	—
Cases (rate)[b]	128 (23.0)	146 (26.9)	163 (30.6)	199 (38.2)	—
Model 1[c]	1.00	1.16 (0.91, 1.47)	1.35 (1.07, 1.70)	1.37 (1.10, 1.72)	1.13 (1.06, 1.21)
Model 2[d]	1.00	1.18 (0.93, 1.50)	1.18 (0.93, 1.50)	1.16 (0.91, 1.48)	1.05 (0.97, 1.13)

CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; Q, quartile; SD, standard deviation

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

Table 13. Associations between accelerometer measures and cancer mortality among cancer survivors in WHAC

Accelerometer variable	Quartiles of exposure			Per 1-SD[a]
	T1 (Low)	T2	T3 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA				
Range (min/day)	<267.2	267.2–333.9	>333.9	—
Cases (rate)[b]	69 (9.9)	73 (10.2)	42 (5.7)	—
Model 1[c]	1.00	1.30 (0.93, 1.81)	0.77 (0.52, 1.14)	0.90 (0.78, 1.05)
Model 2[d]	1.00	1.43 (1.00, 2.05)	0.83 (0.55, 1.27)	0.92 (0.78, 1.08)
MVPA				
Range (min/day)	<36.0	36.0–63.7	>63.7	—
Cases (rate)[b]	94 (14.3)	52 (7.1)	38 (5.0)	—
Model 1[c]	1.00	0.77 (0.53, 1.10)	0.73 (0.47, 1.13)	0.85 (0.70, 1.03)
Model 2[d]	1.00	0.88 (0.59, 1.31)	0.77 (0.47, 1.27)	0.89 (0.71, 1.11)
Total PA				
Range (min/day)	<313.6	313.6–393.1	>393.1	—
Cases (rate)[b]	78 (11.4)	66 (9.2)	40 (5.3)	—
Model 1[c]	1.00	1.03 (0.73, 1.44)	0.76 (0.51, 1.14)	0.88 (0.75, 1.03)
Model 2[d]	1.00	1.09 (0.76, 1.56)	0.81 (0.52, 1.26)	0.90 (0.75, 1.07)
Steps				
Range (steps/day)	<3305	3305–5278	>5278	—
Cases (rate)[b]	96 (14.6)	49 (6.7)	39 (5.1)	—
Model 1[c]	1.00	0.70 (0.49, 1.01)	0.75 (0.49, 1.17)	0.84 (0.69, 1.03)
Model 2[d]	1.00	0.75 (0.50, 1.12)	0.77 (0.46, 1.27)	0.89 (0.71, 1.12)
Sitting time				
Range (min/day)	<536.2	536.2–619.3	>619.3	—
Cases (rate)[b]	41 (5.5)	63 (8.7)	80 (11.7)	—
Model 1[c]	1.00	1.32 (0.88, 1.98)	1.37 (0.92, 2.05)	1.16 (0.99, 1.35)
Model 2[d]	1.00	1.35 (0.90, 2.04)	1.30 (0.84, 2.01)	1.11 (0.93, 1.32)
Sitting bout duration				
Range (min/bout)	<10.9	10.9–14.2	>14.2	—
Cases (rate)[b]	54 (7.3)	64 (9.0)	66 (9.5)	—
Model 1[c]	1.00	1.39 (0.96, 2.00)	1.27 (0.88, 1.83)	1.10 (0.97, 1.25)
Model 2[d]	1.00	1.34 (0.92, 1.94)	1.07 (0.73, 1.58)	1.05 (0.91, 1.20)

CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; SD, standard deviation; T, tertile

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

Table 14. Associations between accelerometer measures and cardiovascular disease mortality among cancer survivors in WHAC

Accelerometer variable	Tertiles of exposure			Per 1-SD[a]
	T1 (Low)	T2	T3 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA				
Range (min/day)	<267.2	267.2–333.9	>333.9	—
Cases (rate)[b]	62 (8.9)	33 (4.6)	24 (3.2)	—
Model 1[c]	1.00	0.79 (0.51, 1.22)	0.63 (0.39, 1.04)	0.86 (0.71, 1.04)
Model 2[d]	1.00	0.91 (0.57, 1.45)	0.76 (0.45, 1.30)	0.97 (0.78, 1.20)
MVPA				
Range (min/day)	<36.0	36.0–63.7	>63.7	—
Cases (rate)[b]	85 (12.9)	26 (3.6)	8 (1.1)	—
Model 1[c]	1.00	0.53 (0.33, 0.85)	0.27 (0.12, 0.60)	0.50 (0.36, 0.69)
Model 2[d]	1.00	0.66 (0.40, 1.08)	0.34 (0.15, 0.79)	0.59 (0.41, 0.84)
Total PA				
Range (min/day)	<313.6	313.6–393.1	>393.1	—
Cases (rate)[b]	66 (9.7)	37 (5.2)	16 (2.1)	—
Model 1[c]	1.00	0.82 (0.54, 1.24)	0.53 (0.30, 0.95)	0.77 (0.62, 0.95)
Model 2[d]	1.00	0.98 (0.62, 1.54)	0.70 (0.37, 1.33)	0.88 (0.69, 1.12)
Steps				
Range (steps/day)	<3305	3305–5278	>5278	—
Cases (rate)[b]	77 (11.7)	34 (4.6)	8 (1.1)	—
Model 1[c]	1.00	0.79 (0.51, 1.22)	0.33 (0.15, 0.72)	0.52 (0.38, 0.72)
Model 2[d]	1.00	1.01 (0.63, 1.62)	0.44 (0.19, 1.02)	0.64 (0.45, 0.93)
Sitting time				
Range (min/day)	<536.2	536.2–619.3	>619.3	—
Cases (rate)[b]	16 (2.1)	34 (4.7)	69 (10.1)	—
Model 1[c]	1.00	1.53 (0.83, 2.81)	2.29 (1.29, 4.07)	1.36 (1.11, 1.68)
Model 2[d]	1.00	1.45 (0.78, 2.72)	2.10 (1.13, 3.91)	1.24 (0.98, 1.56)
Sitting bout duration				
Range (min/bout)	<10.9	10.9–14.2	>14.2	—
Cases (rate)[b]	34 (4.6)	29 (4.1)	46 (8.0)	—
Model 1[c]	1.00	0.96 (0.58, 1.59)	1.42 (0.92, 2.19)	1.17 (1.01, 1.35)
Model 2[d]	1.00	0.94 (0.56, 1.57)	1.22 (0.75, 1.97)	1.10 (0.93, 1.30)

CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; T, tertile; SD, standard deviation

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

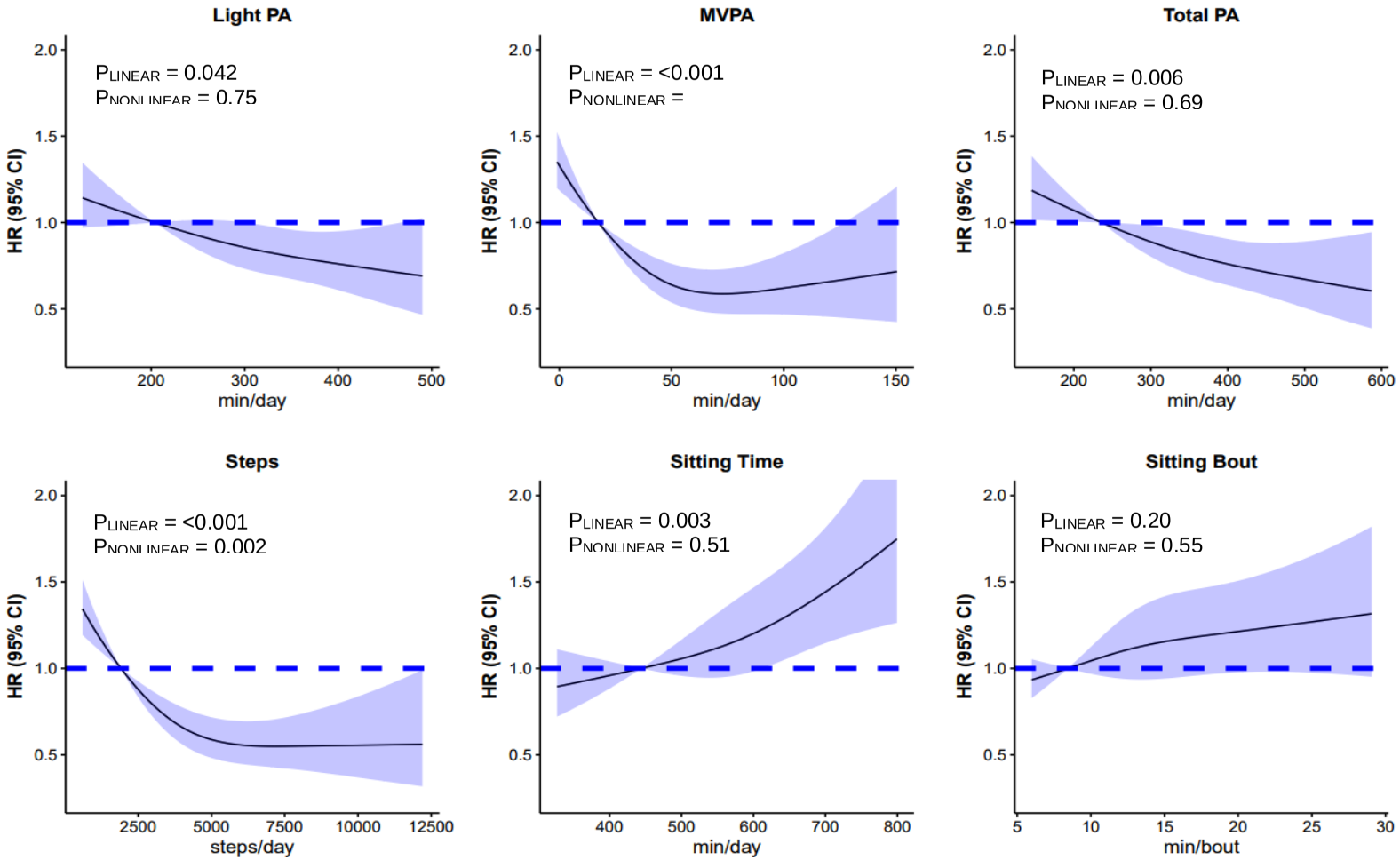

Figure 1. Restricted cubic splines for the hazard of all-cause mortality by accelerometer measures.

Knots were at the 10th (referent), 50th, and 90th percentiles. P-values are for Wald tests at spline components for linear and non-linear associations. Shaded area is the bounds of the 95% confidence limits. Models were 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 years since cancer diagnosis at WHAC baseline.

Table 15. Associations between accelerometer measures and all-cause mortality among cancer survivors

Cohort Group (*n*)	Events *n* (%)	Light PA[a] HR (95% CI)[b]	MVPA[a] HR (95% CI)[b]	Total PA[a] HR (95% CI)[b]
Overall (2,616)	636 (24.3)	0.92 (0.84, 1.00)	0.84 (0.74, 0.96)	0.89 (0.80, 0.98)
Age, years				
<75 (1,487)	179 (12.0)	0.90 (0.77, 1.07)	1.02 (0.86, 1.22)	0.93 (0.78, 1.10)
≥75 (1,129)	457 (40.5)	0.93 (0.83, 1.03)	0.71 (0.59, 0.86)	0.88 (0.78, 0.99)
P-value		0.47	0.02	0.91
Race and Ethnicity				
White (2,251)	520 (23.1)	0.92 (0.84, 1.02)	0.85 (0.74, 0.99)	0.89 (0.80, 1.00)
Other (365)	116 (31.8)	0.86 (0.69, 1.06)	0.85 (0.62, 1.17)	0.84 (0.67, 1.06)
P-value		0.87	0.59	0.95
BMI, kg/m^2				
<30 (2,033)	482 (23.7)	0.87 (0.78, 0.96)	0.83 (0.72, 0.95)	0.83 (0.74, 0.93)
≥30 (583)	154 (26.4)	1.16 (0.95, 1.41)	0.86 (0.61, 1.21)	1.13 (0.91, 1.41)
P-value		0.35	0.13	0.61
Physical function[c], score				
<75 (936)	357 (38.1)	0.97 (0.86, 1.10)	0.87 (0.72, 1.05)	0.95 (0.83, 1.08)
≥75 (1,472)	207 (14.1)	0.88 (0.74, 1.03)	0.92 (0.76, 1.12)	0.86 (0.72, 1.03)
P-value		0.08	0.12	0.04
Years between diagnosis and accelerometry, years				
<2 (355)	104 (29.2)	0.90 (0.71, 1.13)	0.83 (0.59, 1.17)	0.87 (0.67, 1.12)
≥2 (2,261)	532 (23.5)	0.92 (0.83, 1.01)	0.83 (0.72, 0.97)	0.88 (0.79, 0.99)
P-value		0.84	0.22	0.38
Cancer types				
Breast cancer (1,352)	271 (20.0)	0.92 (0.80, 1.05)	0.89 (0.73, 1.07)	0.89 (0.77, 1.04)
Other (1,264)	365 (28.9)	0.87 (0.77, 0.98)	0.79 (0.66, 0.94)	0.83 (0.73, 0.95)
P-value		0.60	0.75	0.76
MVPA, min/day[d]				
<50 (1,328)	477 (35.9)	0.96 (0.86, 1.06)	—	—
≥50 (1,288)	159 (12.3)	0.84 (0.70, 1.02)	—	—
P-value		0.56		
Sitting time, min/day[d]				
<575 (1,311)	239 (18.2)	0.95 (0.80, 1.12)	0.90 (0.76, 1.08)	0.91 (0.76, 1.10)
≥575 (1,305)	397 (30.4)	0.90 (0.79, 1.03)	0.75 (0.60, 0.93)	0.85 (0.73, 0.99)
P-value		0.63	0.17	0.54

Table 15. (cont'd) Associations between accelerometer measures and all-cause mortality among cancer survivors in WHAC, stratified by cohort subgroups

Cohort Group (*n*)	Daily Steps[a]	Sitting Time[a]	Sitting Bout[a]
	HR (95% CI)[b]	HR (95% CI)[b]	HR (95% CI)[b]
Overall (2,616)	0.82 (0.71, 0.94)	1.12 (1.02, 1.23)	1.05 (0.97, 1.13)
Age, years			
<75 (1,487)	0.97 (0.81, 1.17)	1.02 (0.87, 1.19)	0.96 (0.81, 1.14)
≥75 (1,129)	0.70 (0.58, 0.86)	1.16 (1.04, 1.31)	1.08 (0.99, 1.18)
P-value	0.05	0.75	0.72
Race and Ethnicity			
White (2,251)	0.82 (0.71, 0.96)	1.14 (1.02, 1.26)	1.08 (0.99, 1.18)
Other (365)	0.82 (0.59, 1.14)	1.09 (0.89, 1.35)	1.01 (0.86, 1.19)
P-value	0.54	0.43	0.27
BMI, kg/m^2			
<30 (2,033)	0.77 (0.67, 0.90)	1.17 (1.05, 1.31)	1.07 (0.96, 1.19)
≥30 (583)	1.00 (0.72, 1.40)	0.94 (0.77, 1.15)	1.01 (0.89, 1.15)
P-value	0.50	0.78	0.96
Physical function[c], score			
<75 (936)	0.91 (0.74, 1.11)	1.07 (0.94, 1.22)	1.03 (0.93, 1.13)
≥75 (1,472)	0.85 (0.70, 1.04)	1.10 (0.94, 1.29)	1.13 (0.97, 1.31)
P-value	0.02	0.26	0.05
Years between diagnosis and accelerometry, years			
<2 (355)	0.96 (0.69, 1.33)	0.95 (0.72, 1.24)	1.04 (0.81, 1.34)
≥2 (2,261)	0.78 (0.67, 0.92)	1.15 (1.04, 1.28)	1.06 (0.98, 1.15)
P-value	0.04	0.09	0.28
Cancer types			
Breast cancer (1,352)	0.81 (0.66, 1.00)	1.05 (0.91, 1.22)	1.05 (0.93, 1.19)
Other (1,264)	0.79 (0.66, 0.95)	1.19 (1.05, 1.35)	1.09 (0.99, 1.20)
P-value	0.42	0.79	0.64
MVPA, min/day[d]			
<50 (1,328)	0.79 (0.60, 1.02)	1.09 (0.98, 1.22)	1.04 (0.96, 1.13)
≥50 (1,288)	1.02 (0.82, 1.26)	1.09 (0.88, 1.33)	0.98 (0.76, 1.26)
P-value	0.20	0.84	0.60
Sitting time, min/day[d]			
<575 (1,311)	0.83 (0.69, 1.01)	—	—
≥575 (1,305)	0.76 (0.60, 0.96)	—	—
P-value	0.44		

Table 15 (cont'd). Associations between accelerometer measures and all-cause mortality among cancer survivors in WHAC, stratified by cohort subgroups

CI, confidence interval; BMI, body mass index; PA, physical activity; HR, hazard ratio;
[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 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, body mass index, physical function, cancer type, and years since cancer diagnosis at WHAC baseline. Variables were not included in the model when stratifying by the variable.
[c]208 participants excluded for missing physical function data
[d]Estimates not shown for exposures that are comprised of the stratifying variable

Table 16. Sensitivity analysis for all-cause mortality excluding deaths that occurred during the first two years of follow-up.

Accelerometer variable	Quartiles of exposure				Per 1-SD[a]
	Q1 (Low)	Q2	Q3	Q4 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA					
Cases (rate)[b]	198 (38.3)	143 (27.0)	139 (25.8)	103 (18.4)	—
Model 1[c]	1.00	0.90 (0.72, 1.11)	0.87 (0.70, 1.09)	0.67 (0.52, 0.85)	0.86 (0.79, 0.93)
Model 2[d]	1.00	1.02 (0.82, 1.29)	0.98 (0.78, 1.24)	0.82 (0.63, 1.07)	0.92 (0.84, 1.01)
MVPA					
Cases (rate)[b]	268 (56.1)	167 (31.3)	77 (13.7)	71 (12.4)	—
Model 1[c]	1.00	0.82 (0.67, 1.01)	0.43 (0.33, 0.57)	0.55 (0.41, 0.74)	0.72 (0.64, 0.82)
Model 2[d]	1.00	0.97 (0.78, 1.20)	0.56 (0.42, 0.75)	0.72 (0.52, 1.01)	0.85 (0.74, 0.97)
Total PA					
Cases (rate)[b]	228 (45.6)	151 (28.3)	115 (21.1)	89 (15.7)	—
Model 1[c]	1.00	0.84 (0.68, 1.04)	0.68 (0.54, 0.85)	0.61 (0.47, 0.79)	0.81 (0.74, 0.89)
Model 2[d]	1.00	0.93 (0.74, 1.16)	0.78 (0.61, 1.01)	0.75 (0.57, 1.00)	0.89 (0.81, 0.99)
Steps					
Cases (rate)[b]	270 (56.3)	164 (30.9)	82 (14.6)	67 (11.7)	—
Model 1[c]	1.00	0.75 (0.61, 0.92)	0.45 (0.34, 0.59)	0.49 (0.36, 0.66)	0.69 (0.61, 0.79)
Model 2[d]	1.00	0.89 (0.71, 1.10)	0.59 (0.44, 0.79)	0.65 (0.46, 0.92)	0.82 (0.72, 0.96)
Sitting time					
Cases (rate)[b]	101 (17.9)	117 (21.6)	147 (27.2)	218 (43.6)	—
Model 1[c]	1.00	1.12 (0.86, 1.46)	1.21 (0.94, 1.57)	1.56 (1.22, 2.00)	1.21 (1.10, 1.32)
Model 2[d]	1.00	1.06 (0.80, 1.39)	1.11 (0.85, 1.44)	1.27 (0.97, 1.67)	1.11 (1.00, 1.22)
Sitting bout duration					
Cases (rate)[b]	123 (22.1)	130 (24.1)	146 (27.5)	18 (35.4)	—
Model 1[c]	1.00	1.06 (0.83, 1.36)	1.26 (0.99, 1.61)	1.33 (1.05, 1.67)	1.12 (1.04, 1.20)
Model 2[d]	1.00	1.08 (0.84, 1.39)	1.10 (0.86, 1.42)	1.12 (0.88, 1.44)	1.03 (0.95, 1.12)

CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; Q, quartile; SD, standard deviation

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

Table 17. Sensitivity analysis for cancer mortality excluding cancer deaths that occurred during the first two years of follow-up.

	Tertile of exposure			Per 1-SD
	T1 (Low)	T2	T3 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA				
Cases (rate)[b]	59 (8.5)	60 (8.4)	37 (5.0)	—
Model 1[c]	1.00	1.24 (0.86, 1.79)	0.78 (0.51, 1.19)	0.92 (0.78, 1.08)
Model 2[d]	1.00	1.38 (0.93, 2.04)	0.86 (0.55, 1.34)	0.95 (0.80, 1.13)
MVPA				
Cases (rate)[b]	80 (12.2)	43 (5.9)	33 (4.3)	—
Model 1[c]	1.00	0.73 (0.49, 1.08)	0.72 (0.45, 1.15)	0.86 (0.70, 1.07)
Model 2[d]	1.00	0.83 (0.54, 1.27)	0.76 (0.45, 1.28)	0.91 (0.72, 1.15)
Total PA				
Cases (rate)[b]	67 (9.9)	54 (7.6)	35 (4.7)	—
Model 1[c]	1.00	0.97 (0.67, 1.40)	0.76 (0.49, 1.17)	0.89 (0.75, 1.06)
Model 2[d]	1.00	1.02 (0.69, 1.51)	0.82 (0.51, 1.31)	0.93 (0.77, 1.12)
Steps				
Cases (rate)[b]	82 (12.5)	39 (5.3)	35 (4.6)	—
Model 1[c]	1.00	0.64 (0.43, 0.96)	0.77 (0.48, 1.23)	0.87 (0.70, 1.07)
Model 2[d]	1.00	0.67 (0.43, 1.03)	0.78 (0.46, 1.33)	0.92 (0.73, 1.17)
Sitting time				
Cases (rate)[b]	35 (4.7)	55 (7.6)	66 (9.7)	—
Model 1[c]	1.00	1.36 (0.88, 2.09)	1.35 (0.87, 2.08)	1.14 (0.97, 1.36)
Model 2[d]	1.00	1.34 (0.86, 2.09)	1.23 (0.77, 1.98)	1.08 (0.90, 1.31)
Sitting bout duration				
Cases (rate)[b]	51 (6.9)	50 (7.0)	55 (7.9)	—
Model 1[c]	1.00	1.15 (0.78, 1.71)	1.13 (0.77, 1.67)	1.08 (0.94, 1.25)
Model 2[d]	1.00	1.10 (0.73, 1.64)	0.96 (0.63, 1.45)	1.01 (0.87, 1.17)

CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; T, tertile; SD, standard deviation

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

Table 18. Sensitivity analysis for CVD mortality excluding cardiovascular disease deaths that occurred during the first two years of follow-up.

	Tertiles of exposure			Per 1-SD[a]
	T1 (Low)	T2	T3 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA				
Cases (rate)[b]	55 (8.0)	31 (4.3)	24 (3.2)	—
Model 1[c]	1.00	0.82 (0.52, 1.28)	0.69 (0.42, 1.13)	0.87 (0.71, 1.06)
Model 2[d]	1.00	0.95 (0.58, 1.54)	0.84 (0.49, 1.45)	0.98 (0.78, 1.23)
MVPA				
Cases (rate)[b]	77 (11.8)	25 (3.4)	8 (1.1)	—
Model 1[c]	1.00	0.54 (0.33, 0.87)	0.27 (0.12, 0.61)	0.50 (0.36, 0.69)
Model 2[d]	1.00	0.66 (0.39, 1.10)	0.33 (0.14, 0.77)	0.57 (0.39, 0.82)
Total PA				
Cases (rate)[b]	59 (8.7)	35 (4.9)	16 (2.1)	—
Model 1[c]	1.00	0.84 (0.54, 1.29)	0.56 (0.31, 1.01)	0.78 (0.63, 0.96)
Model 2[d]	1.00	0.99 (0.62, 1.59)	0.74 (0.39, 1.42)	0.88 (0.69, 1.14)
Steps				
Cases (rate)[b]	70 (10.7)	32 (4.4)	8 (1.1)	—
Model 1[c]	1.00	0.77 (0.49, 1.21)	0.33 (0.15, 0.73)	0.53 (0.38, 0.74)
Model 2[d]	1.00	0.95 (0.58, 1.55)	0.42 (0.18, 0.98)	0.64 (0.44, 0.93)
Sitting time				
Cases (rate)[b]	16 (2.1)	31 (4.3)	63 (9.3)	—
Model 1[c]	1.00	1.43 (0.77, 2.66)	2.21 (1.24, 3.95)	1.39 (1.12, 1.72)
Model 2[d]	1.00	1.35 (0.71, 2.55)	2.05 (1.10, 3.84)	1.27 (1.00, 1.61)
Sitting bout duration				
Cases (rate)[b]	32 (4.3)	26 (3.7)	52 (7.5)	—
Model 1[c]	1.00	0.92 (0.55, 1.56)	1.44 (0.92, 2.26)	1.20 (1.03, 1.39)
Model 2[d]	1.00	0.90 (0.53, 1.55)	1.25 (0.76, 2.05)	1.13 (0.95, 1.34)

CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; Q, quartile; SD, standard deviation

[a]SD (exposure variable): 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Incidence rate per 1,000 person-years

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

[d]Model 2 is 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 WHAC baseline.

Table 19. Complete case analysis of associations of accelerometer measures with all-cause mortality from Model 2 (n=2384 participants, 78 deaths removed)

	Quartiles of Exposure				Per 1-SD
	Q1 (Low)	Q2	Q3	Q4 (High)	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA	1 (ref)	1.11 (0.88, 1.40)	0.98 (0.77, 1.25)	0.89 (0.68, 1.17)	0.95 (0.86, 1.04)
MVPA	1 (ref)	1.06 (0.85, 1.32)	0.64 (0.48, 0.85)	0.86 (0.61, 1.20)	0.90 (0.79, 1.03)
Total PA	1 (ref)	0.99 (0.79, 1.24)	0.79 (0.61, 1.03)	0.84 (0.63, 1.12)	0.93 (0.84, 1.03)
Daily Steps	1 (ref)	0.93 (0.74, 1.16)	0.62 (0.46, 0.83)	0.75 (0.53, 1.06)	0.88 (0.77, 1.01)
Sitting Time	1 (ref)	0.97 (0.73, 1.29)	1.05 (0.80, 1.38)	1.19 (0.90, 1.56)	1.09 (0.99, 1.21)
MSBD	1 (ref)	1.12 (0.87, 1.45)	1.18 (0.92, 1.52)	1.10 (0.85, 1.41)	1.03 (0.95, 1.11)

Model is adjusted for age, race/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 WHAC baseline.

Table 20. Complete case analysis of associations of accelerometer measures with cancer mortality from Model 2 (n=2384 participants, 12 cancer deaths removed)

	Tertile of Exposure			Per 1-SD
	T1 (Low)	T2	T3	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA	1 (ref)	1.41 (0.96, 2.06)	0.86 (0.56, 1.34)	0.93 (0.79, 1.10)
MVPA	1 (ref)	0.73 (0.48, 1.12)	0.80 (0.47, 1.34)	0.91 (0.72, 1.14)
Total PA	1 (ref)	0.97 (0.66, 1.43)	0.83 (0.53, 1.33)	0.91 (0.76, 1.10)
Daily Steps	1 (ref)	0.63 (0.41, 0.97)	0.81 (0.48, 1.36)	0.94 (0.74, 1.19)
Sitting Time	1 (ref)	1.20 (0.77, 1.86)	1.21 (0.76, 1.91)	1.07 (0.89, 1.28)
MSBD	1 (ref)	1.16 (0.78, 1.72)	0.96 (0.64, 1.44)	1.01 (0.88, 1.16)

Model is adjusted for age, race/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 WHAC baseline.

Table 21. Complete case analysis of associations of accelerometer measures with cancer mortality from Model 2 (n=2384 participants, 12 cancer deaths removed)

	Tertile of Exposure			Per 1-SD
	T1 (Low)	T2	T3	
	Ref	HR (95% CI)	HR (95% CI)	HR (95% CI)
Light PA	1 (ref)	1.08 (0.67, 1.75)	0.76 (0.43, 1.36)	1.03 (0.83, 1.30)
MVPA	1 (ref)	0.78 (0.47, 1.31)	0.33 (0.13, 0.83)	0.60 (0.42, 0.87)
Total PA	1 (ref)	1.07 (0.67, 1.71)	0.73 (0.37, 1.45)	0.95 (0.73, 1.22)
Daily Steps	1 (ref)	1.11 (0.67, 1.82)	0.41 (0.16, 1.05)	0.67 (0.46, 0.98)
Sitting Time	1 (ref)	2.05 (1.01, 4.17)	2.49 (1.23, 5.06)	1.23 (0.97, 1.56)
MSBD	1 (ref)	0.94 (0.54, 1.62)	1.25 (0.76, 2.07)	1.07 (0.90, 1.28)

Model is adjusted for age, race/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 WHAC baseline.

Table 22. Associations of accelerometer measures with cardiovascular disease mortality, by cohort.

	WHS (N=38 deaths)	OPACH (N=81 deaths)
	HR (95% CI)	HR (95% CI)
Light PA		
Model 1	0.85 (0.61, 1.20)	0.88 (0.68, 1.13)
Model 2	0.92 (0.56, 1.52)	0.97 (0.72, 1.31)
MVPA		
Model 1	0.47 (0.28, 0.80)	0.51 (0.33, 0.80)
Model 2	0.53 (0.25, 1.13)	0.61 (0.37, 1.00)
Total PA		
Model 1	0.75 (0.52, 1.07)	0.79 (0.60, 1.05)
Model 2	0.81 (0.47, 1.40)	0.89 (0.64, 1.25)
Daily Steps		
Model 1	0.49 (0.29, 0.82)	0.57 (0.36, 0.90)
Model 2	0.54 (0.25, 1.19)	0.72 (0.43, 1.21)
Sitting Time		
Model 1	1.20 (0.83, 1.73)	1.51 (1.15, 1.99)
Model 2	1.10 (0.64, 1.88)	1.44 (1.06, 1.97)
MSBD		
Model 1	1.26 (0.93, 1.72)	1.18 (0.99, 1.41)
Model 2	1.22 (0.77, 1.92)	1.12 (0.91, 1.39)

Model 1 is adjusted for age and race and ethnicity. Model 2 is 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 WHAC baseline.

Estimates are per 1-SD increment: 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

Table 23. Sensitivity analysis based on competing risk model (Fine-Gray method)

Accelerometer Measure (per SD unit)[a]	**Cancer Mortality**	**CVD Mortality**
Competing Risk Model[b]	**sHR (95% CI)**	**sHR (95% CI)**
Light PA	0.93 (0.79, 1.10)	1.05 (0.84, 1.31)
MVPA	0.90 (0.69, 1.19)	0.61 (0.42, 0.90)
Total PA	0.92 (0.76, 1.10)	0.97 (0.75, 1.25)
Steps	0.94 (0.72, 1.22)	0.69 (0.49, 0.98)
Sitting time	1.05 (0.88, 1.26)	1.17 (0.93, 1.48)
Sitting bout duration	1.00 (0.86, 1.17)	1.03 (0.90, 1.19)
Primary Results	**HR (95% CI)**	**HR (95% CI)**
Light PA	0.92 (0.78, 1.08)	0.97 (0.78, 1.20)
MVPA	0.89 (0.71, 1.11)	0.59 (0.41, 0.84)
Total PA	0.90 (0.75, 1.07)	0.88 (0.69, 1.12)
Steps	0.89 (0.71, 1.12)	0.64 (0.45, 0.93)
Sitting time	1.11 (0.93, 1.32)	1.24 (0.98, 1.56)
Sitting bout duration	1.05 (0.91, 1.20)	1.10 (0.93, 1.30)

CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; PA, physical activity; SD, standard deviation; sHR, subdistribution hazard ratio (Fine-Gray method)

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, body mass index, physical function, cancer type, and number of years since cancer diagnosis at WHAC baseline.

[a]SD units: 78.3 min/day (light PA), 32.9 min/day (MVPA), 96.7 min/day (total PA), 2470 steps/day (steps), 102.3 min/day (sitting time), 4.7 min/bout (sitting bouts)

[b]Competing risk model: for cancer mortality, the competing event was mortality from non-cancer causes. For cardiovascular disease mortality, the competing event was mortality from non-cardiovascular disease causes.

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Chapter 4 Characterizing longitudinal changes in accelerometer-measured physical activity among older women: the Women's Health Initiative Strong and Healthy trial

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Abstract

Background: Engaging in physical activity (PA) can help older women reduce risk of chronic conditions and supports mobility, independence and quality of life. However, PA levels among older women are reported to be low and decline with age. We examined longitudinal changes in accelerometer-measured PA among older women and identified participant characteristics associated with different trajectories.

Methods: Women ages 63–95 years in the Women's Health Initiative Strong and Healthy (WHISH) trial wore an ActiGraph GT3X+ on the hip for ≥4 of 7 days on up to 4 occasions over up to 7 years follow-up. Mixed effects linear regression models estimated PA change over time, and associations between participant characteristics and PA change over time were tested.

Results: A total of 2,033 women with ≥2 adherent accelerometer wear periods were included. PA levels significantly declined over time, with estimated annual change (95% confidence interval) of -3.1 (-3.6, -2.6) min/day for light PA, -3.4 (3.6, -3.3) for MVPA, 6.6 (-7.1, -6.0) for total PA, and -203 (-216, -190) daily steps. Older age, non-drinkers, lower physical function and energy/fatigue scores, higher BMI, and higher waist circumference at baseline were associated with greater declines in PA measures over time. Compared to White women, Black and Hispanic women experienced less decline in light PA, but Black women had greater declines in MVPA.

Conclusion: PA levels among older women decline significantly over time, with the largest relative declines in MVPA and daily steps. Various demographic, psychosocial, socioeconomic, and health-related factors are associated with PA trajectories. These findings can help inform future PA promotion strategies that consider these diverse factors in supporting PA among older women.

Introduction

The proportion of older adults (ages ≥65 years) in the US is growing, with recent projections suggesting that this demographic group will represent nearly 25% of the population in 2060 and over half will be comprised of older women.[46] Currently, older adults account for over a third of all health care spending, which is the largest share of any age group, and per person spending for women is 14% higher than men.[100] Given the rise in the proportion of older adults in the US and that women have longer life expectancies than men[2], public health strategies that delay loss of physical and cognitive function are a societal priority.

Physical activity (PA) reduces risk of premature mortality, the development of many chronic conditions, and can help preserve independence, mobility, and quality of life among older women.[10] However, PA levels among US older women remain low, with 14.4% of women aged 65–69 years and 5.2% of women aged ≥80 years meeting the national recommended levels.[14,15] Understanding which factors (i.e., demographic, psychosocial, socioeconomic, health-related) are associated with PA trajectories in older women may help inform future PA promotion strategies. However, prospective studies that have sought to characterize PA trajectories among older women are scarce and have relied on self-reported measures.[101,102] Compared to accelerometry-derived measures, self-reported PA questionnaires are less accurate[28], poorly measure light intensity PA[50], and are unable to capture daily step counts. Among older adults, most PA is of light intensity[45,70] and walking is a common type of PA.[103] Therefore, understanding what factors are associated with PA change over time is particularly important.

The first aim of this study was to examine changes in accelerometer-measured PA (light PA, moderate-to-vigorous PA [MVPA], total PA, and daily steps) measured 4 times over approximately 7 years of follow-up among older women ages 63–95 years in the Women's Health Initiative (WHI) Strong and Healthy (WHISH) trial. The second aim was to identify whether selected participant characteristics were associated with accelerometer-measured PA trajectories over time.

Methods

Study Population

The WHISH trial design and baseline characteristics of study participants have been published previously.[104] Briefly, WHISH included 49,331 women aged over 65 years who were participating in the nationwide WHI Extension Study and were free of conditions including: living in a nursing home or clinical care facility, dementia, inability to walk, or inability to read English.[105] In 2015, women were randomly assigned to an

intervention arm designed to promote multicomponent PA recommendations for older adults[10,106] or a "usual activity" arm, with major cardiac events as the primary outcome. A subcohort of WHISH participants were invited to join the "WHI Physical Activity Follow-up Study" to provide data on changes in accelerometer-measured PA.[104] These women participated in a previous 2012–2014 WHI ancillary study of accelerometer-measured PA and aging outcomes called the Objective Physical Activity and Cardiovascular Health (OPACH) Study.[56] Surviving OPACH women who had successfully worn and returned accelerometers were mailed invitations and consent forms to participate in the WHISH accelerometer sub-study. A recruitment target of 2,300 was set to achieve balanced groups of at least 1,000 women in both WHISH study arms and 2,356 consented. All women provided written informed consent, and the studies were approved by the Institutional Review Board at the Fred Hutchinson Cancer Research Center.

Measures

Accelerometer Deployment and Measurement

The same accelerometer wear protocol was utilized in both OPACH and WHISH. Consenting participants were mailed a package containing an Actigraph GT3X+ triaxial accelerometer (ActiGraph LLC, Pensacola, FL), an elastic waist band, a sleep journal to track in-bed and out-of-bed times, and instructions for wearing and returning the accelerometer in an addressed express mail return envelope. Participants were asked to wear the accelerometer over the right hip for 24 hours/day for 7 days including during sleep but not when in water;[56] subsequently, the time spent sleeping was removed for all analyses based on times in and out of bed recorded in sleep journals. Participants were given a phone number to call for assistance during the accelerometer wear period, and at least 1 phone call was made to each participant during accelerometer wear to facilitate accurate placement and adherence. Participants were given a $10 gift card upon receipt of their accelerometer and sleep journal. Accelerometers were deployed at three separate time points: during 2015–2016 (i.e., at 6 months post-WHISH intervention baseline), 2016–2017 (18 months), and 2018–2019 (36 months). Along with the OPACH measurement in 2012–2014, women provided up to four separate weeks of accelerometer-measured PA.[104]

Accelerometers recorded three-dimensional raw acceleration signals at 30 Hz, which were aggregated using ActiLife software (V.6) to counts per 15s epochs with the normal filter setting. Accelerometer non-wear time was removed using the validated Choi algorithm.[57,58] Using OPACH calibration-study derived vector magnitude (VM) cutpoints,[33,59] daily average time spent in intensity-specific categories measured from VM/15s cutpoints were defined as follows: light PA 19–518, MVPA ≥519, and total PA ≥19. Steps per day were determined using the

ActiGraph GT3X+ manufacturer's step algorithm. Accelerometer wear adherence was defined as wearing time of ≥10 hours on ≥4 days of device wear at each measurement period, consistent with other protocols.[29,86] Awake wear time was accounted for using the residuals method.[60]

Participant Characteristics

Age, race, ethnicity, and education level were self-reported at enrollment into the original WHI study. Data on a wide array of health behaviors and health conditions were ascertained at baseline and periodically during follow-up. Incident medical conditions and health status changes after baseline were ascertained annually beginning in 2005, and responses from the measure closest in time to OPACH accelerometer baseline were used. Women reported on smoking status, frequency of alcohol use, and whether they lived alone. Self-rated general health was assessed with the question, "In general, would you say your health is excellent, very good, good, fair or poor?" Physical function and energy/fatigue were based on responses to the RAND-36 Item Health survey (scores range from 0 to 100; higher scores reflect better function and a more favorable health state, respectively).[61] The social support construct was based on responses to the Medical Outcomes Study (score ranges from 9 to 45; higher scores indicate more social support)[107] and purpose in life construct was based on responses to the Scales of Psychological Well-Being (score ranges from 9 to 45; higher scores indicate higher sense of purpose in life).[108,109] Vision and hearing impairment was determined by reported trouble with vision or hearing loss that was moderate or severe. Women reported whether they had joint pain or stiffness was mild, moderate, severe, or did not occur. Number of comorbidities was categorized as 0, 1, 2, or ≥3 of 10 prevalent conditions: history of cardiovascular disease, cancer, diabetes, hip fracture, osteoarthritis, chronic obstructive pulmonary disease, cognitive impairment, ≥2 falls in past 12 months, and urinary incontinence.[110] Self-reported weight loss of more than 10 lbs., and having a spouse die within the past year were also examined. Body mass index (BMI) and waist circumference (WC) were measured by examiners during the Long Life Study home visit. BMI was calculated as weight (kg) divided by squared height (m^2). WC (in) was measured level with the iliac crest using an anthropometric tape measure. Variables were grouped into sociodemographic (age, race, ethnicity, education level), health behaviors and health status (smoking status, alcohol use, self-rated general health, physical function, energy/fatigue, vision impairment, hearing impairment, joint pain, number of comorbidities, BMI, WC, lost 10 lb. in the past year, depression), and social and psychological (living alone, social support, purpose in life, spousal death) categories. All participant characteristic variables were selected *a priori* based on evidence in the current literature and were hypothesized to be associated with PA

trajectories. Missingness of one or more of these predictor variables was common; 676 participants (33.3% of analytic sample) were missing at least one variable with the highest proportion observed for purpose in life score (n=162), spousal death (n=136), and social support (n=106).

Analytic Sample

From the 2,356 OPACH participants who consented to WHISH, the following number of women returned the accelerometers with usable data at each WHISH wear period: 1,924 at 6-months post-WHISH baseline ("WHISH 1"), 1,672 at 18 months ("WHISH 2"), and 1,391 at 36 months ("WHISH 3"). Among these women, 2,346 women were adherent at OPACH baseline, 1,896 at WHISH 1, 1,532 at WHISH 2, and 1,289 at WHISH 2. A total of 1,890 women were adherent at two periods, 1,513 at three periods, and 1,199 at all four measurement periods. To be included in the primary analysis of PA trajectories, a minimum of two adherent wear periods was required, resulting in 2,033 women (86.7% of consenting sample) remaining in the analytic dataset. To maximize sample size, participants with missing data for a given characteristic were only excluded from analyses that included the characteristic in the model.

Statistical Analysis

Participant characteristics, expressed as numbers and percentages for categorical variables and means and standard deviations for continuous variables, were estimated for participants with ≥2 adherent wear periods. Characteristics were compared between the analytic sample and excluded participants using chi ($\chi 2$) tests and ANOVA for categorical and continuous variables, respectively. The primary outcomes were changes in light PA (min/day), MVPA (min/day), total PA (min/day), and steps (steps/day). Using data from participants with ≥2 adherent wear periods, overall changes in PA variables were first examined using mixed effects linear regression modeling. Mixed effects linear regression modeling accounts for the correlation of responses within a subject over time by including a subject-specific random intercept in the model. Coefficients and 95% confidence intervals (CIs) were calculated for changes in PA measures over time and linear slopes for trendlines were estimated. Then, participants were grouped into tertiles of baseline accelerometry measurement to examine whether trajectories of change differed by baseline PA levels. Next, we examined the associations between participant characteristics and change in PA variables using mixed effects linear regression modeling. All models included adjustment for study arm, age, race, and ethnicity. To determine which of the remaining characteristics would be included in the multivariable mixed effects linear regression models, the characteristic first must be associated with at least 3 of 4 PA measures in minimally adjusted models. Then, likelihood ratio tests were used to compare models with and

without a given characteristic to determine the model that provides the best fit for our data. The same multivariable model mixed effects linear regression model was used for each PA measure for comparison purposes.

To account for death during the follow-up period and the potential effects on participant PA levels, we used a joint modeling approach that consisted of multivariable mixed effects linear regression models and a Cox proportional hazards model that accounts for potential correlation between the outcomes of both models.[111-114] This approach is appropriate when the longitudinal measurements and survival times are not independent. The Cox models had all-cause mortality as the outcome of interest and contained the same variables as the multivariable mixed effects linear regression models. Follow-up time was set as time from OPACH accelerometry measurement to death, loss to follow-up, or end of follow-up on February 19, 2023, whichever came first. All analyses were conducted in R v4.2 (R Foundation for Statistical Computing; Vienna, Austria).

Results

Descriptive characteristics for the 2,033 women with ≥2 adherent wear periods are displayed in **Table 24**. Among these women, the mean time between OPACH baseline measurement and their final adherent wear period was 5.2 years (standard deviation=1.3, range=1.5–7.0 years). Compared to those excluded, included women were younger, lived alone, had better self-rated health, had higher scores on psychosocial scales, less likely to have sensory impairments, had less joint pain, had fewer comorbidities, were less likely to have lost 10 lbs within the past year, and had higher PA levels at OPACH baseline.

Overall, participants' PA levels decreased over time (**Figure 2)**. On average, the estimated change per year (95% confidence interval was -3.1 (-3.6, -2.6) min/day for light PA, -3.4 (-3.6, -3.3) for MVPA, -6.6 (-7.1, -6.0) for total PA, and -203 (-216, -190) daily steps (all P<0.001). When estimated over the study period, the change per year was -16.0 (-18.5, -13.6) min/day, -17.9 (-18.9, -16.9) min/day, -34.2 (-37.0, -31.3) min/day, and -1055 (-1121, -989) steps/day for light PA, MVPA, total PA, and daily steps, respectively. PA change over time stratified by tertiles is displayed in **Figure 3**. When stratified by tertiles of baseline PA measures, all trajectory groups had significant linear slopes of PA decline except for the lowest tertile for light PA (P= 0.08). Associations estimated from mixed effects linear regression models adjusting for study arm, age, race, ethnicity, and each characteristic separately for each PA measure are shown in **Table 25.** In minimally adjusted models, age, race, ethnicity, alcohol use, self-rated general health, physical function, energy/fatigue, vision impairment, joint pain, number of comorbidities, BMI, WC, weight loss within the last year, and purpose in life were associated with all PA measures. Based on our modeling

strategy, the following characteristics were included in each the fully adjusted mixed effects linear regression model: study arm, age, race, ethnicity, smoking status, alcohol use, self-rated general health, physical function, energy/fatigue, number of comorbidities, BMI, and WC (**Table 426**). In general, older age, being a smoker or non-drinker, lower physical function and energy/fatigue scores, higher BMI, and higher WC were associated greater declines in PA measures over time. Compared to White race, Black race was associated with higher light PA but lower MVPA and daily steps over time. Hispanic ethnicity was associated with higher light and total PA. Compared to excellent or very good health, having good health was associated with higher light and total PA. Last, a higher number of comorbidities was associated with lower MVPA and daily steps.

Results from analyses using joint modeling to account for death during follow-up were generally consistent with those from the mixed effects linear regression models (**Table 27**), indicating that loss-to-follow-up due to death during WHISH did not materially affect estimates of change in PA measures over time.

Discussion

This study examined the changes in accelerometer-measured PA among older women initially aged 63-99 using up to 4 measurements, identified trajectories of PA change, and examined associations with various participant characteristics. Over 5.2 average years of follow-up, women experienced significant declines in all PA measures, including an estimated 16.0 min/day decrease in light PA, 17.9 min/day in MVPA, 34.2 min/day in total PA, and 1,054 fewer steps/day. While the absolute reductions in min/day of light PA and MVPA are comparable, the *relative* decrease from OPACH baseline for MVPA (17.9/58.7 = 30.5%) is over 5 times larger than the decrease in light PA (16.0/298.5 = 5.4%), indicating the largest proportion of PA decline in our sample was in MVPA. When stratified by tertiles of baseline PA measures, women with the highest baseline PA measures experienced the largest declines in all PA measures during the study period. Several factors were associated with different PA trajectories, and public health strategies should consider these identified groups when tailoring interventions aimed at preserving PA levels among older women.

Few studies have examined trajectories of device-measured PA in older women. In a study of older men of a comparable age range (mean age=77.9, SD=4.5 years) and up to three measurements over a two year span, Jefferis et al. reported a 341 steps/day decrease per year, while the proportion of the day spent in light PA and MVPA also decreased by 0.7% and 0.4%, respectively.[115] Notably, the differences in proportional decreases in light and MVPA (3% and 10%) align with our findings. Similarly, Watanabe et al. studied 478 Japanese older women aged 26–85

and observed a decline in light and MVPA beginning around age 70.[116] Our findings add significant evidence to the literature, emphasizing the considerable reductions in PA, especially MVPA and daily steps, that occur in older women over time.

Except for the lowest tertile of baseline light PA, all tertile groups experienced significant decreases in PA levels over time. The magnitude of decline for each PA measure was greatest among women in the highest tertiles of baseline PA measures. While older age was consistently associated with greater PA decline, the associations with race were more complex. Compared to White women, Black and Hispanic race was associated with higher light PA but Black race was associated with lower MVPA over time. While light PA has recently been shown to provide health benefits for older women,[117,118] substantially more health benefits are achieved when engaging in MVPA.[10] Understanding the root causes for differences in PA behavior across sociodemographic groups such as race is crucial for promoting equity in PA promotion.

Some participant characteristics such as low physical function, low energy/fatigue, greater number of comorbidities, high BMI, and high WC were consistently associated with greater PA decline over time in both minimally adjusted (**Table 25**) and fully adjusted (**Table 26)** models. While some of the health characteristics may directly impact an individual's physical ability to engage in PA, other characteristics may be associated with accessibility to places and opportunities to be physically active. For example, older women who live alone might have fewer social interactions or supportive relationships, which are important for maintaining a physically active lifestyle. Women with frailty or weakened physical function may not have access to safe spaces to engage in PA or places with supports for people with chronic conditions to be physically active. Altogether, our findings suggest that PA promotional strategies for older women should be multifaceted. Programs should consider not only physical barriers but also psychosocial, environmental, and health equity factors when seeking to promote PA in older women.

Strengths and Limitations

Our study is the first (to our knowledge) to characterize longitudinal patterns of PA behavior among older women using repeated accelerometry measures. Having up to 4 repeated measures permitted comparisons of PA levels among the same women over time and the identification of different trajectories of PA change. In addition, the average follow-up time of over 5 years allowed for measurement of PA in many women who were near or above 100 years of age, which are an understudied age group. Extensive data on participant health and sociodemographic

characteristics permitted descriptive analyses and characterization of trajectories over time. Unlike most studies of repeated PA measures in older adults, we performed sensitivity analysis using joint modeling to account for death during follow-up and found that our results differed minimally. There are some limitations to our findings. This study is strictly descriptive and causality between participant characteristics and PA trajectories cannot be inferred. The model selection approach was selected to develop a model that adequately fit each PA outcome measure, and other methods such as machine-learning approaches could be considered in future research. As mentioned earlier, there may be survival bias that could be affecting the associations between characteristics and PA. Last, women included in our study differed across several health status variables, including PA levels, from those excluded.

Conclusions

Among over 2,000 older women with up to 4 accelerometry measurements, we observed that PA levels decreased over time and the largest relative declines were for MVPA and daily steps. Several participant characteristics were associated with different PA trajectories. Overall, our findings emphasize the importance of considering various demographic, psychosocial, socioeconomic, and health-related factors in screening for and promoting PA among older women.

Table 24. Participant characteristics, by adherent accelerometer wear during at least 2 periods during WHISH

Characteristic	Adherent ≥2[a]	Adherent <2 or missing	P-value
N	2,033	323	
Age (years), *n (%)*			<0.001
<70	287 (14.1)	28 (8.7)	
70–79	923 (45.4)	132 (40.9)	
80–89	783 (38.5)	144 (44.6)	
≥90	40 (2.0)	19 (5.9)	
Mean (SD)	77.1 (6.6)	78.8 (6.7)	<0.001
Race, *n (%)*			0.741
White	1267 (62.3)	192 (59.4)	
Black	659 (32.4)	111 (34.4)	
American Indian/Alaska Native	3 (0.1)	0 (0.0)	
More than one race	36 (1.8)	6 (1.9)	
Unknown/not reported	68 (3.3)	14 (4.3)	
Ethnicity , *n (%)*			0.387
Non-Hispanic	1721 (84.7)	280 (86.7)	
Hispanic	312 (15.3)	43 (13.3)	
Highest education level, *n (%)*			0.935
High school/GED or less	363 (17.9)	54 (16.7)	
Some college	761 (37.4)	119 (36.8)	
College graduate	896 (44.1)	148 (45.8)	
Missing	13 (0.6)	2 (0.6)	
Current smoker, *n (%)*	41 (2.0)	12 (3.7)	0.087
Alcohol use, *n (%)*			0.077
Non-drinker	674 (33.2)	121 (37.5)	
<1 drink/week	669 (32.9)	99 (30.7)	
≥1 drink/week	609 (30.0)	83 (25.7)	
Missing	81 (4.0)	20 (6.2)	
Living alone, *n (%)*			0.001
Yes	798 (39.3)	141 (43.7)	
No	1097 (54.0)	145 (44.9)	
Missing	138 (6.8)	37 (11.5)	
Self-rated general health, *n (%)*			<0.001
Excellent or very good	1204 (59.2)	148 (45.8)	
Good	726 (35.7)	145 (44.9)	
Fair or poor	101 (5.0)	30 (9.3)	
Missing	2 (0.1)	0 (0.0)	
PF score (range: 0–100)			<0.001
Mean (SD)	74.3 (23.4)	66.6 (25.0)	
Missing (%)	8 (0.4)	1 (0.3)	
Energy score (range: 0–100)			<0.001
Mean (SD)	65.1 (18.1)	60.5 (18.8)	
Missing (%)	115 (5.7)	27 (8.4)	
Social support score (range: 9–45)			0.006
Mean (SD)	38.1 (7.4)	36.8 (7.9)	
Missing (%)	144 (7.1)	38 (11.8)	
Purpose in life score (range: 0–28)			<0.001
Mean (SD)	20.7 (4.7)	19.6 (4.6)	
Missing (%)	208 (10.2)	46 (14.2)	

Table 24. (cont'd) Participant characteristics, by adherent accelerometer wear at ≥2 periods during WHISH

Characteristic	Adherent ≥2[a]	Adherent <2 or missing	P-value[b]
N	2,033	323	
Depression, *n (%)*			0.077
Yes	115 (5.7)	27 (8.4)	
No	1918 (94.3)	296 (91.6)	
Vision impairment, *n (%)*			0.043
Yes	85 (4.2)	22 (6.8)	
No	1810 (89.0)	273 (84.5)	
Missing	138 (6.8)	28 (8.7)	
Hearing impairment, *n (%)*			0.001
Yes	313 (15.4)	73 (22.6)	
No	1582 (77.8)	222 (68.7)	
Missing	138 (6.8)	28 (8.7)	
Joint pain, *n (%)*			0.046
None	339 (16.7)	49 (15.2)	
Mild	923 (45.4)	127 (39.3)	
Moderate	543 (26.7)	103 (31.9)	
Severe	148 (7.3)	23 (7.1)	
Missing	80 (3.9)	21 (6.5)	
Number of comorbidities, *n (%)*			<0.001
None	215 (10.6)	23 (7.1)	
1	650 (32.0)	74 (22.9)	
2	705 (34.7)	115 (35.6)	
≥3	463 (22.8)	111 (34.4)	
Lost ≥10 lbs in the past year			0.004
Yes	380 (18.7)	81 (25.1)	
No	1568 (77.1)	222 (68.7)	
Missing	85 (4.2)	20 (6.2)	
Spouse died in the past year			0.183
Yes	71 (3.5)	14 (4.3)	
No	1775 (87.3)	270 (83.6)	
Missing	187 (9.2)	39 (12.1)	
Body mass index (kg/m^2), *n (%)*			0.642
<18.5	24 (1.2)	4 (1.2)	
18.5-24.9	594 (29.2)	90 (27.9)	
25.0-29.9	699 (34.4)	101 (31.3)	
≥30.0	595 (29.3)	107 (33.1)	
Mean (SD)	28.1 (5.6)	28.8 (6.0)	0.046
Missing	121 (6.0)	21 (6.5)	
Waist circumference			0.341
Mean (SD)	35.3 (5.5)	35.7 (5.7)	
Missing (%)	114 (5.6)	21 (6.5)	
OPACH Accelerometer measures, *mean (SD)*			
Light PA, min/day	298.5 (70.0)	278.1 (72.8)	<0.001
MVPA, min/day	58.7 (35.3)	47.0 (30.3)	<0.001
Total PA, min/day	357.2 (88.4)	325.1 (90.6)	<0.001
Steps/day	4166 (2209)	3363 (1794)	<0.001
Not adherent (%)	7 (0.3)	5 (1.6)	

[a]676 participants who were adherent ≥2 periods are missing data for ≥1 characteristic.
[b]P-value determined from chi ($\chi 2$) tests and ANOVA for categorical and continuous variables, respectively

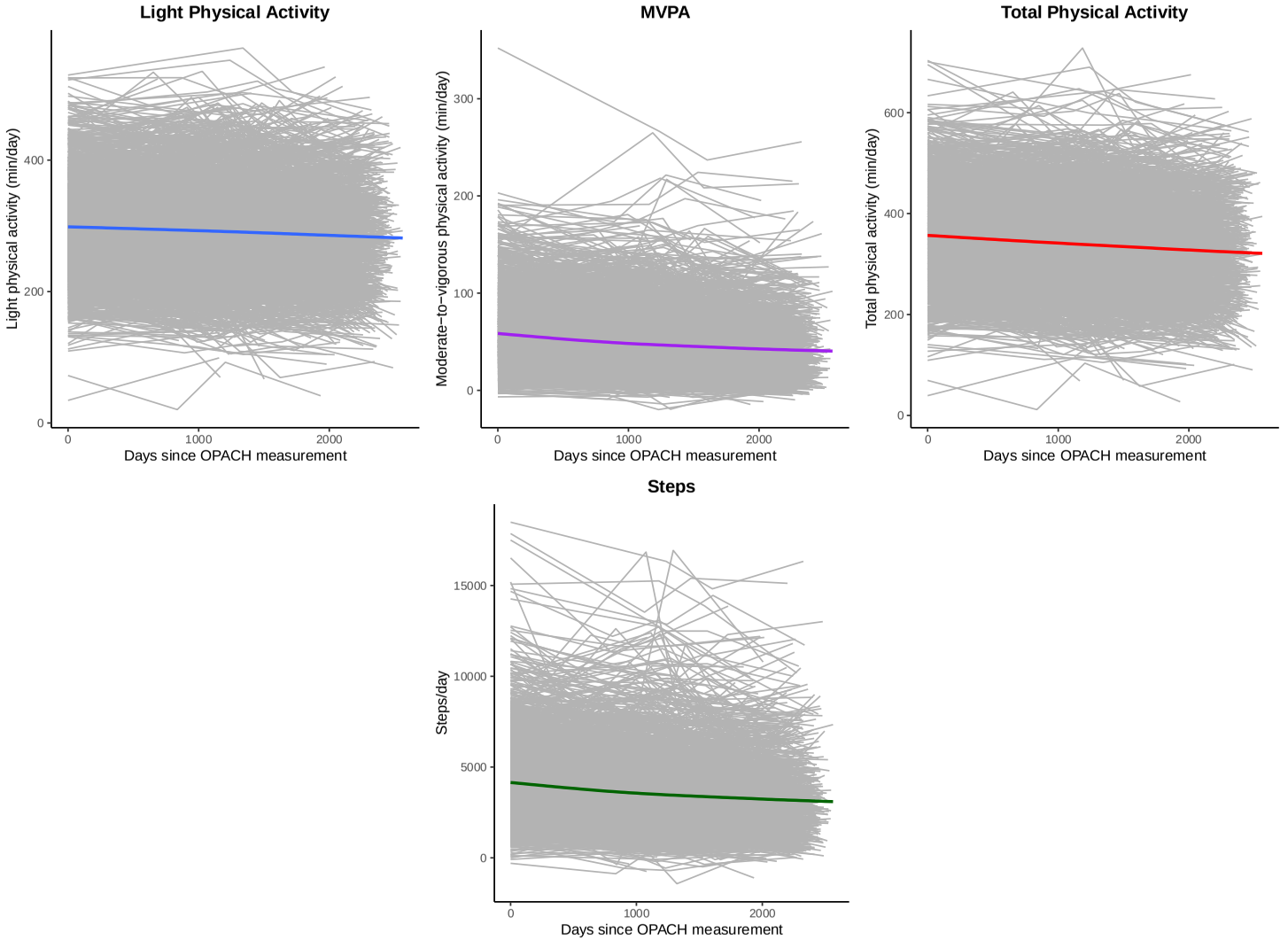

Figure 2. Multiple physical activity measurements among WHISH participants with at least 2 adherent wear periods.

Each gray line represents a single participant. The colored trendlines represent the smoothed estimated mean at each time point. Linear slopes for each of trendlines (estimated change per year) were: -3.1 min/day (light PA), -3.4 min/day for (MVPA), -6.6 min/day (total PA), and -203 (steps/day), all P<0.0001.

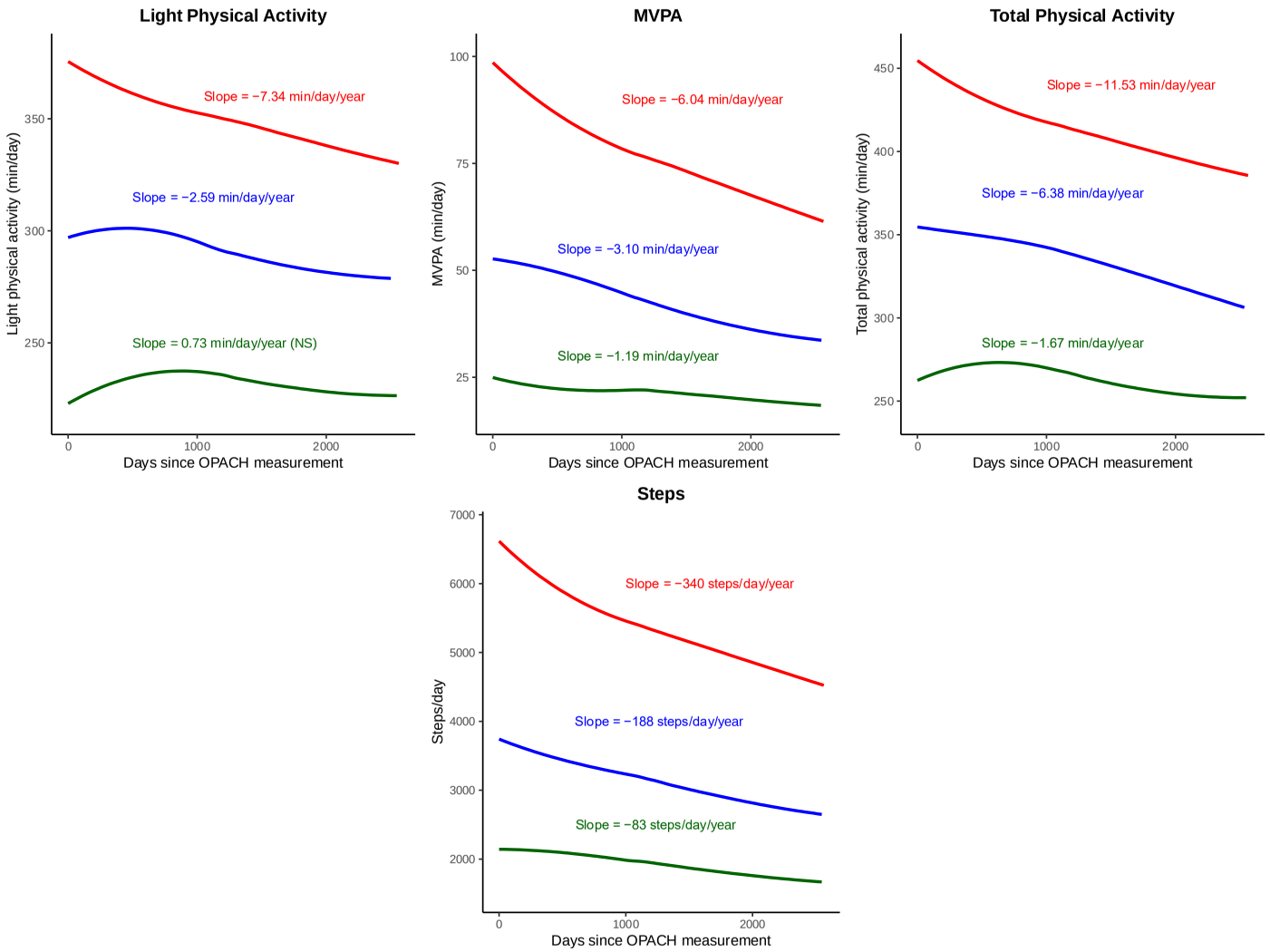

Figure 3. Mean PA and 95% confidence intervals estimated using locally estimated scatterplot smoothing, stratified by tertiles of baseline PA levels.

Slopes (95% CI) estimated from mixed effects linear regression models are shown for each tertile and represent change in daily activity (min/day or steps/day) per year. Red corresponds to tertile 3 (high), blue for tertile 2, and green for tertile 1 (low). NS, linear slope is not significant

Table 25. Longitudinal associations between participant characteristics and changes in physical activity using minimally adjusted repeated measures linear mixed effect models.

Characteristics	LPA	MVPA	Total PA	Steps
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Sociodemographic				
Age (per 6.6 years)	-5.3 (-8.4, -2.1)	-13.6 (-15.0, -12.3)	-19.3 (-23.2, -15.4)	-931 (-1016, -846)
Race (ref=White)				
Black	12.6 (5.7, 19.5)	-12 (-14.9, -9)	0.0 (-8.5, 8.5)	-810 (-995, -625)
American Indian/Alaska Native	77.4 (4.5, 150.3)	-2.6 (-33.1, 27.9)	73 (-16.4, 162.4)	123 (-1797, 2042)
More than one race	-0.4 (-21.8, 21.0)	-10.5 (-19.7, -1.2)	-10.3 (-36.7, 16.1)	-924 (-1501, -345)
Unknown/not reported	3.5 (-13.6, 20.5)	3.9 (-3.4, 11.1)	6.3 (-14.6, 27.3)	-23 (-478, 432)
Ethnicity (ref=Non-Hispanic)				
Hispanic	18.4 (9.2, 27.5)	1.3 (-2.6, 5.2)	19.9 (8.7, 31.2)	270 (25, 514)
Highest education level (ref= High school/GED or less)				
Some college	-2.2 (-10.3, 5.9)	-0.1 (-3.6, 3.4)	-2.2 (-12.2, 7.7)	-29 (-245, 188)
College graduate	1.5 (-6.4, 9.4)	3.1 (-0.3, 6.5)	4.6 (-5.1, 14.3)	309 (98, 521)
Health Behaviors and Health Status				
Current smoker (ref=No)				
Yes	-29.2 (-49.2, -9.3)	-7.5 (-16.2, 1.1)	-36.4 (-61.0, -11.8)	-721 (-1261, -182)
Alcohol use (ref=Non-drinker)				
<1 drink/week	1.1 (-5.8, 7.9)	3.4 (0.4, 6.3)	4.0 (-4.4, 12.4)	284 (103, 465)
≥1 drink/week	16.9 (9.8, 24.1)	8.5 (5.5, 11.5)	25.7 (17.0, 34.4)	768 (581, 956)
Self-rated general health (ref= Excellent or very good)				
Good	-6.5 (-12.5, -0.5)	-9.1 (-11.6, -6.6)	-16.1 (-23.4, -8.8)	-771 (-928, -615)
Fair or poor	-30.2 (-43.3, -17.1)	-14.6 (-20.2, -9.0)	-46.5 (-62.5, -30.4)	-1299 (-1645, -953)
PF score (per 23.4 units)	17.1 (14.2, 20.0)	9.0 (7.8, 10.2)	26.6 (23.1, 30.1)	706 (632, 780)
Energy score (per 18.1 units)	11.0 (8.1, 13.8)	6.1 (4.9, 7.3)	17.5 (14, 20.9)	452 (377, 527)
Vision impairment (ref=No)				
Yes	-16.7 (-30.7, -2.7)	-7.5 (-13.5, -1.4)	-24.8 (-42.0, -7.6)	-579 (-959, -200)
Hearing impairment (ref=No)				
Yes	-2.5 (-10.6, 5.6)	-2.4 (-5.9, 1.1)	-4.6 (-14.6, 5.4)	-180 (-400, 40)

Table 25 (cont'd). Longitudinal associations between participant characteristics and changes in physical activity using minimally adjusted repeated measures linear mixed effect models

Characteristics	LPA	MVPA	Total PA	Steps
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Joint pain (ref=None)				
Mild	-3.0 (-11, 5.1)	-1.5 (-4.9, 1.9)	-4.8 (-14.6, 5.0)	-243 (-452, -33)
Moderate	-10.2 (-19.0, -1.5)	-7 (-10.7, -3.2)	-17.8 (-28.6, -7.1)	-702 (-930, -473)
Severe	-9.9 (-22.4, 2.6)	-10.2 (-15.5, -4.9)	-20.8 (-36.1, -5.5)	-957 (-1284, -631)
Number of comorbidities (ref=None)				
1	-8.7 (-18.6, 1.2)	-6.6 (-10.8, -2.4)	-16.2 (-28.3, -4.2)	-524 (-784, -264)
2	-13.9 (-23.7, -4.0)	-11.7 (-15.9, -7.5)	-26.7 (-38.7, -14.6)	-865 (-1124, -606)
≥3	-25.4 (-35.8, -14.9)	-16.6 (-21.1, -12.2)	-43.4 (-56.2, -30.7)	-1261 (-1537, -986)
Body mass index (per 5.6 kg/m^2)	-24.0 (-26.8, -21.2)	-7.4 (-8.7, -6.2)	-31.8 (-35.2, -28.4)	-599 (-674, -524)
Waist circumference (per 5.5 in)	-22.5 (-25.2, -19.8)	-8.5 (-9.7, -7.3)	-31.4 (-34.7, -28.1)	-614 (-687, -542)
Lost ≥10 lbs in the past year (ref=No)				
Yes	-9.4 (-16.6, -2.2)	-5.4 (-8.5, -2.4)	-15.1 (-23.9, -6.2)	-432 (-623, -241)
Depression (ref=No)				
Yes	-7.5 (-19.6, 4.7)	-4.6 (-9.8, 0.6)	-12.9 (-27.8, 2.0)	-242 (-568, 85)
Social and Psychological				
Living alone (ref=No)				
Yes	-6.7 (-12.7, -0.7)	1.1 (-1.5, 3.7)	-5.2 (-12.5, 2.2)	31.3 (-128, 191)
Social support score (per 7.4 units)	1.0 (-1.9, 3.9)	0.5 (-0.8, 1.7)	1.5 (-2.1, 5.1)	51 (-26, 128)
Purpose in life score (per 4.7 units)	4.4 (1.4, 7.4)	2.7 (1.4, 3.9)	7.3 (3.6, 11.0)	213 (134, 291)
Spouse died in the past year (ref=No)				
Yes	-5.8 (-21.0, 9.5)	-1.3 (-7.9, 5.3)	-6.3 (-25.1, 12.4)	-95 (-508, 318)

All continuous variables were assessed per one standard deviation. All models adjusted for study arm, age, race, and ethnicity. Sample sizes range from 1,825 to 2,033 participants.

Table 26. Longitudinal associations between characteristics and changes in physical activity using full linear mixed effect models

Characteristics	LPA	MVPA	Total PA	Steps
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Demographic				
Age (per 6.6 years)	-5.1 (-8.7, -1.5)	-11.7 (-13.3, -10.1)	-16.9 (-21.2, -12.6)	-799 (-892, -707)
Race (ref=White)				
Black	18.7 (11.3, 26.0)	-9.3 (-12.5, -6.1)	8.9 (0.1, 17.6)	-538 (-726, -351)
American Indian/Alaska Native	76.8 (9.9, 143.8)	4.7 (-24.1, 33.4)	80.7 (0.8, 160.5)	729 (-970, 2428)
More than one race	5.9 (-17.7, 29.4)	-7.7 (-18.0, 2.6)	-0.4 (-28.5, 27.7)	-566 (-1171, 38)
Unknown/not reported	8.2 (-9.4, 25.9)	5.8 (-1.8, 13.4)	13.0 (-8.0, 34.1)	158 (-292, 608)
Ethnicity (ref=Non-Hispanic)				
Hispanic	14.6 (5.1, 24.0)	-1.1 (-5.2, 3.0)	13.6 (2.3, 24.9)	157 (-84, 399)
Health Behaviors and Health Status				
Current smoker (ref=No)				
Yes	-33 (-55.2, -10.8)	-6.9 (-16.7, 2.8)	-39.7 (-66.3, -13.2)	-730 (-1302, -158)
Alcohol use (ref=Non-drinker)				
<1 drink/week	0.6 (-6.3, 7.5)	2.0 (-1.0, 5.0)	2.3 (-6.0, 10.5)	172 (-4, 349)
≥1 drink/week	10.1 (2.8, 17.4)	5.0 (1.9, 8.2)	15.2 (6.5, 23.9)	510 (323, 697)
Self-rated general health (ref= Excellent or very good)				
Good	15.4 (8.4, 22.3)	-0.1 (-3.1, 3.0)	15.5 (7.2, 23.8)	-115 (-293, 64)
Fair or poor	9.8 (-5.8, 25.4)	4.6 (-2.2, 11.4)	14.5 (-4.1, 33.2)	61 (-340, 462)
PF score (per 23.4 units)	7.9 (3.8, 12)	5.0 (3.2, 6.8)	13.2 (8.3, 18.0)	367 (262, 471)
Energy score (per 18.1 units)	4.8 (1.4, 8.2)	2.6 (1.1, 4.1)	7.6 (3.5, 11.6)	145 (58, 231)
Number of comorbidities (ref=None)				
1	-5.8 (-15.9, 4.3)	-2.9 (-7.3, 1.5)	-9.3 (-21.4, 2.7)	-249 (-507, 9)
2	-3.3 (-13.5, 6.9)	-5.4 (-9.9, -1.0)	-9.3 (-21.4, 2.9)	-348 (-609, -87)
≥3	-5.0 (-16.1, 6.1)	-6.9 (-11.7, -2.1)	-12.5 (-25.8, 0.7)	-447 (-731, -163)
Body mass index (per 5.6 kg/m^2)	-12.2 (-17.0, -7.4)	0.4 (-1.7, 2.5)	-11.9 (-17.7, -6.1)	-132 (-255, -8)
Waist circumference (per 5.5 in)	-10.6 (-15.4, -5.9)	-5.5 (-7.6, -3.5)	-16.1 (-21.8, -10.5)	-281 (-403, -159)

All continuous variables were assessed per one standard deviation. Each model included the following variables: study arm, age, race, ethnicity, smoking status, alcohol use, self-rated general health, physical function score, energy/fatigue score, number of comorbidities, body mass index, and waist circumference (n=1,771 women and 6,084 observations).

Table 27. Longitudinal associations of participant characteristics with change in physical activity measures using a joint modeling approach to account for death during follow-up.

Characteristics	LPA	MVPA	Total PA	Steps
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Demographic				
Age (per 6.6 years)	-5.7 (-9.2, -2.2)	-12.1 (-13.6, -10.6)	-17.9 (-22.1, -13.8)	-812 (-902, -723)
Race (ref=White)				
Black	17.5 (10.5, 24.5)	-9.6 (-12.7, -6.6)	7.3 (-1.0, 15.7)	-554 (-735, -372)
American Indian/Alaska Native	74.9 (8.2, 141.6)	3.9 (-24.7, 32.6)	77.8 (-1.6, 157.2)	688 (-1021, 2397)
More than one race	-3.8 (-25.3, 17.7)	-9.8 (-19.1, -0.4)	-12.7 (-38.3, 12.9)	-690 (-1247, -134)
Unknown/not reported	6.9 (-10, 23.9)	7.4 (0.1, 14.8)	13.5 (-6.6, 33.7)	206 (-230, 643)
Ethnicity (ref=Non-Hispanic)				
Hispanic	14.3 (5.3, 23.2)	-1.1 (-5.0, 2.8)	13.2 (2.5, 23.9)	169 (-62, 401)
Health Behaviors and Health Status				
Current smoker (ref=No)				
Yes	-34.2 (-54.6, -13.8)	-6.7 (-15.6, 2.3)	-40.1 (-64.4, -15.8)	-666 (-1195, -137)
Alcohol use (ref=Non-drinker)				
<1 drink/week	-0.4 (-7.0, 6.3)	1.8 (-1.1, 4.7)	1.0 (-6.9, 9.0)	149 (-23, 320)
≥1 drink/week	9.4 (2.3, 16.4)	4.3 (1.3, 7.4)	13.7 (5.3, 22.1)	460 (278, 642)
Self-rated general health (ref= Excellent or very good)				
Good	15.4 (8.7, 22.0)	0.0 (-2.9, 2.9)	15.6 (7.6, 23.5)	-113 (-286, 60)
Fair or poor	9.5 (-5.5, 24.4)	3.6 (-2.9, 10.2)	13.2 (-4.6, 31.0)	22 (-365, 410)
PF score (per 23.4 units)	7.2 (3.3, 11.1)	5.0 (3.3, 6.7)	12.5 (7.8, 17.1)	365 (264, 466)
Energy score (per 18.1 units)	4.9 (1.7, 8.2)	2.5 (1.1, 4.0)	7.7 (3.8, 11.6)	147 (62, 231)
Number of comorbidities (ref=None)				
1	-5.1 (-14.9, 4.7)	-4.0 (-8.2, 0.3)	-9.7 (-21.4, 2.0)	-313 (-566, -59)
2	-2.0 (-11.9, 7.9)	-6.0 (-10.3, -1.7)	-8.7 (-20.5, 3.1)	-403 (-658, -147)
≥3	-4.7 (-15.4, 6.1)	-7.8 (-12.5, -3.2)	-13.2 (-26.0, -0.4)	-498 (-776, -219)
Body mass index (per 5.6 kg/m^2)	-12.2 (-16.9, -7.6)	0.0 (-2, 2.1)	-12.3 (-17.8, -6.7)	-156 (-276, -35)
Waist circumference (per 5.5 in)	-11 (-15.7, -6.4)	-5.7 (-7.7, -3.7)	-16.8 (-22.3, -11.2)	-284 (-404, -164)

All continuous variables were assessed per one standard deviation. All linear mixed effect models and Cox models included the following variables: study arm, age, race, ethnicity, smoking status, alcohol use, self-rated general health, physical function score, energy/fatigue score, number of comorbidities, body mass index, and waist circumference (n=1,771 women).

Chapter 4, in part, is currently being prepared for submission for publication of the material. Hyde, Eric T.; Bandoli, Gretchen E.; Crespo, Noe C.; Parada Jr., Humberto; Zou, Jingjing; LaCroix, Andrea Z. The dissertation author was the primary investigator and author of this paper.

Chapter 5 Discussion

Summary

The proportion of older adults in the US is expected to continue to increase such that they will outnumber children and youth by 2035.[119] Given that older adults comprise over a third of all health care spending and that costs are highest among women,[100] it is crucial to identify strategies that can promote healthy longevity to help minimize the burdens associated with the aging process among older women. Increasing PA and limiting SB is frequently recommended as an effective behavioral strategy for facilitating healthy longevity due to the numerous health benefits that older adults can achieve that include reduced risk of many chronic diseases, management of prevalent conditions, and preservation of independent living and physical function.[10,11,120] However, the epidemiological evidence for the relationships between PA and SB with healthy longevity among older women has suffered from some limitations. These include varied definitions of healthy aging and longevity in prospective studies, limited research examining SB, reliance on self-reported PA measures, a single assessment of PA/SB, and few studies focused specifically on older women. This dissertation addresses these limitations to enhance understanding of the relationships between PA, SB, and the aging process.

In Aim 1, we tested the associations between accelerometer-measured PA, SB, and survival to age 90 with intact mobility among 3,809 women ages 78–89 in WHAC. Our findings suggest that higher PA levels (including light, MVPA, total, and daily steps) and less time spent in SBs were associated with survival to age 90 with and without mobility disability compared to dying before age 90. Our findings expand on the current evidence base by showing that more time spent in accelerometer-determined light PA, which is poorly captured with questionnaire methods[50] and is the most common PA intensity level that older adults engage in,[45,70] was strongly associated with increased odds of survival to age 90 without functional limitations. Another novel finding from this study was that higher daily step counts, which can be taken at any intensity level, were associated with improved odds of healthy longevity. While both sitting time and sitting bout during had a harmful association with the healthy longevity outcomes, the theoretical substitution of sitting time with light PA was associated with increased odds of survival to age 90 with or without mobility disability. This is a significant finding, given that engaging in higher intensity PA may be difficult or even unfeasible for many older women. While this is a statistical estimation and should not be interpreted as causal, these findings align with current PA recommendations for older adults to “move more, sit less”[10] to gain health benefits.

Mobility disability is a common affliction among older adults, with estimates suggesting approximately 25% of older adults have a prevalent mobility disability.[66] In our study, higher PA levels and lower SB levels increased the odds of both survival to age 90 with mobility disability, though the magnitude of the associations for mobility disability were consistently lower than survival with intact mobility. The observed relatively weaker associations may have been due to other age-related factors associated with both PA behaviors and physical function, such as the development of chronic conditions over the follow-up period. Given that documented inverse association between higher PA levels and risk of mobility limitations among older adults,[11,69] our findings underscore the importance of promoting PA of all types to help prolong health span and especially for those with chronic conditions.

While the concept of healthy longevity involves more dimensions of aging than just reducing risk of premature mortality, this portion of the definition is undoubtedly an important piece. In Aim 2, we examined the associations between accelerometer-measured PA and SB with mortality among older women who have survived cancer. The number of older women in US living with cancer is increasing and strategies are needed to help address the unique challenges they face to prolong survivorship and improve quality of life. Existing evidence demonstrates that higher levels of PA are associated with many health benefits for cancer survivors, including lower risk of premature mortality.[11,20,22] However, this evidence is based almost exclusively on self-reported questionnaires of PA behavior, which are biased measures in cancer survivor populations[79,80], and studies on associations of SB with mortality among cancer survivors are scarce. In our study, higher levels of all forms of PA (light PA, MVPA, total PA, and daily steps) and lower levels of SB were associated with reduced risks of all-cause mortality. These findings are generally consistent with previous studies using either questionnaire-measured[91-93] or accelerometer-measured[94,95] PA and SB behaviors, though our findings build upon those of previous studies by observing significant associations for daily steps and sitting time.

For each 2,500 step/day increment higher at baseline, we observed a 18% reduced risk in all-cause mortality which doubled to 36% for cardiovascular disease mortality. Furthermore, our dose-response analysis for steps and all-cause mortality showed that, compared to those who took approximately 2,500 steps/day at baseline, women who took approximately 5,000 steps/day achieved the most health benefits with hazard ratios near 0.50 (**Figure 1**). Daily step counts have garnered interested as a measure of total PA volume for future PA guidelines because they are an intuitive PA measure for the public to understand and measure themselves, can be taken at any

intensity level, and are a measure of walking behavior which is the most common PA performed by adults.[121] These findings suggest that encouraging cancer survivors to increase their daily step counts may help prolong survivorship. To our knowledge, our study was the first to observe an inverse association between more time spent in accelerometer-classified sitting and all-cause mortality in cancer survivors. This findings is particularly important given that cancer survivors are prone to engage in SBs at higher levels than the general population.[98] Combined with our findings for light PA and daily steps, encouraging older cancer survivors to sit less and engage in PA of any intensity may help promote survivorship.

Recently, the risk of non-cancer mortality has begun to surpass risk of cancer mortality among US cancer survivors.[122] Cardiovascular disease mortality has emerged as one of the major causes of non-cancer death in cancer survivors,[18,19] and we observed strong associations for MVPA and daily steps in reducing cardiovascular disease mortality. While cancer mortality remains a significant cause of death and higher levels of self-reported PA have shown associations with reduced risk,[23] we did not observe significant associations between accelerometer-measured PA and SB with cancer mortality. However, our study was limited by a low number of cancer deaths cases and point estimates were similar to those for all-cause mortality. Altogether, the findings from Aim 2 highlight the crucial role of PA in extending lifespan of cancer survivors by reducing risk of mortality overall and also for two of the most common causes of mortality in cancer survivors. It also underscores the risks associated with SBs, providing a strong case for lifestyle modifications as part of cancer survivorship care plans.

The findings from Aim 1 and Aim 2 helped to establish a clear foundation for the role of increasing PA levels to extend healthy longevity for older women. Unfortunately, PA levels among US older women are low and continue to decrease as they enter older ages.[14,15] In Aim 3, we sought to better understand what factors are associated with different PA trajectories over time among older women with multiple accelerometer measurements. Ours was the first study characterize PA trajectories using up to four accelerometer measurements in exclusively older women. Among over 2,000 participants in the WHISH trial with at least two valid accelerometer measurements over an average 5.2 years, the estimated absolute rates of decline over the study period were 16.0 min/day for light PA, 17.9 min/day for MVPA, 34.2 min/day for total PA, and 1,054 steps/day. While the relative rates of decline from OPACH baseline levels were 5.4%, 30.5%, 9.6%, and 25.3% for light, MVPA, total PA, and daily steps, respectively, and this indicates that the largest proportion of PA decline was in MVPA and daily steps. Our analysis identified 3 distinct PA trajectories for each measure, and all but one had significant slopes of decline

over time. Older age, living alone, lower physical function, vision impairments, higher body mass index, and higher waist circumference were associated with lower odds of being in higher PA trajectory groups. Our study highlights the critical need for tailored public health strategies that consider demographic, psychosocial, and physical factors such as those previously listed to maintain or enhance PA levels in older women. Interestingly, compared to White women, Black and Hispanic women had higher odds of higher trajectory groups for light PA, but Black women had *lower* odds of higher trajectory groups for MVPA. These findings underscore that PA behaviors can vary across sociodemographic subgroups, and it is important to understand why these differences exist and how to address them to achieve equity in PA participation.

The findings from this dissertation advances the fields of PA epidemiology, PA measurement, and healthy longevity in older women by highlighting: (1) the significant associations between lower intensity PAs and survival and preventing functional decline, (2) how prolonged sitting time and bout durations are risk factors for premature mortality, (3) that cancer survivors who engaged in any type of PA while reducing sitting behaviors had prolonged survivorship, (4) the significant decline in PA levels over time among women ages 63–99 is largely in higher intensity activities, and (5) the rates of decline differ across several factors that should be considered in future targeted PA screening or intervention strategies.

Recommendations for future research

Future studies investigating the role of PA and SB in promoting healthy longevity in older women can build upon the findings of this dissertation in several ways. First, accelerometer-measured PA and SB levels were measured at one time point for the analyses in Aim 1 and Aim 2. While important insights were gained from these studies, we also learned in Aim 3 that PA levels decline precipitously among older women. Studies on the associations between accelerometer-measured PA/SB and aging outcomes should consider multiple measurements of PA over time, which will provide a clearer representation of these behaviors among older women. Another important finding was the complex differences in PA behaviors that exist among older women of different races and ethnicities. While we attempted to examine multiplicative interaction by race in Aim 2, all non-Hispanic White races were grouped into one category due to sample size limitations. Larger cohorts of older women with more diverse racial and ethnic compositions are needed to identify if the associations between PA/SB and healthy longevity outcomes differ across these groups. Next, our definition of healthy longevity in Aim 1 included survival to old age and mobility disability. Future research can consider including other age-related factors, such as mental health and

quality of life measures, in their definitions of healthy longevity to examine how these changes may affect associations with PA and SB. Lastly, we were unable to examine stage at cancer diagnosis, cancer treatment modalities, and other cancer-specific characteristics among women with cancer in Aim 2. In addition, PA/SB measures during pre-diagnosis and during treatment were not available, and these behaviors are known to change during these time periods. If feasible, future studies on the associations of PA and SB with cancer survivorship should include these measures to provide a better understanding of these dynamic relationships.

Concluding remarks

In conclusion, higher levels of PA and lower levels of SB are associated with beneficial health outcomes in older women. If older women are unable to engage in MVPA, sitting less and participating in higher levels of light PA can still confer substantial health benefits and help facilitate healthy longevity. These insights are applicable to older women in general and extend to cancer survivors specifically to help reduce their risk of premature mortality. PA levels in older women decrease significantly over time, though the trajectory of decline varies across several characteristics. Addressing these differences in future behavioral intervention studies will be vital for achieving equity in PA participation.

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