HHS Public Access
Author manuscript
Cancer. Author manuscript; available in PMC 2023 May 15.

Published in final edited form as:
Cancer. 2023 May 15; 129(10): 1579–1590. doi:10.1002/cncr.34699.

Accelerometer-measured physical activity and postmenopausal breast cancer incidence in the Women's Health Accelerometry Collaboration

Eric T. Hyde, MPH[1,2], **Andrea Z. LaCroix, PhD, MPH**[1], **Kelly R. Evenson, PhD, MS**[3], **Annie Green Howard, PhD**[4,5], **Blake Anuskiewicz, MS**[1], **Chongzhi Di, PhD**[6], **John Bellettiere, PhD, MPH**[1], **Michael J. LaMonte, PhD, MPH**[7], **JoAnn E. Manson, MD, MPH, DrPH**[8,9], **Julie E. Buring, ScD**[8,9], **Eric J. Shiroma, ScD**[10], **I-Min Lee, MBBS, ScD**[8,9], **Humberto Parada Jr., PhD, MPH**[2,11]

[1]Herbert Wertheim School of Public Health and Human Longevity Science, University of California San Diego, San Diego, California, USA

[2]Division of Epidemiology and Biostatistics, School of Public Health, San Diego State University, San Diego, California, USA

[3]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[4]Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[5]Carolina Population Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

[6]Division of Public Health Sciences, Fred Hutchinson Cancer Center, Seattle, Washington, USA

[7]Department of Epidemiology and Environmental Health, School of Public Health and Health Professions, University at Buffalo-SUNY, Buffalo, New York, USA

Correspondence: Eric T. Hyde, San Diego State University/University of California San Diego Joint Doctoral Program (Epidemiology), 9500 Gilman Dr, La Jolla, CA 92093, USA. ehyde@health.ucsd.edu.
The last two authors contributed equally to this article.

AUTHOR CONTRIBUTIONS
Andrea Z. LaCroix: Conceptualization, data curation, methodology, supervision, writing–original draft, and writing–review and editing. **Kelly R. Evenson:** Conceptualization, data curation, methodology, supervision, writing–original draft, and writing–review and editing. **I-Min Lee:** Conceptualization, data curation, methodology, supervision, writing–original draft, and writing–review and editing. **Humberto Parada Jr:** Conceptualization, formal analysis, methodology, supervision, writing–original draft, and writing–review and editing. **Annie Green Howard:** Data curation, methodology, and writing–review and editing. Eric T. Hyde: Formal analysis, methodology, writing–original draft, and writing–review and editing. **Chongzhi Di:** Data curation, methodology, and writing–review and editing. **Blake Anuskiewicz:** Data curation and writing–review and editing. **John Bellettiere:** Data curation and writing–review and editing. **Michael J. LaMonte:** Writing–review and editing. **JoAnn E. Manson:** Writing–review and editing. **Julie E. Buring:** Writing–review and editing. **Eric J. Shiroma:** Writing–review and editing.

CONFLICT OF INTEREST STATEMENT
Kelly R. Evenson reports grant funding from National Institutes of Health. Annie Green Howard reports grant funding from National Institutes of Health. Eric T. Hyde reports grant funding from the National Heart, Lung, and Blood Institute. Andrea Z. LaCroix reports grant funding from the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Institute on Aging. JoAnn E. Manson reports grant funding and other fees from the National Institutes of Health. Chongzhi Di reports grant funding from the National Institutes of Health. The other authors declare no conflicts of interest.

SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

[8]Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

[9]Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, Massachusetts, USA

[10]Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, NIH, Bethesda, Maryland, USA

[11]UC San Diego Health Moores Cancer Center, La Jolla, California, USA

Abstract

Background: Few studies have examined accelerometer-measured physical activity and incident breast cancer (BC). Thus, this study examined associations between accelerometer-measured vector magnitude counts per 15 seconds (VM/15s) and average daily minutes of light physical activity (LPA), moderate-to-vigorous PA (MVPA), and total PA (TPA) and BC risk among women in the Women's Health Accelerometry Collaboration (WHAC).

Methods: The WHAC comprised 21,089 postmenopausal women (15,375 from the Women's Health Study [WHS]; 5714 from the Women's Health Initiative Objective Physical Activity and Cardiovascular Health Study [OPACH]). Women wore an ActiGraph GT3X+ on the hip for ≥4 days and were followed for 7.4 average years to identify physician-adjudicated *in situ* (n = 94) or invasive (n = 546) BCs. Multivariable stratified Cox regression estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for tertiles of physical activity measures in association with incident BC overall and by cohort. Effect measure modification was examined by age, race/ethnicity, and body mass index (BMI).

Results: In covariate-adjusted models, the highest (vs. lowest) tertiles of VM/15s, TPA, LPA, and MVPA were associated with BC HRs of 0.80 (95% CI, 0.64–0.99), 0.84 (95% CI, 0.69–1.02), 0.89 (95% CI, 0.73–1.08), and 0.81 (95% CI, 0.64–1.01), respectively. Further adjustment for BMI or physical function attenuated these associations. Associations were more pronounced among OPACH than WHS women for VM/15s, MVPA, and TPA; younger than older women for MVPA; and women with BMI ≥30 than <30 kg/m^2 for LPA.

Conclusion: Greater levels of accelerometer-assessed PA were associated with lower BC risk. Associations varied by age and obesity and were not independent of BMI or physical function.

Keywords

accelerometer; breast cancer; incidence; physical activity; postmenopause; women's health

INTRODUCTION

In 2023, an estimated 29,770 United States (US) women will be diagnosed with breast cancer (BC), which, except for skin cancer, is the most common cancer diagnosed and the second leading cause of cancer-related death among US women.[1] For postmenopausal breast cancer in particular, it is estimated that approximately one-third of cases are attributable to modifiable risk factors such as physical inactivity.[2] Prospective cohort studies assessing the relationship between self-reported physical activity and postmenopausal BC have consistently reported lower BC risk in association with higher physical activity levels.[3–6] However, self-reported physical activity measures are prone to measurement error, which can be mitigated by using accelerometry.[7,8] Generally, the correlation coefficient for self-reported and accelerometer-measured physical activity is approximately 0.4.[9–11]

To our knowledge, only one study to date has prospectively examined the association between accelerometer-measured physical activity and incident BC.[12] In that study, using data from the United Kingdom Biobank, Guo and colleagues[12] reported an inverse linear association between physical activity and BC risk among postmenopausal women; however, the unit of physical activity measurement used, overall acceleration average, cannot be directly translated into practice (i.e., minutes of physical activity per day or week) or intensities (i.e., light, moderate, and/or vigorous), limiting the ability to understand the extent to which their results support current physical activity guidelines for BC prevention.

To help fill this gap, we examined the prospective associations between physical activity and incident BC among postmenopausal women in the US Women's Health Accelerometry Collaboration (WHAC). We performed a comprehensive assessment using multiple metrics of physical activity including daily vector magnitude counts per 15 seconds (VM/15s), a summary metric of output from the three accelerometer axes (i.e., the vertical [up–down], horizontal [forward-backward], and lateral [left–right] axes) and serves as an indicator of total volume of physical activity and daily time spent in intensity-specific categories of light physical activity (LPA), moderate-to-vigorous physical activity (MVPA), and total physical activity (TPA; LPA + MVPA). We also evaluated whether the associations between physical activity and postmenopausal BC incidence varied according to subgroups defined by age, race/ethnicity, and body mass index (BMI).

MATERIALS AND METHODS

Study population

The WHAC is a consortium of two harmonized prospective cohort studies, the Women's Health Study (WHS) and the Women's Health Initiative (WHI) Objective Physical Activity and Cardiovascular Health (OPACH) Study. Details of each study's history, participant recruitment, and methodology and the WHAC harmonization have been previously described.[13] Briefly, the WHS is a completed randomized trial (1992–2004) that tested aspirin, β-carotene, and vitamin E for the prevention of cardiovascular disease and cancer among 39,876 US women ≥45 years old.[14–16] From 2011 to 2014, 18,289 women participated in an ancillary study that collected accelerometry data, and of these, 17,466 (96%) women returned the accelerometers with usable data.[17] The OPACH study is an ancillary to the WHI Long Life Study, a 2012–2014 study of US postmenopausal women focused on healthy aging,[18] and is a prospective study of accelerometry and chronic disease outcomes including cancer.[19] Among the 9252 women consented to the WHI Long Life Study, 7048 participated in OPACH and, of these, 6489 (92%) women returned accelerometers with usable data.

All study protocols were approved by institutional review boards of each participating institution and all women provided informed consent before participating in the studies.

Physical activity

Physical activity was measured in WHS and OPACH using the ActiGraph GT3X+ triaxial accelerometer (ActiGraph LLC, Pensacola, Florida) worn for up to 7 consecutive days, as previously described.[13] In WHS, women were asked to wear the accelerometer over the right hip, removing it only during sleep or when in water.[17] In OPACH, women were asked to wear the accelerometer over the right hip including during sleep but not when in water[19]; subsequently, the time spent sleeping was removed for all analyses. Mean accelerometer wear time was 14.9 hours/day for both cohorts.[13] For WHS and OPACH, accelerometer wear adherence was defined as wearing time of ≥10 hours on ≥4 days of device wear. Raw acceleration signals at 30 Hz were aggregated using ActiLife software (V.6) to counts per 15-second epochs using the normal filter setting. VM counts were derived by taking the square root of the sum of counts from the three axes squared. Accelerometer nonwear time was removed using the validated Choi algorithm,[20,21] which was applied to VM counts/minute with a 90-minute window, 30-minute stream frame, and 2-minute tolerance. Daily average physical activity volume was summarized as average VM/15s. Using cutpoints derived from a calibration study among women of similar ages,[22] average time spent in intensity-specific categories was defined for LPA as average minutes per day with VM/15s 19–518 and for MVPA as average minutes per day with VM/15s ≥519. TPA time was defined as the sum of the number of minutes spent in LPA and MVPA.

Breast cancer incidence

In WHS and OPACH, participants received annual mailed questionnaires in which they were asked to self-report new cancer diagnoses. Medical records were obtained for all self-reported cancers except nonmelanoma skin cancers.[23] Adjudicators reviewed the medical records and incident cancers. The primary end point of interest for this study was a composite of reported and confirmed incident *in situ* or invasive BCs. In sensitivity analyses, we considered as the outcome invasive BCs only. Time-to-event was computed from the first day of accelerometry to the date of BC diagnosis, with participants right-censored due to death or their last returned annual questionnaire from the time of accelerometer measurement either 2011–2014 in WHS or 2012–2014 in OPACH (i.e., baseline) through December 31, 2021 in WHS or March 31, 2021 in OPACH.

Covariates

For both studies, age, race/ethnicity, and education level were self-reported at enrollment into the original study. Data on health history and health behaviors were ascertained annually, and data from the measure closest in time to accelerometer wear was 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, and history of cancer, diabetes, and confirmed cardiovascular disease. Height and weight were self-reported in WHS and measured by study personnel in OPACH. 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).[24] Number of mammograms received from baseline to date of BC diagnosis and/or censoring was ascertained by self-report annually in OPACH and approximately every 2 years in WHS.

Statistical analysis

Average daily VM/15s and minutes of TPA, LPA, and MVPA variables were residualized to control for differing accelerometer wear times in the statistical models using combined data from both cohorts, as described elsewhere.[25–28] Physical activity variables were categorized into tertiles using cut-points from the overall sample for the primary analysis, and using cohort-specific cut-points for cohort-specific analyses. Multivariable Cox proportional hazards models estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for incident BC in association with each physical activity measure. Models were *a priori* stratified by cohort to allow for baseline hazards of the two cohorts to differ.[29] The proportional hazards assumption was inspected using plots of the Schoenfeld residuals; no violations were evident. We present results adjusted for age-only (model 1) and the fully adjusted model (model 2) that included adjustment for age, race/ethnicity, education level, self-rated general health, smoking status, alcohol use status, postmenopausal hormone therapy use, number of mammograms during follow-up, and history of diabetes, cardiovascular disease, and cancer at the time of accelerometry measurement. We also evaluated the impact of further adjusting model 2 for BMI or physical function, as both measures are presumed confounders or mediators of the association between physical activity and BC. Linear trends (i.e., P_{Trend}) were examined using continuous physical activity measures.

Nonlinear dose–response trajectories were assessed by including in model 2 restricted cubic spline functions for each physical activity measure. Models with three knots placed at the 10th (referent), 50th, and 90th percentiles were evaluated and departures from linearity were examined using χ^2 tests.

To maximize statistical power, continuous physical activity variables (per standard deviation increase) were used to examine associations with *a priori* strata of interest in WHAC including age (<75 vs. ≥75 years), race/ethnicity (White, African American/Black and Hispanic), and BMI (<30 vs. ≥30 kg/m^2). Tests for multiplicative interaction were evaluated using likelihood ratio tests comparing fully adjusted models (model 2) with cross-product terms for continuous physical activity and each of the categorical covariates, with the reduced model without the interaction terms.

To account for missing data, we used multiple imputation using chained equations with predictive mean matching. Overall, missing data was low with physical function having the greatest proportion of missing values (6.5%). Data were imputed separately by cohort. A total of 25 imputations with 20 iterations were used and included all covariates, wear time-standardized physical activity variables, the incident BC indicator, and the Nelson–Aalen estimator of the cumulative hazard.[30] In sensitivity analyses, results from complete-case analyses were compared to those using imputed data sets. All analyses were conducted in R v4.0.2 (R Foundation for Statistical Computing; Vienna, Austria).

From the 23,955 combined participants with accelerometer data (*n* = 17,466 WHS and *n* = 6489 OPACH), we excluded 1087 women (*n* = 724 WHS and *n* = 363 OPACH) with nonadherent accelerometer wear, 1763 women (*n* = 1351 WHS and *n* = 412 OPACH) with a history of BC at the time of accelerometer wear, and 16 WHS women who reported prevalent cancer post-trial randomization. These exclusions resulted in an analytic sample of 21,089 women (*n* = 15,375 WHS and *n* = 5714 OPACH).

RESULTS

Over a mean follow-up time of 7.4 (interquartile range = 6.9–8.6) years, a total of 640 women (3.0%) were diagnosed with incident BC (*n* = 94 in situ, *n* = 546 invasive). Participant baseline characteristics stratified by tertiles of wear-time standardized MVPA are presented in Table 1. Overall, women with higher versus lower levels of MVPA were younger, had lower BMI, and higher frequency of alcohol use, better self-rated general health, and were less likely to have a history of cardiovascular disease, diabetes, or cancer. Cohort-stratified descriptive characteristics are provided in Table S1.

Overall, the average daily VM/15s was 134.2 (SD = 53.8) (mean = 146.3, SD = 52.7 in WHS; mean = 101.8, SD = 42.1 in OPACH). In the fully adjusted model (model 2), women in the highest (vs. lowest) tertile of VM/15s had a BC HR of 0.80 (95% CI, 0.64–0.99) (Table 2). However, this association was attenuated after adjusting for BMI or physical function. By cohort, BC HR estimates were 0.77 (95% CI, 0.61–0.97) in WHS and 0.66 in OPACH (95% CI, 0.43–1.01).

The average daily time spent in wear-time standardized TPA was 369.0 (SD = 92.0) (mean = 380.4, SD = 90.0 in WHS; mean = 338.3, SD = 90.4 in OPACH) minutes/day. As shown in Table 3, women in the highest (vs. lowest) tertile of minutes of daily TPA had a BC HR of 0.84 (95% CI, 0.69–1.02). By cohort, BC HR estimates were 0.81 (95% CI, 0.65–1.02) in WHS and 0.67 (95% CI, 0.44–1.01) in OPACH and were attenuated in both cohorts when adjusting for BMI or physical function.

In WHAC, average daily time spent in wear-time standardized LPA was 287.9 (SD = 67.0) (mean = 288.1, SD = 65.0 in WHS; mean = 287.5, SD = 72.3 in OPACH) minutes/day. None of the associations between LPA and incident BC were statistically significant overall or by cohort (Table S2).

Average daily time spent in wear-time standardized MVPA was 81.0 (SD = 45.6) (mean = 92.3 [SD = 44.3] in WHS; mean = 50.7 [SD = 33.7] in OPACH) minutes/day. As shown in Table 4, women in the highest (vs. lowest) tertile of minutes of daily MVPA had a BC HR of 0.81 (95% CI, 0.64–1.01). By cohort, BC HR estimates were 0.81 (HR, 0.81; 95% CI, 0.63–1.03) in WHS and 0.63 (95% CI, 0.41–0.98) in OPACH and were attenuated when adjusting for BMI or physical function.

In Table 5, we report the results examining effect measure modification by age, race/ethnicity, and BMI using data from both cohorts combined. We observed statistically significant modification by age for MVPA ($P_{\text{Interaction}}$ = 0.03) and by BMI for LPA ($P_{\text{Interaction}}$ = 0.03) and no significant modification by race/ethnicity. Among women <75 years old, a one-standard deviation increase in MVPA was associated with a HR of 0.86 (95% CI, 0.77–0.96) and among women ≥75 years old with a HR of 1.12 (95% CI, 0.92–1.35). Among women with BMI ≥30 kg/m^2, a one-standard deviation increase in LPA was associated with a BC HR of 0.85 (95% CI, 0.73–1.01) and among women with BMI <30 kg/m^2 with a HR of 1.04 (95% CI, 0.94–1.14).

Sensitivity analyses

Sensitivity analyses were generally consistent with the primary findings. Results from the complete-case analysis (Tables S3–S6) and for the outcome definition that included invasive BC only (Tables S7–S10) were not materially different from the main analysis. Dose–response associations between each continuous physical activity variable and incident BC modeled using restricted cubic splines are displayed in Figures S1–S4; inverse associations between higher physical activity levels with lower BC risk were consistent with the primary analyses, although not statistically significant.

DISCUSSION

In this study of over 20,000 US postmenopausal women, higher daily accelerometer vector magnitude counts and greater amounts of time spent in TPA and MVPA were inversely associated BC risk over a mean 7 years of follow-up; however, associations were attenuated and not statistically significant after adjustment for BMI or physical function. Associations of physical activity were stronger among women younger than 75 years than those 75 or older and among women with obesity than among women without obesity. For all accelerometer-based physical activity measures, associations with incident BC were more pronounced in OPACH than in WHS. WHS women had nearly double the amount of average daily MVPA compared to OPACH women. The substantially lower MVPA in OPACH women may partially explain the different estimates observed between cohorts. For example, the amount of average daily MVPA in the OPACH-specific referent tertile (19.0 min/day) was considerably lower than the WHS-specific referent tertile (47.4 min/day), resulting in different cohort-specific hazard ratio estimates. Differences in baseline characteristics between cohorts may further explain these differences; however, we allowed the baseline hazards to differ in the statistical models and adjusted for covariates that differed between the two cohorts.

This study builds on our previous work in OPACH where accelerometer-measured TPA and MVPA were associated with reduced incidence of 13 types of invasive cancers.[31] However, in that study, incident BC could not be examined separately due to small numbers of cases. In a study of postmenopausal women in the United Kingdom Biobank, an increase of 5 milli-gravity assessed using a wrist-worn accelerometer was associated with a 21% reduction in BC risk that attenuated to 16% after adjusting for adiposity.[12] Although their estimates cannot be directly compared to those from our study, our conclusions are in agreement.[12] The only other study that has examined accelerometer-measured physical activity in association with incident BC was a 2012 population-based case-control study of Polish women.[32] In that study, Dallal et al.[32] reported a strong inverse association between MVPA and postmenopausal BC. However, the case-control design may have resulted in biased results because women with BC may engage in greater physical activity following a diagnosis of BC to improve their prognosis or quality of life.[33] Our results are also in line with a number of previous studies that have examined self-reported physical activity and BC risk including previous meta-analyses and systematic reviews.[3,6,34,35]

We observed a 20% reduced risk of BC when comparing women in the highest versus lowest tertiles of accelerometer VM counts. Although a comparable reduction was observed for TPA, the association was not statistically significant. One explanation for the differences observed is that although both these measures are intended to capture a similar construct (i.e., total volume of daily movement), TPA relies on a calibrated cutpoint applied to VM counts and time spent above this cutpoint. Conversely, the raw VM counts include values below this cutpoint threshold, which reflect low intensity movement, but are often classified as sedentary behavior[22]; the inclusion of these movements may have resulted in the observed stronger association for VM counts and incident BC compared to TPA.

Increasing physical activity levels has been shown to play an important role in postmenopausal BC prevention,[36] and the biologic pathways are complex. Physical activity is hypothesized to inhibit breast carcinogenesis through the alterations in sex steroid hormones including estrogens and metabolic hormones.[37] In addition, physical activity reduces inflammation, improves immune system functioning, and reduces adipocity.[38,39] In our study, all associations between physical activity and BC were attenuated when controlling for BMI or physical function, and in analyses stratified by obesity, we observed stronger inverse associations among women with BMI ≥30 kg/m^2. These findings highlight the important role of obesity in the relationship between physical activity and postmenopausal BC risk, as well as a possible role of physical function in preventing physical activity or which may be impacted by obesity. In addition, our findings suggest that physical activity may have a stronger inverse association with breast cancer in women under 75 years compared to women over 75 years. Although evidence for a waning beneficial effect of physical activity on breast cancer with increased age is limited,[6] a possible explanation is that biological pathways that protect against oxidative stress and DNA damage weaken throughout the aging process,[40,41] thereby limiting the protective role of physical activity.

To our knowledge, this study is the first US-based prospective cohort study of accelerometer-assessed physical activity and BC risk. Our study had a number of strengths including the harmonization of physical activity, covariate, and cancer data from OPACH and WHS to create a large and diverse cohort of women.[13] In addition, we used accelerometer cutpoints calibrated for older women.[22] Limitations include having only one physical activity measurement, which prohibited examination of changes in physical activity over time. Furthermore, we did not examine BC subtypes, which may reveal differences that are masked when aggregating all BC subtypes and could provide additional insight into the biological mechanisms by which physical activity impacts BC. Finally, most WHS participants in this study were non-Hispanic White, had a college education, self-rated their health as very good or excellent, and all women were post-menopausal at baseline, which may limit the generalizability of our findings. Notably, the OPACH cohort had greater diversity in race/ethnicity, education, and health status[13]; however, future studies should consider multiple assessments of physical activity and molecular characterization of breast tumors among diverse women.

In conclusion, higher levels of physical activity, and in particular MVPA, measured by accelerometer were associated with lower risk of BC in older women, but these findings were not independent of BMI or physical function. US public health guidelines recommend engaging in physical activity to reduce BC risk,[42] although evidence has been almost exclusively based on studies of self-reported physical activity.[6] Here, we provide evidence on the relationship of device-measured physical activity with postmenopausal BC risk. However, additional studies are needed in large and diverse cohorts of women over a broad age range to further refine physical activity guidelines for the primary prevention of BC.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This work was supported by the National Institutes of Health (NIH), National Cancer Institute (NCI), Office of the Director, Office of Disease Prevention, and Office of Behavioral and Social Sciences Research (5R01CA227122). Women's Health Study is funded by NIH (CA154647, CA047988, CA182913, HL043851, HL080467, and HL099355). The Women's Health Initiative program is funded by the NationalHeart, Lung, and Blood Institute (NHLBI)(75N92021D00001, 75N92021D00002, 75N92021D00003, 75N92021D00004, 75N920 21D00005, and R01HL105065). Eric T. Hyde was supported by the NHLBI (T32HL079891). Michael J. LaMonte was supported by NHLBI (75N92021D00002, HL153462, HL151885, HL150170, and HL130591). Humberto Parada Jr was supported by the National Cancer Institute (K01 CA234317), the San Diego State University/University of California San Diego Cancer Center Comprehensive Partnership (U54 CA132384 and U54 CA132379), and by the Alzheimer's Disease Resource Center for advancing Minority Aging Research at the University of California San Diego (P30 AG059299). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

DATA AVAILABILITY STATEMENT

Access to the WHAC data used in this manuscript or the computer code for replicating these results would require collaboration with the senior authors, approval by the WHS and WHI studies and completion of a data use agreement, and institutional review board approval from the participating institutions.

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TABLE 1

WHAC participant baseline characteristics overall and by tertiles of wear time-standardized average daily MVPA.

Characteristic	Total	Tertiles of MVPA (min/day) <56.8	56.8–96.1	>96.1
N	21,089	7030	7030	7029
Cohort, No. (%)				
WHS	15,375 (72.9)	3342 (47.5)	5583 (79.4)	6451 (91.8)
OPACH	5714 (27.1)	3688 (52.5)	1447 (20.6)	578 (8.2)
Age (years), No. (%)				
<70	7496 (35.5)	1058 (15.0)	2653 (37.7)	3785 (53.8)
70–79	9128 (43.3)	2996 (42.6)	3307 (47.0)	2826 (40.2)
≥80	4465 (21.2)	2976 (42.3)	1070 (15.2)	418 (5.9)
Mean [SD]	73.4 [6.8]	77.5 [7.0]	72.5 [6.0]	70.2 [5.0]
Race/ethnicity, No. (%)				
White	17,500 (83.0)	5089 (72.4)	5954 (84.7)	6457 (91.9)
African American/Black	2132 (10.1)	1331 (18.9)	574 (8.2)	227 (3.2)
Hispanic	1107 (5.3)	512 (7.3)	362 (5.1)	232 (3.3)
Other or unknown	350 (1.7)	98 (1.4)	140 (2.0)	113 (1.6)
Highest education level, No. (%)				
High school/GED or less	1158 (5.5)	790 (11.2)	253 (3.6)	115 (1.6)
Some college	9740 (46.2)	3223 (45.8)	3336 (47.5)	3181 (45.3)
College graduate	9902 (47.0)	2943 (41.9)	3343 (47.6)	3616 (51.4)
Missing	289 (1.4)	74 (1.1)	98 (1.4)	117 (1.7)
Smoking status, No. (%)				
Never	10,905 (51.7)	3608 (51.3)	3657 (52.0)	3641 (51.8)
Former	9406 (44.6)	3068 (43.6)	3129 (44.5)	3208 (45.6)
Current	731 (3.5)	325 (4.6)	230 (3.3)	176 (2.5)
Missing	47 (0.2)	29 (0.4)	14 (0.2)	4 (0.1)
Alcohol use, No. (%)				
Never or rarely	7983 (37.9)	3046 (43.3)	2619 (37.3)	2317 (33.0)
Monthly	3470 (16.5)	1644 (23.4)	1030 (14.7)	797 (11.3)

		Tertiles of MVPA (min/day)		
Characteristic	**Total**	**<56.8**	**56.8–96.1**	**>96.1**
Weekly	6899 (32.7)	1729 (24.6)	2441 (34.7)	2729 (38.8)
Daily	2732 (13.0)	607 (8.6)	939 (13.4)	1186 (16.9)
Missing	5 (0.0)	4 (0.1)	1 (0.0)	0 (0.0)
Body mass index (kg/m^2), No. (%)				
<18.5	386 (1.8)	128 (1.8)	105 (1.5)	153 (2.2)
18.5–24.9	8536 (40.5)	2107 (30.0)	2752 (39.1)	3677 (52.3)
25.0–29.9	7336 (34.8)	2463 (35.0)	2520 (35.8)	2353 (33.5)
≥30.0	4826 (22.9)	2330 (33.1)	1651 (23.5)	845 (12.0)
Missing	5 (0.0)	2 (0.0)	2 (0.0)	1 (0.0)
Mean [SD]	26.8 [5.3]	28.3 [5.9]	26.9 [5.1]	25.2 [4.2]
Self-rated general health, No. (%)				
Excellent or very good	14,487 (68.7)	3676 (52.3)	5058 (71.9)	5753 (81.8)
Good	5662 (26.8)	2724 (38.7)	1771 (25.2)	1168 (16.6)
Fair or poor	915 (4.3)	614 (8.7)	193 (2.7)	107 (1.5)
Missing	25 (0.1)	16 (0.2)	8 (0.1)	1 (0.0)
RAND-36 physical functioning score				
Mean (SD)	77.3 (23.1)	65.6 (25.9)	79.9 (20.4)	86.4 (16.8)
Missing (%)	1376 (6.5)	480 (6.8)	465 (6.6)	431 (6.1)
No. of mammograms[a]				
Mean (SD)	5.9 (2.9)	4.4 (3.1)	6.3 (2.7)	7.0 (2.3)
Missing (%)	30 (0.1)	23 (0.3)	6 (0.0)	1 (0.0)
Current hormone replacement therapy use, No. (%)	1780 (8.4)	379 (5.4)	652 (9.3)	749 (10.7)
Missing (%)	6 (0.0)	2 (0.0)	1 (0.0)	3 (0.0)
History of cardiovascular disease, No. (%)	1227 (5.8)	722 (10.3)	322 (4.6)	183 (2.6)
History of diabetes, No. (%)	2486 (11.8)	1,380 (19.6)	727 (10.3)	379 (5.4)
History of cancer, No. (%)	1271 (6.0)	525 (7.5)	411 (5.8)	334 (4.8)

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

[a]The number of mammograms received from baseline to date of BC diagnosis and/or censoring was ascertained annually by self-report over the follow-up period.

TABLE 2

HRs and 95% CIs for breast cancer incidence and tertiles of wear time-standardized average daily vector magnitude per 15 seconds ($N = 21{,}089$).

	Tertiles of average daily VM/15s			
WHAC	**<106.3**	**106.3–152.3**	**>152.3**	P_{Trend} [a]
Daily VM/15s, mean (SD)	79.3 (19.1)	128.6 (13.1)	194.8 (38.0)	
Breast cancer events, No. (%)	203 (2.9)	226 (3.2)	211 (3.0)	
Person-years	47,769	52,885	55,330	
Incidence rate per 1000 person-years	4.2	4.3	3.8	
Model 1: HR (95% CI)[b]	1.00	0.93 (0.77–1.14)	0.80 (0.65–0.98)	.03
Model 2: HR (95% CI)[c]	1.00	0.93 (0.76–1.14)	0.80 (0.64–0.99)	.04
Model 2 + BMI: HR (95% CI)[d]	1.00	0.97 (0.79–1.19)	0.87 (0.69–1.09)	.22
Model 2 + physical function: HR (95% CI)[e]	1.00	0.98 (0.80–1.20)	0.86 (0.69–1.07)	.17
WHS	**<119.5**	**119.5–163.6**	**>163.6**	
Daily VM/15s, mean (SD)	92.6 (19.4)	141.0 (12.5)	205.4 (37.5)	
Breast cancer events, No. (%)	161 (3.1)	182 (3.6)	147 (2.9)	
Person-years	37,483	39,700	40,794	
Incidence rate per 1000 person-years	4.3	4.6	3.6	
Model 1: HR (95% CI)[b]	1.00	1.05 (0.84–1.30)	0.81 (0.64–1.02)	.13
Model 2: HR (95% CI)[c]	1.00	1.00 (0.81–1.25)	0.77 (0.61–0.97)	.06
Model 2 + BMI: HR (95% CI)[d]	1.00	1.04 (0.84–1.30)	0.84 (0.65–1.07)	.32
Model 2 + physical function: HR (95% CI)[e]	1.00	1.04 (0.83–1.29)	0.81 (0.63–1.03)	.16
OPACH	**<79.5**	**79.5–114.0**	**>114.0**	
Daily VM/15s, mean (SD)	59.9 (14.2)	96.3 (10.0)	149.3 (31.1)	
Breast cancer events, No. (%)	52 (2.7)	51 (2.7)	47 (2.5)	
Person-years	11,603	12,904	13,500	
Incidence rate per 1000 person-years	4.5	4.0	3.5	

WHAC	Tertiles of average daily VM/15s <106.3	106.3–152.3	>152.3	P_{Trend} [a]
Model 1: HR (95% CI)[b]	1.00	0.74 (0.49–1.09)	0.60 (0.40–0.91)	.08
Model 2: HR (95% CI)[c]	1.00	0.73 (0.49–1.10)	0.66 (0.43–1.01)	.22
Model 2 + BMI: HR (95% CI)[d]	1.00	0.75 (0.50–1.13)	0.70 (0.45–1.09)	.37
Model 2 + physical function: HR (95% CI)[e]	1.00	0.82 (0.54–1.25)	0.77 (0.49–1.21)	.64

Abbreviations: BMI, body mass index; CI, confidence interval; GED, General Educational Development; HR, hazard ratio; OPACH, Objective Physical Activity and Cardiovascular Health in Older Women; SD, standard deviation; VM, vector magnitude; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study.

[a] *P* values from χ^2 tests for linear trend using Cox regression models with continuous VM/15s variable.

[b] Model 1 is adjusted for age (years).

[c] Model 2 is adjusted for age (years), race/ethnicity (White, African American/Black, Hispanic, other or unknown), education (high school/GED or less, some college, college graduate), smoking status (never, former, current), alcohol use (never or rarely, monthly, weekly, daily), general health (excellent or very good, good, fair or poor), mammography (number during follow-up period), postmenopausal hormone use (ever or never), history of diabetes (yes or no), confirmed cardiovascular disease (yes or no), and history of cancer at accelerometry measurement (yes or no).

[d] Model is adjusted for model 2 and BMI (<18.5, 18.5–24.9, 25.0–29.9, ≥30 kg/m^2).

[e] Model is adjusted for model 2 and physical function (RAND-36 score).

TABLE 3

HRs and 95% CIs for breast cancer incidence and tertiles of wear time-standardized minutes of daily total physical activity (*N* = 21,089).

	Tertiles of total PA (min/day)			
WHAC	**<326.9**	**326.9–408.2**	**>408.2**	P_{Trend} [a]
Total PA minutes per day, mean (SD)	269.1 (45.9)	367.5 (22.9)	470.3 (50.4)	
Breast cancer events, No. (%)	212 (3.0)	220 (3.1)	208 (3.0)	
Person-years	49,088	52,522	54,374	
Incidence rate per 1000 person-years	4.3	4.2	3.8	
Model 1: HR (95% CI) [b]	1.00	0.94 (0.78–1.14)	0.83 (0.69–1.02)	.10
Model 2: HR (95% CI) [c]	1.00	0.94 (0.77–1.14)	0.84 (0.69–1.02)	.12
Model 2 + BMI: HR (95% CI) [d]	1.00	0.98 (0.81–1.20)	0.92 (0.74–1.13)	.58
Model 2 + physical function: HR (95% CI) [e]	1.00	0.98 (0.81–1.19)	0.89 (0.72–1.09)	.35
WHS	**<339.5**	**339.5–418.3**	**>418.3**	
Total PA minutes per day, mean (SD)	282.7 (45.4)	379.1 (22.5)	479.2 (49.3)	
Breast cancer events, No. (%)	167 (3.3)	172 (3.4)	151 (2.9)	
Person-years	37,952	39,585	40,440	
Incidence rate per 1000 person-years	4.4	4.3	3.7	
Model 1: HR (95% CI) [b]	1.00	0.98 (0.79–1.22)	0.84 (0.67–1.05)	.35
Model 2: HR (95% CI) [c]	1.00	0.95 (0.77–1.18)	0.81 (0.65–1.02)	.22
Model 2 + BMI: HR (95% CI) [d]	1.00	1.00 (0.81–1.25)	0.90 (0.71–1.14)	.86
Model 2 + physical function: HR (95% CI) [e]	1.00	0.98 (0.78–1.21)	0.84 (0.67–1.06)	.40
OPACH	**<296.5**	**296.5–374.5**	**>374.5**	
Total PA minutes per day, mean (SD)	241.2 (42.8)	336.0 (22.7)	438.3 (52.3)	
Breast cancer events, No. (%)	56 (2.9)	48 (2.5)	46 (2.4)	
Person-years	11,812	12,913	13,282	
Incidence rate per 1000 person-years	4.7	3.7	3.5	

WHAC	Tertiles of total PA (min/day) <326.9	326.9–408.2	>408.2	P_{Trend} [a]
Model 1: HR (95% CI)[b]	1.00	0.71 (0.48–1.05)	0.61 (0.41–0.91)	.09
Model 2: HR (95% CI)[c]	1.00	0.73 (0.49–1.09)	0.67 (0.44–1.01)	.22
Model 2 + BMI: HR (95% CI)[d]	1.00	0.76 (0.51–1.14)	0.71 (0.46–1.09)	.39
Model 2 + physical function: HR (95% CI)[e]	1.00	0.80 (0.54–1.20)	0.76 (0.49–1.16)	.59

Abbreviations: BMI, body mass index; CI, confidence interval; GED, General Educational Development; HR, hazard ratio; OPACH, Objective Physical Activity and Cardiovascular Health in Older Women; PA, physical activity; SD, standard deviation; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study.

[a] *P* values from χ^2 tests for linear trend using Cox regression models with continuous total PA variable.

[b] Model 1 is adjusted for age (years).

[c] Model 2 is adjusted for age (years), race/ethnicity (White, African American/Black, Hispanic, other or unknown), education (high school/GED or less, some college, college graduate), smoking status (never, former, current), alcohol use (never or rarely, monthly, weekly, daily), general health (excellent or very good, good, fair or poor), mammography (number during follow-up period), postmenopausal hormone use (ever or never), history of diabetes (yes or no), confirmed cardiovascular disease (yes or no), and history of cancer at accelerometry measurement (yes or no).

[d] Model is adjusted for model 2 and BMI (<18.5, 18.5–24.9, 25.0–29.9, ≥30 kg/m^2).

[e] Model is adjusted for model 2 and physical function (RAND-36 score).

TABLE 4

HRs and 95% CIs for breast cancer incidence and tertiles of wear time-standardized minutes of moderate-to-vigorous intensity physical activity (*N* = 21,089).

	Tertiles of MVPA (min/day)			
WHAC	**<56.8**	**56.8–96.1**	**>96.1**	P_{Trend} [a]
MVPA minutes per day, mean (SD)	34.8 (14.7)	75.6 (11.3)	132.7 (32.6)	
Breast cancer events, No. (%)	194 (2.8)	237 (3.4)	209 (3.0)	
Person-years	47,479	53,050	55,457	
Incidence rate per 1000 person-years	4.1	4.5	3.8	
Model 1: HR (95% CI)[b]	1.00	0.99 (0.81–1.22)	0.81 (0.65–1.01)	.06
Model 2: HR (95% CI)[c]	1.00	0.99 (0.80–1.21)	0.81 (0.64–1.01)	.07
Model 2 + BMI: HR (95% CI)[d]	1.00	1.02 (0.83–1.25)	0.86 (0.68–1.09)	.26
Model 2 + physical function: HR (95% CI)[e]	1.00	1.04 (0.84–1.28)	0.87 (0.69–1.10)	.24
WHS	**<69.2**	**69.2–106.4**	**>106.4**	
MVPA minutes per day, mean (SD)	47.4 (15.9)	87.3 (10.7)	142.0 (31.9)	
Breast cancer events, No. (%)	135 (2.6)	165 (3.2)	130 (2.5)	
Person-years	34,503	36,452	37,483	
Incidence rate per 1000 person-years	3.9	4.5	3.5	
Model 1: HR (95% CI)[b]	1.00	1.14 (0.91–1.41)	0.84 (0.67–1.07)	.22
Model 2: HR (95% CI)[c]	1.00	1.10 (0.88–1.37)	0.81 (0.63–1.03)	.13
Model 2 + BMI: HR (95% CI)[d]	1.00	1.13 (0.91–1.41)	0.87 (0.68–1.11)	.41
Model 2 + physical function: HR (95% CI)[e]	1.00	1.14 (0.91–1.42)	0.85 (0.66–1.08)	.27
OPACH	**<31.7**	**31.7–59.2**	**>59.2**	
MVPA minutes per day, mean (SD)	19.0 (8.7)	44.5 (7.7)	89.0 (27.4)	
Breast cancer events, No. (%)	51 (2.7)	52 (2.7)	47 (2.5)	
Person-years	11,595	12,899	13,514	

	Tertiles of MVPA (min/day)			
WHAC	**<56.8**	**56.8–96.1**	**>96.1**	P_{Trend} [a]
Incidence rate per 1000 person-years	4.4	4.0	3.5	
Model 1: HR (95% CI)[b]	1.00	0.75 (0.49–1.09)	0.59 (0.39–0.90)	.08
Model 2: HR (95% CI)[c]	1.00	0.73 (0.49–1.10)	0.63 (0.41–0.98)	.19
Model 2 + BMI: HR (95% CI)[d]	1.00	0.74 (0.49–1.11)	0.66 (0.42–1.03)	.29
Model 2 + physical function: HR (95% CI)[e]	1.00	0.80 (0.53–1.21)	0.73 (0.46–1.14)	.50

Abbreviations: BMI, body mass index; CI, confidence interval; GED, General Educational Development; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; OPACH, Objective Physical Activity and Cardiovascular Health in Older Women; PA, physical activity; SD, standard deviation; WHAC, Women's Health Accelerometry Collaboration; WHS, Women's Health Study.

[a] *P* values from χ^2 tests for linear trend using Cox regression models with continuous MVPA variable.

[b] Model 1 is adjusted for age (years).

[c] Model 2 is adjusted for age (years), race/ethnicity (White, African American/Black, Hispanic, other or unknown), education (high school/GED or less, some college, college graduate), smoking status (never, former, current), alcohol use (never or rarely, monthly, weekly, daily), general health (excellent or very good, good, fair or poor), mammography (number during follow-up period), postmenopausal hormone use (ever or never), history of diabetes (yes or no), confirmed cardiovascular disease (yes or no), and history of cancer at accelerometry measurement (yes or no).

[d] Model is adjusted for model 2 and BMI (<18.5, 18.5–24.9, 25.0–29.9, ≥30 kg/m^2).

[e] Model is adjusted for model 2 and physical function (RAND-36 score).

TABLE 5

HRs and 95% CIs for breast cancer incidence and tertiles of wear-time standardized average daily vector magnitude per 15 seconds, and minutes of total, light, and moderate-to-vigorous physical activity among cohort subgroups ($N = 21{,}089$).

		VM/15s[a]		Total PA[a]		Light PA[a]		MVPA[a]	
Cohort group	**Cancer events, No. (%)**	**HR (95% CI)[b]**	**$P_{Interaction}$[c]**	**HR (95% CI)[b]**	**$P_{Interaction}$[c]**	**HR (95% CI)[b]**	**$P_{Interaction}$[c]**	**HR (95% CI)[b]**	**$P_{Interaction}$[c]**
Overall	640 (3.0)	0.90 (0.82–0.99)		0.93 (0.86–1.02)		0.96 (0.89–1.04)		0.91 (0.83–1.00)	
Age (years)			.07		.18		.67		.03
<75	462 (3.5)	0.86 (0.78–0.96)		0.91 (0.82–1.00)		0.96 (0.87–1.06)		0.86 (0.77–0.96)	
≥75	178 (2.2)	1.06 (0.87–1.29)		1.00 (0.85–1.18)		0.96 (0.82–1.12)		1.12 (0.92–1.35)	
Race/ethnicity			.42		.70		.99		.32
White	535 (3.1)	0.90 (0.82–1.00)		0.94 (0.86–1.03)		0.97 (0.89–1.06)		0.91 (0.83–1.01)	
AA/Black	70 (3.3)	0.87 (0.61–1.24)		0.81 (0.62–1.06)		0.83 (0.65–1.05)		0.86 (0.58–1.27)	
Hispanic	25 (2.3)	0.94 (0.51–1.76)		1.03 (0.60–1.75)		1.03 (0.63–1.69)		1.00 (0.54–1.86)	
BMI (kg/m^2)			.25		.06		.03		.47
<30	466 (2.9)	0.95 (0.85–1.05)		1.00 (0.91–1.11)		1.04 (0.94–1.14)		0.94 (0.85–1.05)	
≥30	174 (3.6)	0.85 (0.68–1.06)		0.85 (0.71–1.01)		0.85 (0.73–1.01)		0.91 (0.72–1.13)	

Abbreviations: AA, African American; BMI, body mass index; CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; PA, physical activity; VM, vector magnitude.

[a] One-standard deviation unit increment of VM/15s = 53.8, total PA = 92.0 min, light PA = 67.0 min, and MVPA = 45.6 min.

[b] Model is adjusted for age, race/ethnicity, education, general health, smoking status, alcohol use status, postmenopausal hormone use, diabetes, cardiovascular disease, number of mammograms, and cancer at accelerometry measurement.

[c] Interaction evaluated using likelihood ratio tests comparing Cox regression models with cross-product terms for continuous physical activity, and categorical covariates to reduced models without the interaction terms.