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ORIGINAL ARTICLE

Associations of device-measured physical activity and sedentary time with quality of life and fatigue in newly diagnosed breast cancer patients: Baseline results from the AMBER cohort study

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Abstract

Background: This study examined associations of device-measured physical activity and sedentary time with quality of life (QOL) and fatigue in newly diagnosed breast cancer patients in the Alberta Moving Beyond Breast Cancer (AMBER) cohort study.

Methods: After diagnosis, 1409 participants completed the SF-36 version 2 and the Fatigue Scale, wore an ActiGraph device on their right hip to measure physical activity, and an activPAL device on their thigh to measure sedentary time (sitting/lying) and steps. ActiGraph data was analyzed using a hybrid machine learning method (R Sojourn package, Soj3x) and activPAL data were analyzed using activPAL algorithms (PAL Software version 8). Quantile regression was used to examine cross-sectional associations of QOL and fatigue with steps, physical activity, and sedentary hours at the 25th, 50th, and 75th percentiles of the QOL and fatigue distributions.

Results: Total daily moderate and vigorous physical activity (MVPA) hours was positively associated with better physical QOL at the 25th ($\beta = 2.14$, $p = <.001$), 50th ($\beta = 1.98$, $p = <.001$), and 75th percentiles ($\beta = 1.25$, $p = .003$); better mental QOL at the 25th ($\beta = 1.73$, $p = .05$) and 50th percentiles ($\beta = 1.07$, $p = .03$); and less fatigue at the 25th ($\beta = 4.44$, $p < .001$), 50th ($\beta = 3.08$, $p = <.001$), and 75th percentiles ($\beta = 1.51$, $p = <.001$). Similar patterns of associations were observed for daily steps. Total sedentary hours was associated with worse fatigue at the 25th ($\beta = -0.58$, $p = .05$), 50th ($\beta = -0.39$, $p = .06$), and 75th percentiles ($\beta = -0.24$, $p = .02$). Sedentary hours were not associated with physical or mental QOL.

Conclusions: MVPA and steps were associated with better physical and mental QOL and less fatigue in newly diagnosed breast cancer patients. Higher sedentary time was associated with greater fatigue symptoms.

KEYWORDS
accelerometers, breast cancer, fatigue, physical activity, quality of life, sedentary behavior

INTRODUCTION

In Canada, 28,600 women are expected to be diagnosed with breast cancer in 2022, and over 5000 women are expected to die from the disease.[1] In the United States, 287,850 women are expected to be diagnosed with breast cancer in 2022 and 43,250 are expected to die.[2] As breast cancer diagnosis and treatments have improved over time, patient-reported outcomes (PROs), such as quality of life (QOL) and fatigue, remain important outcomes in breast cancer survivorship studies.[3] Most research has explored PROs in the breast cancer context either during or after adjuvant treatments. Few studies have examined PROs before initiating adjuvant therapy or neoadjuvant systemic treatments. This phase in the cancer trajectory is associated with distinct psychosocial needs[4] and is characterized by a series of medical consultations to make often difficult treatment decisions based on the results of recent procedures (e.g., biopsies, imaging). Women often report psychosocial distress, including anxiety and fear regarding upcoming treatments.[4] Psychosocial distress can contribute to poor QOL after diagnosis and may be related to age (<60 years),[5] type of breast surgery (e.g., mastectomy versus breast-conserving surgery), anxiety, depression, and poor sleep quality.[6] QOL and fatigue profiles are poorest at the pretreatment time point and show improvement post adjuvant therapy.[5]

The influence of physical activity on PROs during and after treatments has been studied, and several reviews and meta-analyses have summarized the research examining physical activity and PROs, including QOL and fatigue.[7,8] Less is known about the influence of physical activity and sedentary time on QOL and fatigue before the initiation of adjuvant or neoadjuvant therapies. Few breast cancer studies have reported on physical activity soon after diagnosis or surgery. These studies are limited by small sample sizes[9] and self-reported physical activity.[10] More studies are now using accelerometers and inclinometers to monitor physical activity and other daily movement behaviors among cancer survivors.[11] Accelerometry provides precise, detailed, and reliable measurement across the movement continuum (e.g., light, moderate, vigorous-intensity, sedentary time) and allows the analysis of activity accumulation patterns (e.g., physical activity bouts, activity durations). Accurately measuring the activity patterns of breast cancer patients may provide a better understanding of how these exposures are related to health outcomes such as QOL and fatigue.

To our knowledge, the Alberta Moving Beyond Breast Cancer (AMBER) study is the first and only prospective cohort study designed to examine the role of physical activity, sedentary behavior, and health-related fitness in breast cancer survivorship from the time of diagnosis and into survivorship[12,13] Here, we present baseline data pertaining to physical activity and PROs, including QOL and fatigue in newly diagnosed breast cancer survivors. Data were collected within 90 days of after surgery. The objectives of this study were to (1) examine associations of accelerometer-assessed steps, light, and moderate-to-vigorous intensity physical activity (MVPA) with QOL and fatigue, and (2) examine associations of sitting and lying time during the waking day with QOL and fatigue, in newly diagnosed breast cancer patients. We hypothesized that physical activity (i.e., steps, light, and MVPA) would be associated with better QOL and fatigue, and sedentary time would be associated with poorer QOL and fatigue.

MATERIALS AND METHODS

Study design and participant recruitment

We have previously described the AMBER study design and methods,[12] as well as a baseline description of the full cohort.[13] We recruited participants between July 2012 and July 2019. Women living in Edmonton or Calgary, Alberta, Canada with newly diagnosed breast cancer were eligible if they had histologically confirmed stage I (≥T1c) to stage IIIc breast cancer, were 18–80 years old, were able to complete questionnaires in English, and were not pregnant at the time of recruitment. In Calgary, we identified potential participants through the Alberta Cancer Research Biobank, who approached all breast cancer patients at the time of diagnosis and requested a blood sample for the biobank, and obtained their agreement to be contacted for research studies. These women were contacted for the AMBER cohort study once their clinical and pathology results were available to confirm eligibility. In Edmonton, eligible participants were identified through the Cross Cancer Institute's New Patient Breast Cancer clinics and approached by their treating oncologist at their first visit. Those who expressed interest in AMBER were then further screened for eligibility. In both centers, AMBER recruiters explained the study to the patient. They provided potential participants with a letter and information brochure and followed up via telephone with eligible participants to confirm their interest in the study. We obtained ethics approval through the Health Research Ethics Board of Alberta: Cancer Committee (HREBA.CC-17-0576), and each participant completed a signed consent form.

Timing of assessments and measurements

Participants completed baseline assessments before neoadjuvant therapy or within 90 days after surgery and before adjuvant therapy. To include those who may have started adjuvant treatment soon after surgery, participants were allowed into the cohort if they had completed up to two cycles of chemotherapy or 10 fractions of radiation therapy. In a subset of women who received neoadjuvant treatment, the goal was to complete baseline assessments before initiating adjuvant chemotherapy but always before the third cycle of chemotherapy.

The Baseline Health Questionnaire included participants' sociodemographic characteristics such as age, marital status, ethnicity, education, income, and employment. The questionnaire also assessed patients' menstrual, reproductive and medical history, exogenous hormone and medication use history, family history of cancer, lifetime smoking and alcohol use histories, and comorbidities.

Clinical information about the patient's cancer diagnosis was extracted from medical charts by a trained study staff member. Data extracted included date of diagnosis, tumor stage, grade, histology, surgery type, and treatment(s) received (and dates).

Quality of life was measured using the SF-36 Version 2 (SF-36v2).[14,15] The SF-36v2 is a 36-item generic measure of health status that has been used extensively in both healthy and clinical populations. The measure yields eight health domain scales (i.e., physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health, and self-evaluated transition) that are aggregated to form two distinct component summary measures; physical component summary (PCS) and mental component summary (MCS). These scores represent a summary of the individual's physical and mental health status. In this article, we present the PCS and MCS data. Low PCS scores suggest limitations in physical functioning and poor general health, whereas low MCS scores suggest frequent psychological distress due to emotional problems and poor general health. Based on the original SF-36, Version 2 is a revised measurement tool that has improved item wording and response choice categories. All health domain scales and component summaries are scored using a *T*-score metric. Scoring the SF-36v2 involves the application of proprietary algorithms (QualityMetric, Lincoln, Rhode Island).

Fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F).[16] The FACIT-F includes 13 items, such as "I feel fatigued" and "I feel weak all over." Items are scored on a range from 0 to 52, with higher scores indicating less fatigue. A 3.0-point change on the FACIT-F is considered a clinically important difference,[17] defined as the smallest benefit that is of value to patients.[18]

Physical activity was assessed using the waist-worn ActiGraph GT3X+ (ActiGraph, LLC, Pensacola, Florida). The ActiGraph is a small, lightweight device that records acceleration using a tri-axial accelerometer. Participants wore the monitor on their right hip attached by an elastic belt during all waking hours for 7 consecutive days. Light, moderate, and vigorous-intensity physical activity time were estimated using a hybrid machine learning technique that combined a decision tree and an artificial neural network (R Sojourn package version 1.1.0, Soj3x).[19] We elected to employ the more advanced Soj3x prediction method because it incorporates a broad range of 30 common daily activities in the neural network to predict activity behaviors and their intensity levels, avoiding use of cut-point based methods typically calibrated only to two types of behavior (walking and running) that can substantially underestimate MVPA.[20] This method has also been cross-validated in free-living studies using direct observation[19] and doubly labeled water.[21]

Sedentary time and steps were measured using the thigh-worn activPAL device (PAL Technologies, Glasgow, Scotland). Participants were instructed to adhere the activPAL device to the front-midline portion of the thigh with stretch tape that was provided. Participants enrolling in the study from 2013 to 2017 wore the activPAL during waking hours only for 7 days. However, participants enrolling in the study after 2017 were instructed to wear the device continuously (i.e., for 24 hours per day) for 7 days. Sedentary time (sitting/lying) and steps were calculated using activPAL algorithms (PAL Software version 8). We used the VANE algorithm from the PAL software suite. Data from four participants was excluded due to <10 hours of data for both ActiGraph and activPAL. Previous work has suggested the activPAL yields more accurate step counts compared to the ActiGraph.[22]

Statistical analysis

Descriptive statistics were used to examine demographic, clinical, and behavioral characteristics of the sample. Analyses included preliminary evaluations of the relevant data, including checks for sparsity, distributions, and missingness. We handled missing data on covariates via multivariate imputations through chained equations, which includes all correlated covariates in regression models to avoid reducing the sample size.[23,24] We used quantile regression to examine associations of QOL and fatigue with MVPA, light intensity activity, steps per day, and sedentary time at the 25th, 50th, and 75th percentiles of the dependent variables (i.e., QOL and fatigue). Quantile regression analyzes the data for the entire sample and then provides three different associations across the distribution of data; the 25th, 50th, and 75th percentiles. Quantile regression creates conditional medians of the dependent variables at the identified percentiles. Quantile regression coefficients are interpreted similarly to those of linear regression coefficients, except that a quantile regression coefficient indicates the change in the value at the modeled percentile, not the mean, of the dependent variable.[25] Because the population is not segmented into smaller sample sizes (e.g., quartiles), increased power is gained to better detect any statistically significant differences. All models were adjusted for relevant covariates considered to be potential confounders (based on prior knowledge as well as associations with the dependent variables) with respect to the dependent variables including physical composite score (i.e., age, study location, education, comorbidity, smoking, cancer stage, surgery, total percent body fat, and total caloric intake), mental composite score (i.e., age, study location, smoking, comorbidity, number of first-degree relatives with a breast cancer history, cancer stage, and waist/hip ratio), and fatigue (i.e., age, study location, smoking, comorbidity, cancer stage, waist/hip ratio). Steps per day were analyzed in 1000 steps/day units to provide more meaningful (and interpretable) beta weights. An α of 0.05 was used as a threshold for determining statistical significance. All models were generated using STATA (version 16) (StataCorp, College Station, Texas).

RESULTS

The flow of participants through the study has been presented in detail elsewhere.[13] To summarize, we screened 14,680 newly diagnosed breast cancer patients for eligibility, and 11,007 were ineligible. Of the 1528 recruited into the cohort study, we assessed 884 patients in Calgary and 644 in Edmonton. For this analysis, 1422 participants (93%) had complete QOL, fatigue, and either of ActiGraph and activPAL data. Of those participants, 1409 had complete ActiGraph data and 1396 had complete activPAL data. We collected QOL and fatigue assessments, and accelerometer assessments 55 and 50 days after surgery (median), respectively. Of the sample, 117 (7.7%) patients received neoadjuvant treatment. For participants scheduled to receive chemotherapy, 20% started treatment before their baseline accelerometer assessment. For participants scheduled to receive radiation, 6.6% started radiation before their baseline accelerometer assessment. Table 1 contains descriptive information for sociodemographic and clinical variables. The mean age of this sample was 55.5 years of age (SD = 10.7). Most were Caucasian (87.6%) and had an average body mass index of 27.5 (SD = 5.6). Most participants were diagnosed with stage II or III (55%) breast cancer and 40.9% had a mastectomy.

Descriptive information about steps, physical activity, sedentary time, QOL, and fatigue measures are in Table 2. Participants wore the ActiGraph for an average of 5.5 valid days, for 14 hours each day. Participants wore the activPAL for an average of 5.9 valid days, for 14.2 hours each day. Participants reported a mean PCS of 49.3 (SD = 7.5), MCS of 47.8 (SD = 10.1), and Fatigue Scale score of 39.2 (SD = 9.9).

Steps

Table 3 contains all associations between activity exposures and QOL and fatigue. Participants averaged 7384 steps per day (SD = 3114). Daily average steps (in units of 1000 steps) were positively associated with better physical health at the 25th percentile (β = 0.43, p = <.001), 50th percentile (β = 0.50, p = <.001), and 75th percentile (β = 0.40, $p < .01$). Daily average steps were positively associated with mental health at the 25th percentile (β = 0.34, $p < .05$), 50th percentile (β = 0.27, $p < .05$), and 75th percentile (β = 0.23, $p < .05$). Daily average steps were also positively associated with better fatigue scores at the 25th percentile (β = 0.93, $p < .001$), 50th percentile (β = 0.79, p = <.001), and 75th percentile (β = 0.44, p = <.001). Adjusted and unadjusted models did not differ.

Light intensity physical activity

Participant were engaged in light intensity activity for 4.4 hours per day (SD = 1.2). Daily light intensity activity hours were positively associated with physical health at the 25th percentile (β = 0.60, $p < .01$) and 50th percentile (β = 0.53, $p < .01$), but not at the 75th percentile (β = 0.13, $p > .05$). Light intensity activity hours were positively associated with mental health at the 25th percentile (β = 0.81, $p < .05$), 50th percentile (β = 0.69, $p < .01$), and 75th percentile (β = 0.44, $p < .01$). Light intensity activity hours were positively associated with less fatigue at the 25th percentile (β = 1.75, $p < .001$), 50th percentile (β = 1.14, $p < .001$), and 75th percentile (β = 0.59, $p < .001$). Adjusted and unadjusted models did not differ.

MVPA

Participants engaged in MVPA for an average of 1.02 hours (SD = 0.6) per day. We found positive associations between total daily MVPA hours and better physical health at the 25th percentile (β = 2.14, p = <.001), 50th percentile (β = 1.98, p = <.001), and 75th percentile (β = 1.25, $p < .01$). MVPA hours were positively associated with mental health at the 25th percentile (β = 1.73, $p < .05$) and 50th percentile (β = 1.07, $p < .05$). Total MVPA hours were positively associated with better fatigue scores at the 25th percentile (β = 4.44, $p < .001$), 50th percentile (β = 3.08, p = <.001), and 75th percentile (β = 1.51, p = <.001). For MVPA accumulated in at least 10-minute bouts, associations with physical and mental health were stronger compared to those observed with total MVPA hours (Table 3). The magnitude of the associations between MVPA in 10-minute bouts and fatigue were notably stronger (25th percentile: β = 7.31, p = <.001; 50% percentile: β = 4.93, p = <.001; 75th percentile: β = 2.52, p = <.001). Adjusted and unadjusted models did not differ.

Sedentary time

On average, participants spent 8.9 hours per day (SD = 1.6) either sitting or lying down/reclining during waking hours. Total sedentary hours were not associated with either physical or mental health component summary scores. Total sedentary hours were associated with poorer fatigue scores at the 25th percentile (β = −0.58, p = .05), 50th percentile (β = −0.39, p = .06), and 75th percentile (β = −0.24, p = .02). Adjusted and unadjusted models did not differ.

Sensitivity analysis

We conducted a sensitivity analysis excluding those participants who had already started treatment before their baseline accelerometer assessment (n = 378) and found the associations between accelerometer variables and the physical health and fatigue outcomes were

TABLE 1 Sociodemographic and clinical characteristics of the AMBER cohort participants at baseline, 2012–2019 (*N* = 1422)

Characteristic	No.	%	Mean ± SD
Demographic			
Age at diagnosis, year			55.5 ± 10.7
Study location			
Edmonton	619	43.5	
Calgary	803	56.5	
Marital status			
Married or common-law	1065	74.9	
Widowed/separated/divorced	257	18.1	
Single/never married	100	7	
Ethnicity			
Caucasian	1246	87.6	
Asian	97	6.8	
Indian/South Asian	31	2.2	
Black	9	0.6	
Latino/Hispanic	18	1.3	
First Nations/Indigenous/Metis	13	0.9	
Other	8	0.6	
Education			
High school or below	316	22.2	
College	458	32.2	
University	373	26.2	
Graduate school	275	19.3	
Annual family income, $			
<50,000	227	16	
50,000–100,000	454	31.9	
100,000–150,000	335	23.6	
>150,000	406	28.6	
Employment status			
Works <35 hours/week	950	66.8	
Works ≥35 hours/week	472	33.2	
Clinical			
Body mass index (kg/m^2)			27.5 ± 5.6
Waist circumference (cm)			92.8 ± 13.4
Waist-to-hip ratio (cm)			0.9 ± 0.1
% body fat			43 ± 7.2
Total caloric intake (kcal/day)			1716 ± 745
No. of first-degree relative breast cancer family history			0.3 ± 0.6
Stage			
I	641	45.1	
II	657	46.2	
III	124	8.7	

(Continues)

TABLE 1 (Continued)

Characteristic	No.	%	Mean ± SD
Histology			
Ductal carcinoma	1203	84.6	
Invasive ductal and lobular carcinoma mixed	56	3.9	
Invasive lobular carcinoma	150	10.6	
Other	13	0.9	
Mastectomy			
Yes	581	40.9	
No	841	59.1	
Received neoadjuvant therapy	117	7.7	
Comorbidity score (0–8)			0.9 ± 1.0
Smoking			
Never smoker	820	57.7	
Past smoker	511	35.9	
Occasional smoker	11	0.8	
Current smoker	80	5.6	

Note: Data are presented as the mean (SD) for continuous variables and frequency (percentage) for categorical variables.
Abbreviations: AMBER, Alberta Moving Beyond Breast Cancer; SD, standard deviation.

similar to the full sample analysis (presented above). In the mental health sensitivity analysis, four associations that were statistically significant in the full sample analysis were no longer significant (i.e., MVPA at the 50th percentile, light activity at the 25th percentile, and steps at the 25th and 75th percentile).

We also created an interaction term (i.e., MVPA * sedentary time) to determine if there were joint associations of physical activity and sedentary time. We ran models for physical and mental health, and fatigue, and found there were no significant interactions between MVPA and sedentary time for the three dependent variables (all p values > .30).

DISCUSSION

In our sample, higher MVPA was significantly associated with better physical and mental health, and lower fatigue across all quantiles. Several reviews have confirmed the positive influence MVPA has on multiple QOL outcomes[26] across the breast cancer trajectory. Unstandardized beta weights (Table 3) from our models indicated that for every 1-hour increase in MVPA per day, physical and mental composite scores may improve by approximately two points for participants in the 25th percentile of the sample and approximately 1-point in the highest percentile. The improvement in physical health meets the 2-point threshold for determining a clinically important difference on the physical composite score, but not the three-point threshold for the mental composite score.[15] For fatigue, a 1-hour increase in total MVPA per day was associated with a three-to-four-point improvement in fatigue at the 25th and 50th percentiles of our sample. The steps analyses suggested an increase in 1000 steps was associated with a 1-point improvement in fatigue at the 25th percentile.

We also explored MVPA accumulated in at least 10-minute bouts. MVPA in 10-minute bouts is considered more intentional movement and synonymous with planned and structured physical activity. Recent evidence suggests health benefits are associated with MVPA regardless of how MVPA is accumulated,[27,28] however, our models suggested expected QOL and fatigue improvements doubled when MVPA in 10-minute bouts increased by 1 hour per day. For physical health, the most substantial benefit was found for participants in the lowest percentile of physical health scores. For fatigue, a 1-hour increase in MVPA-10 per day was associated with improvements of 7.3 (25th percentile), 4.9 (50th percentile), and 2.5 (75th percentile) points. These improvements in fatigue met and exceeded the established three-point threshold for determining a minimal clinically important difference[17]; defined as the smallest benefit that is of value to patients.[18] Research has suggested 3000 steps are equal to approximately 30 minutes of walking.[29] For patients at the lower end of the fatigue distribution (i.e., 25% percentile), taking an extra 3000 steps (or walking an extra 30 minutes per day) may lead to a clinically relevant improvement in fatigue (i.e., $\beta = 0.93$ per 1000 steps $\times$ 3). These findings are noteworthy given that fatigue is often reported as the most common and most debilitating symptom for breast cancer survivors. The most recent review of fatigue among breast cancer survivors identified 104 studies where 66% of survivors had reported some degree of fatigue, with up to 30% indicating their fatigue was problematic.[30]

TABLE 2 Descriptive statistics for device-measured physical activity, sedentary time, quality of life, and fatigue in AMBER cohort study participants, 2012–2019 (N = 1422)

Variable	Mean (SD)	Median	IQR
Physical activity			
ActiGraph valid days[a]	5.5 (1.4)	—	—
ActiGraph weartime (hours/day)	14 (1.2)	—	—
Light-intensity physical activity, hours/day	4.4 (1.2)	4.3	1.6
Moderate-intensity physical activity, hours/day	0.86 (0.48)	0.78	0.57
Vigorous-intensity physical activity, hours/day	0.16 (0.18)	0.10	0.19
MVPA			
Hours per day	1.02 (0.6)	0.92	0.71
Hours per day accumulated in 10-min bouts	0.30 (0.33)	0.19	0.40
Sedentary time			
activPAL valid days[b]	5.9 (1.5)	—	—
activPAL weartime	14.2 (1.2)	—	—
Daily steps	7384 (3114)	6983	3974
Sedentary hours/day	8.9 (1.6)	9.0	2.2
Health-related quality of life and fatigue			
Physical composite score	49.3 (7.5)	49.9	10.6
Mental composite score	47.8 (10.3)	50.0	14.0
Fatigue Scale (0–52)	39.2 (9.9)	42.0	14.0
SF-36v2 domains			
Physical function	83.7 (17.2)		
Role, physical	61.1 (27.3)		
Bodily pain	65.6 (23.5)		
General health	72.9 (17.4)		
Vitality	57.4 (19.7)		
Social functioning	70.9 (24.1)		
Role, emotional	77.9 (24.4)		
Mental health	71.87 (17.0)		

Abbreviations: AMBER, Alberta Moving Beyond Breast Cancer; IQR, interquartile range; MVPA, moderate and vigorous intensity physical activity; SD, standard deviation.

[a]ActiGraph: N = 1409.

[b]activPAL: N = 1396.

Few studies have examined the role of light intensity physical activity and sedentary behavior in the breast cancer context. We observed associations between light intensity activity and physical health. These associations were isolated to the lower half of the distribution of physical QOL and suggest light activity may be more important for those participants with poorer physical health. Previous work with breast cancer survivors who have completed treatment has suggested light intensity activity as assessed by devices is negatively associated with anxiety and physical function.[8,31] In our sample, total sedentary time was not associated with physical or mental health. Sedentary time was significantly associated with poorer fatigue scores across all quantiles. Other studies using device-based measures have reported significant associations between sedentary time and QOL. Similar to our study, Nurnazahiah et al.[32] used the activPAL3 device to assess sedentary time in 83 breast cancer survivors (73.5% were at least 5 years post-treatment) and found longer time spent sedentary was associated with reduced functioning score (EORTC QLQ-C30). Using the ActiGraph, Hartman et al.[33] reported total sedentary time was associated with poorer physical QOL but not mental QOL in breast cancer survivors who were, on average, 2 years post diagnosis. Among a sample of 199 breast cancer survivors at least 4 years post treatment, Dore et al.[34] found sedentary time measured by the ActiGraph GT3X was not associated with fatigue.

TABLE 3 Adjusted quantile regression estimates of MVPA, light-intensity physical activity, steps, and sedentary time at the 25th, 50th, and 75th HRQOL and fatigue percentiles at baseline in AMBER cohort study (N = 1422)

	Physical composite score, β (95% CI)[a]		
Activity/sedentary time	**p25**	**p50**	**p75**
MVPA	2.14 (1.39, 2.89)**	1.98 (1.41, 2.54)**	1.25 (0.43, 2.08)**
MVPA, 10-min bouts	3.72 (2.52, 4.91)**	3.12 (1.76, 4.48)**	2.48 (1.13, 3.82)**
Light-intensity physical activity	0.6 (0.22, 0.99)**	0.53 (0.15, 0.91)**	0.13 (−0.3, 0.57)
Steps[d]	0.43 (0.29, 0.57)**	0.50 (0.34, 0.66)**	0.40 (0.24, 0.57)**
Sedentary time	0.01 (−0.30, 0.32)	0.0 (−0.28, 0.28)	−0.12 (−0.43, 0.19)
	Mental composite score, β (95% CI)[b]		
	p25	**p50**	**p75**
MVPA	1.73 (0.03, 3.43)*	1.07 (0.09, 2.05)*	0.68 (−0.17, 1.54)
MVPA, 10-min bouts	−0.16 (−2.55, 2.23)	1.27 (−0.57, 3.1)	0.01 (−1.26, 1.28)
Light-intensity physical activity	0.81 (0.1, 1.52)*	0.69 (0.19, 1.18)**	0.44 (0.11, 0.77)**
Steps	0.34 (0.08, 0.59)*	0.27 (0.08, 0.46)*	0.23 (0.05, 0.41)*
Sedentary time	−0.07 (−0.55, 0.41)	0.07 (−0.34, 0.47)	−0.07 (−0.38, 0.25)
	Fatigue, β (95% CI)[c]		
	p25	**p50**	**p75**
MVPA	4.44 (3.04, 5.84)**	3.08 (2.19, 3.98)**	1.51 (0.97, 2.05)**
MVPA 10-min bouts	7.31 (4.69, 9.92)**	4.93 (3.22, 6.65)**	2.52 (1.41, 3.63)**
Light-intensity physical activity	1.75 (1.20, 2.31)**	1.14 (0.55, 1.74)**	0.59 (0.29, 0.90)**
Steps	0.93 (0.68, 1.19)**	0.79 (0.60, 0.98)**	0.44 (0.31, 0.57)**
Sedentary time	−0.58 (−1.16, 0.01)*	−0.39 (−0.79, 0.02)	−0.24 (−0.45, −0.04)*

Note: Activity models (N = 1409); sedentary time models (N = 1396).

Abbreviations: AMBER, Alberta Moving Beyond Breast Cancer; β, unstandardized regression coefficient, CI, confidence interval; HRQOL, health-related quality of life; MVPA, moderate and vigorous intensity physical activity.

[a]Physical composite model adjusted for age, education, comorbidity, location, smoking, cancer stage, surgery, total percent body fat, and total caloric intake.

[b]Mental composite model adjusted for age, location, smoking, comorbidity, number of first-degree relative breast cancer history, cancer stage, and waist/hip ratio.

[c]Fatigue model adjusted for age, location, smoking, comorbidity, cancer stage, waist/hip ratio.

[d]Steps per day were analyzed in 1000 steps/day units to provide more meaningful (and interpretable) beta weights.

*$p \le .05$, **$p \le .01$.

Several reviews have suggested sedentary time is associated with increased cancer mortality[35,36] but consistent evidence implicating sedentary time in adverse QOL and other PROs has not emerged. Inconsistent results across these studies may be due to key methodological differences. There is considerable variability across these studies which may be attributed to (1) small sample sizes, (2) longer-term breast cancer survivors, and (3) different devices used to measure sedentary time.

In our study, participants spent 1 h per day engaged in MVPA, and only 0.3 hours in 10-minute bouts of MVPA. Our sample was sedentary for almost 9 hours per day. Other studies have used accelerometers to determine MVPA and sedentary time prevalence of breast cancer survivors. In 134 postmenopausal breast cancer survivors, Hartman et al.[33] estimated participants engaged in 21 minutes of MVPA and 8.5 hours of sedentary time per day. In a similar sample of 259 longer-term breast cancer survivors, Boyle et al.[37] reported participants engaged in 32 minutes of MVPA and 8.2 hours of sedentary time. In another sample of 67 women receiving chemotherapy for breast cancer, participants averaged 23 minutes of MVPA per day.[31] Pinto et al.[38] reported longer-term breast cancer survivors engaged in 11 hours of sedentary time per day. Sedentary time estimates are consistent across these studies, and there are some explanations for the differences in MVPA estimates. All of these studies used the ActiGraph device instead of the activPAL device that is superior for estimating sedentary time.[39] The activPAL is considered the gold standard for the measurement of free-living sedentary time in chronic disease populations.[40] Different data processing methods may have also contributed to differences in MVPA estimates. Our study used the Soj3x processing approach[19] that differs from the approaches used in other studies. These studies also sampled breast cancer survivors at different time points of the cancer trajectory, including during treatment[31] and post treatment.[33]

Given that our sample was assessed a median of 50 days (IQR = 32) after diagnosis and 55 days (IQR = 23) after surgery, it may be difficult to compare our study sample to other samples. Aforementioned studies included samples of breast cancer survivors who were receiving chemotherapy, or were several years post treatment. Our study includes a homogeneous sample of newly diagnosed breast cancer patients at a particularly unique (and short) time point. Few studies have examined physical activity and PROs before initiating adjuvant therapy or neoadjuvant systemic treatments. This phase in the cancer trajectory is associated with distinct psychosocial needs[4] and women often report psychosocial distress, including anxiety and fear regarding upcoming treatments.[4] Many studies in the area of physical activity and breast cancer survivorship include longer term survivors (e.g., 5–10 years post treatment) whose QOL has improved and is similar to age-matched controls.[41] Our study is the first in the literature to examine device-measured physical activity and sedentary time in breast cancer patients soon after diagnosis and surgery and before the start of treatment (e.g., chemotherapy, radiation). The period of time between breast cancer diagnosis and the start of adjuvant therapy is an understudied time point. Given the lack of physical activity research studying patients during this time point (and the lack of device-based studies in breast cancer survivors), it is difficult to determine if associations of physical activity and sedentary time with QOL and fatigue are different during this time period. Future research should continue to examine how activity behaviors impact QOL and fatigue after surgery for breast cancer. Given the prospective design of the AMBER Study, our future research will aim to examine these questions.

There are several strengths of this study. Our study has the largest sample of breast cancer patients in the literature to date. ActiGraph and activPAL devices were used to assess physical activity and sedentary time and both provide valid and precise estimates of these daily measures. Another strength is the Soj3x processing approach we used to estimate activity and intensity. The Soj3x is more sophisticated when compared to cut-points as it uses neural network prediction from 30 different activities. A criticism of previous sedentary behavior research with cancer survivors is that most studies used the ActiGraph device. Using the activPAL device allows for a more precise examination of sedentary behavior, which by definition, involves the participant in either a sitting or lying position.[42] Additional strengths include the exclusion of lower stage (<T1c) breast cancer, and the recruitment of breast cancer patients soon after diagnosis and before the start of adjuvant therapy, compared to other samples that are on average several years post diagnosis and treatment.

The main limitation of this study is the cross-sectional design that limits the ability to determine causation. Another limitation to using accelerometers is the lack of information regarding the context within which physical activity and sedentary time are occurring. There is research suggesting physical activity domains (e.g., recreational, sports, commuting) are differently related with QOL in breast cancer survivors,[43] and other studies have considered different domains of sedentary behavior (e.g., watching television or videos) in examining QOL in cancer survivors.[44] We recognize that some participants completed baseline accelerometer assessments after they had already started treatment (n = 378). However, we conducted a sensitivity analysis excluding those participants who had already started treatment and found the associations observed in this sensitivity analyses remained similar to the full sample analyses. Finally, increasing MVPA minutes by 60 minutes per day may not be feasible, however, more realistic increases in MVPA (e.g., 15 minutes per day) may be associated with smaller improvements in QOL. Future research should examine the context of physical activity and sedentary time and associations with QOL and fatigue. Future research should also continue to examine daily activity patterns of activity and sedentary time across the breast cancer trajectory, and their associations with other clinically relevant PROs including depression and anxiety. The AMBER Study's prospective design will allow us to examine changes in activity, sedentary time, and PROs in the years after diagnosis and treatment (i.e., 1, 3, and 5 years).

In conclusion, we observed consistent and significant associations between light intensity activity, MVPA, and QOL and fatigue outcomes in this cohort of newly diagnosed breast cancer patients. For fatigue, associations were stronger when considering MVPA accrued in at least 10-minute bouts. Sedentary time was only significantly associated with fatigue and only among participants in the lower quantiles. These results may be used to inform clinical practice and policies about incorporating physical activity and reducing sedentary time as adjuvant therapy for newly diagnosed breast cancer patients starting treatment.

AUTHOR CONTRIBUTIONS

Jeff K. Vallance: Conceptualization, formal analysis, writing–original draft, and writing–review and editing. **Christine M. Friedenreich:** Conceptualization, methodology, funding acquisition, supervision, and writing–review and editing. **Qinggang Wang:** Data curation, formal analysis, and writing–review and editing. **Charles E. Matthews:** Methodology, software, formal analysis, and writing–review and editing. **Lin Yang:** Writing–review and editing. **Margaret L. McNeely:** Conceptualization, methodology, and writing–review and editing. **S. Nicole Culos-Reed:** Conceptualization, methodology, and writing–review and editing. **Gordon J. Bell:** Conceptualization, methodology, and writing–review and editing. **Andria R. Morielli:** Data curation, writing–review and editing. **Jessica McNeil:** Writing–review and editing. **Leanne Dickau:** Project administration, data curation, and writing–review and editing. **Diane Cook:** Project administration, data curation, and writing–review and editing. **Kerry S. Courneya:** Conceptualization, methodology, funding acquisition, supervision, and writing–review and editing.

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CONFLICTS OF INTEREST

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