

## Associations of objectively assessed physical activity and sedentary time with biomarkers of breast cancer risk in postmenopausal women: findings from NHANES (2003–2006)

Brigid M. Lynch · Christine M. Friedenreich ·  
Elisabeth A.H. Winkler · Geneviève N. Healy ·  
Jeff K. Vallance · Elizabeth G. Eakin · Neville Owen

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**Abstract** Physical activity reduces the risk of postmenopausal breast cancer through multiple inter-related biologic mechanisms; sedentary time may contribute additionally to this risk. We examined cross-sectional associations of objectively assessed physical activity and sedentary time with established biomarkers of breast cancer risk in a population-based sample of postmenopausal women. Accelerometer, anthropometric and laboratory data were available for 1,024 ( $n = 443$  fasting) postmenopausal women in the U.S. National Health and Nutrition Examination Survey 2003–2006. Associations of quartiles of the accelerometer variables (moderate- to vigorous-intensity activity, light-intensity activity and sedentary time per day; average length of active and sedentary bouts) with the continuous biomarkers were assessed using linear regression models. Following adjustment for potential confounders, including sedentary time, moderate- to vigorous-intensity activity had significant ( $P < 0.05$ ), inverse

associations with all biomarker outcomes (body mass index, waist circumference, C-reactive protein, fasting plasma glucose, fasting insulin and homeostasis model assessment of insulin resistance). Light-intensity activity and sedentary time were significantly associated in fully adjusted models with all biomarkers except fasting glucose. Active bout length was associated with a smaller waist circumference and lower C-reactive protein levels, while sedentary bout length was associated with a higher BMI. The associations of objectively assessed moderate- to vigorous-intensity activity with breast cancer biomarkers are consistent with the established beneficial effects of self-reported exercise on breast cancer risk. Our findings further suggest that light-intensity activity may have a protective effect, and that sedentary time may independently contribute to breast cancer risk.

**Keywords** Breast cancer · Physical activity · Sedentary behavior · Biological markers · Postmenopausal women

B. M. Lynch (✉) · C. M. Friedenreich  
Department of Population Health Research, Alberta Health Services, 1331 29th Street NW, Calgary T2N 4N2, Canada  
e-mail: brigid.lynch@albertahealthservices.ca

C. M. Friedenreich  
Departments of Oncology and Community Health Sciences,  
Faculty of Medicine, University of Calgary, Calgary, Canada

E. A.H.Winkler · G. N. Healy · E. G. Eakin · N. Owen  
Cancer Prevention Research Centre, School of Population Health, The University of Queensland, Brisbane, Australia

G. N. Healy · E. G. Eakin · N. Owen  
Baker IDI Heart and Diabetes Institute, Melbourne, Australia

J. K. Vallance  
Faculty of Health Disciplines, Athabasca University, Athabasca, Canada

### Background

There is consistent, epidemiological evidence linking moderate- to vigorous-intensity physical activity with reduced postmenopausal breast cancer risk [1–3]. Multiple, inter-related biologic mechanisms, including adiposity [4], metabolic and sex hormone changes [5–8], and chronic inflammation [9, 10], are hypothesized to underlie this association [1, 11].

Recently, it has been suggested that sedentary behaviors (prolonged sitting or reclining with the absence of whole-body movement [12]) may also contribute to cancer risk, independently of physical activity [13]. Sedentary behavior has been associated with adiposity [14–16] and with

metabolic [17–19] and inflammatory biomarkers [20] that may be implicated in breast cancer pathogenesis. However, few studies have directly examined sedentary behavior and breast cancer risk. Neither self-reported television viewing nor overall sitting time was associated with invasive or in situ breast cancer in the National Institutes of Health—AARP Diet and Health study [21]. Similarly, no statistically significant association between self-reported television viewing and breast cancer was found in a case–control study of 3,739 Indian women [22].

Epidemiological studies of physical activity, sedentary behavior, and breast cancer risk have been limited by the use of self-report measures. Self-report measures of physical activity generally assess moderate- to vigorous-intensity physical activity, thus capturing only a small fraction of an individual's total physical activity [1]. Light-intensity activities (which include routine domestic or occupational tasks [23]) are the predominant determinant of variability in adults' total daily energy expenditure [24], yet are difficult to measure reliably by questionnaire. Assessment of physical activity and sedentary behavior by devices such as accelerometers or heart rate monitors can objectively measure duration, intensity, and frequency, overcoming some of the biases inherent in self-report.

Incorporation of accelerometer measures in the 2003–2004 and 2005–2006 waves of the National Health and Nutrition Examination Survey (NHANES) enabled the objective assessment of physical activity and sedentary time. Here, we report associations of objectively assessed moderate- to vigorous-intensity activity, light-intensity activity, and sedentary time with mechanisms underlying postmenopausal breast cancer, namely adiposity, insulin resistance, and inflammation. We also examine how physical activity and sedentary time were accrued (e.g., over prolonged periods, with few interruptions; or over shorter periods, with more interruptions), and whether this pattern is associated with biomarkers of postmenopausal breast cancer risk.

## Methods

### Sample

NHANES included a representative sample of the civilian, non-institutionalized US population, selected with a complex multi-stage, stratified, clustered probability design, the methods of which are described in detail at: <http://www.cdc.gov/nchs/nhanes.htm> [25]. The starting sample was 5,215 adult women ( $\geq 20$  years) who had completed the examination component of NHANES 2003–2006. Based on information collected during the mobile examination centre interviews, 2,322 women were considered

postmenopausal. Women were categorized as postmenopausal if they: were aged 55 years or older; or, had undergone a bilateral oophorectomy; or, reported no menses during the past 12 months and had not had a hysterectomy; or, were aged 50 or older and had reported no menses during the past 12 month. Regardless of the above criteria, women were not considered postmenopausal if they reported menses or using oral contraceptives in the past 12 months.

Valid accelerometer data (four or more valid days of data including at least one weekend day) were available for 1,515 postmenopausal women. We excluded 264 women who had been told by a doctor that they had diabetes or who reported taking medication for diabetes, and 158 women who reported a previous diagnosis of cancer (excluding basal and squamous cell carcinomas). Finally, if participants were missing outcome data, they were also excluded from the study sample. Data from 1,031 postmenopausal women were available for analyses, with a sub-sample of 467 available for fasting analyses.

### Accelerometer data collection and variable creation

Participants who attended the NHANES mobile examination centers were asked to wear an accelerometer (Actigraph 7164; Actigraph, LLC, Fort Walton Beach, Florida) for seven consecutive days. This device detects and records the magnitude of acceleration or “intensity” of movement, storing data in memory according to a specified time interval or “epoch”. A 1-min epoch was used in NHANES. The accelerometers were programmed to begin recording activity information for successive epochs beginning at midnight on the day of the health examination. At the end of the data collection period, the accelerometers were returned by mail to the NHANES contractor, where data were downloaded.

An automated SAS program developed by the National Cancer Institute [26] was adapted and used to process the data. Intervals of at least 60 consecutive minutes of zero counts, with allowance for up to 2 min of observations of less than 50 counts per minute within the interval, were classed as non-wear time, and were deleted. The remaining accelerometer wear time was considered wear time. To be considered valid, days of data collection required at least 10 h of wear time, no excessive counts ( $>20,000$  counts per minute, cpm) and the accelerometer needed to have been returned in calibration.

For valid days, the average time per day spent at three different intensities was calculated, based on commonly used activity count ranges for moderate- to vigorous-intensity activity ( $\geq 1,952$  cpm) light-intensity activity (100–1,951 cpm) and sedentary time ( $<100$  cpm) [20, 27, 28]. To remove variation in these variables due to variation

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