Published in final edited form as:

Breast Cancer Res Treat. 2012 January ; 131(2): 637–643. doi:10.1007/s10549-011-1770-1.

Meeting the Physical Activity Guidelines and Survival After Breast Cancer: Findings from the After Breast Cancer Pooling Project

Jeannette M. Beasley¹, Marilyn L. Kwan², Wendy Y. Chen³, Erin K. Weltzien², Candyce H. Kroenke², Wei Lu⁴, Sarah J. Nechuta⁵, Lisa Cadmus-Bertram⁶, Ruth E. Patterson⁶, Barbara Sternfeld², Xiao-Ou Shu⁵, John P. Pierce⁶, and Bette J. Caan²

¹Fred Hutchinson Cancer Research Center, Seattle, WA 98109

²Kaiser Permanente Division of Research, Oakland, CA 94612

³Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115; Department of Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA

⁴Shanghai Center for Disease Control and Prevention, Shanghai, China

⁵Vanderbilt University, Nashville, TN 37203

⁶Cancer Prevention and Control Program, Moores UCSD Cancer Center, University of California, San Diego, San Diego, CA 92093

Abstract

The 2008 Physical Activity (PA) Guidelines recommend engaging in at least 2.5 hours (10 MET-hours/week) of moderate intensity PA per week (defined as 4 METs) to reduce risk of morbidity and mortality. This analysis was conducted to investigate whether this recommendation can be extended to breast cancer survivors. Data from four studies of breast cancer survivors measuring recreational PA from semi-quantitative questionnaires a median of 23 months post-diagnosis (interquartile range 18 to 32 months) were pooled in the After Breast Cancer Pooling Project (n=13,302). Delayed entry Cox proportional hazards models were applied in data analysis with adjustment for age, post-diagnosis body mass index, race/ethnicity, menopausal status, TNM stage, cancer treatment, and smoking history. Engaging in at least 10 MET-hours/week of PA was associated with a 27% reduction in all-cause mortality (n=1,468 events, Hazard Ratio (HR) = 0.73, 95% CI, 0.66–0.82) and a 25% reduction in breast cancer mortality (n=971 events, HR=0.75, 95% CI 0.65–0.85) compared to women who did not meet the PA Guidelines (< 10 MET-hours/week). Risk of breast cancer recurrence (n=1,421 events) was not associated with meeting the PA Guidelines (HR=0.96, 95% CI, 0.86–1.06). These data suggest that adhering to the PA Guidelines may be an important intervention target for reducing mortality among breast cancer survivors.

Keywords

physical activity guidelines; breast cancer survival; mortality; epidemiology

Corresponding Author: Jeannette M. Beasley, PhD, MPH, RD, Fred Hutchinson Cancer Research Center, 1000 Fairview Ave N M3-A410, Seattle, WA 98109, (206)667-7771 (phone); (206) 667-4142 (fax), jbeasley@whi.org.

Publisher's Disclaimer: This paper has not been presented or published elsewhere, and we have no disclaimers to report.

Conflict of Interest

The authors declare that they have no conflict of interest.

Introduction

Physical activity (PA), one of the major determinants of energy balance, is inversely associated with all-cause mortality[1]. The 2008 PA Guidelines from the United States Department of Health and Human Services recommend 2.5 hours per week of moderate to vigorous intensity activity to lower risk of all-cause mortality, coronary heart disease, stroke, hypertension, and type 2 diabetes, including older adults[1]. Intensity of PA is often expressed as metabolic equivalents (METs), and analytic guidelines for international PA questionnaires recommend defining moderate activity as 4 METs and vigorous activity as 8 METs [2,3]. These values are consistent with the PA Guidelines that define 3 to 5.9 METs as moderate and ≥ 6 METs as vigorous PA[1].

Among breast cancer survivors, the data are less definitive. A recent review reported that higher PA was associated with improved survival in four studies while no association was found in three studies, leading to an equivocal conclusion[4]. Meta-analyses combining estimates across published studies have been complicated by study design issues, including differences in eligibility criteria, timing of exposure measurement, method of PA assessment, and adjustment of covariates. Pooling individual level data provides the ability to apply similar analytic criteria across cohorts.

Therefore, we evaluated the association of PA with all-cause mortality, breast cancer-specific mortality, and breast cancer recurrence using data from over 13,000 breast cancer survivors in the After Breast Cancer Pooling Project (ABCPP). The ABCPP pooled data from four epidemiological studies recruited from multiple US sites and Shanghai, China[5]. PA was measured 18 to 48 months post-diagnosis. We compared outcomes for women in the pooled cohort who did versus those who did not meet the 2008 PA Guidelines[1]. We adjusted for similar covariates across studies and tested for effect modification by key characteristics (body mass index (BMI), menopausal status, and hormone receptor (ER/PR) status).

Methods

Study Population

Detailed information about each of the four prospective cohorts of breast cancer survivors[6–9] as well as the overall ABCPP is described elsewhere[5]. Briefly, the Life After Cancer Epidemiology (LACE) Study consists of information on 2,265 women diagnosed with invasive breast cancer between 1997 and 2000 and who were recruited primarily from the Kaiser Permanente Northern California Cancer Registry (83%) and the Utah Cancer Registry (12%) from 2000–2002. The Nurses' Health Study (NHS) contributed 8,075 breast cancer cases diagnosed between 1976 and 2004 from an ongoing prospective cohort study that enrolled 121,700 female registered U.S. nurses aged 30 to 55 years in 1976. The Shanghai Breast Cancer Survival Study (SBCSS) is a population-based, prospective cohort study of 4,886 Chinese women diagnosed with primary invasive breast cancer between 2002 and 2006 conducted in Shanghai, China. The Women's Healthy Eating and Living (WHEL) Study enrolled 3,088 breast cancer survivors diagnosed between 1991 and 2000 from seven institutions in the Southern and Western regions of the U.S.

Outcome Ascertainment

Outcomes of interest included: all-cause mortality, breast cancer-specific mortality, and breast cancer recurrence, defined as a local/regional recurrence, distant recurrence/metastasis or development of a new breast primary.

PA Ascertainment

This analysis included recreational PA only (Table 1). PA was assessed in the LACE Study with a questionnaire adapted from the Arizona Activity Frequency Questionnaire assessing recreational activity, which has been validated against doubly labeled water[10]. Therefore, LACE data were restricted to information related to recreational activities. Recreational PA was assessed in the NHS by querying level of participation in a range of commonly reported recreational activities[11]. This questionnaire was validated against PA diaries and was found to accurately rank participants for recreational PA[12]. In the SBCSS, PA information was collected using a validated PA questionnaire during in-person interviews[13]. Study participants were asked if they participated in recreational exercise regularly (at least twice a week) or not since diagnosis. Information on frequency and duration were obtained for all exercise activities. For the WHEL Study, the Women's Health Initiative (WHI) PA Questionnaire, which has been validated using accelerometry[14], assessed frequency, duration, and speed of walking outside the home and frequency and duration of participation in each of three intensity levels of exercise (mild, moderate, or strenuous).

This analysis focused on summary PA data between 18 and 48 months post-diagnosis that combined information on intensity in terms of metabolic equivalents (METs)[15] with frequency and duration. Meeting PA Guidelines was defined as engaging in ≥ 10 MET-hours/week, equivalent to 2.5 hours of moderate PA per week (4 METs) or to 1.25 hours of vigorous PA (8 METs) per week [3]. PA was also categorized into quintiles based on the pooled data set.

Covariates

Comparable data pooled across cohorts that may be related to both PA levels and survival after breast cancer include: age at diagnosis in years, TNM stage (I, II, III), joint ER/PR status (ER+/PR+, ER+/PR-, ER-/PR+, ER-/PR-), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Asian, Hispanic, Other), menopausal status (premenopausal, postmenopausal), smoking (never, past, current), and BMI (kg/m^2). To evaluate effect modification, BMI was categorized using the classifications of underweight ($<18.5 \text{ kg}/\text{m}^2$), normal weight (18.5 to $24.9 \text{ kg}/\text{m}^2$), overweight (25 to $29.9 \text{ kg}/\text{m}^2$), and obese ($\geq 30 \text{ kg}/\text{m}^2$).

Analysis

We excluded women with stage IV cancer at diagnosis, missing date of first survey/enrollment or lacking follow-up time, or missing PA exposure, resulting in 13,302 women in the final analytic sample. Levels of PA were summarized overall and by cohort. Frequency distributions were calculated for categorical variables and means with standard deviations (SD) for continuous variables according to whether women met the PA Guidelines (>10 MET-hours/week)[1]. Follow-up ended at date of death or date of recurrence, depending on the outcome, or date of last contact (i.e., date of last follow-up survey or date of last registry linkage, whichever was most recent).

The multivariate-adjusted analysis involved two initial stages, followed by an aggregated (pooled individual data) analysis. First, we conducted individual study analyses using delayed entry Cox proportional hazards models to estimate hazard ratios (HR) and 95% confidence intervals (CI), with time since diagnosis as the time scale. The entry date was the date of the baseline survey for LACE and WHEL, second follow-up survey at 18 months for SBCSS, or the date of the first survey after diagnosis for the NHS. Second, we conducted meta-analyses with the study-specific hazards ratios using inverse-variance weights in random-effects models[16]. The Q test statistic was used to test for heterogeneity in risk estimates across studies[17]. Due to no evidence of heterogeneity ($P>0.05$), individual data

from the four cohorts were combined, and a pooled analysis was conducted for the exposure-disease associations of interest using delayed entry Cox proportional hazards models stratified by study.

Covariates included age, post-diagnosis BMI, race/ethnicity, menopausal status, TNM stage, cancer treatment, and smoking. We evaluated possible effect modification in the associations between PA, recurrence, and survival by BMI category, menopausal status, and ER/PR status. Statistical significance of interaction terms was estimated by the Wald test, including a cross-product term of the exposure and the potential effect modifier in the delayed entry Cox models.

Sensitivity analyses were conducted including: 1) cases diagnosed after 1990 only; 2) women having a PA assessment within two years of diagnosis; 3) women who survived beyond two years of the post-diagnosis physical activity assessment; and 4) study participants with missing data. For this latter analysis, we included a missing data indicator category for each covariate. Recurrence analyses were repeated restricting the outcome to distant (versus local) recurrences.

Each contributing study received Institutional Review Board approval and informed consent was obtained for all study participants.

Results

Median PA was 10.0 MET-hours/week (interquartile range 2.3–21.3), the equivalent of engaging in 2.5 hours of moderate intensity PA per week (Table 2). Approximately half (range 48.3% in NHS to 53.2% in WHEL) of the women in each cohort met the PA Guidelines. Women who met the PA Guidelines (10 MET-hours/week) were younger, had earlier stage disease, were less likely to smoke, and were more likely to be in the “normal” weight category (BMI 18.5–24.9 kg/m²) (Table 3, $P < 0.05$ for all comparisons).

Engaging in at least 10 MET-hours/week of PA was associated with a 27% (HR = 0.73, 95% CI, 0.66–0.82) reduction in all-cause mortality ($n = 1,468$ events) compared to women who did not meet PA Guidelines (< 10 MET-hours/week) (Table 4). Higher levels of PA were associated with lower risk of death from any cause. A greater risk reduction was conferred with each increasing quintile of PA (10%, 23%, 29%, and 40% relative to the lowest quintile, Table 4). For breast cancer mortality, significant protective associations were observed for quintiles four (median 18.7 MET-hours/week) and five (median 36.5 MET-hours/week), but not at lower levels of activity. Being physically active was not associated with breast cancer recurrence, and no association remained after further restricting the analysis to women who had a distant recurrence. All associations with recurrence were null across the spectrum of PA levels, i.e. meeting the PA Guidelines or engaging in the highest category of PA.

There was no evidence for effect modification by BMI category, menopausal status or ER/PR status in the associations between physical activity and all outcomes (all-cause mortality, breast cancer mortality, breast cancer recurrence, Table 5), as defined by P for interaction < 0.05 . Each of the sensitivity analyses was consistent with the primary analyses.

Discussion

In this large pooling project of breast cancer survivors, we observed a reduction in death from any cause and death from breast cancer for women who met the PA Guidelines of 10 MET-hours/week 18 to 48 months post-diagnosis. We also found that engagement of PA at levels higher than those recommended conferred even further benefit.

These data are consistent with a growing body of evidence suggesting that participation in PA after breast cancer diagnosis is a modifiable behavior that can improve prognosis. Two recent meta-analyses reported PA assessed at varying time points (pre-diagnosis, at diagnosis, post-diagnosis) was associated with 29%¹⁹ and 41% (HR=0.59, 95% CI, 0.53 to 0.65)[18,19] lower mortality, summarized from 15,886 (n=9 studies)¹⁹ and 12,108 (n=6 studies)²⁰ breast cancer survivors, respectively. The smaller meta-analyses excluded one study due to not having a summary variable of total PA[20], a second study (WHEL) because it was a dietary intervention[21], and provided no rationale for excluding the third study[22]. The WHI also reported that PA of nine or more MET-hours/week after breast cancer diagnosis was associated with lower overall mortality (HR = 0.54, 95% CI 0.38–0.79) among 4,643 postmenopausal women[23].

Prior studies have also consistently demonstrated inverse associations between PA and mortality from breast cancer. The meta-analysis of six studies restricted to those reporting on mortality from breast cancer, reported that post-diagnosis PA reduced breast cancer death by 34% (HR = 0.66, 95% CI 0.57–0.77)[19], while the more inclusive meta-analysis of nine studies did not differentiate all cause from breast cancer-specific mortality[18]. Similarly, WHI reported PA of nine or more MET-hours/week after diagnosis was associated with lower breast cancer mortality (HR = 0.61, 95% CI, 0.35–0.99)[23].

Data are equivocal regarding the association between PA and breast cancer recurrence. There was no association between PA and breast cancer recurrence (HR=0.96, 95% CI, 0.86–1.06) in our pooled analysis of LACE, NHS, WHEL, and SBCSS. The meta-analysis including the LACE, NHS, and WHEL studies reported no association between PA and breast cancer recurrence[18], whereas the other meta-analysis that only included LACE and NHS[19] did report a reduced risk of recurrence with higher PA (HR=0.76, 95% CI, 0.66–0.87)[19]. Measurement error in the recurrence outcome likely explains the lack of a consistent signal.

The previous literature suggests that the mechanisms by which PA lowers risk of mortality in the general population might apply to breast cancer survivors[24]. Those mechanisms, summarized in the national PA Guidelines[1], include improved physical fitness (aerobic capacity, strength, and flexibility), and enhanced physical and cognitive function. Changes that result from PA reflect greater physiological capability and reserve for responding to the stresses of disease and aging and result in better cardiorespiratory, metabolic, hormonal, neurological, muscular, and cognitive outcomes and translate to lower overall risk of mortality[25].

Our observed protective association was evident in normal and overweight women, but no significant benefit of PA on survival among obese women was found. This finding is similar to those reported by other studies that differentiated BMI categories between overweight (25–29.9 kg/m²) and obese (≥30 kg/m²)[23,26]. In contrast, studies that combined overweight and obese into one category reported no differences in effect by BMI category, i.e. associations were similar to the normal weight category [27,11]. Possible explanations for this result include that we may not have had sufficient power to detect inverse associations in the obese subgroup, or differential misclassification in the exposure assessment by obesity status.

Strengths of this analysis include post-diagnosis PA assessment assessed at a similar time point across studies and adjustment for similar covariates in four prospective studies of breast cancer survivors. This adjustment minimized heterogeneity between studies that complicates interpretation of meta-analyses. Another major strength was improved power to

detect differences in the association between PA and health outcomes by key characteristics such as menopausal status, hormone receptor status, and BMI.

When considering these findings, limitations should be noted. We did not evaluate change in PA over time as these data were not available for all cohorts. Recent data from WHEL suggests that the usual pattern of PA is more predictive of better health outcomes than the trajectory of PA[28]. Underlying health status influences both the propensity to exercise and to die, but the inverse association between PA and mortality in our study was still observed in analyses restricted to women who survived at least two years beyond the PA assessment. Data on PA were missing for more than ten percent of the cohort, but analyses including missing values as a separate category were concordant with the complete case analyses. It is highly probable that levels of PA were over reported, as half of women met PA Guidelines. However, we were able to detect a dose-response in the association between amount of PA and survival, suggesting that the ranking of PA levels was conserved.

In conclusion, we observed a 27% reduction in risk of death from any cause among women who adhered to the PA Guidelines 18 to 48 months post-diagnosis, but there was no evidence that this reduction was associated with decreased risk of breast cancer recurrence. Studies are still needed to help disentangle the mechanisms by which PA may improve survival among breast cancer survivors. Nonetheless, PA appears to confer important physiological benefits to breast cancer survivors, which may ultimately improve and extend overall survival after a diagnosis of breast cancer[25]. Therefore, methods to promote PA among women after a breast cancer diagnosis should be pursued.

Acknowledgments

Joan Schwalbe contributed substantively to the data analysis. This study was supported by the National Cancer Institute (Grant number 3R01CA118229-03S1). The parent grants for each individual cohort included in the After Breast Cancer Pooling Project are: LACE (National Cancer Institute, R01 CA129059), NHS (P01 CA87969), SBCSS (Department of Defense, DAMD 17-02-1-0607 and National Cancer Institute, R01 CA118229), and WHEL (Susan G. Komen Foundation, #KG100988).

References

1. Physical Activity Guidelines Advisory Committee report, 2008. To the Secretary of Health and Human Services. Part A: executive summary. *Nutr Rev.* 2008; 67(2):114–120.
2. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ)— Short and Long Forms. 2005. <http://www.ipaq.ki.se/scoring.pdf>. Accessed September 15 2010
3. WHO Global Physical Activity Questionnaire (GPAQ) Analysis Guide. Department of Chronic Diseases and Health Promotion, World Health Organization. http://www.who.int/chp/steps/resources/GPAQ_Analysis_Guide.pdf. Accessed September 15 2010
4. Cheifetz O, Moore L, Brooks E, Barbaric M. Effects of Physical Activity on Cancer Survival: A Systematic Review. *Physiotherapy Canada.* 2010; 62(1):25–34. [PubMed: 21197176]
5. Nechuta SJ, Caan BJ, Chen WY, Flatt SW, Lu W, Patterson RE, Poole EM, Kwan ML, Chen Z, Weltzien E, Pierce JP, Shu XO. The After Breast Cancer Pooling Project: rationale, methodology, and breast cancer survivor characteristics. *Cancer causes & control.* 2011; CCC 22(9):1319–1331. [PubMed: 21710192]
6. Caan B, Sternfeld B, Gunderson E, Coates A, Quesenberry C, Slattery ML. Life After Cancer Epidemiology (LACE) Study: a cohort of early stage breast cancer survivors (United States). *Cancer Causes Control.* 2005; 16(5):545–556. [PubMed: 15986109]
7. Pierce JP, Faerber S, Wright FA, Rock CL, Newman V, Flatt SW, Kealey S, Jones VE, Caan BJ, Gold EB, Haan M, Hollenbach KA, Jones L, Marshall JR, Ritenbaugh C, Stefanick ML, Thomson C, Wasserman L, Natarajan L, Thomas RG, Gilpin EA. A randomized trial of the effect of a plant-

- based dietary pattern on additional breast cancer events and survival: the Women's Healthy Eating and Living (WHEL) Study. *Control Clin Trials*. 2002; 23(6):728–756. [PubMed: 12505249]
8. Colditz GA, Hankinson SE. The Nurses' Health Study: lifestyle and health among women. *Nat Rev Cancer*. 2005; 5(5):388–396. [PubMed: 15864280]
 9. Shu XO, Zheng Y, Cai H, Gu K, Chen Z, Zheng W, Lu W. Soy food intake and breast cancer survival. *JAMA*. 2009; 302(22):2437–2443. [PubMed: 19996398]
 10. Staten LK, Taren DL, Howell WH, Tobar M, Poehlman ET, Hill A, Reid PM, Ritenbaugh C. Validation of the Arizona Activity Frequency Questionnaire using doubly labeled water. *Med Sci Sports Exerc*. 2001; 33(11):1959–1967. [PubMed: 11689750]
 11. Holmes MD. Physical Activity and Survival After Breast Cancer Diagnosis. *JAMA: The Journal of the American Medical Association*. 2005; 293(20):2479–2486. [PubMed: 15914748]
 12. Wolf AM, Hunter DJ, Colditz GA, Manson JE, Stampfer MJ, Corsano KA, Rosner B, Kriska A, Willett WC. Reproducibility and validity of a self-administered physical activity questionnaire. *International journal of epidemiology*. 1994; 23(5):991–999. [PubMed: 7860180]
 13. Matthews CE, Shu XO, Yang G, Jin F, Ainsworth BE, Liu D, Gao YT, Zheng W. Reproducibility and validity of the Shanghai Women's Health Study physical activity questionnaire. *American Journal of Epidemiology*. 2003; 158(11):1114–1122. [PubMed: 14630608]
 14. Johnson-Kozlow M, Rock CL, Gilpin EA, Hollenbach KA, Pierce JP. Validation of the WHI brief physical activity questionnaire among women diagnosed with breast cancer. *Am J Health Behav*. 2007; 31(2):193–202. [PubMed: 17269909]
 15. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. Compendium of physical activities: classification of energy costs of human physical activities. *Medicine and science in sports and exercise*. 1993; 25(1):71–80. [PubMed: 8292105]
 16. Smith-Warner SA. Methods for Pooling Results of Epidemiologic Studies: The Pooling Project of Prospective Studies of Diet and Cancer. *American Journal of Epidemiology*. 2006; 163(11):1053–1064. [PubMed: 16624970]
 17. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986; 7(3):177–188. [PubMed: 3802833]
 18. Patterson RE, Cadmus LA, Emond JA, Pierce JP. Physical activity, diet, adiposity and female breast cancer prognosis: a review of the epidemiologic literature. *Maturitas*. 2010; 66(1):5–15. [PubMed: 20097494]
 19. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. *Medical Oncology*. 2010
 20. Borugian MJ, Sheps SB, Kim-Sing C, Van Patten C, Potter JD, Dunn B, Gallagher RP, Hislop TG. Insulin, macronutrient intake, and physical activity: are potential indicators of insulin resistance associated with mortality from breast cancer? *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2004; 13(7):1163–1172.
 21. Pierce JP, Stefanick ML, Flatt SW, Natarajan L, Sternfeld B, Madlensky L, Al-Delaimy WK, Thomson CA, Kealey S, Hajek R, Parker BA, Newman VA, Caan B, Rock CL. Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. *Journal of Clinical Oncology : official journal of the American Society of Clinical Oncology*. 2007; 25(17):2345–2351. [PubMed: 17557947]
 22. Friedenreich CM, Gregory J, Kopciuk KA, Mackey JR, Courneya KS. Prospective cohort study of lifetime physical activity and breast cancer survival. *International journal of cancer Journal international du cancer*. 2009; 124(8):1954–1962. [PubMed: 19123472]
 23. Irwin ML, McTiernan A, Manson JE, Thomson CA, Sternfeld B, Stefanick ML, Wactawski-Wende J, Craft L, Lane D, Martin LW, Chlebowski R. Physical activity and survival in postmenopausal women with breast cancer: results from the women's health initiative. *Cancer Prev Res (Phila)*. 2011; 4(4):522–529. [PubMed: 21464032]
 24. McTiernan A, Irwin M, VonGruenigen V. Weight, Physical Activity, Diet, and Prognosis in Breast and Gynecologic Cancers. *Journal of Clinical Oncology*. 2010; 28(26):4074–4080. [PubMed: 20644095]

25. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, Pinto BM, Irwin ML, Wolin KY, Segal RJ, Lucia A, Schneider CM, von Gruenigen VE, Schwartz AL. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. *Medicine and science in sports and exercise*. 2010; 42(7):1409–1426. [PubMed: 20559064]
26. Sternfeld B, Weltzien E, Quesenberry CP, Castillo AL, Kwan M, Slattery ML, Caan BJ. Physical Activity and Risk of Recurrence and Mortality in Breast Cancer Survivors: Findings from the LACE Study. *Cancer Epidemiology Biomarkers & Prevention*. 2009; 18(1):87–95.
27. Holick CN, Newcomb PA, Trentham-Dietz A, Titus-Ernstoff L, Bersch AJ, Stampfer MJ, Baron JA, Egan KM, Willett WC. Physical activity and survival after diagnosis of invasive breast cancer. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology*. 2008; 17(2): 379–386.
28. Bertram LA, Stefanick ML, Saquib N, Natarajan L, Patterson RE, Bardwell W, Flatt SW, Newman VA, Rock CL, Thomson CA, Pierce JP. Physical activity, additional breast cancer events, and mortality among early-stage breast cancer survivors: findings from the WHEL Study. *Cancer causes & control*. 2011; CCC 22(3):427–435. [PubMed: 21184262]

Table 1

Description of Measures of Physical Activity (PA), After Breast Cancer Pooling Project

Study ^a	PA Measure	Description
LACE	Recreational PA (adapted from Arizona Activity Frequency Questionnaire)	Running, swimming, biking for exercise, stairmaster, aerobics, sit-ups, yoga, cross-country skiing, downhill skiing, hiking, walking for exercise, volleyball, tennis, soccer, baseball, golf, horseback riding, fishing, dancing, ballet
NHS	Recreational PA	Walking or hiking outdoors, jogging or running, bicycling, swimming, tennis, calisthenics, aerobics, squash or racquetball); In 1992, lower intensity exercise (yoga, stretching, and toning) and other vigorous activities (i.e. lawn mowing) were added to the questionnaire.
SBCSS	Recreational PA	Type and duration of any recreational physical activity
WHEL	Women's Health Initiative PA Questionnaire	Walking and duration/frequency of strenuous, moderate, mild exercise

^aLACE (Life After Cancer Epidemiology Study), NHS (Nurses' Health Study), (SBCSS (Shanghai Breast Cancer Survival Study), WHEL (Women's Healthy Eating and Living Study)

Table 2
Combined and Cohort-Specific Descriptive Measures of Physical Activity (PA), After Breast Cancer Pooling Project

	Combined	LACE	NHS	SBCSS	WHEL
Median PA (IQR^a), MET-hours/week	(n=13,302) 10.0 (2.3–21.3)	(n=1,634) 9.3 (1.7–21.8)	(n=4,598) 9.2 (2.9–21.5)	(n=4,397) 10.1 (0–20.6)	(n=2,673) 10.8 (3.3–22.0)
Meets PA Guidelines, n (%)	6673 (50.2)	795 (48.7)	2222 (48.3)	2233 (50.8)	1423 (53.2)
PA, MET-hours/week, median (IQR)					
Quintile 1	0 (0–0.2)	0 (0–0.4)	0.4 (0.2–0.8)	0 (0–0)	0 (0–0)
Quintile 2	3.7 (2.3–4.9)	3.7 (2.3–5.3)	3.3 (2.3–4.6)	3.9 (2.7–5.2)	3.8 (2.3–5.0)
Quintile 3	10.0 (8.0–11.9)	10.2 (8.3–12.3)	9.7 (7.9–11.5)	10.1 (8.3–12.0)	10.0 (8.0–12.5)
Quintile 4	18.7 (16.2–21.4)	18.0 (16.0–21.0)	18.2 (15.9–20.9)	19.0 (16.3–21.5)	18.9 (16.4–22.0)
Quintile 5	36.5 (29.7–48.0)	38.3 (30.0–54.0)	37.9 (30.9–53.1)	35.0 (28.9–45.5)	34.8 (28.7–43.9)

^aIQR=inter-quartile range

Table 3

Characteristics of Women by Adherence to Physical Activity (PA) Guidelines (10 MET-hours/week), After Breast Cancer Pooling Project

	PA ≥10 MET-hours/week (n=6,673)		PA <10 MET-hours/wk (n=6,629)	
	n	Column (%)	n	Column (%)
Age at diagnosis (years)				
< 55	3,355	50.3	3,261	49.2
≥ 55	3,318	49.7	3,368	50.8
Race/ethnicity				
Non-Hispanic White	3,999	59.9	3,930	59.3
Non-Hispanic Black	80	1.2	135	2.0
Asian	2,347	35.2	2,272	34.3
Hispanic	116	1.7	156	2.4
Other	130	2.0	135	2.0
Menopausal status				
Pre-menopausal	2,212	34.4	2,189	34.3
Post-menopausal	4,217	65.6	4,192	65.7
Smoking				
Never	4,337	65.1	4,193	63.3
Past	2,039	30.6	1,935	29.2
Current	287	4.3	496	7.5
Body mass index, kg/m ²				
<25	3,546	53.7	2,913	44.5
25.0–29.9	2,189	33.2	2,170	33.1
≥ 30	865	13.1	1,465	22.4
TNM Stage ^a				
I	3,045	47.1	2,922	45.7
II	2,637	40.7	2,595	40.5
III	789	12.2	886	13.8
ER/PR status				
ER+/PR+	3,807	60.6	3,724	60.2
ER-/PR+	311	4.9	297	4.8
ER+/PR-	932	14.8	814	13.2
ER-/PR-	1,236	19.7	1,352	21.9
Surgery				
None	7	0.1	12	0.2
Lumpectomy	2,143	32.3	1,929	29.4
Mastectomy	4,399	66.3	4,511	68.7
Other	90	1.3	118	1.8
Chemotherapy				
No	2,249	34.4	2,272	35.4

	PA ≥ 10 MET-hours/week (n=6,673)		PA <10 MET-hours/wk (n=6,629)	
	n	Column (%)	n	Column (%)
Yes	4,284	65.6	4,143	64.6
Radiotherapy				
No	3,391	51.1	3,489	53.2
Yes	3,240	48.9	3,073	46.8
Endocrine therapy				
No	2,222	34.0	2,343	36.5
Yes	4,320	66.0	4,077	63.5

^a AJCC 6th edition criteria

Table 4

Risk^a of breast cancer recurrence, breast cancer mortality, and all-cause mortality by meeting physical activity (PA) guidelines and quintiles of PA, After Breast Cancer Pooling Project

PA Quintile, HR (95% CI)	Recurrence, n=10, 685 (1,421 events)	Breast Cancer Mortality, n=11,282 ^b (971 events)	All-Cause Mortality, n=11,315 (1,468 events)
Meets PA Guidelines, HR (95% CI)	0.96 (0.86–1.06)	0.75 (0.65–0.85)	0.73 (0.66–0.82)
PA Quintile, HR (95% CI)			
Q2 vs. Q1	1.00 (0.84–1.18)	1.00 (0.83–1.21)	0.90 (0.77–1.04)
Q3 vs. Q1	1.07 (0.90–1.26)	0.87 (0.71–1.06)	0.77 (0.66–0.90)
Q4 vs. Q1	1.00 (0.84–1.18)	0.74 (0.60–0.91)	0.71 (0.60–0.84)
Q5 vs. Q1	0.95 (0.80–1.14)	0.73 (0.59–0.91)	0.60 (0.51–0.72)
Test for Trend	0.60	0.0001	<0.0001

^aDelayed entry Cox models stratified by study and adjusted for age at diagnosis, race, menopausal status, TNM stage, hormone receptor status, treatment (chemotherapy/radiation/both), post-diagnosis body mass index, and smoking status

^bParticipants were not included in cause-specific death models if cause of death was unspecified (n=31).

Table 5

Risk^a of Breast Cancer Recurrence, Breast Cancer Mortality, and All-cause Mortality by Meeting (versus not meeting) Physical Activity Guidelines by BMI category, Menopausal Status, and Hormone Receptor Status, After Breast Cancer Pooling Project

	Recurrence	p ^b	Breast Cancer Mortality*	p ^b	All-Cause Mortality, HR	p ^b
Body Mass Index, kg/m²		0.82		0.75		0.21
<25	0.93 (0.81–1.07)		0.72 (0.61–0.86)		0.72 (0.62–0.83)	
25.0–29.9	0.98 (0.85–1.14)		0.78 (0.65–0.94)		0.69 (0.59–0.81)	
≥ 30	0.96 (0.77–1.19)		0.72 (0.61–0.86)		0.86 (0.70–1.06)	
Menopausal Status		0.61		0.28		0.16
Pre-menopausal	0.92 (0.77–1.10)		0.82 (0.66–1.02)		0.84 (0.68–1.03)	
Post-menopausal	0.98 (0.85–1.11)		0.71 (0.60–0.83)		0.70 (0.62–0.79)	
ER/PR Status		0.49		0.44		0.88
ER+/PR+	0.94 (0.82–1.07)		0.75 (0.63–0.89)		0.72 (0.63–0.83)	
ER-/PR+	0.72 (0.45–1.14)		0.74 (0.44–1.24)		0.72 (0.44–1.18)	
ER+/PR-	1.05 (0.80–1.37)		0.91 (0.44–1.24)		0.81 (0.62–1.06)	
ER-/PR-	1.03 (0.81–1.31)		0.64 (0.49–0.84)		0.72 (0.57–0.91)	

^a Delayed entry Cox models stratified by study and adjusted for age at diagnosis, race, menopausal status, TNM stage, hormone receptor status, treatment (chemo/radiation/both), post-diagnosis BMI, and smoking status

^b p for interaction evaluated by the Wald test, estimated by including a cross-product of the exposure and the stratification variable in delayed entry Cox models