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Pain in long-term breast cancer survivors: The role of body mass index, physical activity, and sedentary behavior

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Abstract

Although pain is common among post-treatment breast cancer survivors, studies that are longitudinal, identify a case definition of clinically meaningful pain, or examine factors contributing to pain in survivors are limited. This study describes longitudinal patterns of pain in long-term breast cancer survivors, evaluating associations of body mass index [BMI], physical activity, sedentary behavior with mean pain severity and above-average pain. Women newly diagnosed with stages 0–IIIA breast cancer (N=1183) were assessed, on average, 6 months (demographic/clinical characteristics), 30 months (demographics), 40 months (demographics, pain), 5 years (BMI, physical activity, and sedentary behavior) and 10 years (demographics, pain, BMI, physical activity, and sedentary behavior) post-diagnosis. This analysis includes survivors who completed pain assessments 40 months post-diagnosis (N=801), 10 years post-diagnosis (N=563), or both (N=522). Above-average pain was defined by SF-36 bodily pain scores 1/2 standard deviation worse than age-specific population norms. We used multiple regression models to test unique associations of BMI, physical activity, and sedentary behavior with pain adjusting for demographic and clinical factors. The proportion of survivors reporting above-average pain was higher at 10 years than at 40 months (32.3% vs. 27.8%, $p<0.05$). Approximately one-quarter of survivors reported improved pain, while 9.0% maintained above-average pain and 33.1% reported worsened pain. Cross-sectionally at 10 years, overweight and obese survivors reported higher pain than normal-weight survivors and women meeting physical activity guidelines were less likely to report above-average pain than survivors not meeting these guidelines ($p<0.05$). Longitudinally, weight gain ($>5\%$) was positively associated, while meeting physical activity

guidelines was inversely associated, with above-average pain (OR, 95% CI= 1.76, 1.03–3.01 and 0.40 (0.20–0.84, respectively) ($p<0.05$). Weight gain and lack of physical activity place breast cancer survivors at risk for pain long after treatment ends. Weight control and exercise interventions should be tested for effects on long-term pain in these women.

Keywords

cancer; pain; body mass index; physical activity; sedentary behavior

Background

Pain is common among post-treatment breast cancer survivors, even many years post-treatment.[7, 12, 17, 19, 25, 36, 57] Prevalence estimates vary widely: 9–72% of breast cancer survivors report pain[14] and 12–29% of those 5 years post-diagnosis report pain attributed to cancer.[12, 55] Pain is associated with numerous negative sequelae in cancer survivors, [16, 19, 25, 31] Increased knowledge about pain and strategies for prevention or mitigation among survivors, given their risk for multiple comorbid conditions, physical and psychosocial complaints, and functional limitations[59, 63], can contribute to optimal functioning after breast cancer.

The course of pain over time and factors affecting pain in specific cancer populations are not well understood.[41] Longitudinal studies are few in number and focus on average pain severity without defining the vulnerable subgroup of survivors who experience pain. Research suggests that pain resolves for only certain survivors[36, 57]. [36] More research is needed that examines the trajectories of pain over time for individuals. Further, a case definition for clinically meaningful pain would facilitate research synthesis.[2]

Documentation of modifiable factors associated with pain in post-treatment survivors may identify survivors at risk for poor outcomes and interventions to mitigate pain. Body mass index (BMI)[8, 30, 46, 53, 58, 62, 69] and physical activity[29, 46, 56] have been associated with pain in the general population. Furthermore, physical activity[1, 4, 6, 20, 32, 42, 52, 60] and, to a lesser extent, BMI[47, 52] have been associated with pain in survivors specifically. Research examining associations between sedentary behavior and pain have been mixed,[10] but few studies define sedentary behavior as the amount of waking time spent sitting/reclining rather than the absence of physical activity. A better understanding of the unique effects of BMI, physical activity, and sedentary behavior on pain in long-term survivors is needed.

This study examined the course and predictors of pain in long-term breast cancer survivors using a multicenter, multiethnic, prospective cohort. Specifically, we aimed to (1) describe pain at 40 months and 10 years post-diagnosis by examining mean pain scores, identifying survivors with above-average pain (used as a proxy for a case definition of pain), and comparing observed pain scores to population norms; (2) identify patterns of change in pain over time; and (3) test associations between BMI, physical activity, sedentary behavior with pain in three different ways: (a) testing associations cross-sectionally at 10-years post-diagnosis, (b) testing associations between changes in BMI, physical activity, and sedentary

behavior (5 to 10 years post-diagnosis) and pain at 10 years post-diagnosis, and (c) testing associations between changes in BMI, physical activity, and sedentary behavior with changes in pain (40 months to 10 years post-diagnosis). We hypothesized that BMI and sedentary behavior would be positively associated with pain, and that physical activity would be inversely associated with pain, cross-sectionally and longitudinally.

Methods

Study Design

Participants in this study were women enrolled in the Health, Eating, Activity, and Lifestyle (HEAL) Study, a population-based, multicenter, multiethnic, prospective study of women newly diagnosed with stages 0–IIIA breast cancer. HEAL participants are being followed to determine the impact of weight, physical activity, diet, hormones, and other exposures on breast cancer prognosis.[43] Written or documented verbal informed consent was obtained from each participant for all assessments. All study protocols were approved by the Institutional Review Board of each participating center, in accordance with an assurance filed with and approved by the United States Department of Health and Human Services.

Eligibility, recruitment, and data collection

Eligibility, recruitment, and retention of HEAL participants are described in detail elsewhere.[43] Briefly, patients diagnosed with their first primary breast cancer (N=1,183) were recruited from three Surveillance Epidemiology and End Results (SEER) registries in New Mexico, Western Washington, and Los Angeles County, California. In New Mexico, we recruited 615 women aged 18 years or older diagnosed with in situ to regional breast cancer between 1996 and 1999, living in Bernalillo, Santa Fe, Sandoval, Valencia, or Taos counties. In Western Washington, we recruited 202 women aged 40–64 years diagnosed with in situ to regional breast cancer between 1997 and 1998, living in King, Pierce, or Snohomish counties. The age range for the Washington patients was restricted to avoid overlap with eligibility requirements of other accruing studies. In Los Angeles County, we recruited 366 black women diagnosed with in situ to regional breast cancer between May 1995 and May 1998 who had participated in the Los Angeles portion of the Women's Contraceptive and Reproductive Experiences (CARE) Study[44, 51] or who had participated in a parallel case-control study of in situ breast cancer.[37–38] These two studies were limited to women ages 35–64 years.

Data were drawn from 5 assessments (Figure 1): (1) baseline/6 months post-diagnosis (in-person interview or self-administered questionnaire; stable demographics and clinical variables); (2) 30 months post-diagnosis (in-person interview or self-administered questionnaire; time-dependent demographics); (3) 40 months post-diagnosis (telephone or self-administered questionnaire; time-dependent demographics, pain); (4) 5 years post-diagnosis (telephone or self-administered questionnaire; BMI, physical activity, sedentary behavior); and (5) 10 years post-diagnosis (telephone or self-administered questionnaire; pain, BMI, physical activity, sedentary behavior).

Measures

We used the Bodily Pain subscale of the Medical Outcomes Study short form 36 (SF-36), [22, 68] which is commonly used to measure quality of life (QOL).[24] Considerable psychometric analyses have indicated high internal consistency for the pain subscale.[68] Pain scores are standardized on a T-score metric (overall U.S. general population mean=50, standard deviation=10); higher scores indicate less pain. Because pain interference increases with age,[64] we utilized age-stratified population norms.[68] In the absence of a case definition for pain in cancer survivors, we defined survivors with above-average pain as those with pain scores ≥ 1 standard deviation below the age-specific population mean. One-half standard deviation is considered the minimally important difference across QOL studies.[49] Based on a normal distribution, 30.9% of survivors would be expected to meet criteria for above-average pain.

Change in pain (40-month to the 10-year assessment) was defined by two dimensions of pain: severity (whether pain was considered low versus above-average) and magnitude of change (≥ 1 standard deviation versus no change). Four distinct longitudinal patterns emerged: (1) maintained low pain (no pain change, low pain at both times), (2) pain improved (change with increased pain scores), (3) pain worsened (change with decreased pain scores), and (4) maintained above-average pain (no pain change, above-average pain at both times). Survivors with pain scores that fluctuated around the cut-point for above-average pain with no change in pain were not classified into a pain change group.

Body mass index (BMI, kg/m²) was computed from clinic-measured height (baseline) and self-reported weight (5-year and 10-year follow-up). Self-reported height was substituted for 144 participants missing clinic-measured height, including all participants from Los Angeles County for whom baseline clinic measures were not collected ($r=0.94$ between clinic-measured and self-reported height among participants with both measures). *Change in BMI* was also calculated from these height and weight values (increased $\geq 5\%$, decreased $\geq 5\%$, maintained within $<5\%$).

Physical activity was evaluated (5 and 10 years post-diagnosis) using the Modifiable Activity Questionnaire, which has been shown to be reliable and valid.[28, 54] This questionnaire assessed the type, duration, and frequency of activities performed in the prior year. Given observed associations with breast cancer prognosis and QOL,[1, 23] we focused on moderate-vigorous sports/recreational activity. Hours/week spent in each activity were estimated by multiplying frequency by duration. A variable representing activity relative to current physical activity guidelines for US adults (≥ 150 minutes/week moderate activity or ≥ 75 minutes/week vigorous activity)[66] was created: no activity (0 minutes/week), activity not meeting guidelines (>0 and <150 minutes/week moderate activity) or meeting guidelines. *Change in physical activity* was defined by four distinct longitudinal patterns: (1) stayed inactive (not meeting physical activity guidelines at either assessment), (2) active to inactive (meeting guidelines at 5-year follow-up but not at 10-year follow-up), (3) inactive to active (not meeting guidelines at 5-year follow-up, meeting guidelines at 10-year follow-up), and (4) stayed active (meeting guidelines at both assessments).

Sedentary behavior (5- and 10-year follow-ups) was operationally defined by television time (self-reported hours spent sitting while watching television/videos during a typical 24-hour period on weekdays and weekends) in the past year.[28] Similar measures of television watching have been used in public health research,[11] but we did not have direct evidence of validity or reliability of the questions asked in this study.

We calculated continuous television time/day ((weekday median daily time spent watching television $\times$ 5/7) + (weekend median time spent watching television $\times$ 2/7)). In the absence of reliable groupings for television time associated with mortality or QOL,[18] we used a median split (high versus low television time). *Change in television time* was defined by four distinct longitudinal patterns: (1) maintained low television time (<median at both assessments), (2) decreased television time (>median at 5-year follow-up, <median at 10-year follow-up), (3) increased television time (<median at 5-year follow-up, >median at 10-year follow-up), and (4) maintained high television time (>median at both assessments). Change patterns were based on the median at 5 and 10 years to identify those who changed relative to their peers (more than typical age-related changes).

Baseline demographic and clinical characteristics included self-reported measures of *education* and *race/ethnicity/study site* (combined due to colinearity); furthermore, *stage of disease*, *estrogen receptor and progesterone receptor status*, *breast cancer treatment* and *number of nodes examined* were abstracted from medical records and/or SEER. *Age*, *lymphedema* (ever versus never experienced), and *general health status* were self-reported at the 40-month and 10-year follow-ups. *Menstruation* (still menstruating versus stopped menstruating) and *smoking status* were self-reported at the 30-month and 10-year follow-ups. *Comorbidity burden* (0, 1, or 2 self-reported medical conditions that limited activities) was assessed in the 30-month follow-up only. *Tamoxifen use* (ever versus never) was assessed at 40 months. Because new chemoprevention agents became available, *selective Estrogen Receptor Modulator use* (ever versus never used tamoxifen, raloxifene, or toremifene) and *aromatase inhibitor use* (ever versus never) were self-reported at the 10-year follow-up.

Analysis

All analyses were conducted using Stata 11.2. Changes in mean pain severity and in the proportion of women reporting above-average pain were tested using a paired-samples t-test and McNemar's test, respectively. We tested associations between BMI, physical activity, and sedentary behavior with pain cross-sectionally at 10 years two ways. First, linear regression models were fit with continuous pain scores as the dependent variable and BMI, physical activity, and sedentary behavior each individually fit as the independent variable. Next, BMI, physical activity, and sedentary behavior were modeled simultaneously. Second, logistic regression models were fit with the same independent variables but using the dichotomous above-average pain variable as the dependent variable. We evaluated associations between changes in BMI, physical activity, and sedentary behavior (5 to 10 years post-diagnosis) and pain at 10 years with pain treated both continuously and dichotomously. These analyses were conducted using linear regression and logistic

regression approaches with BMI, physical activity, and sedentary behavior each fit separately and with a combined model that included all three factors.

For each model described above, potential confounders (age, education, race/ethnicity, hormone receptor status, breast cancer stage, cancer treatment type, nodes examined, time since cancer diagnosis, SERM use, AI use, and smoking status) were modeled using backward elimination, with a 10% change in the coefficient for BMI, physical activity, or sedentary behavior indicating confounding.[45, 65] We adjusted for comorbidities after identifying other confounders because of probable reciprocal associations between BMI, physical activity, and sedentary behavior with comorbidities.

We tested associations of changes in BMI, physical activity, and sedentary behavior with changes in pain. Because we anticipated small cell sizes, we planned separate unadjusted logistic regression models comparing those who increased versus decreased BMI, physical activity, or sedentary behavior on likelihood of being classified in each pain change group (maintained above-average pain, pain improved, pain worsened) in separate models relative to maintaining low pain.

Results

Participant characteristics

Most HEAL participants were Non-Hispanic White (61%)(Table 1). The average age was 58.9 years at the 40-month assessment. More than half of the women had locally-staged breast cancer; approximately 22% had in situ cancers. Most women were treated with surgery and radiation (37%) or surgery, radiation, and chemotherapy (22%).

The sample available for analyses at 40-months, 10 years, and changes in pain includes 68%, 48%, and 44% of women who completed the baseline assessment, respectively (Figure 1). Compared to the entire HEAL sample, survivors who completed sufficient follow-up assessments to be included in any of the current analyses were younger, achieved higher education, had less advanced cancer at diagnosis, and were less likely to be ER- or PR- (all $p < 0.05$). Mean pain severity and above-average pain at 40 months were similar among women who did and did not complete the 10-year assessment ($p > 0.05$).

Pain at the 40-month and 10-year follow-ups and changes in pain

Mean pain scores and above-average pain stratified by age are shown in Table 2. At 40 months and 10 years, the overall mean pain score was 50.1 (sd=10.8) and 48.0 (sd=11.0), respectively. The overall proportion of survivors reporting above-average pain was 27.8% and 32.3%, respectively.

Mean pain scores worsened over time ($t=3.99$, $p=0.0001$). The proportion of women reporting above-average pain was higher at 10 years ($\chi^2(1)=5.30$, $p=0.02$). From 40 months to 10 years post-diagnosis, almost 10% of survivors maintained above-average pain, nearly 25% reported improved pain and another one-third reported worsened pain (Figure 2). There were no associations between pain change groups and demographic/clinical

variables except that women who maintained above-average pain reported higher comorbidity burden ($p<0.05$).

Cross-sectional associations: BMI, physical activity, sedentary behavior and pain (10-year follow-up)

In individual models, women who were overweight or obese reported significantly higher pain (lower pain scores) than normal weight survivors ($p<0.05$, Table 3). High television time was also associated with higher pain ($p<0.05$). In the combined model, the effects of overweight and obese BMI remained significant, while the effect of television time was attenuated.

In individual models, obese women were more likely to report above-average pain than normal weight survivors ($p<0.05$, Table 3). Survivors meeting physical activity guidelines were approximately half as likely as inactive women to report above-average pain ($p<0.01$). In the combined model, only the effect of meeting physical activity guidelines remained significant.

Changes in BMI, physical activity, and sedentary behavior (5- to 10-year follow-up) and pain (10-year follow-up)

Always active survivors reported lower pain than always inactive survivors in the individual and combined models ($p<0.05$, Table 4). In individual models, women who gained $>5\%$ BMI were more likely, and survivors who were always active were less likely, to report above-average pain (all $p<0.05$, Table 4). Both associations were similar in the combined model.

Adjustment for comorbidities

Additional adjustment for comorbidities attenuated some associations: the cross-sectional associations with pain scores at 10 years for overweight BMI ($\beta=-1.66$, $p=0.13$) and television time ($\beta=-1.03$, $p=0.26$) in individual models and for overweight BMI in the combined model ($\beta=-1.73$, $p=0.12$), the cross-sectional association between obese BMI and above-average pain at 10 years (OR=1.56, 95% CI=0.96–2.56, $p=0.08$), and the association between being ‘always active’ and pain scores in the combined model ($\beta=2.04$, $p=0.14$).

Changes in BMI, physical activity, and sedentary behavior (5 to 10-year follow-up) and changes in pain (40-month to 10-year follow-up)

Survivors who decreased BMI were less likely than those who increased BMI to be in the pain worsened group (25.6% versus 39.8%; OR, 95% CI: 0.45, 0.23–0.88, $p=0.02$). No other associations were observed between changes in BMI, physical activity, or sedentary behavior with pain change groups (data not shown, all $p>0.05$).

Discussion

Approximately one-third of survivors reported above-average pain relative to their same aged-peers at both 40 months and 10 years post-diagnosis, which is consistent with expectations based on population norms.[68] Other research has suggested that pain is more

common or severe among survivors than the general population,[3, 55] but these studies measured pain continuously or as present versus absent. More research is needed to establish a reliable, valid, and clinically relevant case definition of pain to determine whether pain is different in survivors compared to the general population. Nonetheless, examination of survivors with above-average pain is a first step toward identifying the subgroup most in need of intervention. Nearly 10% of women maintained above average pain, approximately one-third reported increased pain, and the likelihood of above-average pain was greater further out from cancer diagnosis. These results suggest that pain is a common and perhaps an increasingly important complaint many years post-diagnosis.

Consistent with observational studies in the general population[8–9, 30, 46, 53, 58, 62, 69] and in cancer survivors,[47] excess weight was uniquely associated with higher pain 10 years after breast cancer; moreover, weight gain was positively associated with above-average pain and worsened pain over time. Several studies failed to find cross-sectional associations between BMI and pain among cancer survivors[5, 21, 36, 55], again perhaps due to a focus on the presence versus absence of pain[36, 55] or on average pain severity[5, 21] rather than a case definition of meaningful pain. Additionally, building on a previous HEAL study demonstrating associations between physical activity and pain up to 40 months post-diagnosis,[1] meeting physical activity guidelines at 10 years post-diagnosis and consistently over time was uniquely associated with a lower likelihood of above-average pain. Although this prospective observational study cannot fully determine whether changes in physical activity caused or were a consequence of reduced pain, intervention studies show that short-term physical activity programs reduce pain in cancer survivors.[6, 32, 42] Taken together, these results document that BMI and physical activity are independently associated with pain in breast cancer survivors, both acutely and prospectively, over the course of long-term survivorship.

Consistent with a previous cross-sectional HEAL analysis on sedentary behavior and QOL 3.5 years post-diagnosis,[18] sedentary behavior was not uniquely associated cross-sectionally or longitudinally with pain in this sample. The attenuation of the cross-sectional association between television time and pain after adjustment for BMI and physical activity suggests sedentary behavior may not be uniquely associated with pain among breast cancer survivors. Alternatively, the self-report nature of our television watching measure or the definitions we chose for change in sedentary behavior may have resulted in exposure misclassification. Even if sedentary behavior is not a predictor of pain, sedentary behavior is common[39] and associated with obesity among breast cancer survivors[34] and with biomarkers of postmenopausal breast cancer risk[35] and mortality[13, 15, 26, 40, 50, 61, 67] among adults without cancer. Additional studies of sedentary behavior and QOL in cancer survivors with validated, comprehensive self-report measures of sedentary behavior, complemented by objective monitoring of sedentary behavior where feasible, would be helpful towards understanding the role of sedentary behavior and health of cancer survivors.

Strengths of this study include a large group of breast cancer survivors recruited through population-based cancer registries, a prospective study design with follow-up through 10 years post-diagnosis, repeat measures of pain, examination of above-average pain and pain change patterns, and assessment of the unique role of BMI, physical activity, and sedentary

behavior. However, several limitations should be considered. Data on BMI, physical activity, and sedentary behavior were self-reported using multiple modes of administration of unknown comparability. Participants may have difficulty accurately recalling activities over the past year. Data for total sedentary time were not available, thus time spent on computers or in sedentary employment was not captured. Our operational definitions for above-average pain, high television time, and changes in BMI, physical activity, and sedentary behavior may be mis-specified. Due to sample size constraints, we were unable to examine a more stringent case definition for pain. Data were not available at 10 years to control for all possible confounders (e.g., pain medication use) or fully assess the role of comorbidities as a confounder or a moderator. We cannot examine the course of pain prior to 40 months post-diagnosis, thus pain cannot be attributed to cancer, and the extent to which changes in BMI and physical activity were a cause or a consequence of pain is unclear. Small cell sizes likely limited power for analyses associating changes in BMI, physical activity, and sedentary behavior with changes in pain. Selection bias due to differential attrition may reduce the generalizability of our findings. Finally, given racial/ethnic differences in associations between obesity, physical activity, and pain in breast cancer survivors,[33, 52] future research should examine pain in more diverse samples.

This study suggests that pain remains or becomes a significant complaint among some long-term breast cancer survivors and that excess weight and lack of physical activity place survivors at continuing risk for pain long after cancer treatment ends. Assessment and treatment of pain are already considered standard for quality care during cancer treatment, [48] but they should continue to be a routine part of long-term survivorship care. Future research should determine the directionality and causal mechanisms for associations of BMI and physical activity with pain, as well as examine the unique role of BMI and physical activity in symptom clusters (e.g., pain, depression, fatigue, sleep disturbances)[27]. Associations between BMI and pain are strongest among older women[62]; thus, if weight control and physical activity interventions are supported by randomized controlled trials, these interventions may be particularly relevant for preventing or mitigating pain among older long-term breast cancer survivors.

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Figure 1.
Participant flow and recruitment

Figure 2.

Patterns of pain change in breast cancer survivors (40-month to 10-year follow-up, N=522)

Note:

Maintained low pain: Reported low pain at both time points and pain change $<1/2$ standard deviation.

Maintained above-average pain: Reported above-average pain at both time points and pain change $<1/2$ standard deviation.

Pain improved: Pain scores improved by $>1/2$ standard deviation. Of these, 76 (14.6% of total sample) reported above-average pain at 40 months and low pain at 10 years, 81 (15.5% of total sample) reported low pain at both time points and 11 (2.1% of total sample) reported above-average pain at both time points.

Pain worsened: Pain scores worsened by $>1/2$ standard deviation. Of these, 47 (9.0% of total sample) reported low pain at 40 months and above-average pain at 10 years, 65 (12.5% of total sample) reported low pain at both time points and 3 ($<1\%$ of total sample) reported above-average pain at both time points.

Unclassified: Pain change $<1/2$ standard deviation but reported above-average pain at 40 months and low pain at 10 years or vice-versa.

Table 1

Characteristics of HEAL participants

	Available for 40-month analyses (N=801)	Available for 10-year analyses (N=563)	Available for pain change analyses (N=522)			
	n	% ^a	n	%		
<i>Baseline variables</i>						
Race/ethnicity/study site						
Non-Hispanic White (New Mexico)	341	42.6	257	45.6	239	45.8
Non-Hispanic White (Western Washington)	144	18.0	104	18.5	101	19.3
Hispanic	95	11.9	62	11.0	53	10.2
Black	197	24.6	127	22.6	116	22.2
Other	24	3.0	13	2.3	13	2.5
Education						
High school or less	205	25.6	123	21.8	112	21.5
Some college	291	36.3	210	37.3	194	37.2
College graduate	156	19.5	104	18.5	101	19.3
Graduate school	148	18.5	126	22.4	115	22.0
Stage at diagnosis						
in situ	178	22.2	130	23.1	119	22.8
Local	453	56.6	320	56.8	302	57.9
Regional	170	21.2	113	20.1	101	19.3
Treatment type						
Surgery only	259	32.3	176	31.3	163	31.2
Surgery/Radiation	295	36.8	211	37.5	197	37.7
Surgery/Chemotherapy	73	9.1	49	8.7	46	8.8
Surgery/Radiation/Chemotherapy	174	21.7	127	22.6	116	22.2
Number of nodes examined						
0 (no axillary surgery)	203	25.3	142	25.2	133	25.5
1 to 9	171	21.3	122	21.7	113	21.6

	Available for 40-month analyses (N=801)		Available for 10-year analyses (N=563)		Available for pain change analyses (N=522)	
	n	% ^a	n	%	n	%
10+	410	51.2	288	51.2	267	51.1
Hormone receptor status						
ER+	453	56.6	315	56.0	295	56.5
ER−	125	15.6	85	15.1	81	15.5
ER borderline or unknown	223	27.8	163	29.0	146	28.0
PR+	363	45.3	257	45.6	241	46.2
PR−	169	21.1	108	19.2	105	20.1
PR borderline or unknown	269	33.6	198	35.2	176	33.7
Months since diagnosis (mean ± SD)						
Diagnosis to baseline	6.0 ± 2.2		5.9 ± 2.2		5.9 ± 2.2	
Diagnosis to 30-month follow-up	30.2 ± 3.5		30.0 ± 3.5		29.9 ± 3.4	
Diagnosis to 40-month follow-up	40.0 ± 6.9		39.8 ± 7.0		39.8 ± 7.0	
Diagnosis to 5-year follow-up			67.4 ± 4.2		67.3 ± 3.8	
Diagnosis to 10-year follow-up			123.1 ± 8.1		122.8 ± 8.3	
<i>Time dependent characteristics, 40-month follow-up</i>						
Age (years)						
<44	62	7.7			32	6.1
45–54	250	31.2			170	32.6
55–64	274	34.2			196	37.5
65–74	146	18.2			100	19.2
75+	69	8.6			24	4.6
(mean ± SD)	(58.9 ± 10.5)				(58.1 ± 9.2)	
Menstruation ^b						
Still menstruating	142	17.7			96	18.4
Stopped menstruating or unknown	695	53.7			426	81.6
History of lymphedema						

	Available for 40-month analyses (N=801)		Available for 10-year analyses (N=563)		Available for pain change analyses (N=522)	
	n	% ^a	n	%	n	%
No	638	79.7	413	77.8	413	79.1
Yes	163	20.3	109	16.5	109	20.9
General health						
Fair/poor	135	16.9			68	13.0
Good/Very Good/Excellent	666	83.1			454	87.0
Comorbidity index ^c (# of comorbidities that limit activities) ^b						
0	604	75.4	438	77.8	406	77.8
1	136	17.0	93	16.5	88	16.9
2+	61	7.6	32	5.7	28	5.4
Tamoxifen use						
Never/unknown	379	47.3			247	47.3
Ever	422	52.7			275	52.7
Smoking status ^b						
Never	364	45.4			242	46.4
Former	319	39.8			216	41.4
Current	91	11.4			52	10.0
Marital status						
Married/living as married	449	56.1			312	59.8
Not married	322	40.2			195	37.4
<i>Time dependent characteristics, 10 year follow-up</i>						
Age (years)						
<44			2	0.4	2	0.4
45–54			78	13.9	68	13.0
55–64			221	39.3	204	39.1
65–74			183	32.5	172	33.0
75+			79	14.0	76	14.6

	Available for 40-month analyses (N=801)		Available for 10-year analyses (N=563)		Available for pain change analyses (N=522)	
	n	% ^a	n	%	n	%
(mean ± SD)	(64.9 ± 9.2)					
Menstruation						
Still menstruating			20	3.6	19	3.6
Stopped menstruating			543	96.4	503	96.4
History of lymphedema						
No			437	77.6	406	77.8
Yes			126	22.4	116	22.2
General health						
Fair/poor			77	13.7	77	14.8
Good/Very Good/Excellent			486	86.3	445	85.2
Selective Estrogen Receptor Modulator use						
Never/unknown			254	45.1	230	44.1
Ever			309	54.9	292	55.9
Aromatase inhibitor use						
Never/unknown			508	90.2	472	90.4
Ever			55	9.8	50	9.6
Smoking status						
Never			265	47.1	249	47.7
Former			242	43.0	226	43.3
Current			37	6.6	33	6.3
Marital status						
Married/living as married			299	53.1	278	53.3
Not married			260	46.2	240	46.0
<i>BMI, physical activity, and sedentary behavior (10 year follow-up)</i>						
Body Mass Index						
Normal weight (>18 kg/m ² & <25 kg/m ²)			220	39.1	203	38.9

	Available for 40-month analyses (N=801)		Available for 10-year analyses (N=563)		Available for pain change analyses (N=522)	
	n	% ^a	n	%	n	%
Overweight (≥ 25 kg/m ²)			167	29.7	159	30.5
Obese (≥ 30 kg/m ²)			174	30.9	158	30.3
Physical activity						
No activity (0 min/week)			242	43.0	222	42.5
Activity not meeting guidelines (>0 min/week & <150 min/week)			188	33.4	175	33.5
Meeting guidelines (≥ 150 min/week)			121	21.5	113	21.6
Television time						
Low (<2.5 hours/day)			302	53.6	283	54.2
High (≥ 2.5 hours/day)			259	46.0	237	45.4
(mean $\pm$ SD)			(2.7 $\pm$ 1.7)		(2.6 $\pm$ 1.7)	
Range			0 – 9		0 – 9	
<i>Change in BMI, physical activity, and sedentary behavior (5 year follow-up to 10 year follow-up)</i>						
Change in Body Mass Index (BMI)						
Maintained BMI within 5%					267	51.1
Increased $>5\%$					98	18.8
Decreased $>5\%$					137	26.2
Change in physical activity						
Always inactive (below guidelines at both time points)					273	52.3
Active to inactive (met guidelines at 5-year follow-up only)					110	21.1
Inactive to active (met guidelines at 10-year follow-up only)					26	5.0
Always active (met guidelines at both time points)					82	15.7
Change in television time						
Maintained low television time (low at 5 and 10 years)					201	38.5
Decreased television time (high at 5 years, low at 10 years)					70	13.4
Increased television time (low at 5 years, high at 10 years)					69	13.2

	Available for 40-month analyses (N=801)		Available for 10-year analyses (N=563)		Available for pain change analyses (N=522)	
	n	% ^a	n	%	n	%
Maintained high television time(high at 5 and 10 years)			160		30.7	

^aPercentages do not add to 100% due to missing data.

^bData were collected at 30-month interview

^cComorbidities assessed included angina, arthritis, osteoporosis, chronic lung disease, diabetes, gall bladder disease, myocardial infarction, heart failure, hypertension, endometriosis, liver disease, kidney disease, deep vein thrombosis, pulmonary embolism, stroke, thyroid disease, cancers other than breast

Table 2
SF-36 bodily pain scores and proportion reporting above-average pain at 40-month and 10-year follow-up

	Breast Cancer Survivors				
	General Population ^a	40-month Follow-up (N=801)		10-year Follow-up (N=563)	
		Mean (SD) ^b	Mean (SD)	% with above-average pain ^c	Mean (SD)
44 years	49.95 (9.64)	51.48 (11.29)	27.4	-- ^d	--
45 to 54 years	48.07 (10.29)	50.96 (9.80)	24.0	49.91 (10.84)	29.5
55 to 64 years	47.73 (11.09)	49.82 (11.38)	28.8	47.53 (10.76)	34.4
65 to 74 years	47.33 (10.38)	48.93 (11.15)	32.9	48.32 (11.10)	31.7
75 years	44.87 (11.07)	48.98 (10.77)	27.5	46.71 (11.59)	29.1
Total	50.00 (10.00)	50.07 (10.81)	27.8	48.02 (11.02)	32.2

^a General population norms stratified by age reported by Ware et al. (1993) [68]

^b SF-36 Bodily Pain scores are standardized on a T=score metric with on overall US general population mean score of 50 (standard deviation=10); higher scores indicate less pain.

^c Above average pain defined as SF-36 bodily pain scores $\geq 1/2$ standard deviation below the mean for same-aged peers. Expected percent $>1/2$ SD below the mean based on a normal distribution=30.9%.

^d Only 2 survivors were <44 years old at 10-year follow-up

Table 3

Multiple regression models: Associations between BMI, physical activity, and sedentary behavior with pain at 10-year follow-up

		SF-36 Bodily Pain scores		Above-average pain [§]	
		β	(95% CI)	OR	(95% CI)
		(no confounders)		(no confounders)	
Individual Models	BMI				
	Normal weight	--	--	--	--
	Overweight	-2.26	(-4.45, -0.06)*	1.36	(0.83, 2.34)
	Obese	-4.32	(-6.50, -2.16)***	1.81	(1.12, 2.91)*
		<i>a, c, g, h, l, k, m</i>		<i>c</i>	
	Physical activity				
	No activity	--	--	--	--
	Activity not meeting guidelines	-0.23	(-2.49, 2.03)	0.94	(0.59, 1.48)
	Meeting guidelines	1.98	(-0.59, 4.56)	0.41	(0.22, 0.75)**
		<i>m</i>		<i>m</i>	
	Television time				
Combined Model	Low (<2.5 hours/day)	--	--	--	--
	High (2.5 hours/day)	-1.85	(-3.70, -0.01)*	1.15	(0.76, 1.72)
		<i>f, i, m</i>		<i>c, m</i>	
	BMI				
	Normal weight	--	--	--	--
	Overweight	-2.21	(-4.45, -0.03)*	1.42	(0.84, 2.41)
	Obese	-3.26	(-5.56, -0.97)**	1.69	(0.99, 2.88)
	Physical activity				
	No activity	--	--	--	--
	Activity not meeting guidelines	-0.58	(-2.71, 1.55)	0.99	(0.61, 1.59)
	Meeting guidelines	1.09	(-1.38, 3.56)	0.46	(0.24, 0.86)*
	Television time				
	Low (<2.5 hours/day)	--	--	--	--
	High (2.5 hours/day)	-1.31	(-3.22, 0.60)	1.00	(0.65, 1.56)

* p<0.05,

** p<0.01,

*** p<0.001

[§] Above average pain defined as SF-36 bodily pain scores 1/2 standard deviation below the mean for same-aged peers.

a – *n* indicate confounders included in the model: ^a age, ^b education, ^c race/ethnicity, ^d ER status, ^e PR status, ^f time since diagnosis (months), ^g stage, ^h number of nodes examined, ⁱ treatment history, ^j use of Aromatase inhibitors, ^k use of Selective Estrogen Receptor Modulators, ^m smoking history, ⁿ number of comorbidities

Multiple regression models: Associations between changes in BMI, physical activity, and sedentary behavior (5 to 10-year follow-up) and pain at 10-year follow-up

Table 4

		SF-36 Bodily Pain scores		Above-average pain [§]	
		β	(95% CI)	OR	(95% CI)
		<i>a, c, f, h, i, k, m</i> (no confounders)			
BMI					
Maintained BMI within 5%		--	--	--	--
BMI increased >5%		-2.17	(-4.65, 0.31)	1.93	(1.17, 3.17)*
BMI decreased >5%		-0.34	(-2.60, 1.92)	1.01	(0.64, 1.61)
		<i>c, i</i>			
Physical activity					
Always inactive		--	--	--	--
Active to inactive		2.27	(-0.07, 4.61)	0.90	(0.54, 1.48)
Inactive to active		2.78	(-1.57, 7.14)	0.36	(0.10, 1.28)
Always active		3.39	(0.72, 6.06)*	0.38	(0.19, 0.78)**
		<i>c, i, m</i>			
TV time					
Maintained low TV time		--	--	--	--
Decreased TV time		1.22	(-1.69, 4.13)	1.11	(0.58, 2.11)
Increased TV time		-1.37	(-4.32, 1.58)	0.95	(0.48, 1.88)
Maintained high TV time		-1.41	(-3.66, 0.84)	1.30	(0.79, 2.14)
		<i>c, h, i, m</i>			
BMI					
Maintained BMI within 5%		--	--	--	--
BMI increased >5%		-1.89	(-4.37, 0.64)	1.76	(1.03, 3.01)*
BMI decreased >5%		0.01	(-2.22, 2.25)	0.89	(0.52, 1.53)
Physical activity					
Always inactive		--	--	--	--

SF-36 Bodily Pain scores		Above-average pain [§]	
	β	(95% CI)	OR (95% CI)
Active to inactive	2.21	(-0.21, 4.64)	0.77 (0.454, 1.338)
Inactive to active	2.91	(-1.53, 7.35)	0.36 (0.10, 1.28)
Always active	2.81	(0.05, 5.57)*	0.40 (0.20, 0.84)*
TV time			
Maintained low TV time	--	--	--
Decreased TV time	1.24	(-1.76, 4.24)	1.09 (0.55, 2.16)
Increased TV time	-0.76	(-3.80, 2.27)	0.84 (0.41, 1.71)
Maintained high TV time	-1.24	(-3.56, 1.08)	1.15 (0.68, 1.94)

* p<0.05,
** p<0.01,
*** p<0.001

[§] Above average pain defined as SF-36 bodily pain scores 1/2 standard deviation below the mean for same-aged peers.

a – n indicate confounders included in the model: ^a age, ^b education, ^c race/ethnicity, ^d ER status, ^e PR status, ^f time since diagnosis (months), ^g stage, ^h number of nodes examined, ⁱ treatment history, ^j use of Aromatase inhibitors, ^k use of Selective Estrogen Receptor Modulators, ^m smoking history, ⁿ number of comorbidities