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### Changes in body fat and weight after a breast cancer diagnosis: Influence of demographic, prognostic and lifestyle factors

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#### Abstract

**Purpose**—Obese women and women who gain weight after a breast cancer diagnosis are at a greater risk for breast cancer recurrence and death compared with lean women and women who do not gain weight. In this population-based study, we assessed weight and body fat changes from within the first year of diagnosis to within the third year after diagnosis, and whether any changes in weight and body fat varied by demographic, prognostic, and lifestyle factors in 514 women with incident Stage 0–IIIA breast cancer.

**Methods**—Women were participants in the Health, Eating, Activity, and Lifestyle (HEAL) Study. Weight and body fat (via DEXA) were measured during the baseline visit and two years later at a follow-up visit. Analysis of covariance methods were used to obtain mean weight and body fat changes adjusted for potential cofounders.

**Results**—Women increased their weight and percent body fat by  $1.7 \pm 4.7$  kg and  $2.1 \pm 3.9$  %, respectively, from within their first year of diagnosis to within their third year of diagnosis. A total of 68% and 74% gained weight and body fat. Greater increases in weight were observed among women diagnosed with a higher disease stage, younger age, being postmenopausal, and women who decreased their physical activity from diagnosis to within 3 years after diagnosis (p for trend < 0.05).

**Conclusions**—Weight and body fat increased in the post-diagnosis period. Future research should focus on the effect of physical activity on weight and fat loss and breast cancer prognosis.

#### Keywords

obesity; physical activity; diet; prognosis; treatment

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#### INTRODUCTION

Weight gain and obesity are common occurrences in women diagnosed with breast cancer (1–6). Gains in weight usually range from 2.0 to 6.0 kg during the first year of diagnosis; however, greater gains are not uncommon. Evidence exists that post-diagnosis weight gain may adversely affect survival among breast cancer survivors (7–9), and obesity at the time of diagnosis is a negative prognostic factor that is associated with recurrent disease and decreased survival (10–14). Both weight gain and obesity adversely affect risk for cardiovascular disease, hypertension, and diabetes (15–17), conditions for which women who have been diagnosed with breast cancer are at increased risk (18,19).

Multiple reasons for post-diagnosis weight gain in breast cancer survivors have been suggested, including receiving chemotherapy, being or becoming postmenopausal after diagnosis, decreased physical activity, and increased total caloric intake, although these explanations have not been extensively studied (1–6). Most studies that have examined changes in body weight after a diagnosis of breast cancer and factors associated with weight gain have been of short study duration (e.g., only during treatment or within the first year) and with small sample sizes (2,3,5,20,21). Few studies have measured body weight (most rely on self-report) and even fewer studies have measured changes in body fat. Studies with a larger number of patients, with a longer follow-up, using valid measures of body composition are necessary so as to better define the real prognostic impact of gains in body fat and weight in this setting.

To further investigate changes in body composition in the post diagnosis period, we examined changes in body fat and weight from diagnosis to within three years after diagnosis in 514 breast cancer survivors enrolled in the Health, Eating, Activity, and Lifestyle (HEAL) Study, a population-based prospective cohort study. We also examined the associations of demographic, prognostic, and lifestyle factors with changes in body fat and weight.

#### METHODS

#### Study Setting, Subjects, and Recruitment

The HEAL study is a population-based, multi-center, multi-ethnic prospective cohort study that has enrolled 1,223 breast cancer survivors who are being followed to determine whether weight, physical activity, diet, sex hormones, and other exposures affect breast cancer prognosis (22–24). Women were recruited into the HEAL study through Surveillance, Epidemiology, End Results (SEER) registries in New Mexico, Los Angeles County (CA), and Western Washington. Details of the aims, study design, and recruitment procedures have been published previously (22–24). Comparable data on body weight collected at both visits were available only for New Mexico and Washington. Therefore these analyses were limited to participants from those two sites.

Briefly, in New Mexico, 654 women, aged 18 years or older, diagnosed with *in situ* to Stage IIIA breast cancer between July 1996 and March 1999, and living in Bernalillo, Sante Fe, Sandoval, Valencia, or Taos Counties were recruited for the HEAL Study. In Western Washington, 202 women, between the ages of 40 and 64 years, diagnosed with *in situ* to Stage IIIA breast cancer between September 1997 and September 1998, and living in King, Pierce, or Snohomish Counties were recruited. In both New Mexico and Washington, stage of disease was based on the American Joint Committee on Cancer (AJCC) stage groupings: 0 (*'in situ'*), I, IIA, IIB, IIIA, which are based on the tumor-node-metastasis system (25). During the years of 1996 through 1999 when these women were diagnosed, there were no major changes in the AJCC codes within SEER.

Participants completed in-person interviews at baseline (within their first year after diagnosis,  $6 \pm 2$  months from diagnosis) and two-years after the baseline visit (within their

diagnosis,  $6 \pm 2$  months from diagnosis) and two-years after the baseline visit (within their third year after diagnosis,  $31 \pm 4$  months from diagnosis). Among the 856 women enrolled at baseline, a total of 39 women had a previous breast cancer diagnosis, a total of 47 women did not have a baseline body weight measure; 220 women did not have a follow-up body weight measure, 6 women did not complete the physical activity questionnaire at baseline, and a total of 30 women had a recurrence of breast cancer between the two visits. Our analyses are based on the remaining 514 women. Analyses involving body fat include a reduced sample size of 132 women because of limited funds available to perform DEXA scans. Women who had a DEXA scan were similar to the cohort of women included in the full analyses in terms of baseline characteristics. Written informed consent was obtained from each subject. The study was performed with the approval of the Institutional Review Boards of participating centers, in accord with an assurance filed with and approved by the U.S. Department of Health and Human Services.

#### **Data Collection**

**Anthropometrics**—Trained staff measured weight and height in a standard manner at the clinic visit. With the women wearing light indoor clothing and no shoes, weight was measured to the nearest 0.1 kg using a balance-beam laboratory scale. Height was measured, also without shoes, to the nearest 0.1 cm using a stadiometer. All measurements were performed and recorded twice in succession, averaged for a final value for analyses. Body mass index (BMI) was computed as weight in kg divided by height in m<sup>2</sup>. Three mutually exclusive BMI groups were created: lean weight (BMI < 25 kg/m<sup>2</sup>), overweight (25 kg/m<sup>2</sup> ≤ BMI < 30.0 kg/m<sup>2</sup>), and obese (BMI ≥ 30.0 kg/m<sup>2</sup>) (26).

Percent body fat was measured from whole-body scans using a dual-energy x-ray absorptiometry (DEXA) scanner (Lunar model DPX [GE Medical Systems, Milwaukee, WI] in New Mexico; Hologic model QDR 1500 [Hologic Inc, Waltham, MA] in Washington).

**Physical Activity Assessment**—We collected information on physical activity using an interview-administered questionnaire at a visit scheduled within the first and third years after diagnosis. The questionnaire was based on the Modifiable Activity Questionnaire developed by Kriska and colleagues, which was designed to be easily modified for use with different populations, and which has been shown to be reliable and valid (27). The type, duration, and frequency of activities performed in the past year were assessed. The sports/ recreation and household activity section of the questionnaire addressed 29 popular activities.

We then estimated hours per week for each activity by multiplying frequency and duration together. Two mutually exclusive groups were created based on type of activity, sports/ recreation including walking or household/gardening. Each activity was also categorized as light (< 3 METs)-, moderate (3–6 METs)-, or vigorous (> 6 METs)-intensity based on Ainsworth et al's 'Compendium of Physical Activities' (28,29).

**Stage of Disease and Cancer Treatment**—We obtained data on disease stage from the local SEER registries prior to recruitment of women into the HEAL Study (30). Adjuvant treatment was categorized into three mutually exclusive groups: surgery only (including those taking or not taking tamoxifen), surgery + radiation (including those taking or not taking tamoxifen), or any chemotherapy (including surgery, those taking or not taking tamoxifen, as well as those having radiation or not). We also were interested in looking at tamoxifen use (adjusted for treatment group), thus two mutually exclusive groups were created: not taking tamoxifen and taking tamoxifen.

**Other Variables**—Standardized questionnaire information was collected on medical history, reproductive histyor, family history of cancer, physician-diagnosed type 2 diabetes, smoking status, and selected demographic data. Information on diet was collected via a food frequency questionnaire (31).

#### **Statistical Analyses**

Means and standard deviations of physiological and demographic characteristics of the study sample were calculated by study site, and differences in means were compared using t-tests for continuous variables and chi-square analyses for categorical variables. We also examined the proportion of breast cancer survivors gaining or losing body weight or body fat over the two-year follow-up period.

We used analysis of covariance methods to estimate least squares means and test for differences in body weight and body fat across categories of disease stage, adjuvant treatment, age, menopausal status, tamoxifen use, BMI, study site, ethnicity, smoking status, changes in total caloric intake, and changes in physical activity. Each analysis was adjusted for the other factors except the variable of interest; for example, in comparing body weight across disease stage, we adjusted for the other factors, but not disease stage. We used Tukey's Honestly Significant Difference (HSD) test to identify statistically significant differences between groups with the overall level of statistical significance constrained to 5%.

#### RESULTS

The mean age and BMI of participants were  $56.3 \pm 10.5$  years and  $26.3 \pm 5.3$  kg/m<sup>2</sup>, respectively (Table I). Sixty-nine percent of women were postmenopausal. Seventy-eight percent of the women had completed 12 years of high school, and 85% and 15% of the women were non-Hispanic White and Hispanic White, respectively. Twenty-five percent, 57%, and 18% of the patients were diagnosed with *in situ*, Stage I, and Stage II to III-A breast cancer, respectively.

The mean weight and percent body fat change of participants were  $1.7 \pm 4.7$  kg and  $2.1 \pm 3.9\%$ , respectively with 68% of the sample gaining weight (mean weight gain =  $3.9 \pm 3.7$  kg) and 74% gaining percent body fat (mean percent body fat gain =  $3.6 \pm 3.0\%$ ) (Figure I). Among the 68% of women who gained weight, 31% gained less than 2.5 kg, 19% gained between 2.5 and 4.9 kg, and 18% gained 5 kg or more (Figure II). Among the 74% of women who gained body fat, 36% gained less than 2.5%, 17% gained between 2.5 and 4.9%, and 21% gained 5% or more (Figure II).

We observed a statistically significant trend of increasing gains in weight with increasing category of disease stage (p for trend = .0039), younger age groups (p for trend = .0001), postmenopausal women (p < .05), and decreasing sports/recreational physical activity from baseline to within 3 years after diagnosis (p for trend = .032) (Table II). Because of the observation of increasing weight gain among younger women, yet also with postmenopausal women, we further examined changes in body weight stratified by both age groups and menopausal status, and by age groups among only postmenopausal women (Table III). Postmenopausal women had greater weight gain compared to premenopausal women and women who became postmenopausal after diagnosis for all age groups. When examining weight gain by age groups among only postmenopausal women, we observed a significant trend of greater weight gain among younger postmenopausal women compared to older postmenopausal women, p for trend = .0020 (Table III).

In unadjusted analyses, we observed greater weight gain among women receiving chemotherapy than women receiving just surgery or surgery plus radiation (p < .05). However, when we adjusted for potential confounders, weight gain was no longer greater among women receiving chemotherapy compared to the other two treatment groups. To determine which variables were the strongest confounders in the treatment and weight change association, we analyzed the treatment data by adding each adjustment variable one at a time as well as by examining the effect of treatment on weight change stratified by each adjustment variable. No one variable significantly changed the treatment – weight change association. However, when we stratified the analyses by menopausal status, in postmenopausal women we observed nonsignificantly greater weight gain among women receiving chemotherapy than women receiving just surgery or surgery plus radiation, but not among premenopausal women or women who became postmenopausal after diagnosis (data not shown). Further, when we stratified the analyses by change in sports/recreational physical activity from baseline to within 3 years after diagnosis, in women who did not increase their physical activity from baseline to within 3 years after diagnosis, we observed greater weight gain among women receiving chemotherapy than women receiving just surgery or surgery plus radiation (p = .061 and p = .048, respectively), but not among women who increased their activity from baseline to within 3 years after diagnosis (data not shown). This latter group actually had less weight gain among those receiving chemotherapy compare to the two other treatment groups (p < .05). Thus, it appears that menopausal status and physical activity had the strongest effect on the treatment and weight change association. Lastly, we also examined the effect of type of chemotherapy (i.e., those taking anthracycline-based chemotherapy vs. those not taking anthracycline-based chemotherapy) on change in body weight. In unadjusted and adjusted analyses, we observed similar amounts of weight gain in both chemotherapy groups (p = .68).

No significant associations were observed between changes in weight and family history of breast cancer, family history of type 2 diabetes, physician-diagnosed type 2 diabetes, cardiovascular disease, and education (data not shown).

We observed a statistically significant trend of increasing gains in body fat with decreasing categories of BMI (p for trend = .050) and sports/recreational physical activity from baseline to within 3 years after diagnosis (p for trend = .051) (Table IV). The trend of increasing gains in body fat associated with decreasing age approached significance (p for trend = .061). No statistically significant associations were observed between changes in body fat and disease stage, treatment, menopausal status, tamoxifen use, ethnicity, and change in total caloric intake.

#### DISCUSSION

On average, breast cancer patients in our study gained 1.7 kg of weight and 2.1% body fat over 2 years. More than 68% and 74% of the women experienced gains in weight and percent body fat, respectively. The mean increases for those who gained weight and percent body fat were 3.9 kg and 3.6%, with a range of 0.1 kg to 27.0 kg and 0.1% to 15.0%. The weight gain that we observed is comparable to that reported by others in women with recently diagnosed breast cancer. Goodwin et al (4) reported that 84% of 535 breast cancer patients gained weight in the first year after diagnosis, with a mean weight gain of 1.6 kg overall. In a study by Rock et al (1), 60% of 1116 women enrolled in the WHEL Study reported weight gain from one year before diagnosis to within four years after diagnosis. The mean weight gain was 2.7 kg.

The weight gain we and others have observed in breast cancer survivors is larger than that observed by others in healthy women. Williamson et al (32) studied weight gain over a 10-

year period in the 1970's in 6,135 women who participated in the NHANES I Study. Over 10 years, women aged 45 to 55 years gained only 0.79 kg (0.08 kg/yr), whereas those aged 55 years and older lost weight. Our findings cannot be compared directly with the NHANES I study, however, women with breast cancer may experience a greater weight gain than women in the general population.

The effects of weight gain on breast cancer recurrence have been debated in the literature. Some (7–9), but not all (33–37) investigators have associated weight gain with an earlier disease recurrence. Camoriano et al (8) followed 646 breast cancer patients for a median of 6.6 years and found that premenopausal women who gained more than 5.9 kg were 1.5 times more likely to relapse and 1.6 times more likely to die of their breast cancer than were women gaining less weight.

Although it remains to be determined whether post-diagnosis weight gain influences risk for progressive disease, it is known that weight gain adversely affects risk for cardiovascular disease, hypertension, and diabetes (15–17). Furthermore, many studies have identified obesity as an important negative prognostic factor for breast cancer survival (10–14). In a review by Chlebowski et al (10), 17 of 26 studies found increased weight to be a significant risk factor for recurrent disease and decreased survival; seven studies produced null findings; and two studies found an inverse association between weight and recurrence. In the studies that found a significant positive association between overweight and progressive disease, women categorized in the higher vs. lower levels of obesity exhibited a 30% to 540% increased risk of death. Data from the National Surgical Adjuvant Breast and Bowel Project in 3,385 women indicated that while obesity did not increase risk for breast cancer recurrence or death, obesity did increase risk of overall death, risk of other cancers, and death from cardiac disease (38). It is currently unknown whether post-diagnosis weight reduction modifies the relationship between obesity and breast cancer recurrence and mortality.

Several mechanisms have been proposed to explain the adverse effect of adiposity and weight gain on breast cancer prognosis. One mechanism rests on greater peripheral conversion of androstenedione to estradiol and inhibition of synthesis of sex hormone binding globulin with an increase in free estradiol which stimulates neoplastic cells (39), especially in postmenopausal women (23). We have previously reported an association between increased adiposity and increased concentrations of estrone, estradiol, and free estradiol in the HEAL cohort of breast cancer survivors (23). Another mechanism relates to insulin and IGF-1 and the interactions of these hormones with adiposity (40). Insulin and IGFs exhibit mitogenic effects that influence both premalignant and cancerous stages of cell growth. Both insulin and IGF-1 stimulate the synthesis of sex steroids, and thus, their cancer-promoting effects in the progression of breast cancer may be mediated by an effect on sex hormones. Another explanation for poorer survival may be associated with obese women failing to respond to treatment as a result of the common practice of chemotherapy capping at a body surface area of 2 m<sup>2</sup>, which may offer suboptimal treatment benefit (41).

In our study, higher disease stage, being postmenopausal, and less participation in physical activity were significantly related to gains in body weight. Receiving chemotherapy was also associated with greater weight gain, however this observation was limited to postmenopausal women and women who did not increase their physical activity from baseline to within 3 years after diagnosis. Goodwin et al. (4) examined factors associated with weight gain during the subsequent year after diagnosis in 535 newly diagnosed breast cancer survivors. In multivariate analysis, onset of menopause and administration of chemotherapy were independent predictors of weight gain.

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A study by Demark-Wahnefried studied energy balance over the first year after breast cancer diagnosis in 53 premenopausal women (2). Weight gain during chemotherapy was associated with an increase in fat mass and decrease in lean body mass, a pattern consistent with sarcopenic obesity. This form of obesity is associated with reduced physical activity, aging, and menopause. A significantly lower level of physical activity throughout the year of observation was demonstrated. The authors conclude that reduced physical activity is the primary factor responsible for weight gain during chemotherapy for breast cancer. Demark-Wahnefried et al's results are also consistent with a report by Rock et al (1) stating that physical activity predicted weight stability in 1116 breast cancer survivors participating in the WHEL Study.

Despite strong evidence suggesting that regular physical activity can protect against gains in body fat and weight, only 32% of breast cancer survivors enrolled in the HEAL Study engaged in the recommended level of physical activity defined as 150 min per week of moderate- to vigorous-intensity physical activity (24). This percentage is similar to the proportion of healthy U.S. women (27%) meeting the current recommendation (29). Recently, we reported that women diagnosed with breast cancer were significantly less physically active within their first year after diagnosis than they were one year before diagnosis (22). While physical activity levels reported three years after diagnosis increased to pre-diagnosis levels for approximately 50% of the sample, this was mostly limited to nonobese women (24). Exercise interventions and physical activity programs focused on increasing physical activity among breast cancer survivors with the ultimate goal of testing the effects on prognosis are needed. Previous research has also shown beneficial effects of dietary interventions on breast cancer prognosis in breast cancer survivors (42,43). Studies examining the combination of diet and physical activity on prognosis are also needed.

The HEAL Study has several strengths. It is one of a handful that has examined changes in measured body weight for a relatively long follow-up period, and the largest study reporting changes in body fat measured via DEXA. However, a limitation of our study is that we were unable to measure weight and percent body fat at other time points (e.g., within the second year after diagnosis). Women may have initially gained and then lost weight during this time. Thus, we are unable to report the maximal gains in body weight and body fat within three years after a breast cancer diagnosis. Another limitation of the study is that some women were recruited into the study while undergoing treatment, while others had not begun treatment or had completed treatment. Some women may have already experienced changes in weight or body fat after diagnosis, but prior to enrollment in the study. Lastly, our sample was highly educated and mostly non-Hispanic White, therefore, we cannot be sure that these findings pertain to all breast cancer survivors.

Weight gain is a concern of many women after a diagnosis of breast cancer. In a community-based study (44), the majority of breast cancer survivors were dissatisfied with their weight and stated that they were ready to take steps necessary to reduce their weight. A study conducted among 531 breast cancer survivors found that 52% wanted nutritional guidance at the time of diagnosis or soon after, although few reported having ever received dietary recommendations from their physicians (45).

In conclusion, over two-thirds of women in our study gained weight and body fat within the first three years after a diagnosis of breast cancer, and to a greater degree than that previously reported in studies of healthy women. Weight and body fat gains were greatest in women who reported less participation in physical activity. Since higher levels of body fat are associated with increased breast cancer recurrence and decreased survival, it is imperative that research be conducted on the prognostic effect of physical activity and weight loss in overweight and obese breast cancer survivors.

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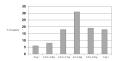
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80		-	
60			
40		_	-
20	32% 29% Lost Weight Lost Fut	3.9 ± 3.74	3.6 ± 3.0%
0	2822640 -2122.0%	675.	74%
20		Cairod weight	Cared Fat

#### Figure I.

Body weight (N = 514) and fat changes (N = 132) from baseline to within 3 years. Overall mean weight change =  $1.7 \pm 4.7$ kg (-13.2 to 27.0 kg); Overall mean fat change =  $2.1 \pm 3.9$ % (-14.5 to 15.0%)



#### Figure II.

Distribution of weight changes from baseline to within 3 years (n = 514).

40	
35	
30	
25	
20	
15	
10	
5	
0 419 479 449 4	5 29245 239495 25-

#### Figure III.

Distribution of body fat changes from baseline to within 3 years (n = 132).

#### Table I

Baseline characteristics of breast cancer survivors in the HEAL Study by study site (N = 514).

	All	Washington	New Mexico
	(N = 514)	(N = 161)	(N = 353)
	Mean ± SD	Mean ± SD	Mean ± SD
Age, years, mean ± SD	$56.3\pm10.5$	$52.4\pm 6.3$	58.1 ± 11.5*
Postmenopausal at baseline	69%	63%	71%
Education, % High School graduates	96%	99%	95%
Months from diagnosis to initial interview, mean $\pm$ SD	$6\pm 2$	$7\pm2$	$6\pm 2$
Ethnicity			
Non-Hispanic White	85%	98%	79% <sup>*</sup>
Hispanic White	15%	2%	21%
Stage of Disease			
0, in situ	25%	32%	21%*
Ι	57%	49%	61%
II – IIIA	18%	19%	18%
Treatment			
Surgery only	30%	25%	33%*
Surgery $\pm$ Radiation only	42%	49%	43%
Any chemotherapy	27%	19%	24%
Tamoxifen users	48%	53%	46%
Weight, kg, mean $\pm$ SD	$69.8 \pm 15.0$	$73.8 \pm 16.3$	$68.0 \pm 14.0^{*}$
Height, cm, mean ± SD	$162.9\pm6.9$	$164.2\pm6.6$	$162.4\pm6.9$
Body mass index, $kg/m^2$ , mean $\pm$ SD	$26.3\pm5.3$	$27.3\pm5.7$	$25.8\pm5.1$
Baseline sports/recreational activity levels, hrs/wk, mean $\pm$ SD	$2.4\pm3.5$	$2.2\pm3.3$	$2.5\pm3.6$
Baseline total daily caloric intake, mean $\pm$ SD	$1545\pm562$	$1597\pm576$	$1503\pm591$
Current smokers	9%	8%	10%
Physician-diagnosed type 2 diabetes	6%	2%	7% *
Family history of breast cancer	25%	21%	27%*

significantly different from Washington (p < .05).

## Table II

Weight change (kg) from baseline assessment to assessment conducted during year three following diagnosis in HEAL breast cancer survivors (N = 514).

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Disease Stage		2		nmenfnt	
Disease Stage		Mean ± SE	% Change ± SE	Mean ± SE	% Change ± SE
In Situ	127	$1.3 \pm 0.4$	$1.8\%\pm0.6$	$0.9 \pm 0.5$	$1.3\%\pm0.7$
Stage I	294	$1.4 \pm 0.3$	$2.3\% \pm 0.4$	$1.7 \pm 0.3$	$2.5\%\pm0.4$
Stage II – IIIA	93	$3.1\pm0.5^{*}\varPhi$	$4.5\%\pm0.7^{*}\varPhi$	$3.2\pm0.5^{*}$ $\Phi$	$4.5\%\pm0.7^{*}\varPhi$
P for trend		.0036	.0031	.0039	.0037
Treatment					
Surgery only	156	$1.5 \pm 0.4$	$2.3\% \pm 0.5$	$2.0 \pm 0.5$	$3.0 \pm 0.6$
Surgery + Radiation	217	$1.1 \pm 0.3$	$1.6\% \pm 0.4$	$1.5\pm0.3$	$3.2 \pm 0.4$
Any Chemotherapy	141	$3.0\pm0.4^{*}$ $\Phi$	$4.3\% \pm 0.5^* \Phi$	$2.0\pm0.5$	$3.0\pm0.7$
<u>Age Group</u>					
40 – 49 years	142	$2.8\pm0.4$	$4.3\% \pm 0.5$	$3.7\pm0.5$	$5.6\%\pm0.7$
50 – 59 years	194	$2.1 \pm 0.3$	$2.9\% \pm 0.5^{*}$	$1.8 \pm 0.3$	$2.5\%\pm0.5^{*}$
60 + years	178	$0.5\pm0.3^{*}\varPhi$	$0.9\pm0.5$ $^{*}$ $\Phi$	$0.3\pm0.4^{*}$ $\varPhi$	$0.4\%\pm0.6~^{*}\varPhi$
P for trend		.0001	.0001	.0001	.0001
<u>Menopausal Status</u>					
Premenopausal	84	$1.6\pm0.5$	$2.4\% \pm 0.7$	$0.3 \pm 0.6$	$0.3\%\pm0.8$
Pre to Postmenopausal	LL	$3.0\pm0.5^{*}$	$4.1\%\pm0.8$	$1.5 \pm 0.6$	$2.0\%\pm0.8$
Postmenopausal	353	$1.5\pm0.2$ $\Phi$	$2.3\%\pm0.4~\varPhi$	$2.2\pm0.3^*$	$3.3\%\pm0.4^*$
Tamoxifen Use					
No Tamoxifen	267	$1.8\pm0.3$	$2.7\% \pm 0.4$	$1.9 \pm 0.3$	$2.8\%\pm0.4$
Tamoxifen	247	$1.7 \pm 0.3$	$2.4\% \pm 0.4$	$1.7 \pm 0.3$	$2.4 \% \pm 0.4$
Body Mass Index					
< 25.0 kg/m2	239	$1.7 \pm 0.3$	$2.9\%\pm0.4$	$1.7 \pm 0.3$	$3.0\%\pm0.4$
25.0 – 29.9 kg/m2	167	$1.5 \pm 0.4$	$2.1\%\pm0.5$	$1.7 \pm 0.3$	$2.4\%\pm0.5$
≥ 30.0 kg/m2	108	$2.2 \pm 0.4$	$2.5\%\pm0.6$	$1.8 \pm 0.4$	$2.0\%\pm0.6$
P for trend		.34	.60	.92	.20

	z	Un	Unadjusted	Ad	Adjusted <sup>I</sup>
		Mean ± SE	% Change ± SE	Mean ± SE	% Change ± SE
Ethnicity					
Non-Hispanic White	436	$1.9 \pm 0.2$	$2.7\% \pm 0.3$	$1.9\pm0.2$	$2.8\% \pm 0.3$
Hispanic White	78	$1.0\pm0.5$	$1.7\%\pm0.7$	$1.1\pm0.5$	$1.9\%\pm0.8$
Change in total caloric intake					
<-270 kcals	113	$1.1 \pm 0.4$	$1.6\% \pm 0.6$	$1.0 \pm 0.4$	$1.5\%\pm0.6$
-270 to 100 kcals	113	$2.7 \pm 0.4$	$3.8\%\pm0.6^*$	$3.0\pm0.4^*$	$4.0\%\pm0.6^*$
> 100 kcals	112	$2.1 \pm 0.4$	$3.2\%\pm0.6$	$2.1 \pm 0.4$	$3.2\% \pm 0.6^{*}$
P for trend		.14	.072	.083	.040
Change in sports hrs/wk					
≤0 hr/wk	204	$1.9 \pm 0.3$	$2.7\% \pm 0.5$	$2.2 \pm 0.3$	$3.2\%\pm0.5$
0.1 - 1.5 hr/wk	155	$2.1 \pm 0.4$	$3.0\% \pm 0.6$	$1.9 \pm 0.4$	$2.8\%\pm0.5$
$\geq 1.5 hr/wk$	155	$1.3 \pm 0.4$	$2.0\%\pm0.5$	$1.2\pm0.3^{*}$	$1.8\%\pm0.5^*$
P for trend		.18	.29	.032	.048

<sup>1</sup>Adjusted for disease stage, treatment, study site, smoking status, body mass index, tamoxifen use, age, menopausal status, change in total physical activity, change in total caloric intake, time from diagnosis to baseline interview, months from completing treatment, ethnicity, education, completed treatment, family history of breast cancer, family history of type 2 diabetes, physician-diagnosed type 2 diabetes, cardiovascular disease.

\* significantly different from first level and

 $\phi$  significantly different from second level using Tukey's Honestly Significant Difference with overall level of statistical significance constrained at 0.05.

## Table III

Weight change from baseline assessment to assessment conducted during year three following diagnosis in breast cancer survivors (N = 514).

	z	Unac	Unadjusted	Ρġ	Adjusted <sup>I</sup>
		Mean ± SE	% Change ± SE	Mean ± SE	% Change ± SE
<u>40 – 49 years</u>					
Premenopausal	72	$1.7 \pm 0.6$	$2.6\%\pm0.9$	$1.8 \pm 0.6$	$2.6\%\pm0.9$
Pre to Postmenopausal	46	$3.4 \pm 0.8$	$4.8\%\pm1.1$	$3.1 \pm 0.8$	$4.5\% \pm 1.1$
Postmenopausal	24	$5.2\pm1.0^{*}$	$8.4\%\pm1.5^{\ast}\varPhi$	$5.7\pm1.1^{*}$	$9.2\%\pm1.6^{*}\varPhi$
50-59 years					
Premenopausal	12	$0.8 \pm 1.3$	$1.6\%\pm1.8$	$0.1 \pm 1.4$	$0.4\% \pm 2.0$
Pre to Postmenopausal	31	$2.4 \pm 0.8$	$3.0\% \pm 1.1$	$1.7 \pm 0.9$	$2.1\% \pm 1.3$
Postmenopausal	151	$2.1 \pm 0.4$	$2.9\%\pm0.5$	$2.3 \pm 0.4$	$3.2\% \pm 0.5$
60 + years					
Premenopausal	0	NA	NA	NA	NA
Pre to Postmenopausal	0	NA	NA	NA	NA
Postmenopausal	178	$0.5\pm0.3$	$0.9\%\pm0.4$	$0.6 \pm 3.0$	$1.0\% \pm 0.4$
<u>Age (postmenopausal women only)</u>					
40 – 49 years	24	$5.2 \pm 1.4$	$8.4\% \pm 1.4$	$5.2 \pm 1.4$	$8.6\% \pm 1.4$
50 – 59 years	151	$2.1\pm0.4^{*}$	$2.9\%\pm0.6^{*}$	$2.1\pm0.4^{*}$	$2.9\%\pm0.6^*$
60 – 69 years	116	$0.8\pm0.4^{*}{\Phi}$	$1.2\%\pm0.6^{*}$	$1.0\pm0.4^{*}$	$1.4\% \pm 0.6^{*}$
70 – 79 years	47	$-0.1 \pm 0.6$ * $\Phi$	$0.1\%\pm0.9^{*}\varPhi$	$0.4\pm0.7$	$0.5\%\pm1.0^{*}$
80 + years	15	$0.5\pm1.1^{*}$	$1.0\%\pm1.6^*$	$0.5\pm1.2^{*}$	$0.8\%\pm1.7^*$
P for trend		.006	.0002	.002	.0003

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diagnosis to baseline interview, months from completing treatment, ethnicity, education, completed treatment, family history of breast cancer, family history of type 2 diabetes, physician-diagnosed type 2 Adjusted for disease stage, treatment, study site, smoking status, body mass index, tamoxifen use, age, menopausal status, change in total physical activity, change in total caloric intake, time from diabetes, cardiovascular disease

\* significantly different from first level;

 $\phi$  significantly different from second level using Tukey's Honestly Significant Difference with overall level of statistical significance constrained at 0.05.

# Table IV

Percent body fat change from baseline assessment to assessment conducted during year three following diagnosis in HEAL breast cancer survivors (N = 132).

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	Z	Un	Unadjusted	ΡV	Adjusted <sup>I</sup>
		$Mean \pm SE$	% Change ± SE	Mean ± SE	% Change $\pm$ SE
Disease Stage					
In Situ	28	$1.1 \pm 0.7$	$4.5\% \pm 2.7$	$1.3 \pm 0.8$	$4.6\% \pm 2.0$
Stage I	85	$2.1 \pm 0.4$	$8.0\%\pm1.6$	$2.4 \pm 0.4$	$9.0\%\pm1.5$
Stage II – IIIA	19	$3.2 \pm 0.9$	$10.3\% \pm 3.3$	$1.8 \pm 1.0$	$5.8\% \pm 3.7$
P for trend		.078	.18	.68	.82
Treatment					
Surgery only	39	$1.9 \pm 0.6$	$7.0\% \pm 2.3$	$2.2 \pm 0.7$	$8.4\pm2.6$
Surgery + Radiation	62	$1.6\pm0.5$	$6.7\%\pm1.9$	$2.0 \pm 0.5$	$8.3\pm1.8$
Any Chemotherapy	31	$3.2 \pm 0.7$	$10.0\% \pm 2.6$	$2.2 \pm 1.0$	$5.6 \pm 3.5$
Age Group					
40 – 49 years	36	$3.3\pm0.6$	$11.5\% \pm 2.4$	$3.4 \pm 0.8$	$10.3\%\pm2.9$
50 – 59 years	47	$2.1 \pm 0.6$	$8.5\% \pm 2.1$	$1.9 \pm 0.6$	$8.4\%\pm2.1^*$
60 + years	49	$1.2\pm0.5^*$	$3.8\pm2.0$	$1.3\pm0.6$	$5.2\%\pm2.2$
P for trend		.013	.017	.061	.21
<u>Menopausal Status</u>					
Premenopausal	21	$2.5 \pm 0.8$	$10.9\% \pm 3.1$	$2.0 \pm 0.9$	$5.0\%\pm3.9$
Pre to Postmenopausal	23	$3.4 \pm 0.8$	$12.6\% \pm 3.0$	$2.8 \pm 0.9$	$8.4\% \pm 3.4$
Postmenopausal	88	$1.6 \pm 0.4$	$5.5\% \pm 1.5$	$1.9 \pm 0.4$	$8.1\%\pm1.7$
Tamoxifen Use					
No Tamoxifen	LL	$2.1 \pm 0.4$	$8.7\% \pm 1.7$	$1.9 \pm 0.4$	$7.5\% \pm 1.6$
Tamoxifen	55	$1.9 \pm 0.5$	$6.0\% \pm 2.0$	$2.3\pm0.5$	$7.9 \% \pm 1.9$
<b>Body Mass Index</b>					
< 25.0 kg/m2	57	$3.3 \pm 0.5$	$13.9\%\pm1.8$	$3.2 \pm 0.6$	$13.3\%\pm2.0$
25.0 – 29.9 kg/m2	52	$1.1 \pm 0.5$	$2.9\%\pm1.9^*$	$1.2\pm0.6^{*}$	$3.5\%\pm2.0^{*}$
≥ 30.0 kg/m2	23	$1.1\pm0.8^*$	$2.4\% \pm 2.8^{*}$	$1.2\pm0.9^*$	$3.2\% \pm 3.1^{*}$
P for trend		.019	.00080	.050	.010

	Z	Un	Unadjusted	Ad	Adjusted <sup>I</sup>
		Mean ± SE	% Change ± SE	Mean ± SE	% Change $\pm$ SE
Ethnicity					
Non-Hispanic White	105	$2.2 \pm 0.4$	$8.4\%\pm1.4$	$2.0 \pm 0.4$	$8.0\% \pm 1.3$
Hispanic White	27	$1.3 \pm 0.7$	$4.3\% \pm 2.8$	$2.2 \pm 0.8$	$6.4\% \pm 2.8$
Change in total caloric intake					
< -200 kcals	28	$0.9 \pm 0.8$	$3.9\% \pm 3.0$	$1.0 \pm 0.9$	$3.9\% \pm 3.0$
-200 to 50 kcals	28	$3.1 \pm 0.8$	$12.7\% \pm 3.0^{*}$	$3.5 \pm 0.9$	$12.6\% \pm 3.0^{*}$
> 50 kcals	28	$2.4 \pm 0.8$	$7.3\% \pm 3.0$	$1.9 \pm 0.9$	$7.1\% \pm 3.0$
P for trend		.21	.42	.52	.49
Change in sports hrs/wk					
0 hr/wk	4	$3.1 \pm 0.6$	$12.1\% \pm 2.2$	$2.9 \pm 0.6$	$11.12\% \pm 2.2$
0.1 - 1.5 hr/wk	44	$1.5\pm0.6^{*}$	$4.2\% \pm 2.2^{*}$	$2.0\pm0.6$	$6.8\% \pm 2.1$
≥ 1.5 hr/wk	44	$1.6\pm0.6^{*}$	$6.5\%\pm2.2$	$1.3 \pm 0.6$	$5.2\% \pm 2.0^{*}$
P for trend		.051	.067	.051	.047

<sup>1</sup>Adjusted for disease stage, treatment, study site, smoking status, body mass index, tamoxifen use, age, menopausal status, change in total physical activity, change in total caloric intake, time from diagnosis to baseline interview, months from completing treatment, ethnicity, education, completed treatment, family history of breast cancer, family history of type 2 diabetes, physician-diagnosed type 2 diabetes, cardiovascular disease.

\* significantly different from first level;  $\phi$  significantly different from second level using Tukey's Honestly Significant Difference with overall level of statistical significance constrained at 0.05.