

# A Prospective Study of Weight Gain in Women Diagnosed with Early-Stage Invasive Breast Cancer, Ductal Carcinoma *In Situ*, and Women Without Breast Cancer

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## Abstract

**Background:** Weight gain after breast cancer has been associated with recurrence and mortality. We therefore examined factors associated with  $\geq 5\%$  weight gain over 2-year follow-up of a cohort of newly diagnosed early-stage invasive breast cancer (EIBC) and ductal carcinoma *in situ* (DCIS) patients and age-matched controls without a breast cancer history.

**Materials and Methods:** We interviewed participants 4–6 weeks after definitive surgical treatment (patients) or a negative/benign screening mammogram (controls). Multivariable logistic regression models were used to identify socioeconomic, psychosocial, and treatment factors associated with  $\geq 5\%$  weight gain over 2-year follow-up.

**Results:** Overall, 88 (24%) of 362 EIBC patients, 31 (17%) of 178 DCIS patients, and 82 (15%) of 541 controls had  $\geq 5\%$  weight gain during follow-up. EIBC patients were more likely to experience  $\geq 5\%$  weight gain than DCIS patients (Odds ratio [OR] = 2.16; 95% confidence interval [95% CI] = 1.19–3.95) and controls (OR = 1.76; 95% CI = 1.23–2.51). Among EIBC patients, older patients (OR = 0.96; 95% CI = 0.93–0.99), patients who underwent endocrine therapy (OR = 0.43; 95% CI = 0.19–0.95), smokers (OR = 0.35; 95% CI = 0.14–0.86), and African Americans (OR = 0.23; 95% CI = 0.09–0.58) were less likely to have  $\geq 5\%$  weight gain than their respective counterparts. Among DCIS patients, older patients (OR = 0.94; 95% CI = 0.89–0.99) were less likely to have  $\geq 5\%$  weight gain. Among controls, smokers were more likely to have  $\geq 5\%$  weight gain (OR = 3.03; 95% CI = 1.49–6.17).

**Conclusions:** EIBC patients were more likely than DCIS patients and controls to experience  $\geq 5\%$  weight gain over follow-up. Studies are necessary to elucidate mechanisms of weight gain in early-stage breast cancer survivors.

**Keywords:** breast cancer, weight gain, ductal carcinoma *in situ* (DCIS), early-stage breast cancer (EIBC), estrogen receptor

## Introduction

WEIGHT GAIN IS common following breast cancer treatment.<sup>1</sup> Weight gain in breast cancer patients is of particular concern because of its impact on prognosis, self-image, and quality of life.<sup>2</sup> Prior studies have shown that the onset of menopause and the receipt of adjuvant chemotherapy are risk factors for weight gain in breast cancer patients, with the most significant weight gain observed in women undergoing cytotoxic therapies and women treated with

both chemotherapy and hormonal treatment.<sup>2–4</sup> Proposed mechanisms of breast cancer-related weight gain include chemotherapy-related amenorrhea and insulin resistance.<sup>5,6</sup> In addition, declines in physical activity or inactivity after diagnosis may also contribute significantly to weight gain.<sup>5,6</sup> As studies have shown that patients are unlikely to return to prediagnosis weight after gaining weight,<sup>5,7</sup> it has become increasingly important to identify at-risk patients and potential targets for interventions to combat weight gain in breast cancer patients.

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Patients with incident ductal carcinoma *in situ* (DCIS) have a clinical diagnosis distinct from patients with early-stage invasive breast cancer (EIBC). DCIS patients also have a much better prognosis than EIBC patients, irrespective of treatment administered.<sup>8,9</sup> Although some longitudinal studies have compared weight gain in breast cancer patients and women without a history of breast cancer, results are mixed,<sup>3,10,11</sup> and few have evaluated whether there are differences in weight gain between DCIS and EIBC patients. We hypothesize that EIBC patients would gain more weight over time than both DCIS patients and cancer-free women. Therefore, the purpose of this study was to (a) examine differences in weight gain over 2 years in EIBC patients, DCIS patients, and an age-matched control group of women without a history of breast cancer, and (b) to identify sociodemographic, psychosocial, and treatment factors associated with weight gain within these three groups. Identifying risk factors within each of the three groups of participants will allow for the development of strategies to minimize weight gain after a breast cancer diagnosis.

## Materials and Methods

### Participants

We conducted a secondary analysis of data collected for a study which was designed to examine changes in quality of life in a cohort of first primary DCIS (stage 0) and EIBC (stages 1–2A) cases and of age-matched women without a history of any breast cancer.<sup>12</sup> Between October 2003 and June 2007, study participants were recruited from two sites in St. Louis, Missouri: Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine and Saint Louis University School of Medicine. Breast cancer stage was determined by surgical pathology. We included women at least 40 years of age without a breast cancer history; we excluded patients who had received neoadjuvant chemotherapy and who did not speak English. Age-matched controls were identified within 2 weeks of a negative or benign screening mammogram. The study enrolled a total of 365 EIBC patients, 184 DCIS patients, and 547 controls.

Participants completed four, 45–60 minutes computer-assisted telephone interviews at 4–6 weeks after definitive surgical treatment (patients) or screening mammogram (controls) and then at 6-, 12-, and 24-month follow-up. Detailed recruitment and interview procedures have been published previously.<sup>12,13</sup> Informed consent was obtained from all participants, and the study was approved by the Institutional Review Boards at both institutions.

### Measures

For this analysis, the primary outcome of interest was  $\geq 5\%$  weight gain after 2 years of follow-up. At each interview, weight was ascertained using a question from the CDC Behavioral Risk Factor Surveillance System.<sup>14</sup> Study participants were asked “About how much do you weigh without shoes?” Weight gain was calculated using percent weight change ( $[24\text{-month weight} - \text{baseline weight}] / \text{baseline weight} \times 100$ ), and analyzed as a dichotomous outcome:  $\geq 5\%$  versus  $< 5\%$  weight gain. Weight gain of  $\geq 5\%$  is considered clinically significant,<sup>15,16</sup> and this cut-point has been widely

used in previous studies of weight gain and health outcomes in breast cancer survivors.<sup>7,17</sup>

Sociodemographic information collected from interviews included age at enrollment, race, marital status, education, health insurance status, employment status, household income, menopausal status at enrollment, body mass index (BMI), and smoking status. Using a validated questionnaire based on the Charlson comorbidity index, we determined the severity of comorbidity.<sup>18,19</sup> Social support was assessed using the Medical Outcomes Study (MOS) Social Support Survey, with higher scores indicating more social support.<sup>20</sup> Elevated depressed mood was defined as a Center for Epidemiologic Studies-Depression score of 16 or higher.<sup>21,22</sup> We used the eight subscales (physical functioning, role limitations due to physical problems, role limitations due to emotional health, vitality, emotional well-being, social functioning, pain, and general health) of the RAND 36-Item Health Survey subscales to evaluate quality of life.<sup>23–25</sup> Patients’ clinical data obtained from medical records included estrogen receptor (ER) status (positive or negative), cancer stage, surgery type (lumpectomy or mastectomy), and receipt of adjuvant endocrine therapy, adjuvant radiation or chemotherapy during the study. We evaluated surgical side effects severity using a list of eight commonly reported side effects derived from the literature, which we previously validated.<sup>13</sup>

### Statistical analyses

Chi-square and Kruskal–Wallis tests were used to compare baseline characteristics across the three diagnostic groups: EIBC, DCIS, and controls. Multivariable logistic regression was first used to evaluate the association between diagnostic group and  $\geq 5\%$  weight gain, estimating adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for  $\geq 5\%$  weight gain for each patient group relative to controls. Potential confounders included the sociodemographic factors, psychosocial factors and treatment such as radiation, chemotherapy, and endocrine therapy. We used directed acyclic graphs to determine the minimally sufficient set of confounders.<sup>26,27</sup> Thus, the adjusted models included BMI (obese [ $\geq 30 \text{ kg/m}^2$ ] and overweight [ $25$  to  $< 30 \text{ kg/m}^2$ ]), race (African American vs. white, excluding 13 participants from other racial/ethnic groups because of small numbers), marital status (married/partnered vs. not married/not partnered), education (high school graduate or less education vs. more than high school), annual household income ( $< \$50,000$  and refused to answer, each vs.  $\geq \$50,000$ ), smoking status (current, former, vs. never), age at enrollment, and the vitality subscale of the RAND SF-36 Health Survey (hereafter referred to as vitality), an established measure of energy/fatigue, with higher scores indicating more energy and less fatigue (range 0–100).

We further evaluated weight gain among the three diagnostic groups (EIBC, DCIS and controls) separately using stratified logistic regression models to identify independent predictors within each group. For the patient (EIBC and DCIS) groups, models were further adjusted for treatment received (endocrine therapy, radiation, and chemotherapy). Weight gain in postmenopausal women is a risk factor for cancer-related outcomes.<sup>28,29</sup> Thus, we further stratified EIBC models by menopausal status to investigate potential differences

TABLE 1. CHARACTERISTICS OF THE STUDY SAMPLE BY DIAGNOSTIC GROUP

	<i>EIBC</i> N = 362	<i>DCIS</i> N = 178	<i>Control</i> N = 541	p <sup>a</sup>
	Median (IQR)			
Age	58 (51, 66)	55 (49, 64)	55 (49, 64)	<b>0.04</b>
Vitality	52.5 (35, 70)	55 (40, 75)	65 (50, 80)	<b>&lt;0.001</b>
	N (%) <sup>b</sup>			
Weight change				<b>0.002</b>
Weight gain ≥5% body weight	88 (24.3)	31 (17.4)	82 (15.2)	
Weight gain <5% body weight	274 (75.7)	147 (82.6)	459 (84.8)	
BMI				0.87
Obese (≥30 kg/m <sup>2</sup> )	121 (33.4)	63 (35.4)	171 (31.6)	
Overweight (25 to <30 kg/m <sup>2</sup> )	113 (31.2)	53 (29.8)	165 (30.5)	
Normal weight (<25 kg/m <sup>2</sup> )	128 (35.4)	62 (34.8)	205 (37.9)	
Race				<b>0.01</b>
African American	69 (19.1)	32 (18.0)	143 (26.4)	
White	293 (80.9)	146 (82.0)	398 (73.6)	
Marital status				0.59
Married	214 (59.1)	112 (62.9)	336 (62.1)	
Not married	148 (40.9)	66 (37.1)	205 (37.9)	
Education				<b>0.04</b>
≤High school	116 (32.0)	52 (29.2)	135 (25.0)	
>High school	246 (68.0)	126 (70.8)	405 (75.0)	
Income				<b>0.03</b>
<\$50,000	183 (50.6)	84 (47.2)	223 (41.2)	
Refused	30 (8.3)	12 (6.7)	36 (6.7)	
≥\$50,000	149 (41.2)	82 (46.1)	282 (52.1)	
Smoking status				0.47
Current smoker	52 (14.4)	18 (10.1)	64 (11.8)	
Former smoker	111 (30.7)	63 (35.4)	189 (34.9)	
Never smoker	199 (55.0)	97 (54.5)	288 (53.2)	
Menopausal status <sup>c</sup>				0.17
Premenopausal	88 (24.3)	54 (30.3)	147 (27.2)	
Postmenopausal	273 (75.7)	122 (69.3)	393 (72.8)	
Surgery type				0.16
Breast-conserving surgery	242 (66.9)	108 (60.7)	—	
Mastectomy	120 (33.2)	70 (39.3)	—	
Estrogen receptor status <sup>d</sup>				<b>&lt;0.0001</b>
ER-positive	282 (80.1)	85 (75.9)	—	
ER-negative	70 (19.9)	27 (24.1)	—	
Radiation				<b>0.02</b>
Yes	243 (67.1)	101 (56.7)	—	
No	119 (32.9)	77 (42.3)	—	
Chemotherapy and Endocrine therapy <sup>e</sup>				<b>&lt;0.0001</b>
Both	80 (22.2)	0 (0)	—	
Chemotherapy only	54 (15.0)	0 (0)	—	
Endocrine therapy only	182 (50.4)	77 (44.3)	—	
No	45 (12.5)	97 (55.8)	—	

<sup>a</sup>p value derived from Kruskal–Wallis test for continuous variables and Chi-square tests for categorical variables. Bold type indicates statistical significance at  $p < 0.05$ .

<sup>b</sup>Percentages may not sum up to 100% due to rounding.

<sup>c</sup>Data for menopausal status were missing for four patients (one DCIS, one EIBC, and two Controls).

<sup>d</sup>Data for estrogen receptor status were missing for 76 patients (66 DCIS and 10 EIBC).

<sup>e</sup>Data for endocrine therapy or chemotherapy were missing for five patients (four DCIS and one EIBC).

EIBC, early-invasive breast cancer; DCIS, ductal carcinoma *in situ*; IQR, interquartile range; BMI, body mass index.

in associations with weight gain as reported in previous studies.<sup>30–32</sup> Finally, sensitivity analyses were performed by excluding patients who experienced  $\geq 5\%$  weight loss between baseline and 2 years. Stata version 14 was used for all statistical analyses. Two-tailed tests of significance at  $p < 0.05$  were considered significant.

## Results

### Characteristics of the study sample

The sample's baseline characteristics are described in Table 1. Median age at enrollment for EIBC patients was higher than for DCIS patients and controls, while baseline vitality scores were lower for EIBC patients than for DCIS patients and controls. In addition, greater proportions of EIBC patients reported  $\leq$  high school education and annual household income  $< \$50,000$  compared with DCIS patients and controls. A higher percentage of DCIS patients reported lower education and lower household income than the control group. EIBC patients (80%) were more likely to have ER-positive tumors than DCIS patients (76%). A greater proportion of EIBC patients (67%) received radiation compared with DCIS patients (57%). Approximately 14% of EIBC patients received only chemotherapy treatment, whereas DCIS patients did not receive chemotherapy. BMI, marital status, smoking status, and menopausal status did not differ significantly among the three diagnostic groups at baseline.

### Weight gain among EIBC patients, DCIS patients, and controls

At the 2-year follow-up,  $\sim 24\%$  of EIBC patients, 17% of DCIS patients, and 15% of controls gained  $\geq 5\%$  body weight during follow-up (Fig. 1). In multivariable models, EIBC patients were 1.8 times more likely to experience  $\geq 5\%$  weight gain than controls (Table 2). In addition, EIBC patients were

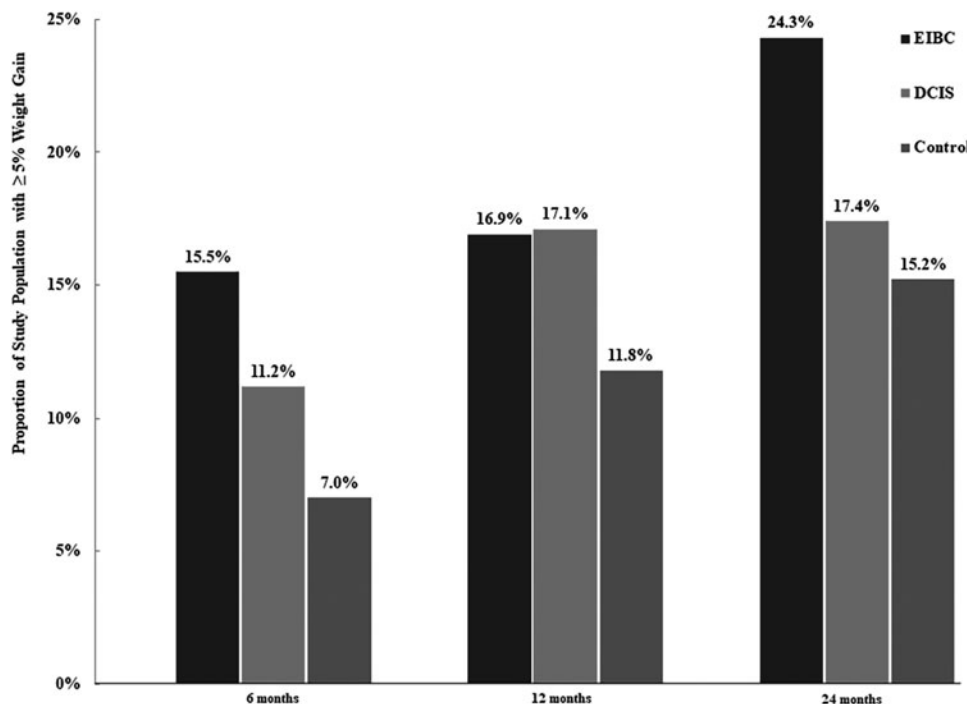
2.2 times more likely to experience  $\geq 5\%$  weight gain compared with DCIS patients (OR = 2.16, 95% CI = 1.19–3.95). Patients who underwent radiation were more likely to experience  $\geq 5\%$  weight gain than those who did not (OR = 1.74, 95% CI = 1.06–2.87). African American women were 55% less likely to have  $\geq 5\%$  weight gain than white women (Table 2). Results of the sensitivity analysis excluding patients who experienced  $\geq 5\%$  weight loss were robust and consistent with the results from the primary model. (Supplementary Table 1).

As shown in Table 3, among EIBC patients, older patients, African American (vs. white) patients, and current (vs. never) smokers were less likely to have  $\geq 5\%$  weight gain. EIBC patients who underwent endocrine therapy were also less likely to experience  $\geq 5\%$  weight gain. Among DCIS patients, age was inversely associated with weight gain. Among controls, current (vs. never) smokers were three times more likely to gain weight than never smokers. For EIBC patients, sensitivity analysis further confirmed the effects of age, race, and endocrine therapy on weight gain (Supplementary Table 2).

### Menopausal status and weight gain in EIBC patients

Approximately 17% ( $n=62$ ) of EIBC patients changed from pre- to postmenopausal over the follow-up period; 22 (35%) of these patients experienced  $\geq 5\%$  weight gain. Women who became postmenopausal during follow-up were twice as likely to experience  $\geq 5\%$  weight gain as women who were postmenopausal at study onset (OR = 2.04, 95% CI = 1.04–4.01, data not shown). Because of small numbers, we were unable to further evaluate factors associated with weight gain among premenopausal women and women who experienced menopause during the study period.

Among postmenopausal EIBC patients, African American (vs. white) women were less likely to have  $\geq 5\%$  weight gain,



**FIG. 1.** Proportion of Study Population with  $\geq 5\%$  Weight Gain by Diagnostic Group.

TABLE 2. LOGISTIC REGRESSION FOR THE RELATIONSHIP BETWEEN SELECTED CHARACTERISTICS AND  $\geq 5\%$  WEIGHT GAIN

	Weight gain $\geq 5\%$ body weight (N = 201)	No weight gain <5% body weight (N = 880)	All groups OR (95% CI) <sup>a</sup> (N = 1,081)	EIBC vs. DCIS OR (95% CI) <sup>b</sup> (N = 540)
Age, median (IQR)	55 (49, 62)	57 (50, 65.5)	<b>0.97 (0.95–0.99)</b>	<b>0.96 (0.93–0.98)</b>
Vitality, median (IQR)	55 (40, 75)	60 (45, 75)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
N (%) <sup>c</sup>				
Diagnostic group				
EIBC	88 (43.8)	274 (31.1)	<b>1.76 (1.23–2.51)</b>	<b>2.16 (1.19–3.95)</b>
DCIS	31 (15.4)	147 (16.7)	1.08 (0.68–1.72)	Reference
Control	82 (40.8)	459 (52.2)	Reference	—
BMI				
Obese ( $\geq 30$ kg/m <sup>2</sup> )	66 (32.8)	289 (32.8)	1.12 (0.75–1.65)	0.88 (0.52–1.50)
Overweight (25 to <30 kg/m <sup>2</sup> )	61 (30.4)	270 (30.7)	1.13 (0.77–1.67)	1.00 (0.58–1.73)
Normal weight (<25 kg/m <sup>2</sup> )	74 (36.8)	321 (36.5)	Reference	Reference
Race				
African American	30 (14.9)	214 (24.3)	<b>0.45 (0.28–0.72)</b>	<b>0.28 (0.13–0.60)</b>
White	171 (85.1)	666 (75.7)	Reference	Reference
Marital status				
Married	119 (59.2)	543 (61.7)	0.78 (0.53–1.15)	0.87 (0.51–1.50)
Not married	82 (40.8)	337 (38.3)	Reference	Reference
Education				
$\leq$ High school	52 (25.9)	251 (28.6)	0.93 (0.64–1.37)	0.90 (0.53–1.48)
>High school	149 (74.1)	628 (71.4)	Reference	Reference
Income				
<\$50,000	93 (46.3)	397 (45.1)	1.24 (0.82–1.87)	1.65 (0.95–2.87)
Refused	14 (7.0)	64 (7.3)	1.25 (0.65–2.38)	2.04 (0.87–4.78)
$\geq$ \$50,000	94 (46.8)	419 (47.6)	Reference	Reference
Smoking status				
Current smoker	30 (14.9)	104 (11.8)	1.19 (0.73–1.95)	<b>0.37 (0.17–0.81)</b>
Former smoker	67 (33.3)	296 (33.6)	1.10 (0.77–1.55)	0.98 (0.61–1.58)
Never smoker	104 (51.7)	480 (54.6)	Reference	Reference
Radiation				
Yes	85 (71.4)	259 (61.5)	—	<b>1.74 (1.06–2.87)</b>
No	34 (28.6)	162 (38.5)	—	Reference
Chemotherapy and endocrine therapy				
Both	20 (17.2)	60 (14.3)	—	0.52 (0.23–1.17)
Chemotherapy only	17 (14.7)	37 (8.8)	—	1.01 (0.43–2.37)
Endocrine therapy only	49 (42.2)	210 (50.1)	—	0.55 (0.30–1.01)
No	30 (25.9)	112 (26.7)	—	Reference

<sup>a</sup>Adjusted for age, vitality, BMI, race, marital status, education, income, and smoking status. Bold type indicates statistical significance at  $p < 0.05$ .

<sup>b</sup>Adjusted for age, vitality, BMI, race, marital status, education, income, smoking status, and treatment type. Bold type indicates statistical significance at  $p < 0.05$ .

<sup>c</sup>Percentages may not sum up to 100% due to rounding.

OR, odds ratio; CI, confidence interval.

and patients who underwent endocrine therapy were less likely to have  $\geq 5\%$  weight gain (Table 4). In addition, lower (<\$50,000) income was associated with an increased likelihood of  $\geq 5\%$  weight gain. Sensitivity analysis confirmed the effects of race, income, and endocrine therapy for postmenopausal EIBC patients (Supplementary Table 3).

## Discussion

In this 2-year study of newly diagnosed early-stage breast cancer patients and age-matched controls, we found that

EIBC patients were 1.8 times more likely than controls without a history of breast cancer and twice as likely as DCIS patients to report  $\geq 5\%$  weight gain. There was no significant difference in likelihood of  $\geq 5\%$  weight gain between DCIS patients and controls, and vitality was not associated with weight gain. We also observed that African American participants were 55% less likely to report  $\geq 5\%$  weight gain over the 2-year follow-up period than white participants. We discuss our findings in the context of the literature to date regarding differences in weight gain by diagnostic group, race/ethnicity, smoking, and treatment.

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION MODELS FOR THE RELATIONSHIP BETWEEN SELECTED CHARACTERISTICS AND  $\geq 5\%$  WEIGHT GAIN, STRATIFIED BY DIAGNOSTIC GROUP

	EIBC			DCIS			Controls		
	Weight gain $\geq 5\%$ (N=88)	Weight gain <5% (N=274)	OR (95% CI) <sup>a</sup>	Weight gain $\geq 5\%$ (N=31)	Weight gain <5% (N=147)	OR (95% CI) <sup>a</sup>	Weight gain $\geq 5\%$ (N=82)	Weight gain <5% (N=459)	OR (95% CI) <sup>b</sup>
	Median (IQR)			Median (IQR)			Median (IQR)		
Age	56 (49, 62)	59 (51, 67)	<b>0.96 (0.93–0.99)</b>	53 (47, 59)	56 (50, 65)	<b>0.94 (0.89–0.99)</b>	54.5 (48, 62)	55 (49, 65)	0.98 (0.96–1.01)
Vitality	50 (35, 70)	55 (35, 70)	1.00 (0.99–1.01)	50 (25, 70)	55 (40, 75)	0.99 (0.97–1.01)	62.5 (50, 80)	65 (50, 80)	1.00 (0.99–1.02)
	N (%) <sup>c</sup>			N (%) <sup>c</sup>			N (%) <sup>c</sup>		
BMI									
Obese ( $\geq 30$ kg/m <sup>2</sup> )	24 (27.3)	97 (35.4)	0.81 (0.43–1.51)	13 (41.9)	50 (34.0)	1.84 (0.60–5.64)	29 (35.4)	142 (30.9)	1.64 (0.89–3.08)
Overweight (25 to <30 kg/m <sup>2</sup> )	25 (28.4)	88 (32.1)	0.66 (0.35–1.24)	10 (32.3)	43 (29.3)	1.70 (0.54–5.37)	26 (31.7)	138 (30.3)	1.50 (0.81–2.76)
Normal weight ( $< 25$ kg/m <sup>2</sup> )	39 (44.3)	89 (32.5)	Reference	8 (25.8)	54 (36.7)	Reference	27 (32.9)	178 (38.8)	Reference
Race									
African American	9 (10.2)	60 (21.9)	<b>0.23 (0.09–0.58)</b>	3 (9.7)	29 (19.7)	0.47 (0.12–1.87)	18 (22.0)	125 (27.2)	<b>0.49 (0.25–0.98)</b>
White	79 (89.8)	214 (78.1)	Reference	28 (90.3)	118 (80.3)	Reference	64 (78.0)	334 (72.8)	Reference
Marital status									
Married	51 (58.0)	163 (59.5)	0.74 (0.39–1.42)	21 (67.7)	91 (61.9)	1.67 (0.57–4.88)	47 (57.3)	289 (63.0)	0.63 (0.35–1.13)
Not married	37 (42.1)	111 (40.5)	Reference	10 (32.3)	56 (38.1)	Reference	35 (42.7)	170 (37.0)	Reference
Education									
$\leq$ High school	24 (27.3)	92 (33.6)	0.74 (0.40–1.36)	9 (29.0)	43 (29.3)	1.20 (0.45–3.23)	19 (23.2)	116 (25.3)	1.04 (0.56–1.96)
>High school	64 (72.7)	182 (66.4)	Reference	22 (71.0)	104 (70.8)	Reference	63 (76.8)	342 (74.7)	Reference
Income									
<\$50,000	45 (51.1)	138 (50.4)	1.73 (0.89–3.36)	16 (51.6)	68 (46.3)	1.89 (0.66–5.43)	32 (39.0)	191 (41.6)	0.72 (0.37–1.42)
Refused	8 (9.0)	22 (8.0)	1.95 (0.73–5.20)	2 (6.5)	10 (6.8)	2.03 (0.31–13.18)	4 (4.9)	32 (7.0)	0.68 (0.22–2.10)
$\geq$ \$50,000	35 (39.8)	114 (41.6)	Reference	13 (41.9)	69 (47.9)	Reference	46 (56.1)	236 (51.4)	Reference
Smoking status									
Current smoker	9 (10.2)	43 (25.7)	<b>0.35 (0.14–0.86)</b>	3 (9.7)	15 (10.2)	0.75 (0.17–3.70)	18 (22.0)	46 (10.0)	<b>3.03 (1.49–6.17)</b>
Former smoker	29 (33.0)	82 (29.9)	1.03 (0.59–1.82)	10 (32.3)	53 (36.1)	0.88 (0.34–2.27)	28 (34.2)	161 (35.1)	1.33 (0.76–2.30)
Never smoker	50 (56.8)	149 (54.4)	Reference	18 (58.1)	79 (53.7)	Reference	36 (43.9)	252 (54.9)	Reference
Radiation									
Yes	65 (73.9)	178 (65.0)	1.71 (0.95–3.09)	20 (64.5)	81 (55.1)	1.37 (0.50–3.75)	—	—	—
No	23 (26.1)	96 (35.0)	Reference	11 (35.5)	66 (44.9)	Reference	—	—	—
Chemotherapy and endocrine therapy									
Both	20 (23.0)	60 (21.9)	0.44 (0.18–1.11)	0	0	—	—	—	—
Chemotherapy	17 (19.5)	37 (13.5)	0.88 (0.34–2.29)	0	0	—	—	—	—
Endocrine therapy	36 (41.4)	146 (53.3)	<b>0.43 (0.19–0.95)</b>	13 (44.8)	64 (44.1)	0.99 (0.37–2.65)	—	—	—
No	14 (16.1)	31 (11.3)	Reference	16 (55.2)	81 (55.9)	Reference	—	—	—

<sup>a</sup>Adjusted for age, vitality, BMI, race, marital status, education, income, smoking status, and treatment type. Bold type indicates statistical significance at  $p < 0.05$ .<sup>b</sup>Adjusted for age, vitality, BMI, race, marital status, education, income, and smoking status. Bold type indicates statistical significance at  $p < 0.05$ .<sup>c</sup>Percentages may not sum up to 100% due to rounding.

TABLE 4. LOGISTIC REGRESSION FOR THE RELATIONSHIP BETWEEN SELECTED CHARACTERISTICS AND  $\geq 5\%$  WEIGHT GAIN IN POSTMENOPAUSAL EARLY-INVASIVE BREAST CANCER PATIENTS

	Weight gain $\geq 5\%$ (N=59)	Weight gain $< 5\%$ (N=214)	OR (95% CI) <sup>a</sup>
	Median (IQR)		
Age	61 (56, 68)	62 (56, 69)	0.97 (0.93–1.01)
Vitality	50 (40, 75)	55 (35, 70)	1.00 (0.99–1.02)
	N (%) <sup>b</sup>		
BMI			
Obese ( $\geq 30$ kg/m <sup>2</sup> )	16 (27.1)	80 (37.4)	0.51 (0.23–1.12)
Overweight (25 to $< 30$ kg/m <sup>2</sup> )	17 (28.8)	73 (34.1)	0.66 (0.31–1.41)
Normal weight ( $< 25$ kg/m <sup>2</sup> )	26 (44.1)	61 (28.5)	Reference
Race			
African American	6 (10.2)	46 (21.5)	<b>0.26 (0.09–0.77)</b>
White	53 (89.8)	168 (78.5)	Reference
Marital status			
Married	31 (52.5)	125 (58.4)	0.81 (0.37–1.77)
Not married	28 (47.5)	89 (41.6)	Reference
Education			
$\leq$ High school	39 (66.1)	134 (62.6)	0.77 (0.39–1.54)
$>$ High school	20 (33.9)	80 (37.4)	Reference
Income			
$<$ \$50,000	36 (61.0)	111 (51.9)	<b>2.34 (1.03–5.31)</b>
Refused	7 (11.9)	20 (9.4)	2.04 (0.67–6.15)
$\geq$ \$50,000	16 (27.1)	83 (38.8)	Reference
Smoking status			
Current smoker	9 (15.3)	31 (14.5)	0.66 (0.24–1.79)
Former smoker	22 (37.3)	68 (31.8)	1.14 (0.59–2.24)
Never smoker	28 (47.5)	115 (53.7)	Reference
Radiation			
Yes	42 (71.2)	144 (67.3)	1.19 (0.59–2.40)
No	17 (28.8)	70 (32.7)	Reference
Chemotherapy			
Both	12 (20.7)	40 (18.7)	0.54 (0.18–1.59)
Chemotherapy only	9 (15.5)	23 (10.8)	0.92 (0.29–2.85)
Endocrine therapy only	25 (43.1)	126 (58.9)	<b>0.40 (0.17–0.95)</b>
No	12 (20.7)	25 (11.7)	Reference

<sup>a</sup>Adjusted for age, vitality, BMI, race, marital status, education, income, smoking status, and treatment type. Bold type indicates statistical significance at  $p < 0.05$ .

<sup>b</sup>Percentages may not sum up to 100% due to rounding.

We are aware of only three studies comparing weight gain in early-stage breast cancer patients with cancer-free controls. Two previous studies of weight gain after 6 months<sup>3</sup> and 6 years<sup>10</sup> of follow-up found no significant differences in weight gain between women with breast cancer and women without breast cancer. In a cohort study of women with a family history of breast cancer, breast cancer survivors had an increased likelihood for  $\geq 5\%$  weight gain over 4 years of follow-up than controls without breast cancer.<sup>11</sup> To our knowledge, our study is the first to examine differences in weight gain among EIBC and DCIS patients and controls without a history of breast cancer. While EIBC patients were more likely to report  $\geq 5\%$  weight gain compared with controls, the odds of  $\geq 5\%$  weight gain experienced by DCIS patients over 2-year follow-up was similar to that of controls.

In our study, a higher proportion of African American than white women were obese at enrollment (54% and 27%, respectively), similar to higher obesity rates observed in black

and Hispanic women compared with white women in the United States.<sup>33</sup> African American women in our study were less likely to have  $\geq 5\%$  weight gain than white women, which was observed in the model with all three diagnostic groups, and this inverse association was statistically significant in the stratified model that included only EIBC patients. Some, but not all, studies have reported that nonwhite women from various racial/ethnic groups were less likely than white women to gain weight following breast cancer diagnosis and treatment. A retrospective cohort study of 1,282 long-term ( $> 5$  years) breast cancer survivors treated in Houston, TX observed that Asian women had a lower risk of  $\geq 5\%$  weight gain than white women.<sup>31</sup> Across the four U.S. sites of the ENERGY trial, Hispanic women had a lower odds of gaining  $\geq 5\%$  of body weight than non-Hispanic white women after an average of 2.65 years of follow-up; and in this study, Hispanic women had higher rates of obesity than non-Hispanic white women.<sup>34</sup> Race was not a significant predictor of  $\geq 5\%$

weight gain in either the WHEL study or the SUNSHINE study.<sup>7,10</sup> Furthermore, these studies evaluating the relationship between race and  $\geq 5\%$  weight gain in breast cancer survivors were conducted with samples of women residing in southern and southwestern regions of the United States. Results from our study in the Midwest suggest that further research of racially/ethnically diverse samples in different regions across the United States may be warranted to identify possible geographic variation in  $\geq 5\%$  weight gain in specific groups of breast cancer survivors and explanatory factors amenable to intervention.

In the stratified model among EIBC patients in our study, weight gain varied by smoking status; patients who were current smokers at diagnosis were less likely to experience  $\geq 5\%$  weight gain than patients who had never smoked. These results contrast with those of the ENERGY trial, in which, among patients, smoking at diagnosis was associated with a 2.7-fold increased risk for  $\geq 5\%$  weight gain when compared to never smokers.<sup>34</sup> This finding from the ENERGY trial is similar to our findings among the controls, who were three times more likely than never smokers to experience  $\geq 5\%$  weight gain. Due to the small sample of EIBC patients who were current smokers at time of diagnosis and experienced  $\geq 5\%$  weight gain ( $n=9$ ), our results should be interpreted with caution. Continued smoking after a breast cancer diagnosis has been discouraged because of associations with treatment toxicity, cancer recurrence, and breast cancer mortality.<sup>35,36</sup> If women in our study quit smoking after diagnosis in adherence to survivorship recommendations, this might explain our findings. Previous studies have shown that smoking cessation is associated with weight gain in women.<sup>37–39</sup> However, we were unable to examine the relationship between postdiagnosis smoking patterns and weight gain due to limitations of small sample size.

Several studies have examined the relationship between various treatments and weight gain after breast cancer with mixed results.<sup>7,10,11,34,40–49</sup> We and others have found that chemotherapy was not an independent predictor of  $\geq 5\%$  weight gain.<sup>10,34</sup> Although we did not observe any significant relationships between adjuvant radiation and chemotherapy and weight gain in EIBC patients, we found that endocrine therapy was inversely associated with  $\geq 5\%$  weight gain in models that adjusted for these other treatments. Patients with ER-negative tumors, for whom endocrine therapy is not indicated, have been found to have significant weight gain after diagnosis.<sup>11,30</sup> Although most breast tumors are hormone-receptor-positive subtypes (about 80% are estrogen- and/or progesterone-receptor positive),<sup>50</sup> women with ER-negative tumors are at elevated risk of adverse cancer-related outcomes, which might be true especially for survivors with significant weight gain. For example, women with ER-negative tumors who experienced postdiagnosis weight gain were reported to be at increased risk for subsequent contralateral breast cancer.<sup>30,51</sup>

A novel finding of our study is that income was associated with  $\geq 5\%$  weight gain in postmenopausal EIBC patients. Lower income ( $< \$50,000$ ) EIBC patients were twice more likely to report  $\geq 5\%$  weight gain than higher income patients. A potential mechanism between low-income status and postdiagnosis weight gain may be environmental stress. Neighborhood environmental factors (*i.e.*, adverse socioeconomic conditions and the built environment), for example, have

been associated with weight gain among women in the general U.S. population.<sup>52,53</sup> However, it is unknown whether neighborhood-level factors influence weight gain in breast cancer patients in addition to individual-level (*e.g.*, psychosocial, clinical, and treatment) factors. Further work should examine the role of environmental factors in weight gain after breast cancer.

Strengths of our study include the longitudinal study design, the large samples of women with incident EIBC and DCIC, and the inclusion of a large, age-matched control group of women without a breast cancer history. Our diverse study sample (22% African American and 44% with annual income  $< \$50,000$ ) allowed for sociodemographic subgroup comparisons. We collected detailed data about participants' sociodemographic, psychosocial, clinical, and treatment characteristics from medical records, which allowed us to examine relationships between these factors and weight gain. Nevertheless, our study also has limitations. All participants were recruited from two academic medical centers, and one is a National Cancer Institute-designated comprehensive cancer center; thus, findings may not be generalizable to patients recruited from community or rural hospitals or from other regions in the United States. We did not collect information about diet and physical activity, and therefore, could not evaluate potential confounding by these factors. Due to the extensive lack of height and weight information in the medical record, we relied on self-reported information for these variables to compute BMI, which can lead to misclassification related to social desirability or recall bias.<sup>54</sup>

## Conclusions

EIBC patients, but not DCIS patients, were more likely to experience  $\geq 5\%$  weight gain after 2-year follow-up compared with women without a history of breast cancer. Compared with patients with advanced breast cancer, EIBC patients have a lower risk of complications, recurrence, and mortality.<sup>1,2</sup> However, their more favorable prognoses may be hampered by significant postdiagnosis weight gain and obesity,<sup>1,55</sup> which seems especially important for patients with ER-negative tumor subtypes.<sup>30,51</sup> Future work should evaluate the long-term influence of postdiagnosis weight gain on patients' health. Also, the biological mechanisms linking invasive breast cancer to weight gain remain unclear. Further research is necessary to elucidate modifiable factors affecting weight gain in this growing population of cancer survivors.

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No competing financial interests exist.

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## Supplementary Material

Supplementary Table S1  
 Supplementary Table S2  
 Supplementary Table S3

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