Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Melissa Anne Taylor Date

Quality of Life Factors Influencing Post-Diagnosis Change in BMI in a Cohort of Breast Cancer Patients

By

Melissa Anne Taylor

Master of Public Health

Epidemiology

Terry Hartman, PhD, MPH, RD

Faculty Thesis Advisor

Quality of Life Factors Influencing Post-Diagnosis Change in BMI in a Cohort of Breast Cancer Patients

By

Melissa Anne Taylor

B.A., University of Colorado at Boulder, 2012

Faculty Thesis Advisor: Terry Hartman, PhD, MPH, RD

An abstract of

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Epidemiology

2018

Abstract

Introduction and Objectives : Weight gain during breast cancer treatment is well documented in the literature and has been associated with chemotherapy treatment, hormone therapy, age, stage at diagnosis, and menopause status. The effects of quality of life factors on post-diagnosis weight gain have not been well studied. We examined the effect of measures of quality of life on post-diagnostic weight gain in breast cancer patients treated with radiation and surgery.

Methods: We enrolled 140 female breast cancer patients receiving radiation treatment at the Emory University Winship Cancer Institute in Atlanta, GA from March 2010-November 2011. Body mass index (BMI) was recorded at five different time points during the study, from baseline to one year post diagnosis and percent BMI change was measured from baseline to the end of follow-up. Quality of life was measured by the validated 36-Short Form Survey (SF-36) at the same time points as BMI to assess trends and overall change. The association between quality of life measures and BMI change was evaluated in multivariate linear regression models after adjustment for confounders.

Results: The individual SF-36 component scores were not statistically significant determinants of baseline BMI. A modest inverse association between the physical functioning component score and baseline BMI and was borderline significant (P=0.06). A one unit higher physical functioning score was associated with a lower BMI (-0.05 95% CI= -0.11-0.003). None of the other component scores were significantly associated with baseline BMI and no SF-36 scores were associated with BMI change.

Conclusions: In this study population there was little or no association between quality of life and either baseline BMI or breast cancer treatment associated change in BMI.

Quality of Life Factors Influencing Post-Diagnosis Change in BMI in a Cohort of Breast Cancer Patients

By

Melissa Anne Taylor

B.A., University of Colorado at Boulder, 2012

M.D, Emory University School of Medicine 2018

MPH Emory Rollins School of Public Health 2018

Faculty Thesis Advisor: Terry Hartman, PhD, MPH, RD

A thesis submitted to the Faculty of the

Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of

Master of Public Health

in Epidemiology

2018

Acknowledgements

I would like to thank my advisor, Dr. Terry Hartman for her guidance and patience throughout this process. I would also like to thank Dr. Mylin Torres, MD for allowing the use of her original dataset for this thesis. I would also like to thank my family and friends for their encouragement and support through this and throughout my overall education.

Table of Contents

Background

Breast cancer is the most common cancer diagnosis and the second leading cause of cancer-related death among women in the United States. The American Cancer Society estimated that in 2017 there were 63,410 new in situ cases diagnosed, 252,710 new diagnoses of invasive breast cancer, and 40,610 deaths due to breast cancer in the United States [1]. Due to advances in treatment, including new chemotherapy and immunotherapy drugs, radiation therapy, surgical options, and advancements in early detection, there are more women living as breast cancer survivors than ever before. This presents a new challenge to understand the physical and mental consequences of breast cancer treatment and the effect these consequences have on overall health and quality of life.

It is well documented that weight gain throughout life increases the risk for breast cancer. A study published in JAMA in 2015 examined the association between obesity and risk of invasive breast cancer in postmenopausal women. The study consisted of a cohort of 67,42 women enrolled from 1993-1998 with 13-year follow up and found that women with a BMI defined as obese (30+) had an increased risk of invasive breast cancer compared to those with a normal BMI (18.5-24.9) (HR 1.58, 95% CI= 1.40-1.79), especially estrogen receptor positive cancer (HR 1.86, 95% CI= 1.60-2.17) [3]. Another study from 2005-2010 involving over 5,000 women found that those who experienced a change in BMI from normal or overweight to obese had two times higher odds of developing breast cancer compared to those who did not have a change in BMI or those who only increased from a normal BMI to an overweight BMI classification [2]. There are many hypotheses for the mechanism behind the association of breast cancer and obesity, such as the effect of hormones and inflammatory cytokines on cellular apoptosis, increased level of adipose tissue causing aromatisation and driving estrogen receptor

linked tumor growth, and a high level of insulin and insulin like growth factor leading to cellular proliferation [4]. Increased serum insulin concentration during and after treatment has been directly linked to disease recurrence and death [4]. Additionally, there are non-biological mechanisms behind the association between breast cancer and obesity that are less well defined including socioeconomic and racial factors, inferior predictability of screening mechanisms like mammography and self-exams in overweight and obese women [5]. There is some evidence that obese women undergoing chemotherapy and radiation may be under dosed which results in decreased therapeutic response [6]. When clinical factors of breast cancer are examined obesity has been associated with larger tumor size and later stage of cancer at diagnosis, worse response to chemotherapy treatment, and higher risk of recurrence [7].

BMI changes following diagnosis have also been associated with breast cancer outcomes. It has been well documented that women experience weight gain during treatment with chemotherapy and radiation and in the years following treatment with an average weight gain between 2.9-4.4kg [8]. Weight gain during treatment is a significant issue of clinical and public health concern because studies have demonstrated an association with post diagnosis weight gain and increased all-cause mortality. A meta-analysis of twelve studies (n=23,832) examining weight gain following breast cancer diagnosis and all-cause mortality reported weight gain of >=5% of body weight was associated with an increased all-cause mortality (HR 1.12, 95% CI=1.03-1.22) and a weight gain of >=10% showed even greater increased risk (HR 1.23, 95% CI=1.09-1.39) compared with age-matched women without breast cancer [9]. Another study using data from the Breast Cancer Pooling Project prospective cohort of 18,333 breast cancer survivors across multiple sites in the United States and Shanghai found that 37% of women reported post diagnosis weight gain [10]. Women who were premenopausal were more likely to

report weight gain than post-menopausal women. Women who were normal weight at diagnosis and experienced a weight gain of ≥10% were found to have a higher risk of all-cause mortality (HR 1.24, 95% CI=0.98-1.56) compared to women who similar weight gain but were overweight at the time of diagnosis (HR 1.04, 95% CI=0.98-1.56) [10].

The mechanisms that lead to weight gain after breast cancer diagnosis are not clear, but many studies have shown an association between various factors and post diagnosis weight gain, such as differences in chemotherapy and hormone treatment, baseline BMI, menopause status, age, physical activity, and social support [11]. A study conducted by Caan et al. in 2006 looked at participants from the two large studies, WHEL (n=1,473) and LACE (n=1,742), to examine if weight gain after diagnosis affects risk of recurrence. Women were enrolled between 1995-2002 and had a breast cancer diagnosis within 48 months of enrollment. Weight change between one-year pre-diagnosis and enrollment was reported with 44% of participants reporting weight gain. Height, lower pre-diagnosis BMI, younger age, treatment with chemotherapy, premenopausal status, and estrogen receptor positive tumors were significantly associated with weight gain during this period [12]. Weight gain during breast cancer treatment is an important clinical and public health concern because studies have shown that a gain in BMI above 0.5kg/m^2 was associated with a higher risk of recurrence [7] and that a gain of 5kg during treatment increased breast cancer specific mortality by 13% [14].

Chemotherapy has been shown to be associated with weight gain when compared with Tamoxifen. The Women's Healthy Eating and Living Study (WHEL) looked at 3,088 breast cancer survivors and showed that chemotherapy was positively related to weight gain (OR 1.65 95% CI =1.12-2.43) while Tamoxifen was not associated with weight gain (OR 1.03 95% CI=0.71-1.51) This weight gain also persisted over time with only 10% returning to their pre-

cancer weight after the first year [15]. Chemotherapy is shown to change body composition such that there is an increase in fat mass and a decrease in lean body mass; however, this also occurs as a result of the natural process of aging [16]. Studies have shown that weight gain occurs regardless of the specific type of chemotherapy with non-significant differences between regimens. There has not yet been a study comparing different durations of treatment for the same regimen, thus, it remains to be seen whether this is a contributing factor.

It is well documented that weight gain during and after treatment for breast cancer increases the risk of recurrence, breast cancer related mortality, and all-cause mortality. This has prompted many studies to examine demographic and clinical predictors of weight gain during breast cancer treatment, yet much less is known about how quality of life influences weight gain during treatment. A recent study by Hart et. al. looked at patients diagnosed with ductal carcinoma in situ and the effects of post-diagnosis health behaviors on quality of life. The study surveyed 1,448 women treated for DCIS in the Wisconsin in Situ Cohort using the Short Form (SF)-36 questionnaire to assess for quality of life outcomes. The results determined that women who were classified as being overweight or obese after diagnosis reported lower physical quality of life scores on the SF-36 compared to those with normal weight BMI; however, there were no differences in the mental component of quality of life scores [17].

The aim of this study is to describe the association between quality of life factors and change in BMI one year after diagnosis for patients being treated with radiation for localized breast cancer. The factors examined include demographic, socioeconomic, and clinical factors as well as results from the validated SF-36 questionnaire survey. These results may assist health care providers to identify those patients at greatest risk of weight gain during treatment to intervene on potentially modifiable quality of life measures.

Materials and Methods

Population characteristics

The study combined two groups of breast cancer patients (n=60, n=80) treated with radiation therapy at the Emory University Winship Cancer Institute in Atlanta, GA (total n=140). Women were recruited from March 2010 to November 2011 from the Emory University Department of Radiation Oncology. Eligibility criteria included age between 18 and 75 years old, breast cancer stage between 0 and IIIA, and breast conservation surgery with or without neoadjuvant or adjuvant chemotherapy. Exclusion criteria included a known history of major psychiatric disorders including schizophrenia, bipolar disorder, or substance about within the past year. Patients with uncontrolled cardiovascular, metabolic, renal, pulmonary, or autoimmune disease were also excluded. Patients who were pregnant were not included in the study. The study was limited to Caucasian and African American patients due to the small number of other racial and ethnic participants in the source population. The study procedures were approved a priori by the Emory University Institutional Review Board, and all participants provided written informed consent.

Assessment of Weight Outcomes

At each visit the subjects weight and height was recorded and BMI (kg/m^2) was calculated. BMI and height were recorded at five time points, at baseline, at the start of radiation therapy, at the end of radiation therapy (six weeks after radiation), six months after diagnosis, and one year after diagnosis. Participants who did not have BMI recorded for at least three time points were not included in the study resulting in a final count of 122 study participants eligible for final analysis. BMI change was examined using both total change and percentage of BMI change from baseline

to end of follow-up at (one year after initial visit), baseline to end of radiation treatment, and end of radiation treatment to end of follow-up.

Assessment of Quality of Life Measures

Our exposure consisted of quality of life variables that were quantified using the RAND 36-Item Short Form Survey (SF-36). This survey has been validated and widely used for assessing overall physical and mental function in clinical studies with quality of life outcomes including general health, social functioning, vitality, physical pain, mental health, physical functioning, and physical and emotional roles. The physical components include physical functioning, general health, pain, and physical role, while the emotional components include mental health, emotional roles, vitality, and social functioning. The raw data from these eight components are normalized to a range from 0-100 with a higher score meaning a better state of health (19). The SF-36 was given to the subjects at each visit and a total score was calculated. The change in total SF score was determined by subtracting the initial score obtained at the first visit before radiation therapy and the final score at one-year post treatment.

Covariates

Covariates such as age, race, menopause status, smoking status, income, marital status, and educational level were all self-reported. Clinical covariates such as estrogen, progesterone , and HER2 receptor status were determined from histopathology. TNM stage was determined by pathological, clinical and radiographic findings. Chemotherapy induction (yes or no), chemotherapy agent, hormone therapy status, and choice of hormone therapy were based on recommended treatment guidelines and coded for analyses.

Statistical Analysis

Statistical analyses were performed with the use of SAS 9.4 (SAS Institute). Our outcome, BMI change, was analyzed both as continuous and categorical variables. Participants were divided into three groups based on BMI classification with normal BMI being <25 kg/m^2 (this included two subjects who were classified as underweight with a BMI <18.5 kg/m^2), overweight BMI between 25-29.9 kg/m^2, and obese BMI of 30.0 kg/m^2 or greater for descriptive statistics. Baseline demographic and clinical characteristics of the study population were evaluated across categories of BMI (Table 1). Differences in characteristics were tested using analysis of variance for continuous variables and chi square/Fisher's Exact tests for categorical variables.

The association between quality of life measures and weight change was evaluated in multivariate linear regression models after adjustment for confounders. Selection of potential confounders was based on prior literature review and on our descriptive analyses. Backwards selection was used to guide the selection of confounders and other variables of interest. Final models were adjusted for menopause status (premenopausal vs. postmenopausal), race (African American vs. Caucasian), smoking history (yes vs. no), education status (high school graduate, college graduate, or professional school graduate), chemotherapy status (not received vs. adjuvant), and hormonal agents taken during treatment (none, tamoxifen, Arimidex, or other).

Each of the eight components of the SF-36 were entered into a separate model controlling for the potential confounders previously mentioned. The total SF-36 score as well as the total for the four emotional components and the four physical components were also entered into individual multivariable regression models for each outcome of interest (Table 5 and Table 6). Results are reported as betas, standard errors (SE) and p-values and model statistics (total r-squared). All statistical tests were two-sided and p-value < 0.05 were considered statistically significant.

Results

Demographic and Clinical

The 122 study participants eligible for analysis were dived into three groups based on baseline BMI value, normal BMI (18.5-24.9 kg/m^2) (n=27), overweight BMI (25-29.9 kg/m^2) (n=43), and obese BMI (≥30 kg/m^2) (n=52). The participants (table 1) included 70 Caucasian and 52 African American women, 82 post-menopausal women and 37 pre-menopausal women. The preponderance of participants had college or graduate degrees (64%). The majority of the participants presented with early stage cancer with only 8 women presenting with stage T3 or T4. Most of the women received adjuvant hormone therapy (57%) with nearly 40% receiving Tamoxifen. In contrast, only 23% of the participants received chemotherapy as part of the treatment plan. The normal BMI group tended to be younger at diagnosis compared to the overweight and obese group ($p=0.06$). Race was an important variable with more African American women in the obese BMI group (67.3% African American vs. 32.6% Caucasian) and more Caucasian women in the normal BMI group (81.5% Caucasian vs. 18.5% African American) ($p <0.001$). Occupation (labor/managerial, professional, homemaker, and other) was also found to differ between BMI groups ($p=0.02$). Stage of cancer at diagnosis varied across BMI groups ($p=0.01$) with a greater percentage of obese women diagnosed at a later stage than women with normal BMI. Finally, normal weight BMI women were more likely to be taking Herceptin compared to overweight or obese women ($p=0.02$).

Weight and BMI change

The weight and BMI change values by baseline BMI group are described in table 2. The average baseline BMI for all study participants was 29.9 kg/m^2. The average baseline BMI for the normal, overweight, and obese BMI groups was 22.3kg/m^2, 27.6kg/m^2, and 35.7kg/m^2,

respectively. The average total percent BMI change from baseline to the end of follow-up one-year post diagnosis was 0.65% overall and less than 1% in all groups. Weight gain during breast cancer therapy did occur in this study; however, the amount of weight gain was minimal. Figure 1 shows the mean BMI at each timepoint during the study and it demonstrates negligible change in BMI from baseline to end of treatment in all three BMI groups.

Quality of Life Factors

The main exposure of the study was quality of life factors as determined by the SF-36 survey. Table 3 shows the mean baseline SF-36 score by each of the eight components and the total physical and emotional scores by BMI group. Mean physical functioning score and mean general health score tended to differ across BMI groups (p=0.06). The obese BMI group reported a mean physical functioning score of 64.9 (±26.6) compared to the normal BMI group mean of 77.1 (±28.l2) and overweight BMI group of 76.6 (±23.5). In the general health category, the obese BMI group also reported a lower mean baseline score compared to the normal and overweight BMI groups (61.8(±22.0) vs. 70.6 (±21.3) and 71.4 (±18.4)).

The study also examined the change in SF-36 score in the eight component scores as well as the total physical component and total emotional component from baseline to end of follow up by baseline BMI group (Table 4). Mean bodily pain showed some variability between BMI groups with the overweight BMI group reporting an overall decrease of -2.3 (±17.6) points compared to a gain of 9.2 (±25.7) points in the obese group and a gain of 7.9 (±17.7) points in the normal BMI group (p=0.04). The total score for the physical component scores also showed some evidence of variability across BMI groups (p=0.05) with the overweight group experiencing the smallest mean increase in scores of 17.4 (±63.9) points compared to an increase

of 53.8 (±83.5) points and 50.8 (±66.5) points in the obese and normal weight groups, respectively.

Final Models

The multivariate regression analyses of the relationship between the outcome of baseline BMI as a continuous variable and the exposure of baseline SF-36 component scores is displayed in Table 5. The individual SF-36 component scores were not statistically significant determinants of the baseline BMI. A modest inverse association between the physical functioning component score and baseline BMI and was borderline significant (P=0.06). A one unit higher physical functioning score was associated with a lower BMI (-0.05 95% CI= -0.11-0.003). None of the other component scores were significantly associated with baseline BMI.

In addition, we found no evidence of association between the percent change in BMI from baseline to end of follow up and each of the eight SF-36 component scores as well as the total for the physical scores and the total for the emotional scores (Table 6).

Discussion

The aim of this study was to examine the association between quality of life factors as measured by the SF-36 survey and change in BMI during breast cancer treatment. Weight gain during breast cancer treatment has been well documented in the literature and this study also demonstrated an increase in BMI during breast cancer therapy across all three BMI groups, normal, overweight, and obese, although the increase was minimal ($p=0.77$). In this study population the SF-36 component scores were not a good predictor of baseline BMI and the change in SF-36 scores was not a good predictor of change in BMI from baseline to end of follow up. We found no clear evidence of association between baseline BMI and baseline total and component SF-36 scores after adjustment for demographic and clinical factors. The multivariate regression analysis of the relationship between change in BMI and change in SF-36 component scores from baseline to end of treatment also showed essentially no association between these variables.

Quality of life among breast cancer patients diagnosed with ductal carcinoma in-situ at two years post diagnosis is similar to age matched controls without a diagnosis of breast cancer [20]. Previous studies of the role of quality of life in BMI change among breast cancer patients have been equivocal. In a study by Hart et.al. breast cancer patients with obese or overweight BMI reported lower physical functioning quality of life compared with breast cancer patients of normal weight BMI [17]. This is similar to our study in that obese women reported lower scores for the physical components of the SF-36 that the women with normal BMI. This differed from our study in that the overweight BMI reported higher physical quality of life scores compared with women of normal BMI in all but one physical category, physical functioning, and even then, the mean scores differed by half a point. Another study by Xia et.al. examined the

association between quality of life and BMI in a cohort of 10,708 breast cancer survivors in China Overweight breast cancer survivors reported significantly ($P<0.05$) better QOL in almost all domains compared with underweight, normal weight and obese survivors. When the cohort was stratified by comorbidity status (none vs ≥1) the same association was shown ($P<0.05$) [21].

One explanation for our findings may be that the average weight gain in our study one year post diagnosis was 0.39kg which was less than most studies in the literature. A literature review paper by Makari-Judson et.al. looked at post-diagnosis weight gain in breast cancer patients and found the mean weight gain to be between 1-3.9kg at one year post-diagnosis with women who received chemotherapy reporting a greater weight gain [22].

Limitations

Our study had some limitations which should be mentioned. The modest sample size likely limited our ability to observe potential associations between measures of quality of life and BMI outcomes. Some of the demographic and clinical variables had many categories for coding that had to be combined into fewer categories for analyses. This required making assumptions for combining categories within variables, but this also could have resulted in inaccurate representation of some of the study subjects. Study subjects with ≥3 values recorded for BMI were included in the final analysis. There was a large number of subjects who did not have BMI values recorded for at least three visits and were excluded, which may have compromised our ability to accurately capture the full picture of weight and BMI change during the study period. The study participants were recruited at Emory University, a large academic tertiary care center, where patients must have insurance to be treated. This excludes some patients of lower socioeconomic status without insurance and the final results may be less generalizable to the rest of the population. The majority of patients presented at early stages (I or II) so there were fewer

patients who received chemotherapy, which could limit the ability to fully assess quality of life or weight changes during treatment or extrapolate to other breast cancer patients. Lastly, the SF-36 study was not originally designed to be used in breast cancer patients specifically, so it may not be the most appropriate test for determining quality of life within this population.

Future directions

In the literature a gain of ≥5% of BMI during treatment for breast cancer therapy is clinically significant for increase in recurrence and all-cause mortality [9]. Preliminary analysis in this study revealed that only 22 women experienced a BMI increase of ≥5% from baseline BMI to end of follow-up so further analysis for this specific outcome was not performed due to the limited sample size. In future studies it would be useful to look at the role of quality of life measured by the SF-36 survey among this specific group of women who experience greater increases in BMI during treatment and are at greater risk for morbidity and mortality. In the future it would be beneficial to assess post-diagnosis weight gain in chemotherapy vs. no chemotherapy given that the literature suggests that weight gain is more prevalent among breast cancer patients who received chemotherapy. Finally, examining women from a more diverse socioeconomic background would be advantageous in future studies to ensure that the results can be extrapolated across a broader segment of breast cancer survivors.

Conclusion

In this study population there was not a statistically significant relationship between quality of life and either baseline BMI or breast cancer treatment associated change in BMI. Future research in larger and more diverse populations of breast cancer patient populations is warranted.

Tables and Figures

Figure 1: Mean BMI at Each Visit by BMI Group

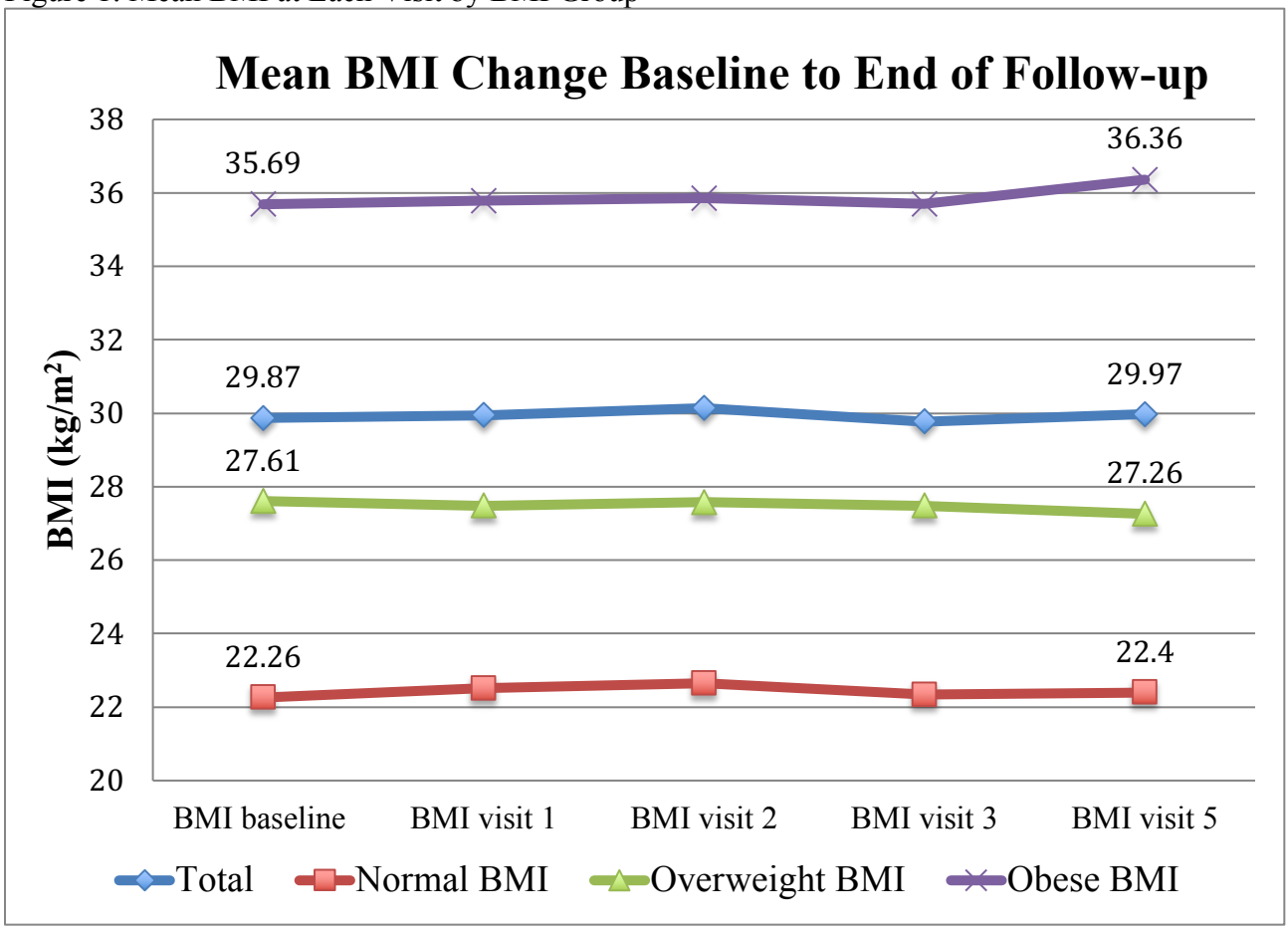

Table 1: Participant Demographic and Clinical Characteristics by BMI Group

Demographic	**Total**	**(%)**	**BMI (18.5-24.9)**	**(%)**	**BMI (25-29.9)**	**(%)**	**BMI (30+)**	**(%)**	**P Value**
	n = 122	100	n=27	22.13	n=43	35.25	n=52	42.62	
Age									0.06
<50	32	26.23	13	48.15	6	13.95	13	25.00	
50-59	42	34.43	7	25.93	15	34.88	20	38.46	
60-69	37	30.33	5	18.52	16	37.21	16	30.77	
70+	11	9.02	2	7.41	6	13.95	3	5.77	
Race									<0.001
Black	52	42.62	5	18.52	12	27.91	35	67.31	
White	70	57.38	22	81.48	31	72.09	17	32.60	
Marital Status									0.39
Single	38	31.15	5	18.52	12	27.91	21	40.38	
Married	65	53.28	20	74.07	22	51.16	23	44.23	
Divorced/Widowed	19	15.57	2	7.41	9	20.93	8	15.38	
Smoking History									0.23
Yes	22	18.03	2	7.41	8	18.60	12	23.08	
No	100	81.97	25	92.59	34	79.07	40	76.92	
Menopause Status									0.06
Premenopausal	37	30.33	12	44.44	8	18.60	17	32.69	
Postmenopausal	82	67.21	14	51.85	34	79.07	34	65.38	
Occupation									0.02
Labor/managerial	20	16.39	3	11.11	5	11.63	12	23.08	
Professional	54	44.26	11	40.74	21	48.84	22	42.31	
Homemaker	15	12.30	9	33.33	4	9.30	2	3.85	
Other	16	13.11	3	11.11	5	11.63	8	15.38	
Education									0.12
High school	42	34.43	4	14.81	15	34.88	23	44.23	
College	38	31.15	11	40.74	15	34.88	12	23.08	
Professional	40	32.79	11	40.74	12	27.91	17	32.69	
Income									0.06
<$40,000	32	26.23	10	37.04	11	25.58	11	21.15	
$40,000-$79,999	40	32.79	3	11.11	14	32.56	23	44.23	
>= $80,000	37	30.33	11	40.74	13	30.23	13	25.00	
Clinical									

Chemo Induced									
Yes	23	18.85	8	29.63	4	9.30	40	76.92	
No	97	79.51	18	66.67	39	90.70	11	21.15	
T									0.08
T1	60	49.18	18	66.67	15	34.88	27	51.92	
T2	31	25.41	6	22.22	11	25.58	14	26.92	
T3-T4	8	6.56	2	7.41	4	9.30	2	3.85	
T in situ	23	18.85	1	3.70	13	30.23	9	17.31	
N									0.16
N0	76	62.30	20	74.07	28	65.12	28	53.85	
N1	38	31.15	6	22.22	11	25.58	21	40.38	
Stage									0.01
0	23	18.85	1	3.70	13	30.23	9	17.31	
I	38	31.15	14	51.85	9	20.93	15	28.85	
II	54	44.26	10	37.04	18	41.86	26	50.00	
ER									0.92
Positive	91	74.59	20	74.07	33	76.74	38	73.08	
Negative	31	25.41	7	25.93	10	23.26	14	26.92	
PR									0.76
Positive	79	64.75	18	66.67	26	60.47	35	67.31	
Negative	43	35.25	9	33.33	17	39.53	17	32.69	
HER2									0.70
Positive	25	20.49	7	25.93	9	20.93	9	17.31	
Negative	75	61.48	19	70.37	22	51.16	34	65.38	
Herceptin									0.02
Yes	14	11.48	20	74.07	4	9.30	3	5.77	
No	108	88.52	7	25.93	39	90.70	49	94.23	
Hormone status									0.36
None	38	31.15	9	33.33	10	23.26	19	36.54	
Adjuvant	70	57.38	17	62.96	26	60.47	27	51.92	
Adjuvant + Radiation	13	10.66	1	3.70	7	16.28	5	9.62	
Hormone agents									0.59
N/A	14	11.48	3	11.11	5	11.63	6	11.54	
Tamoxifen	48	39.34	11	40.74	19	44.19	18	34.62	
Arimidex	23	18.85	6	22.22	6	13.95	11	21.15	
Other	9	7.38	1	3.70	6	13.95	2	3.85	
Chemotherapy status									0.71
None	55	45.08	11	40.74	20	46.51	24	46.15	
N/A	39	31.97	11	40.74	11	25.58	17	32.69	
Adjuvant	28	22.95	5	18.52	12	27.91	11	21.15	

Table 2: Mean (SD) Weight and BMI, Weight and BMI Change, and Percent Weight and BMI Change by BMI group

Weight Measurement	**Total n= 122 Mean (SD)**	**BMI (18.5-24.5) n=27 Mean (SD)**	**BMI (25-29.9) n=43 Mean (SD)**	**BMI (30+) n=52 Mean (SD)**	**P value**
Weight (kg) baseline	80.58 (19.16)	62.15 (6.20)	73.87 (6.30)	95.70 (19.17)	<0.001
Weight (kg) visit 1	80.69 (19.05)	62.81 (6.70)	73.46 (6.34)	95.73 (18.98)	<0.001
Weight (kg) visit 2	81.24 (19.31)	62.40 (6.70)	73.71 (6.22)	96.46 (18.72)	<0.001
Weight (kg) visit 3	80.19 (19.32)	62.41 (7.03)	73.23 (6.59)	95.63 (19.42)	<0.001
Weight (kg) visit 5	80.48 (20.01)	62.32 (7.47)	72.81 (7.54)	96.83 (19.78)	<0.001
BMI (kg/m^2) Baseline	29.87 (6.92)	22.26 (1.91)	27.61 (1.93)	35.69 (6.36)	<0.001
BMI (kg/m^2) visit 1	29.95 (6.93)	22.51 (1.98)	27.48 (1.43)	35.78 (6.62)	<0.001
BMI (kg/m^2) visit 2	30.14 (7.00)	22.65 (2.11)	27.58 (1.43)	35.85 (6.52)	<0.001
BMI visit (kg/m^2) 3	29.77 (7.08)	22.34 (2.31)	27.48 (1.76)	35.70 (6.70)	<0.001
BMI (kg/m^2) visit 5	29.97 (7.45)	22.40 (2.35)	27.26 (27.26)	36.36 (6.97)	<0.001
Weight change total (kg)	0.39 (5.70)	0.62 (3.16)	0.08 (5.24)	0.67 (7.03)	0.80
Weight change total (%)	0.63 (6.95)	0.93 (4.96)	-0.02 (6.92)	1.03 (7.90)	0.77
BMI (kg/m^2) change total	0.19 (2.14)	0.22 (1.08)	0.01 (1.95)	0.32 (2.67)	0.77
BMI change total (%)	0.65 (6.99)	0.91 (4.92)	0.12 (7.04)	0.96 (7.89)	0.83
BMI change end of treatment to follow up (%)	-0.63 (5.62)	-0.38 (3.37)	-1.57 (6.09)	0.05 (6.07)	0.42
BMI change baseline to end of treatment (%)	0.21 (3.40)	0.72 (3.67)	-0.03 (3.92)	0.14 (3.08)	0.70

Table 3: Mean Baseline SF-36 Component Score by BMI Group

SF-36 Component Baseline Score	Total (n=122) Mean (SD)	BMI (18.5-24.9) n=27 Mean (SD)	BMI (25-29.9) n=43 Mean (SD)	BMI (30+) n=52 Mean (SD)	P-Value
Physical Functioning	71.7 (26.3)	77.1 (28.2)	76.63 (23.5)	64.90 (26.6)	0.06
Physical Role	51.6 (42.9)	50.0 (39.7)	59.4 (44.8)	45.8 (42.6)	0.33
Bodily Pain	63.7 (23.9)	66.3 (22.8)	67.8 (19.8)	59.0 (27.0)	0.19
General Health	67.1 (20.9)	70.6 (21.3)	71.4 (18.4)	61.8 (22.0)	0.06
Vitality	56.9 (23.9)	60.0 (26.4)	58.5 (23.5)	54.1 (23.0)	0.53
Social Functioning	72.4 (26.9)	72.9 (28.0)	77.2 (24.0)	68.2 (28.5)	0.30
Emotional Role	70.5 (41.4)	80.6 (36.7)	74.2 (38.9)	62.5 (44.9)	0.17
Mental Health	75.9 (19.0)	76.5 (20.9)	79.5 (13.2)	72.6 (21.6)	0.23
Total Physical component	254.0 (94.5)	264.0 (94.9)	275.1 (88.6)	231.5 (96.0)	0.08
Total Emotional Component	275.8 (92.3)	290.0 (97.7)	289.4 (76.9)	257.4 (99.7)	0.19

Table 4: Change in SF-36 Component Score from Baseline to end of Follow-up by BMI Group

SF-36 Component Change in Score	Total (n=122) Mean (SD)	BMI (18.5-24.9) n=27 Mean (SD)	BMI (25-29.9) n=43 Mean (SD)	BMI (30+) n=52 Mean (SD)	P-value
Physical Functioning	7.5 (23.0)	8.8 (24.7)	2.3 (20.3)	11.2(23.8)	0.19
Physical Role	26.1 (41.2)	30.2 (36.1)	18.8 (39.1)	30.2 (45.0)	0.37
Bodily Pain	4.8 (21.9)	7.9 (17.7)	-2.3 (17.6)	9.2 (25.7)	0.04
General Health	1.7 (14.5)	4.0 (14.7)	-1.4 (10.6)	3.2 (16.8)	0.23
Vitality	6.5 (19.9)	5.2 (18.7)	5.8 (20.9)	7.7 (19.8)	0.85
Social Functioning	13.4 (24.0)	11.5 (18.8)	9.1 (25.9)	18.0 (24.3)	0.20
Emotional Role	11.3 (38.4)	-1.4 (34.7)	10.8 (32.4)	18.1(43.5)	0.13
Mental Health	5.0 (17.4)	4.5 (15.2)	1.80(15.7)	8.0 (19.6)	0.25
Physical Component Total	40.1 (74.8)	50.8 (66.5)	17.4(63.9)	53.8 (83.5)	0.05
Emotional Component Total	36.2 (73.5)	19.8 (56.3)	27.5 (71.6)	51.7 (80.6)	0.14

Table 5: Multivariate Regression Analyses of the Relationship between Baseline BMI (continuous) and Baseline SF-36 Component Score (continuous)

Variable	Estimate (SE)	p-value	Model R^2
Physical Functioning	-0.0547 (0.0288)	0.06	23.08%
Physical Role	-0.0088 (0.0189)	0.64	19.53%
Bodily pain	-0.0197 (0.0339)	0.56	19.66%
General Health	-0.0580 (0.0362)	0.11	22.04%
Vitality	-0.0382 (0.0325)	0.24	20.79%
Social Functioning	-0.0165 (0.0293)	0.58	19.64%
Emotional Role	-0.0298 (0.0204)	0.15	21.58%
Mental Health	-0.0248 (0.0425)	0.56	19.67%
Physical Component Total	-0.0102 (0.0083)	0.22	20.96%
Emotional Component Total	-0.0110 (0.0089)	0.22	20.97%

*All models adjusted for menopause status (pre or post-menopausal), race (African American or Caucasian), education level (high school, college, or professional school graduate), chemotherapy status (none, neoadjuvant, or adjuvant), smoking History (yes or no), hormone therapy agents (none, Tamoxifen, Arimidex, other).

Table 6: Multivariate Regression Analyses of the Relationship between Percent Change in BMI (continuous) from Baseline to End of Follow-up with Change in SF-36 Component Score from Baseline to end of Follow-up (continuous)

Variable	Estimate (SE)	P-value	Model R^2
Physical Functioning	-0.0193 (0.0322)	0.55	11.83%
Physical Role	0.0152 (0.0193)	0.66	12.14%
Bodily Pain	-0.0060 (0.0365)	0.87	11.42%
General Health	-0.0729 (0.0535)	0.18	13.62%
Vitality	-0.0671 (0.0412)	0.11	14.54%
Social Functioning	0.0080 (0.0310)	0.80	11.47%
Emotional Role	-0.0187 (0.0206)	0.37	12.40%
Mental Health	-0.0334 (0.0455)	0.47	12.05%
Physical Component Total	-0.0009 (0.0105)	0.94	11.40%
Emotional Component Total	-0.0119 (0.0114)	0.30	23.31%

*All models adjusted for menopause status (pre or post-menopausal), race (African American or Caucasian), education level (high school, college, or professional school graduate), chemotherapy status (none, neoadjuvant, adjuvant), smoking History (yes or no), hormone therapy agents (none, Tamoxifen, Arimidex, other), and baseline BMI.

References

1. American Cancer Society. Breast Cancer Facts & Figures 2017-2018. Atlanta: American Cancer Society,Inc. 2017

2. Wambui G. Gathirua-Mqangi, Zollinger, T. Murage, M. Pradhan, K. Champion, V. (2015). Adult BMI change and risk of Breast Cancer: National Health and Nutrition Examination Survey (NHANES) 2005-2010. *Breast Cancer*, 22:648-656.

3. Neuhouser, M. L., Aragaki, A. K., Prentice, R. L., Manson, J. E., Chlebowski, R., Carty, C. L., .Anderson, G. L. (2015). Overweight, Obesity, and Postmenopausal Invasive Breast Cancer Risk. *JAMA Oncology, 1*(5), 611.

4. Goodwin PJ, Ennis M, Pritchard KI, Trudeau ME, Koo J, Madarnas Y, Hartwick W, Hoffman B, Hood N: (2002) Fasting insulin and outcome in early-stage breast cancer: results of a prospective cohort study. *J Clin Oncol* 20: 42–51.

5. Chan, D. S., Vieira, A. R., Aune, D., Bandera, E. V., Greenwood, D. C., Mctiernan, A., . . . Norat, T. (2014). Body mass index and survival in women with breast cancer—systematic literature review and meta-analysis of 82 follow-up studies. *Annals of Oncology, 25*(10), 1901-1914.

6. Madarnas Y, Sawka CA, Franssen E, Bjarnason GA: (2001). Are medical oncologists biased in their treatment of the large woman with breast cancer? *Breast Cancer Res Treat* 66: 123–133.

7. Kroenke, C. Chen, W., Rosener, B. Holmes, M., (2005). Weight, Weight gain, and survival after breast cancer diagnosis. *Journal of Clinical Oncology*. 23(7), 1370-1378

8. Vance V, Mourtzakis M, McCargar L, et al. (2011) Weight gain in breast cancer survivors: prevalence, pattern and health consequences. *Obes Rev.*12(4):282–294.

9. Playdon, M., Bracken, M. Sanft, T., Ligibel J., Harrigan, M., Irwin, M., (2015) Weight gain after breast cancer diagnosis and all-cause mortality: systemic review and meta-analysis. *Journal of the National Cancer Institute.* 107(12): 1-15.

10. Caan BJ, Kwan ML, Shu XO, et al. (2012) Weight change and survival after breast cancer in the after breast cancer pooling project. *Cancer Epidemiology Biomarkers Prev.* ;21(8):1260–1271.

11. Irwin ML, McTiernan A, Baumgartner RN, et al (2005). Changes in body fat and weight after a breast cancer diagnosis: influence of demographic, prognostic, and lifestyle factors. *Journal of Clinical Oncology*.23(4):774–782.

12. Caan, B. J., Emond, J. A., Natarajan, L., Castillo, A., Gunderson, E. P., Habel, L., Pierce, J. P. (2006). Post-diagnosis weight gain and breast cancer recurrence in women with early stage breast cancer. *Breast Cancer Research and Treatment, 99*(1), 47-57.

13. 22. Caan BJ, Kwan ML, Hartzell G et al. (2008). Pre-diagnosis body mass index, post-diagnosis weight change, and prognosis among women with early stage breast cancer. *Cancer Causes Control* 19: 1319–1328.

14. Nichols HB, Trentham-Dietz A, Egan KM et al. (2009). Body mass index before and after breast cancer diagnosis: associations with all-cause, breast cancer, and cardiovascular disease mortality. *Cancer Epidemiol Biomarkers Prev*; 18: 1403–1409.

15. Saquib N, Flatt SW, Natarajan L et al. (2007). Weight gain and recovery of pre-cancer weight after breast cancer treatments: evidence from the women's healthy eating and living (WHEL) study. *Breast Cancer Res Treat*; 105: 177–186.

16. Gadéa, E., Thivat, E., Planchat, E., Morio, B., & Durando, X. (2011). Importance of metabolic changes induced by chemotherapy on prognosis of early-stage breast cancer patients: a review of potential mechanisms. *Obesity Reviews, 13*(4), 368-380.

17. Hart, V., rentham-Dietz, A., Berkman, A., et al. (2018). The association between post-diagnosis health behaviors and long-term quality of life in survivors of ductal carcinoma in situ: a population-based longitudinal cohort study. *Quality of Life Research;* Online publication

18. Serra, M. C., Goldberg, A. P., & Ryan, A. S. (2016). Increased depression and metabolic risk in postmenopausal breast cancer survivors. *Diabetology & Metabolic Syndrome, 8*(1).

19. Ware, J.E., Jr., & Sherbourne, C.D. (1992) The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual Framework and Item Selection, *Medical Care*, 30:473-483.

20. Hart, V., Sprague, B., Lakoski, S., Hampton, J., Newcomb, P., Gangnon, R., Trentham-Dietz, A., (2016). Trends in Health-Related Quality of Life After a Diagnosis of Ductal Carcinoma in Situ. *Journal of Clinical Oncology.* 34(12) 1323-1329.

21. Xia, J., Tang, Z., Deng, Q., Wang, J., Yu, J., (2018) Being slightly overweight is associated with a better quality of life in breast cancer survivors. *Nature: Scientific Reports*, 8(3022) 1-8.

22. Makari-Judson, G., Braun, B., Jerry, JD., Mertens, WC. (2014).Weight gain following breast cancer diagnosis: Implication and proposed mechanisms. *World Journal of Clinical Oncology.* 5(3), 272-282.