

Washington University School of Medicine

Digital Commons@Becker

---

Biostatistics Faculty Publications

Division of Public Health Sciences Faculty  
Publications

---

2016

## Correlates of quality of life in overweight or obese breast cancer survivors at enrollment into a weight loss trial

Bilge Pakiz

*University of California - San Diego*

Patricia A. Ganz

*University of California, Los Angeles*

Rebecca L. Sedjo

*University of Colorado*

Shirley W. Flatt

*University of California - San Diego*

Wendy Demark-Wahnefried

*University of Alabama, Birmingham*

*See next page for additional authors*

Follow this and additional works at: [https://digitalcommons.wustl.edu/biostats\\_pubs](https://digitalcommons.wustl.edu/biostats_pubs)

---

### Recommended Citation

Pakiz, Bilge; Ganz, Patricia A.; Sedjo, Rebecca L.; Flatt, Shirley W.; Demark-Wahnefried, Wendy; Liu, Jingxia; Wolin, Kathleen Y.; and Rock, Cheryl L., "Correlates of quality of life in overweight or obese breast cancer survivors at enrollment into a weight loss trial" (2016). *Biostatistics Faculty Publications*. Paper 6. [https://digitalcommons.wustl.edu/biostats\\_pubs/6](https://digitalcommons.wustl.edu/biostats_pubs/6)

This Article is brought to you for free and open access by the Division of Public Health Sciences Faculty Publications at Digital Commons@Becker. It has been accepted for inclusion in Biostatistics Faculty Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact [vanam@wustl.edu](mailto:vanam@wustl.edu).

---

**Authors**

Bilge Pakiz, Patricia A. Ganz, Rebecca L. Sedjo, Shirley W. Flatt, Wendy Demark-Wahnefried, Jingxia Liu, Kathleen Y. Wolin, and Cheryl L. Rock

***This is the pre-peer reviewed version of the following article:***

Pakiz, B., Ganz, P. A., Sedjo, R. L., Flatt, S. W., Demark-Wahnefried, W., Liu, J., Wolin, K. Y., and Rock, C. L. (2016) Correlates of quality of life in overweight or obese breast cancer survivors at enrollment into a weight loss trial. *Psycho-Oncology*, 25: 142–149. doi: [10.1002/pon.3820](https://doi.org/10.1002/pon.3820).

***which has been published in final form at [10.1002/pon.3820](https://doi.org/10.1002/pon.3820). This article may be used for non-commercial purposes in accordance with [Wiley Terms and Conditions for Self-Archiving](#).***

**Correlates of quality of life in overweight or obese breast cancer survivors at enrollment into a weight loss trial**

Bilgé Pakiz,<sup>1\*</sup> Patricia A. Ganz,<sup>2</sup> Rebecca L. Sedjo,<sup>3</sup> Shirley W. Flatt,<sup>1</sup> Wendy Demark-Wahnefried,<sup>4</sup> Jingxia Liu,<sup>5</sup> Kathleen Y. Wolin,<sup>6</sup> Cheryl L. Rock<sup>1</sup>

<sup>1</sup> Department of Family Medicine and Public Health, School of Medicine, University of California, San Diego, La Jolla, California, USA

<sup>2</sup> Jonsson Comprehensive Cancer Center, and the UCLA Fielding School of Public Health, University of California, Los Angeles, California, USA

<sup>3</sup> Department of Community and Behavioral Health, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

<sup>4</sup> Department of Nutrition Sciences, University of Alabama at Birmingham, Birmingham, Alabama, USA

<sup>5</sup> Division of Biostatistics, Washington University School of Medicine, St. Louis, Missouri, USA

<sup>6</sup> Coeus Health LLC, Scale Down LLC, and the Department of Preventive Medicine, Northwestern University, Chicago, IL, USA

\* Correspondence to: Bilge Pakiz, EdD, UC San Diego Moores Cancer Center, 3855 Health Sciences Dr., Office 3076, La Jolla, California, USA 92093-0901; Telephone: 858-822-6160; Fax 858-822-6166; email: bpakiz@ucsd.edu

**Short title:** Quality of life in overweight survivors in a weight loss trial

**Word Count:** Abstract 241; Text 3281

## ABSTRACT

*Objective:* To examine the correlates of the physical and psychosocial domains of quality of life (QOL) in a cohort of breast cancer survivors participating in a weight loss intervention trial.

*Methods:* Correlates of QOL and psychosocial functioning were examined in 692 overweight/obese breast cancer survivors at entry into a weight loss trial. QOL was explored with three measures: Short-form 36 (SF-36); Impact of Cancer Scale (IOCv2); and the Breast Cancer Prevention Trial (BCPT) Symptom Scales. Available data included information on weight and physical activity, as well as demographic and medical characteristics. Multivariate analyses were used to identify associations adjusted for other characteristics.

*Results:* In multivariate analysis, younger age was associated with higher negative impact scores ( $p < 0.0001$ ). Hispanic, African-American and Asian women had higher positive IOC impact scores compared to white non-Hispanic women ( $p < 0.01$ ). Increased number of co-morbidities was associated with lower physical and mental QOL scores ( $p < 0.01$ ). BMI was not independently associated with QOL measures. Physical activity was directly associated with physical and mental QOL and IOC positive impact, and inversely related to IOC negative impact and BCPT symptom scales.

*Conclusions:* QOL measures in breast cancer survivors are differentially associated with demographic and other characteristics. When adjusted for these characteristics, degree of adiposity among overweight/obese women does not appear to be independently associated with QOL. Among overweight/obese breast cancer survivors, higher level of physical activity is associated with higher QOL across various scales and dimensions.

**Key Words:** breast cancer; quality of life; overweight; physical activity; oncology  
psychological measures

## Introduction

Breast cancer diagnosis and treatment is associated with adverse health effects in physical and psychosocial domains, and thus, can have a negative impact on quality of life (QOL) [1]. Although most symptoms show improvement over time [2], some may be long-term, lasting for up to 10 years after surgery and completion of treatment [3]. Among psychosocial correlates, depression and anxiety are often associated with poorer QOL either as indicators [4] or determinants. Sleep problems and fatigue have also been identified as being associated with poorer QOL [5], as well as weight gain after treatment [6], and often these symptoms are interrelated [7].

In a systematic review, Chopra and Kamal [8] concluded that age, ethnicity, and type of treatment influence different aspects of QOL. Similarly, differential effects of treatment on QOL have been noted for race/ethnicity, and age [9-12]. Based on a comprehensive literature review, Yanez et al. [13] concluded that Latina survivors experience worse QOL than non-Latina whites, but White et al. [14] caution that racial differences may be better explained by the variance in levels of engagement in healthy behaviors. Concerns and adverse effects may be particularly notable for younger survivors who report more adverse psychosocial and health outcomes [3, 15]. Premature menopause is thought to exacerbate the effects of treatment among these younger women [16].

Obesity and weight gain, as indicated by high body mass index (BMI), has been associated with worse QOL among breast cancer survivors [15, 17]. Post-diagnosis physical activity has been identified as a protective factor that may mitigate common side effects such as fatigue and weight gain [18] and improve overall QOL [19]. In a



large randomized clinical trial of breast cancer survivors, participants who exercised at least 150 minutes/week of moderate-paced walking reported significantly higher levels of QOL independent of race/ethnicity [11].

The purpose of this analysis was to examine the correlates of QOL and psychosocial functioning in overweight or obese breast cancer survivors using data collected upon entry into a weight loss intervention trial. The multi-center Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) study is the largest weight loss study in this patient population to date, enrolling 692 overweight or obese women who had been diagnosed and treated for early stage breast cancer [20]. Within this large and well-characterized sample, different aspects of QOL were explored with three measures: the Short-form 36 (SF-36) [21] as a general measure of physical and mental QOL; Impact of Cancer Scale (IOCv2) to assess QOL and both positive and negative aspects of cancer survivorship [10]; and the Breast Cancer Prevention Trial (BCPT) Symptom Scales to evaluate side effects of treatment [22]. We hypothesized that responses on the QOL measures would be differentially distributed across level of adiposity, as well as age, race/ethnicity, cancer stage and treatment, number of co-morbidities, and level of physical activity.

## **Methods**

### **Participants and study procedures**

A total of 692 overweight or obese breast cancer survivors were enrolled into a randomized controlled trial of a weight loss intervention, the Exercise to Enhance Recovery and Good Health for You (ENERGY) trial, at four sites (San Diego, CA; Denver, CO; St. Louis, MO; and Birmingham, AL). Inclusion criteria were: age  $\geq 21$

years; a history of breast cancer (stages I [ $\geq 1$  cm], II, or III) diagnosed within the previous five years; completion of initial therapies not including endocrine therapy; BMI 25-45 kg/m<sup>2</sup>; and ability to comply with study procedures. Exclusion criteria included: history of malignancies other than initial breast cancer with the exception of non-melanoma skin cancer, serious psychiatric illness, and any medical condition substantially limiting moderate physical activity, such as severe orthopedic conditions. The study was reviewed and approved by the Institutional Review Boards of all sites, and participants provided written informed consent. A detailed description of the study procedures and intervention has been published previously [20].

## **Measures**

### **Demographic and other characteristics**

Data included self-reported age, race/ethnicity, education level, marital status, and medical history (including co-morbidities). Anthropometric measurements (height, weight) were conducted by trained study staff using standard procedures and were used to calculate BMI [23]. Medical record review was conducted to obtain information on breast cancer diagnosis including stage and date of diagnosis and treatment and to verify eligibility.

Physical activity was measured using the modified Godin Leisure-Time Exercise Questionnaire (GLTEQ) which has been validated previously in cancer research [24]. The modified GLTEQ consists of three questions regarding the frequency and duration of mild, moderate, and strenuous exercise performed during free time in a typical week.

Risk for depression was measured with the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is comprised of 20 items and assesses risk for

depression in the general population [22]. Measures of internal consistency are high in the general population (0.85) and in psychiatric samples (0.90). Test-retest correlations are reported to be in the moderate range (0.45-0.70). Validity has been established with other self-report measures, correlations with clinical ratings of depression, and by construct validity [25]. It has also been used in other studies of cancer survivors [26].

Self-reported information on co-morbidities was collected with a questionnaire modeled after the Self-Administered Co-morbidity Questionnaire [27]. Number of reported co-morbidities (e.g., heart disease, hypertension, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, anemia, depression, osteoarthritis, back pain, rheumatoid arthritis, or other) was summed.

### **Psychosocial QOL measures**

The SF-36 is a multi-purpose, brief health survey, which is used as a general measure of physical and mental QOL [21, 28]. It is comprised of an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures. There is considerable evidence for the reliability of the SF-36 (Cronbach's  $\alpha > 0.85$ , reliability coefficient  $> 0.75$ ) [28, 29]. It has been used extensively with breast cancer survivors [5, 6, 26].

The BCPT Symptom Scales have been used to measure concurrent and late side effects of medical interventions to prevent and treat breast cancer [22]. Factor analysis with this instrument [22] has revealed eight symptom clusters corresponding to physical symptoms associated with cancer treatment, chemoprevention, menopause, and normal aging: hot flashes, nausea, bladder control, vaginal problems, musculoskeletal pain, cognitive problems, weight problems, and arm problems.

The IOC was developed specifically to measure the impact of cancer on aspects of QOL in long term survivors (i.e. > 5 years since diagnosis) [10]. Recent refinement of this instrument in a large sample of long-term breast cancer survivors (ref 10) yielded a factor structure relating IOC items to psychosocial impact domains that exhibited high factor loadings (factor-item correlations of 0.59-0.94) and high internal consistency (Cronbach's  $\alpha=0.76-0.89$ ). The scales consist of a Positive Impact Summary Scale with four subscales (altruism and empathy, health awareness, meaning of cancer, and positive self-evaluation), a Negative Impact Summary Scale with four subscales (appearance concerns, body change concerns, life interferences, and worry), and subscales for Employment and Relationship Concerns.

### **Statistical analysis**

For the five overall QOL outcome measures (summary scores for physical and mental QOL, IOC positive and negative impact scales, and mean severity averaged across all 18 symptoms on the BCPT questionnaire), bivariate analyses were used to examine associations with the *a priori* hypothesized influencing variables (BMI, age, race/ethnicity, cancer stage and treatment, number of co-morbidities, and level of physical activity) and exploratory variables (education, marital status, and time since diagnosis). We hypothesized that greater degree of adiposity (higher BMI), younger age, higher stage, chemotherapy, and number of co-morbidities would be associated with worse physical and mental QOL, higher IOC negative impact, and greater BCPT symptoms. We also hypothesized that higher physical activity would be inversely associated with these measures.

Continuous variables (age, BMI, number of co-morbidities, weekly hours of moderate/vigorous activity, and CES-D score) were modeled in continuous ANOVA. Categorical variables (race/ethnicity, cancer stage, chemotherapy, endocrine therapy, education, marital status) were compared using categorical ANOVA where the first category was the referent. Implementing a conservative strategy, we used a significance level of  $\alpha = 0.01$  for the bivariate models, and  $p \leq 0.05$  in the multivariate model, without further adjustment for multiple comparisons. All tests were two-sided.

Multivariate models for four of the main outcomes (physical and mental QOL and IOC positive and negative impact scale) used regression models to examine relationships between the predictors jointly and outcomes. The multivariate analyses included all variables that were *a priori* hypothesized predictors, as well as the 8 BCPT symptom clusters, but did not include the exploratory variables. Dependent variables were log transformed to reduce skew in their distributions.

We also evaluated the four subscales each from the IOC Positive and Negative Impact Scales separately. We set significance at  $p < 0.01$  for the subscale analyses. Analyses were conducted using SAS version 9.3 (Cary, NC).

## Results

Participants were 692 overweight or obese breast cancer survivors with a mean (SD) age of 56 (9) years at enrollment. Characteristics of the study sample and distribution of scores across the QOL measures are shown in Tables 1 and 2. The majority of the sample was non-Hispanic white, and BMI at study entry was 31.4 (4.7) kg/m<sup>2</sup>. On average, time since diagnosis was 2.7 years (range 0.25-5.8 years). A

majority of the women had been diagnosed with stage II cancer (52%), and 30% and 18% had stage I and stage III cancer, respectively.

In bivariate analysis, responses on the QOL measures were differentially distributed across categories of demographic characteristics, as shown in Table 1. QOL measures differed across age, BMI, and race/ethnicity categories. Compared to white, non-Hispanic participants, Hispanic, African-American and Asian participants all reported higher scores on the IOC positive impact scale ( $p < 0.01$ ). Responses on the QOL measures also were differentially distributed across categories of medical and cancer-related factors, as shown in Table 2. Having more co-morbidities was associated with lower physical and mental QOL scores ( $p < 0.01$ ).

Differential responses on the QOL measures across physical activity and CES-D score categories are shown in Table 3. Being moderately active, as is recommended for weight management [30], was associated with better scores on the physical and mental QOL scales ( $p < 0.01$ ), and a dose-response effect was observed. Higher level of physical activity was associated with lower scores on the IOC negative impact scale ( $p < 0.01$ ) and with lower scores on the BCPT symptoms scales ( $p < 0.01$ ). The reverse was true for those who had higher scores ( $\geq 16$ ) on the CES-D. Those at higher risk for depression had lower scores on physical and mental QOL and higher scores on the BCPT symptom scales ( $p < 0.01$ ).

Table 4 shows the associations for the *a priori* hypothesized variables when adjusted for other influencing variables in the multivariate models. Younger age was associated with higher IOC negative impact scale ( $p < 0.0001$ ). Hispanic, African-American and Asian women had higher scores on the IOC positive impact scale

compared to white, non-Hispanic women, and African-American women scored lower on the IOC negative impact scale ( $p < 0.01$ ). Number of co-morbidities and several BCPT symptom clusters were associated with lower physical and mental QOL ( $p < 0.02$ ), when adjusted for other variables.

Contrary to our hypothesis, BMI was not independently associated with any of the QOL measures in the multivariate models. As hypothesized, level of physical activity was associated with physical and mental QOL ( $p < 0.01$ ). Women with higher levels of depressive symptoms on the CES-D had significantly lower physical QOL, lower IOC positive impact and higher IOC negative impact scores ( $p < 0.001$ ).

As shown in Table 4, the BCPT symptom scale for nausea was inversely associated with both physical and mental QOL ( $p < 0.01$ ). The BCPT scale for bladder control was inversely associated with mental QOL, and the musculoskeletal pain scale was inversely associated with physical and mental QOL ( $p < 0.02$ ). Cognitive problems were inversely associated with mental QOL, and directly associated with both IOC positive and negative impact scores. The BCPT symptom scale for weight problems was inversely associated with mental QOL and directly associated with the IOC negative impact scores ( $p < 0.01$ ). The BCPT arm problems scale was inversely associated with physical QOL scores, meaning lower severity of arm problems was associated with better physical QOL scores, and directly associated with the IOC negative impact scale ( $p < 0.001$ ). Two of the symptom scales (vasomotor and vaginal problems) were not significantly associated with any of the QOL outcomes.

Associations with the subscales of the IOC negative and positive impact score also were examined (data not shown), and cancer stage was directly associated with

scores for each negative impact subscale ( $p < 0.01$ ). In contrast, age and African-American ethnicity were inversely associated with every subscale score. Age was inversely associated with altruism and meaning of cancer subscale scores. African-American, Asian and Hispanic race/ethnicity were all directly associated with health awareness and positive self-concerns subscales. In addition, being African-American was associated with greater meaning of cancer, while being Asian was associated with altruism. Chemotherapy was directly associated with scores for all four IOC positive impact subscales ( $p < 0.01$  for all).

## **Discussion**

We found that various dimensions and measures of QOL in breast cancer survivors are differentially associated with demographic and medical characteristics. After adjusting for these characteristics, contrary to our hypotheses, degree of adiposity had no relationship to any of the QOL outcomes in the multivariable models, although BMI was inversely associated with physical (but not mental) QOL when unadjusted for other influencing variables. However, we found that among overweight or obese breast cancer survivors, higher level of physical activity correlates with higher mental and physical QOL and does so in a dose-dependent manner.

This analysis presents a multifaceted approach to examining QOL in a large and geographically-diverse sample of overweight or obese breast cancer survivors. By utilizing several different measurement constructs, this study provides a global examination of the psychosocial and physical QOL associations in this target population. In particular, this is the first study, to our knowledge, to have used the IOC in shorter-term breast cancer survivors, along with the SF-36 and the BCPT symptom



scales. In addition to the large sample, the diversity of the sample also allowed analysis of findings for various subgroups, such as older versus younger survivors or those with different racial/ethnicity and cancer characteristics.

The characteristics that were found to impact QOL in the current study can be compared to those reported in other studies with breast cancer survivors, and confirm and expand upon what has been observed in other reports. Using the SF-36, Bowen et al. [9] concluded that participants in the HEAL study were doing relatively well two years after diagnosis, even though some racial/ethnic and socioeconomic differences were identified as important determinants of QOL. Utilizing the BCPT Symptom Scales, Ganz et al. [1] noted that even though overall functioning improved after breast cancer treatment, those who received chemotherapy reported more severe physical symptoms such as vaginal and weight problems.

In this study, age at diagnosis and non-white race/ethnicity (Hispanic, African-American or Asian) were identified as independently associated with QOL in breast cancer survivors, with younger women experiencing more negative impact from the cancer and non-white women noting more meaning and positive impact from the cancer experience. This is consistent with other studies in the literature, although this study is notable for assessing these issues in a group of women earlier in the post-treatment phase of survivorship. Although younger participants noted some positive outcomes from their experience on the IOC measure (i.e., becoming more health aware, valuing their relationships more), our results suggest that their overall outlook on body changes was more negative, and they reported more health-related worries and treatment-related symptoms. This observation held true in IOC subscale analysis as well. In another

sample of breast cancer survivors, Crespi et al. [11] also found younger women to have somewhat higher scores on both positive and negative IOC scores, and results from previous studies indicate that survivors <50 years of age report concerns about premature menopause and infertility, physiologic symptoms such as night sweats and hot flashes, weight gain, and adverse psychosocial outcomes, such as depressive symptoms [15, 16]. Future studies that focus on identifying effective strategies to improve QOL in this vulnerable group of survivors are clearly warranted.

Racial/ethnic minority participants reported higher IOC positive and negative impact scores which may indicate willingness to see cancer as a positive life challenge, such as having more health awareness and positive self-concerns as identified by IOC subscale analysis. Other studies have noted greater meaning and personal growth among African-American breast cancer survivors [31, 32], and better QOL. Different levels of QOL for survivors with diverse racial and ethnic backgrounds have been identified in prior studies [13].

The association between degree of adiposity (reflected in the BMI) and better physical QOL in the bivariate analysis did not remain significant in the multivariate model, although at enrollment in this study, none of the participants was in the healthy weight range. In another sample of breast cancer survivors, higher BMI was associated with higher IOC negative impact and subscales [11], but that observation was not adjusted for other influencing factors as in the present study. There is evidence in the literature that maintaining a healthy weight is an independent factor for better prognosis of breast cancer [33, 34], as well as for better overall physical functioning and management of treatment side effects such as sleep and mood problems [6]. However,

results of this analysis suggest that in overweight or obese women, co-morbidities and other factors are crucial determinants of QOL.

As in the present study, Ashing-Giwa and Lim [35] found that having fewer co-morbidities were related to better mental and physical QOL in a diverse group of breast cancer survivors. This is an important finding because it suggests that overweight or obese breast cancer survivors who can lose enough weight to impact co-morbidities, even if they do not achieve an optimal weight, may improve QOL. Ganz et al. [1] found that even though physical and social functioning improves after treatment, physical symptoms persist for those who have received chemotherapy for up to a year. Similarly, in the current study, participants indicated experiencing lower mental and physical QOL in association with a myriad of symptoms such as nausea, bladder control issues, and musculoskeletal and arm problems. That these factors are contributing to lower mental and physical QOL is an important finding, and attention to symptom control could be important for improving QOL outcomes.

Multivariate models in this study revealed that more physical activity in these overweight or obese women was related to better overall QOL, having a more positive outlook on life, as well as having fewer health-related worries and treatment-related symptoms. In fact, our observations suggest that any amount of exercise is better than none. In contrast, higher depressive symptomatology scores were associated with lower physical QOL scores, as well as lower positive impact and higher negative impact IOC scores, as previously observed in this target population [11]. Although this analysis uses cross-sectional data that cannot imply causality, previous interventions have shown that exercise has positive impact on overall QOL [36] and also depressive

symptoms [37, 38] and fatigue [39]. Regular physical activity after breast cancer diagnosis and treatment also may mitigate common side effects of adjuvant therapy, such as weight gain and fatigue [36], depression, reduced QOL, as well as decreased muscular strength [40].

Results of this study present important evidence of symptom burden following treatment in overweight or obese breast cancer survivors. However, this study also has limitations. Even though the large sample size allowed for subgroup analysis, the study sample was nonetheless largely homogeneous, so results may not be entirely representative of the general population of breast cancer survivors. Nevertheless, most breast cancers are diagnosed in overweight or obese women, and our sample had more diversity than most other studies in this research area. It is important to examine these constructs in an even more diverse sample of breast cancer survivors, particularly among those across an even wider range of BMI, including lean women. Additionally, we have not addressed all potential confounding influences, such as income [35], location of treatment (e.g., academic centers, community- or hospital-based practices), or rural vs. urban environment. Finally, the relationship between depression and QOL is not straightforward, and future research should examine the impact of these variables on QOL. Future research is needed to examine this complex association in cancer survivors to determine if depression is an indicator or determinant of QOL.

These baseline findings set the stage for the longitudinal evaluation of QOL outcomes in this study sample. In future analyses we can examine whether increased physical activity and weight loss have a positive impact on QOL and improve long term functionality in this group of overweight or obese breast cancer survivors.

**Acknowledgements**

This study was supported by National Cancer Institute grant CA148791. The ENERGY Trial Group investigators: *University of California, San Diego*: Cheryl Rock, PhD, RD, Bilge Pakiz, EdD, Barbara Parker, MD; *University of California, Los Angeles*: Patricia Ganz, MD; *University of Colorado, Denver*: Tim Byers, MD, MPH, Rebecca Sedjo, PhD, Holly Wyatt, MD, Anthony Elias, MD, James Hill, PhD; *Washington University in St. Louis*: Graham Colditz, MD, Kathleen Wolin, ScD, Jingxia Liu, PhD, Michael Naughton, MD; and *University of Alabama at Birmingham*: Wendy Demark-Wahnefried, PhD, RD, Helen Krontiras, MD, Maria Azrad, PhD, RD.

**Conflict of Interest**

The authors declare that they have no conflicts of interest.

## References

1. Ganz PA, Kwan L, Stanton AL, Bower JE, Belin TR. Physical and psychosocial recovery in the year after primary treatment of breast cancer. *J Clin Oncol* 2011, **29**:1101-1109.10.1200/JCO.2010.28.8043.3083865.
2. Hsu M-C, Tu C-H. Improving quality-of-life outcomes for patients with cancer through mediating effects of depressive symptoms and functional status: a three-path mediation model. *Journal of Clinical Nursing* 2013:n/a-n/a.10.1111/jocn.12399.
3. Koch L, Jansen L, Herrmann A, Stegmaier C, Holleczeck B, Singer S, *et al.* Quality of life in long-term breast cancer survivors - a 10-year longitudinal population-based study. *Acta Oncol* 2013, **52**:1119-1128.10.3109/0284186X.2013.774461.
4. Hutter N, Vogel B, Alexander T, Baumeister H, Helmes A, Bengel J. Are depression and anxiety determinants or indicators of quality of life in breast cancer patients? *Psychol Health Med* 2013, **18**:412-419.10.1080/13548506.2012.736624.
5. Meeske K, Smith AW, Alfano CM, McGregor BA, McTiernan A, Baumgartner KB, *et al.* Fatigue in breast cancer survivors two to five years post diagnosis: a HEAL Study report. *Qual Life Res* 2007, **16**:947-960.10.1007/s11136-007-9215-3.
6. Imayama I, Alfano CM, Neuhouser ML, George SM, Wilder Smith A, Baumgartner RN, *et al.* Weight, inflammation, cancer-related symptoms and health related quality of life among breast cancer survivors. *Breast Cancer Res Treat* 2013, **140**:159-176.10.1007/s10549-013-2594-y.3772666.
7. Alfano CM, Lichstein KL, Vander Wal GS, Smith AW, Reeve BB, McTiernan A, *et al.* Sleep duration change across breast cancer survivorship: associations with symptoms and health-related quality of life. *Breast Cancer Res Treat* 2011, **130**:243-254.10.1007/s10549-011-1530-2.3929112.
8. Chopra I, Kamal KM. A systematic review of quality of life instruments in long-term breast cancer survivors. *Health Qual Life Outcomes* 2012, **10**:14.10.1186/1477-7525-10-14.3280928.
9. Bowen DJ, Alfano CM, McGregor BA, Kuniyuki A, Bernstein L, Meeske K, *et al.* Possible socioeconomic and ethnic disparities in quality of life in a cohort of breast cancer survivors. *Breast Cancer Res Treat* 2007, **106**:85-95.10.1007/s10549-006-9479-2.2999962.
10. Crespi CM, Ganz PA, Petersen L, Castillo A, Caan B. Refinement and psychometric evaluation of the impact of cancer scale. *J Natl Cancer Inst* 2008, **100**:1530-1541.10.1093/jnci/djn340.2586823.
11. Paxton RJ, Phillips KL, Jones LA, Chang S, Taylor WC, Courneya KS, *et al.* Associations among physical activity, body mass index, and health-related quality of life by race/ethnicity in a diverse sample of breast cancer survivors. *Cancer* 2012, **118**:4024-4031.10.1002/cncr.27389.3330155.
12. Paskett ED, Alfano CM, Davidson MA, Andersen BL, Naughton MJ, Sherman A, *et al.* Breast cancer survivors' health-related quality of life. *Cancer* 2008, **113**:3222-3230.10.1002/cncr.23891.

13. Yanez B, Thompson EH, Stanton AL. Quality of life among Latina breast cancer patients: a systematic review of the literature. *J Cancer Surviv* 2011, **5**:191-207.10.1007/s11764-011-0171-0.3096762.
14. White A, Pollack LA, Smith JL, Thompson T, Underwood JM, Fairley T. Racial and ethnic differences in health status and health behavior among breast cancer survivors--Behavioral Risk Factor Surveillance System, 2009. *J Cancer Surviv* 2013, **7**:93-103.10.1007/s11764-012-0248-4.
15. Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. *J Natl Cancer Inst* 2012, **104**:386-405.10.1093/jnci/djr541.
16. Rosenberg SM, Partridge AH. Premature menopause in young breast cancer: effects on quality of life and treatment interventions. *J Thorac Dis* 2013, **5**:S55-61.10.3978/j.issn.2072-1439.2013.06.20jtd-05-S1-S55 [pii].3695534.
17. Binkley JM, Harris SR, Levangie PK, Pearl M, Guglielmino J, Kraus V, *et al*. Patient perspectives on breast cancer treatment side effects and the prospective surveillance model for physical rehabilitation for women with breast cancer. *Cancer* 2012, **118**:2207-2216.10.1002/cncr.27469.
18. Hayes SC, Rye S, Disipio T, Yates P, Bashford J, Pyke C, *et al*. Exercise for health: a randomized, controlled trial evaluating the impact of a pragmatic, translational exercise intervention on the quality of life, function and treatment-related side effects following breast cancer. *Breast Cancer Res Treat* 2013, **137**:175-186.10.1007/s10549-012-2331-y.
19. Smith AW, Alfano CM, Reeve BB, Irwin ML, Bernstein L, Baumgartner K, *et al*. Race/ethnicity, physical activity, and quality of life in breast cancer survivors. *Cancer Epidemiol Biomarkers Prev* 2009, **18**:656-663.10.1158/1055-9965.EPI-08-0352.3031117.
20. Rock CL, Byers TE, Colditz GA, Demark-Wahnefried W, Ganz PA, Wolin KY, *et al*. Reducing breast cancer recurrence with weight loss, a vanguard trial: the Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) Trial. *Contemp Clin Trials* 2013, **34**:282-295.S1551-7144(12)00262-5 [pii] 10.1016/j.cct.2012.12.003.3593786.
21. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992, **30**:473-483.
22. Stanton AL, Bernaards CA, Ganz PA. The BCPT symptom scales: a measure of physical symptoms for women diagnosed with or at risk for breast cancer. *J Natl Cancer Inst* 2005, **97**:448-456.10.1093/jnci/dji069.
23. Lohman TG, Roche AF, Martorell R. *Anthropometric standardization reference manual*. Champaign, IL: Human Kinetics Books; 1988.
24. Milne HM, Wallman KE, Gordon S, Courneya KS. Effects of a combined aerobic and resistance exercise program in breast cancer survivors: a randomized controlled trial. *Breast Cancer Res Treat* 2008, **108**:279-288.10.1007/s10549-007-9602-z.

25. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement* 1977, **1**:385-401.10.1177/014662167700100306.
26. Ganz PA, Rowland JH, Desmond K, Meyerowitz BE, Wyatt GE. Life after breast cancer: understanding women's health-related quality of life and sexual functioning. *J Clin Oncol* 1998, **16**:501-514.
27. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The self-administered comorbidity questionnaire: A new method to assess comorbidity for clinical and health services research. *Arthritis Care & Research* 2003, **49**:156-163.10.1002/art.10993.
28. Brazier J, Usherwood T, Harper R, Thomas K. Deriving a preference-based single index from the UK SF-36 Health Survey. *J Clin Epidemiol* 1998, **51**:1115-1128.
29. Ware J. *SF-36 Health Survey update*. In Maruish ME, ed. *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment*. 3rd edn. Mahwah (NJ): Lawrence Erlbaum Associates; 2004.
30. Institute Of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. The National Academies Press; 2001.
31. Ganz PA, Guadagnoli E, Landrum MB, Lash TL, Rakowski W, Silliman RA. Breast cancer in older women: quality of life and psychosocial adjustment in the 15 months after diagnosis. *J Clin Oncol* 2003, **21**:4027-4033.10.1200/JCO.2003.08.097.
32. Ganz PA, Desmond KA, Leedham B, Rowland JH, Meyerowitz BE, Belin TR. Quality of life in long-term, disease-free survivors of breast cancer: a follow-up study. *J Natl Cancer Inst* 2002, **94**:39-49.
33. Bradshaw PT, Ibrahim JG, Stevens J, Cleveland R, Abrahamson PE, Satia JA, et al. Postdiagnosis change in bodyweight and survival after breast cancer diagnosis. *Epidemiology* 2012, **23**:320-327.10.1097/EDE.0b013e31824596a1.3586208.
34. Demark-Wahnefried W, Campbell KL, Hayes SC. Weight management and its role in breast cancer rehabilitation. *Cancer* 2012, **118**:2277-2287.10.1002/cncr.27466.
35. Ashing-Giwa KT, Lim JW. Examining the impact of socioeconomic status and socioecologic stress on physical and mental health quality of life among breast cancer survivors. *Oncol Nurs Forum* 2009, **36**:79-88.10.1188/09.ONF.79-88.
36. Ligibel JA, Partridge A, Giobbie-Hurder A, Campbell N, Shockro L, Salinardi T, et al. Physical and psychological outcomes among women in a telephone-based exercise intervention during adjuvant therapy for early stage breast cancer. *J Womens Health (Larchmt)* 2010, **19**:1553-1559.10.1089/jwh.2009.1760.
37. Fuscaldo JM. Prescribing physical activity in primary care. *W V Med J* 2002, **98**:250-253.
38. Kesaniemi YK, Danforth E, Jr., Jensen MD, Kopelman PG, Lefebvre P, Reeder BA. Dose-response issues concerning physical activity and health: an evidence-based symposium. *Med Sci Sports Exerc* 2001, **33**:S351-358.



39. Winningham ML, MacVicar MG, Bondoc M, Anderson JI, Minton JP. Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. *Oncol Nurs Forum* 1989, **16**:683-689.
40. Loprinzi PD, Cardinal BJ. Effects of physical activity on common side effects of breast cancer treatment. *Breast Cancer* 2012, **19**:4-10.10.1007/s12282-011-0292-3.

**Table 1.** Quality of life (QOL) measures within demographic and anthropometric categories (N = 692)<sup>a</sup>

	N	QOL Physical	QOL Mental	IOC Positive Impact Scale	IOC Negative Impact Scale	BCPT Symptom Scales
Age at enrollment (yrs)						
<50	173	70.4 (19.5)	73.4 (19.2)	3.9 (0.5)*	2.9 (0.8)*	2.1 (0.6)*
50-64	372	71.8 (18.4)	76.0 (18.0)	3.8 (0.6)*	2.7 (0.7)*	2.1 (0.5)*
≥65	147	67.7 (17.8)	77.2 (16.4)	3.7 (0.5)*	2.4 (0.7)*	1.9 (0.5)*
Body mass index (kg/m <sup>2</sup> )						
25-29.99	285	72.3 (17.9)*	75.9 (17.9)	3.8 (0.6)	2.7 (0.7)	2.0 (0.5)
30-34.99	243	70.5 (18.8)*	74.7 (18.5)	3.8 (0.6)	2.6 (0.7)	2.0 (0.5)
35-45	164	67.6 (19.2)*	76.3 (17.5)	3.8 (0.6)	2.6 (0.7)	2.1 (0.6)
Race/ethnicity						
White, non-Hispanic	547	70.8 (17.7)	75.9 (17.3)	3.8 (0.5)	2.7 (0.7)	2.0 (0.5)
Hispanic	46	68.9 (19.2)	70.3 (21.5)	4.0 (0.5)*	2.8 (0.7)	2.1 (0.6)
African-American	71	67.9 (24.3)	75.2 (21.1)	4.0 (0.6)*	2.5 (0.8)	2.2 (0.6)
Asian	11	76.8 (13.9)	82.1 (11.5)	4.3 (0.3)*	2.8 (0.6)	1.7 (0.3)
Mixed/other	15	74.1 (18.4)	76.3 (17.7)	3.9 (0.6)	2.7 (0.7)	1.9 (0.4)
Education						
Not a college graduate	282	70.6 (18.5)	76.0 (17.5)	3.9 (0.5)*	2.6 (0.7)	2.1 (0.5)
College graduate	410	70.5 (18.7)	75.3 (18.3)	3.7 (0.6)*	2.7 (0.7)	2.0 (0.6)
Marital status						
Married/partnered	463	72.0 (17.7)	77.1 (17.5)	3.8 (0.6)	2.7 (0.7)	2.1 (0.5)
Not married or partnered	228	67.6 (20.1)*	72.5 (20.4)*	3.8 (0.6)	2.7 (0.8)	2.0 (0.5)

<sup>a</sup> Values shown are mean (SD).

\*  $p < 0.01$ ; continuous variables (age and body mass index) were modeled in continuous ANOVA, and categorical variables were compared using categorical ANOVA where the first category was the referent.

**Table 2.** Quality of life (QOL) measures within medical and cancer-related categories (N = 692)<sup>a</sup>

	N	QOL Physical	QOL Mental	IOC Positive Impact Scale	IOC Negative Impact Scale	BCPT Symptom Scales
Time since diagnosis						
<1 year	76	66.1 (21.1)*	70.5 (21.2)*	3.9 (0.6)	2.7 (0.7)	2.1 (0.6)
1-2.9 years	325	69.5 (18.9)*	75.0 (17.6)*	3.8 (0.6)	2.7 (0.7)	2.1 (0.5)
≥3 years	291	72.9 (17.2)*	77.5 (17.2)*	3.8 (0.6)	2.6 (0.7)	2.0 (0.6)
Cancer stage						
I	210	73.3 (17.5)	77.2 (17.6)	3.7 (0.6)	2.5 (0.7)	2.0 (0.5)
II	358	70.7 (18.8)	75.4 (18.0)	3.8 (0.6)*	3.0 (0.7)*	2.1 (0.6)
III	124	65.4 (18.8)*	73.3 (18.4)	3.9 (0.5)	2.9 (0.7)*	2.1 (0.5)*
Chemotherapy						
No	165	73.5 (17.5)	76.6 (18.3)	3.6 (0.6)	2.5 (0.7)	1.9 (0.5)
Yes	527	69.6 (18.8)	75.3 (17.9)	3.9 (0.5)*	2.7 (0.7)*	2.1 (0.6)*
Endocrine therapy						
None	179	69.0 (19.6)	74.2 (19.3)	3.8(0.6)	2.8 (0.8)	2.0 (0.5)
Anti-estrogen only	147	71.5 (20.4)	75.4 (17.5)	3.9 (0.5)	2.7 (0.7)	2.1 (0.6)
Aromatase inhibitor	366	70.9 (17.3)	76.3 (17.5)	3.8 (0.6)	2.6 (0.7)	2.1 (0.6)
Co-morbidities <sup>b</sup>						
None	253	75.7 (16.2)*	78.2 (16.0) *	3.9 (0.5)	2.6 (0.7)	2.0 (0.6)*
1	240	70.5 (18.2)*	76.2 (17.3)*	3.7 (0.6)	2.7 (0.7)	2.0 (0.5)*
2	119	67.5 (18.4)*	74.0 (18.6)*	3.8 (0.6)	2.6 (0.7)	2.9 (0.5)*
3 or more	80	59.0 (21.1)*	67.7 (22.2)*	3.8 (0.6)	2.7 (0.8)	2.2 (0.6)*

<sup>a</sup> Values shown are mean (SD).

<sup>b</sup> Co-morbidities assessed are current treatment for heart disease, hypertension, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, anemia, depression, osteoarthritis, back pain, rheumatoid arthritis and other conditions.

\*  $p < 0.01$ , continuous variables were modeled in continuous ANOVA, and categorical variables (cancer stage, chemotherapy, and endocrine therapy) were compared using categorical ANOVA where the first category was the referent.

**Table 3.** Quality of life (QOL) measures within strata of behavioral and psychosocial covariates (N = 692)<sup>a</sup>

	<b>N</b>	<b>QOL Physical</b>	<b>QOL Mental</b>	<b>IOC Positive Impact Scale</b>	<b>IOC Negative Impact Scale</b>	<b>BCPT Symptom Scales</b>
Moderate/vigorous activity, hrs/wk						
None	284	65.9 (19.6)*	72.3 (19.0)*	3.8 (0.6)	2.7 (0.7)*	2.1 (0.5)*
0.1-0.9	70	69.0 (18.8)*	73.8 (17.0)*	3.8 (0.5)	2.9 (0.7)*	2.1 (0.6)*
1-2.9	208	73.6 (16.6)*	77.1 (16.7)*	3.8 (0.6)	2.6 (0.7)*	2.0 (0.5)*
3 or more	130	76.6 (16.8)*	81.3 (16.8)*	3.9 (0.6)	2.6 (0.7)*	1.9 (0.6)*
CES-D score						
Not depressed (0-15)	555	73.9 (16.6)*	81.0 (12.6)*	3.8 (0.6)	2.5 (0.6)*	1.9 (0.5)*
At risk for depression ( $\geq 16$ )	137	57.1 (20.1)*	53.7 (19.8)*	3.8 (0.6)	3.3 (0.8)*	2.5 (0.5)*

<sup>a</sup> Values shown are mean (SD).

\* $p < 0.01$ .

**Table 4.** Multivariate models for quality of life (QOL) measures in overweight/obese breast cancer survivors (N = 692)<sup>a</sup>

	QOL Physical R <sup>2</sup> =0.43		QOL Mental R <sup>2</sup> =0.30		IOC Positive Impact Scale R <sup>2</sup> =0.11		IOC Negative Impact Scale R <sup>2</sup> =0.39	
	$\beta$ Coefficient	<i>p</i> Value	$\beta$ Coefficient	<i>p</i> Value	$\beta$ Coefficient	<i>p</i> Value	$\beta$ Coefficient	<i>p</i> Value
Age	-.001	.55	.002	.15	-.004	.12	-.011	<b>&lt;.0001</b>
Body mass index	-.003	.20	.003	.28	-.000	.95	-.009	.08
Race/ethnicity								
African-American	.002	.94	-.027	.50	.269	<b>.0002</b>	-.396	<b>&lt;.0001</b>
Asian	.018	.81	.018	.84	.538	<b>.001</b>	.173	.33
Hispanic	-.003	.94	-.056	.22	.233	<b>.006</b>	.090	.32
Cancer stage	-.027	.10	-.013	.49	-.003	.92	.125	<b>.0008</b>
Chemotherapy	.022	.40	.037	.22	.233	<b>&lt;.0001</b>	.023	.69
Any endocrine therapy	.032	.16	.029	.28	.046	.34	-.092	.08
No. of co-morbidities	-.040	<b>&lt;.0001</b>	-.032	<b>.006</b>	-.012	.58	.024	.30
Moderate/vigorous activity	.012	<b>.006</b>	.014	<b>.01</b>	.010	.29	-.002	.82
CES-D Score*	-.009	<b>&lt;.0001</b>	x	x	-.012	<b>.001</b>	.031	<b>&lt;.0001</b>
BCPT symptom clusters								
Hot flashes	-.005	.55	.002	.84	.015	.44	.010	.63
Nausea	-.083	<b>.002</b>	-.086	<b>.005</b>	-.061	.27	.031	.60
Bladder control	.011	.36	-.028	<b>.05</b>	.003	.91	.021	.45
Vaginal problems	.013	.12	.006	.53	.001	.94	.021	.28
Musculoskeletal pain	-.128	<b>&lt;.0001</b>	-.032	<b>.02</b>	-.001	.96	.048	.09
Cognitive problems	-.016	.23	-.124	<b>&lt;.0001</b>	.081	<b>.004</b>	.064	<b>.04</b>
Weight problems	-.006	.54	-.041	<b>.0009</b>	-.012	.60	.112	<b>&lt;.0001</b>
Arm problems	-.046	<b>.001</b>	.008	.60	.002	.95	.088	<b>.006</b>

<sup>a</sup> Values shown are  $\beta$  coefficients and  $p$  values for associations with each of the four outcomes, when controlled for all variables tabulated. Quality of life outcomes were log transformed

\* CES-D score was omitted as a predictor for *QOL Mental* because of high correlation between the two ( $\rho = -0.72$ ).