Diet Quality and Weight Maintenance in Rural Breast Cancer Survivors

BY

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Abstract

Purpose: Obesity and diet quality are two factors associated with increased risk of recurrence and morbidity/mortality among breast cancer survivors. The purpose of this study was to explore the importance of diet quality on weight maintenance in a cohort of rural breast cancer survivors after an intense weight loss intervention.

Methods: Study participants were overweight/obese breast cancer survivors who had previously lost ≥5% of their body weight in an intense 6 month weight loss intervention. Participants were randomized into two intervention arms during a 12-month weight maintenance period: 1) a mailed information group or 2) a phone counseling group. All participants in this study provided 24-hour dietary recall information at the beginning and end of the weight loss intervention, as well as 24-hour dietary recall information at the end of the weight maintenance intervention. The recalls were entered into the Nutrition Data System for Research (NDSR) and Healthy Eating Index (HEI) 2010 scores were calculated. A logistic regression was run to examine the relationship between HEI-2010 scores at the end of the weight loss intervention, weight maintenance at the end of the weight maintenance intervention, and randomization to weight maintenance intervention. ANOVA analysis was used to examine differences between randomization arm and HEI-2010 scores at the end of the weight maintenance intervention, as well as differences between HEI-2010 scores at the end of weight loss and the end of weight maintenance. Multiple linear regression was used to predict HEI-2010 scores at the end of weight maintenance from diet quality change during the weight loss intervention, HEI-2010 scores at the end of weight loss, and the interaction between diet quality change during weight loss and HEI-2010 scores at the end of weight loss.

Results: There was no relationship between the HEI-2010 scores at the end of the 6 month weight loss intervention and the HEI 2010 scores at the end of the 12 month weight maintenance period (64.2 vs. 64.5, p = 0.69). There was also no difference in 12 month scores between the randomization arms (phone 64.8 vs mail 64.2, p = 0.72). The interaction between diet quality change and HEI-2010 scores at the end of the weight loss intervention to predict HEI-2010 scores at the end of weight maintenance was insignificant (p=0.10), although HEI-2010 score at the end of weight loss was shown to be significant in predicting HEI-2010 score at the end of weight maintenance (p=0.01). Participants were predicted to increase their odds of maintaining weight loss by 3.1% for every 1-point higher HEI-2010 score at the end of the weight loss period (point estimate 1.031, 95% CI 0.99-1.07), although this finding was not statistically significant (p=0.13). Additionally, randomization to the phone intervention during weight maintenance was predicted to increase chances of weight maintenance by ~ 181% (point estimate 2.81, 95% CI 1.30-6.05, p=0.01).

Conclusions: Diet quality improvements during weight loss have a lasting effect on diet quality during weight maintenance, regardless of intervention type during weight maintenance. However, type of counseling during weight maintenance does play an important role in maintaining weight loss.

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Chapter 1: Introduction

Breast cancer is a major chronic disease among women, with the American Cancer Society estimating nearly 300,00 new cases being diagnosed in 2015 (1). It is estimated that over 40,000 women will die from breast cancer in 2016 alone (1). However, survival rates for women diagnosed with breast cancer are high. Five year cause-specific breast cancer survival rates range from 92% (for Asian-American women) to 80% (for African-American women) (1). Obesity (body-mass index (BMI) score $\geq$ 30.0 kg/m^2) has been linked with breast cancer diagnosis in post-menopausal women and cancer recurrence in both pre- and post-menopausal women. Research has shown decreased rates of cancer recurrence and death among post-menopausal breast cancer survivors who maintain a healthy BMI ($\geq$18.5 and $\leq$ 24.9 kg/m^2) (2-4). However, an elevated BMI has been correlated with reduced risk for breast cancer among pre-menopausal women (4). The relationship between obesity and breast cancer may be further compounded in rural areas, as obesity rates continue to increase in rural populations (5), and rates of rural breast cancer diagnosis continue to increase (6-8).

Researchers have also examined possible correlations between various diet quality indices and the recurrence of breast cancer, but with mixed results. Diet quality scores have had little correlation with breast cancer recurrence (9-13), although some research shows a possible negative correlation between diet quality scores and breast cancer risk (14). However, higher diet quality indices scores have been linked with a reduction in chronic diseases such as cardiovascular disease (15-17) and obesity (18) in all populations, and a reduced risk of death from causes other than cancer in breast cancer survivors (11, 13). Research examining a correlation between diet quality indices and weight maintenance among breast cancer survivors has been very limited.

Statement of Purpose

The purpose of this study was to examine the relationship between a diet quality index, the Healthy Eating Index 2010 (HEI-2010), and 12 months of weight maintenance in a cohort of rural breast cancer survivors who had previously participated in a structured 6 month weight loss intervention. In addition, we examined the difference between HEI-2010 scores after 12 months of weight maintenance and the type of maintenance intervention, to determine if type of weight maintenance intervention had a significant effect on HEI-2010 scores. Finally, we examined the relationship between diet quality change during the weight loss intervention, HEI-2010 scores at the end of the weight loss intervention, and HEI-2010 scores at the end of the weight maintenance intervention, to determine whether HEI-2010 scores at the 6 month weight loss intervention timepoint predicted HEI-2010 scores at the 18 month weight maintenance intervention timepoint.

Research Questions.

1. Is there a relationship between HEI-2010 scores at the end of a six month weight loss intervention and weight maintenance at the end of a 12 month weight maintenance intervention?
2. Is there a statistically significant difference in HEI-2010 scores after 12 months of weight maintenance intervention between the two different interventions (group phone counseling vs bi-weekly newsletters)?

3. Is there a statistically significant difference in mean HEI-2010 score after 6 months of weight loss intervention and mean HEI-2010 score after 12 months of weight maintenance intervention?
4. Does diet quality change during the weight loss intervention, HEI-2010 scores at 6 months, and the interaction of diet quality change during the weight loss intervention and HEI-2010 scores at 6 months predict HEI-2010 scores at 18 months?

Chapter 2: Literature Review

Obesity Description

Obesity is a chronic disease diagnosed by an individual having a body-mass index (BMI) score $\geq$ 30 kg/m^2. BMI scores are a ratio of weight to height and are determined by dividing weight in kilograms by height in meters^2. Obesity classifications are based on BMI scores and have been labeled as Stage I (BMI 30.0-34.9), Stage II (BMI 35.0-39.9) and Stage III (BMI $\geq$ 40) (19).

Obesity has been linked to increased risk for developing type 2 diabetes, hypertension, stroke, cardiovascular disease, and certain cancers (20). The causes of obesity are complex, and include both genome and environmental factors such as poor diet and physical inactivity (19). In a study by Mokdad et al (21), poor diet and lack of physical activity was the second leading cause of death in the United States (US) in 2000, related to 400,000 deaths. Obesity has been linked to the development of breast cancer. Increased BMI in post-menopausal women is shown to increase the risk for breast cancer development, although BMI and breast cancer risk in pre-menopausal women is shown to be inversely related. The mechanisms responsible for this are unclear (4).

Obesity Prevalence

The prevalence of obesity in the US has grown dramatically since 1980. In 1980, the US obesity rate was 15% (22). By 1994, adult obesity rates grew to 22.5% (23). In 2012, the obesity rate had increased to 34.9% (24). Rural obesity rates exceed urban rates (25). In 1998, the rural obesity rate was 20.4%, compared to 17.8% in urban settings (26). By 2008 the gap between rural and urban obesity rates had increased (39.6% vs 33.4%) (27). In 2014, the update to the

Rural-Urban Chartbook showed obesity rates increase as population density decreases, a sign that rural obesity rates outpace urban rates (5). Rural communities face unique barriers to preventing and treating obesity, which may explain these increased rates.

Definition of Rurality

Definitions of rurality vary from study to study. In Befort's study on rural obesity prevalence (27), urban influence codes were used to define rurality. These codes describe the population of a county in relation to larger metropolises in the same county (28). Rural-urban commuting area codes are another method used to define rurality. These codes use measures of population density, urbanization, and commuting distance to judge rurality (28). In the 2014 update of the Rural-Urban Chartbook (5), rurality was described as micropolitan (10,000-49,999 per county) or non-core (less than 10,000 per county). Another study (29) described rurality as the number of people per square mile. The Center for Disease Control defines frontier rural areas as having a population of $\leq$ 7 people per square mile (30). Since definitions for rurality vary, the results of these studies may not be generalizable. Currently, rural populations account for 19.8% of the total US population (30).

What is Different about Rural Obesity

There are many possible reasons that rural obesity rates are higher than urban rates. The combination of economics, personal beliefs, and little access to physical activity resources, health professionals, and healthy foods has been partially responsible for obesity increases in this population. These rural-related causes differ in scope from urban-related causes and require further explanation.

Lower socioeconomic status (SES) has been associated with increased rates of obesity and mortality. In a study by Lantz et al (31), increased prevalence of obesity and higher risk of early mortality were associated with lower SES levels. Individuals who earned < $10,000/year had the highest prevalence of overweight, at 24.4%, while middle income individuals who earned between $10,000 and $29,999 had an overweight rate of 18%. When controlling for smoking status, alcohol consumption, BMI, and physical activity, lower SES individuals had a 177% greater risk of early mortality, while middle SES individuals had a 114% greater risk. Sobel et al (32) showed rural populations have lower incomes that their urban counterparts, which may play a role in increased obesity rates in rural populations. Befort (27), in her study of rural obesity prevalence, showed that rural populations have lower reported incomes, which is linked to increased obesity rates. Over half (54.6%) of rural subjects reported incomes below $45,000, compared to 42% of urban subjects. Befort also found obesity rates are higher in rural populations across many demographics, including age, race, and sex.

Low physical activity (PA) levels also play a role in obesity. PA has been linked to weight loss/weight maintenance and reduced mortality/morbidity from chronic diseases (33), but a majority of the US (60%) is physically inactive (26). Patterson et al (26) stated that rural inactivity rates (62.8%) outpace urban rates (59.3%), and also showed that rural obesity rates are higher than urban rates. Similar results were found in other studies (5, 34). One reason rural populations are less active are a lack of activity spaces and increased distances to the activity spaces available. In a cross-sectional study, Casey et al (34) found that only 24% of rural obese individuals in Tennessee, Missouri, and Arkansas felt there are adequate PA areas in their community. These individuals also stated a lack of sidewalks in their communities, far distances to activity areas, and a feeling their communities are not "activity-friendly". Another study by

Moore et al (35) showed similar results. In this study, focus groups comprised of both parents and children living in rural areas of eastern North Carolina were interviewed about their perceptions of access to PA, and these results were compared to those from urban focus groups. The rural participants stated the major obstacles to PA are distance to PA areas, transport and activity program costs, lack of sidewalks, and a lack of community groups such as the YMCA that help promote activity. These obstacles show how PA may be limited in rural populations.

Another contributor to elevated rural obesity rates is the food environment. Grocery stores are limited in rural areas, with convenience stores in greater numbers. Convenience stores have fewer healthy options, and these options are usually more expensive than grocery store options. In a study of the rural food environment, Liese et al (36) found that convenience stores greatly outnumber grocery stores and supermarkets in rural communities (74% vs 26%), while urban populations have more grocery stores (36%-57%) than convenience stores (8%-41%). These stores also had fewer healthy options. When looking at the availability of eggs, low-fat/nonfat milk products, apples, and high-fiber bread products, it was found that only 4%-29% of rural convenience stores carried these items. These items were also more expensive at convenience stores than in grocery stores. Food preparation and/or food intake also play a role in rural obesity. Befort (27) showed that rural subjects consumed a greater percentage of their calories from fat when compared to urban subjects. This increased fat consumption could lead to excess energy intake, a major contributor to obesity. Another study (37) found less emphasis on healthy food preparation techniques and more emphasis on “country cooking” among rural communities. The combination of poor diet and lack of access to healthy foods can lead to increased obesity rates in this population.

In addition, there is less access to medical services in rural settings when compared to urban settings, and the distance to medical services is greater in rural settings. In Rural Healthy People 2010 (38), Gamm and Van Norstrand state that only 10% of all physicians practice rurally, although nearly 20% of the population is rural. This leads to overworked doctors and difficulty in scheduling appointments. Another study (25) found the average distance to medical services in rural settings is 10 miles. Rural subjects were more likely to not have a primary care provider (PCP), and to have to travel longer to see a doctor. This may lead to fewer visits to a physician, who could diagnose and begin treatment for obesity.

Rural Breast Cancer Rates Compared to Urban Rates

Much like obesity, breast cancer rates are higher in rural populations than in urban populations. Many of the reasons for these increased rates are related to the difficulties accessing medical care, lower SES, lower PA, and diet quality, all described earlier. Williams and colleagues, (8) report increased rates of late-stage breast cancer diagnosis in rural Missouri women, especially in the Caucasian community. Late stage breast cancer diagnosis rates in rural Caucasian women between 2006-2008 were 36.4%, compared to ~ 30% for metropolitan Caucasian women. Possible explanations for these increased rates are increased rates of poverty and a lack of medical resources; both of these are also related to increased obesity rates in rural populations. These authors also found the average travel time to access mammography services in rural Missouri counties is 45 minutes, thus decreasing rural availability for health resources. In rural communities, the first contact for health services is a primary care physician (PCP). The PCP is usually the first to diagnose breast cancer and/or obesity in a patient. With a lack of access to PCPs, rural populations have reduced chances of diagnosing these chronic diseases before they grow to advanced stages.

BMI and Breast Cancer

Weight gain has been linked to treatment of breast cancer. In a study by Goodwin, et al (39), breast cancer patients undergoing adjuvant treatment reported weight gains of 1.3 kg for tamoxifen treatment and 2.5 kg for chemotherapy treatment. Post-treatment overweight and obesity have been linked to increased chances of cancer recurrence in both pre- and post-menopausal women. Ewertz et al (3), documented that overweight women (BMI 25-29.9 kg/m^2) had a 42% increased risk of recurrence 5-10 years post-treatment and obese women (BMI $\geq$30 kg/m^2) had a 46% increased risk of recurrence over the same time period. In addition, breast cancer recurrence after ten years of remission increased by 31% in obese women. In the Women's Intervention Nutrition Study, Chlebowski and colleagues (2) showed a correlation between decreased dietary fat intake, weight loss, and reduced risk of cancer recurrence. Participants randomized to a reduced dietary fat intervention lost an average of 2.7 kg and reduced their risk of breast cancer recurrence by 24%. These studies have shown the importance of weight loss and maintenance in the prevention of breast cancer recurrence.

Diet Quality Indices

There are many different measures used to assess the quality of a diet. Three common indices used are the Healthy Eating Index, the alternative Healthy Eating Index, and the alternative Mediterranean Diet Score. Although these indices measure many similar dietary components, each examines an individual's diet in different ways.

The HEI was first crafted in 1995 by the United States Department of Agriculture (USDA) in response to the Dietary Guidelines for Americans. It is used as a tool to examine adherence to the current Dietary Guidelines, and thus serves as an indicator of diet quality. The HEI was modified following the release of the 2010 Dietary Guidelines for Americans to better mirror current dietary recommendations from the USDA. HEI-2010 guidelines include 9 categories focusing on adequacy and 3 categories focusing on moderation. HEI-2010 categories include vegetables, fruits, dairy, fish, meat, protein foods, fat ratios (PUFA+MUFA/SFA), sodium, whole, grains, refined grains, and empty calories. Scoring is determined by serving amounts per 1000 kcal. Scores range from zero points to ten points (40). There has been a positive link shown between increased HEI-2010 scores and a reduction in cancer death risk (10),

Other diet quality indices have also been linked to preventing chronic diseases. The alternative Healthy Eating Index (aHEI) is a modification of the HEI-2010. The aHEI-2010 categories focus on vegetables, whole grains, sugar-sweetened beverages/fruit juice, nuts/legumes, red/processed meat, *trans* fat, n-3 fatty acids (DHA/EPA), polyunsaturated fatty acids (PUFA), sodium, and alcohol. Scoring is done based on servings/day consumed, and is scored from zero to ten. The aHEI-2010 had been linked to reduced rates of CVD, diabetes, ER-breast cancer, and other major chronic diseases (41).

Previous studies have shown the effectiveness of a Mediterranean-style diet on reducing risks of major chronic diseases (42). Trichopoulou et al (16) used these data to create a dietary quality index for Greek population. The alternative Mediterranean Diet score (aMED) is an adaptation of Trichpoulou’s index, modified for a Western-style background diet. Dietary intake is divided into nine categories: vegetables, legumes, fruit/nuts, dairy, cereals, meat/meat products, fish, alcohol, and monounsaturated/saturated fat ratio. Scoring is based on median intake among the measured population: one point is given if consumption is above the population median. The aMED has also been linked to a reduction in chronic disease risk (15).

Diet Quality Indices and Chronic Disease/Cancer

The use of dietary modification in the treatment of chronic diseases, including different cancers, has grown in recent years. Increased knowledge of the effects of diet on the body and symptoms of chronic diseases has spurred increased rates of dietary modification in patients suffering from these diseases (43). Different dietary quality indices have been used to assess the diets of individuals or participants to assess their risks of developing chronic diseases, as well as symptoms from these diseases. In one study (15), alternative Healthy Eating Index (aHEI) 2010 and alternative Mediterranean Diet (aMED) scores were inversely correlated to inflammatory biomarker production, potentially leading to reduced risks for cardiovascular disease and type 2 diabetes. Other studies have shown links between diet quality scores and decreased risk of chronic diseases such as type 2 diabetes, cardiovascular disease, and cancer (41, 44).

Correlations between diet quality and breast cancer are less certain. In a study by George, et al (45), breast cancer survivors were assessed for diet quality at 30 months post-diagnosis using food frequency questionnaires, and then assessed for fatigue levels via questionnaire at 41 months post-diagnosis. Those who scored higher on the HEI-2010 had decreased levels of fatigue. Subjects who had higher-quality diets and met physical activity goals had significantly lower scores for behavioral severity fatigue (3.2 vs 4.7, p-contrast 0.002) and sensory fatigue (3.8 vs 4.8, p-contrast 0.006). However, a link between diet quality indices and breast cancer recurrence is unclear. Another study by George (11) showed higher HEI-2005 scores were significantly linked to reduced risk of death from all causes (26%, p-trend 0.043) and causes other than breast cancer (42%, p-trend 0.011). Survivors who had estrogen receptor (ER) + breast cancer had decreased risks of death from all causes (45%, p-trend 0.0009) compared to ER- breast cancer survivors, although there was no significant link between diet quality and reduced risk of death from recurrent breast cancer, Similarly, Fung, et al (9) found a link between aHEI-2010 and aMED and reduced risk of death in ER- breast cancer survivors. ER- subjects with higher aHEI-2010 scores had a 22% reduced risk of death, while subjects with higher aMED scores had a 21% reduced risk. ER+ subjects had no reduction in risk of death; again, both groups had no reduction in the risk of cancer death. Similar findings were made by Izano, et al in 2013 (13), where higher aHEI-2010 scores were not linked to a reduced risk of death in post-menopausal breast cancer survivors. However, all-cause mortality risk was reduced by 43%. Kim et al (12) also showed no link between diet quality and reduced risk of death by cancer, although higher aMED scores were linked to decreased non-cancer death rates in women with low physical activity (0.39 RR, p-trend 0.0004). Chiuve and colleagues (41) found no link between diet quality and decreased death risk from cancer. Overall cancer mortality rates were reduced 20%-23% in those subjects that scored highly on the HEI-2010, aMED, and DASH dietary quality indices, but not on the aHEI-2010 (11) in another study by George, et al. Although the link between diet quality and cancer prevention is unclear, it is clear that all-cause mortality is reduced in those who follow a higher-quality diet.

Diet Quality Indices and BMI/Obesity

Although the relationship between increased diet quality scores and decreases in chronic disease risk has been well documented, the relationship between diet quality scores and

BMI/obesity are less clear. Increased HEI-2010 scores have been linked to decreased body fat (BF) percentage in American college-aged women, although this association is no longer statistically significant when adjusted for physical activity (46). Another study (47) found an association between HEI-2010 scores and BF percentage, independent of physical activity, but only in men. This could be accounted for in the male subjects' lower HEI-2010 scores at baseline. Associations between increased HEI-2005 and HEI-1995 scores and decreased BMI have been observed, but only in Caucasian populations (48). Using dietary recall data and anthropometric measures from the third National Health and Nutrition Examination Survey (NHANES III), Guo et al (49) associated poor HEI-2000 scores with increased rates of obesity. Increases in HEI-2005 scores have been inversely associated with several cardiovascular risk factors, including obesity (50, 51). In a study by Tardivo et al (52), HEI-2005 scores <80 were linked to increased BF percentage; this study was limited to post-menopausal women, so generalizability is limited. Other studies have shown mixed associations between diet quality scores and BMI (53-55); however, these studies devised their own dietary intake categories, which are greatly different from established standards such as the HEI.

Conclusion

Breast cancer has been linked to obesity in post-menopausal women, and overweight/obesity has been linked to cancer recurrence in all categories of breast cancer survivors. Breast cancer rates and obesity rates are shown to be higher in rural populations. These rates are higher in rural populations for a variety of reasons. Reducing weight and maintaining that weight loss has been shown to reduce risk for breast cancer recurrence. Diet quality has been linked to reduced risk for chronic disease, although a link between diet quality and cancer is unclear. Studies have shown mixed results for diet quality and ER+/ER- breast cancer survivors, and no study has shown a definitive link between diet quality and breast cancer recurrence. Many diet quality indices are used to assess the diets of study subjects, with the HEI-2010 and aMED indices being closely related to a reduced risk for chronic disease. The HEI-2010 is a commonly used diet quality index, developed by the USDA from the 2010 Dietary Guidelines for Americans; thus it is the tool used in this study to access diet quality.

Chapter 3: Methods

Overview

This study used data collected as part of a weight loss/weight maintenance study conducted by Befort, et al at the University of Kansas Medical Center (56). In Befort's study, the primary endpoint was to examine weight maintenance for 12 months after a weight loss intervention lasting 6 months. Weight maintenance was defined as $<\pm 3\%$ weight regain from previous weight loss. $<+3\%$ weight regain has been shown to be clinically significant, and has been used previously in other studies examining weight maintenance (57).

Sample

Befort' study recruited post-menopausal female breast cancer survivors ≤ 75 years old with a BMI score between 27 and 45 kg/m^2. All participants had to have been diagnosed with Stage 0 – Stage 3c breast cancer within the last 10 years, and had to have completed therapy at least 3 months prior to joining the study. Participants received clearance from their oncologist to participate in a weight-loss program. Other inclusion criteria included: residency in a rural area as determined by Rural-Urban Commuting Area (RUCA) Codes, Urban Influence Codes, agricultural income, and/or commuting patterns, the ability to walk briskly without assistance, telephone access, and weight stability over the previous three months. Exclusion criteria included any serious cardiac/pulmonary conditions (such as congestive heart failure), insulin-dependent diabetes, current participation in any weight loss programs or drug therapy related to weight loss, a history of bariatric surgery, any serious food allergies or special diets, and any current history of substance abuse, major depression, binge eating disorder, or other serious psychological conditions.

Participants were recruited between October 2011 and September 2013. Eleven regional cancer centers, hospitals, or clinics throughout Kansas, Nebraska, and Iowa worked in collaboration with the University of Kansas Medical Center in the recruiting process. Each site supplied names and addresses of breast cancer survivors over the previous ten years. Study brochures and a cover letter from a treating physician were mailed to potential subjects living in rural zip codes detailing the goals of the study. Other recruitment strategies included newspaper advertisements in three of the site locations, presentations within the site area, doctor referral, state-wide media coverage of the study, and a mailing of the study brochure by the Susan G. Komen Foundation.

Initially, 721 interested women were screened for eligibility. From this number, 210 women completed all baseline tests and inclusion requirements, and were enrolled in the study. Study participants were then randomized 1:1 to two different arms. Stratification based on cohort and metformin use was used in the randomization process. Blinding of both participants and investigative staff to cohort designation was maintained through the 6 month weight-loss intervention. A requirement of weight loss $\geq$ 5% of body weight and attendance of a 6-month assessment was enforced for inclusion in the second phase of the study.

The study design was reviewed and approved by the Institutional Review Board (IRB) at the University of Kansas Medical Center for each site, and HIPPA waivers were granted for each site by the IRB.

Intervention

The first phase of the study spanned 6 months and focused on weight loss. The participants' weight loss goal was 10% total body weight. All participants received identical 60 minute group counseling sessions via conference call focusing on problem-solving and weight loss education tailored to this population. Participants were also instructed to follow a reduced-calorie diet (1200-1500 kcal/day) which included $\geq$ 5 servings of fruits and vegetables/day, <25% of total kcal from fat, and 20-30 grams of fiber/day. Participants were instructed to consume two pre-packages meals (each <350 kcal and <9 g fat) or their equivalent per day, to drink two meal replacement shakes/day as well as calorie-free beverages, and to increase consumption of fruits and vegetables. Participants were also instructed to gradually increase their daily physical activity, starting at 15 minutes/day, 3 days/week and increasing to 225 minutes/week. Finally, all participants were instructed to maintain detailed records of their daily consumption of fruits/vegetables, prepackaged meals/unplanned snacks, meals away from home, physical activity minutes, and pedometer steps. This information was transmitted to group study leaders once a week. Detailed food journals with calorie counts were kept one week/month and submitted to group study leaders for analysis.

At the end of the 6 month weight loss intervention, participants who lost $\geq$ 5% body weight were randomized into the 12 month weight maintenance intervention. During the 12 month weight maintenance period, the active arm received bi-weekly 60 minute group counseling sessions via conference call, while the control arm received bi-weekly newsletters promoting weight maintenance. Measurements taken include height (at baseline), weight (at baseline and throughout the study), diet (two 24-hour dietary recalls administered at baseline, 6-, 18-, and 24 months), physical activity (via self-reports and physical activity-based surveys), and various surveys measuring quality of life, physical symptoms related to breast cancer remission, body image/relationships, and social problem-solving (administered at baseline, 6- and 18 months). Serum samples were assessed for sex hormones, fasting insulin, adipokines, and inflammatory markers.

During the final 6 months of the study, both groups stopped receiving counseling/mailings, but were encouraged to continue self-monitoring, and submitting these records to their group leaders.

Measures

Demographics: Participant age and education level were collected at baseline.

Weight, height, and BMI: Study nurses measured participant height using a standiometer and weight using a calibrated digital scale (+0.1 lb, Befour, Inc). Weight/height measurements were taken in duplicate at each timepoint. BMI was calculated using height/weight measurements.

Dietary Assessment: Dietary intake measurements included two 24-hour recalls conducted by trained staff at baseline, 6 months (the end of the weight loss intervention), 18 months (the end of the 12 month weight maintenance intervention) and 24 months (end of the study). Recalls were conducted using the USDA multiple-pass approach (58) and were collected on one random weekday and one weekend day. The recalls were entered into the Nutrition Data System for Research (NDS-R, 2010) and analyzed for food group and nutrient intake.

Healthy Eating Index 2010: The Healthy Eating index 2010 (HEI-2010) is a scoring system based on the Dietary Guidelines for Americans, and is used to assess dietary quality (59). HEI-

2010 calculates diet quality scores based on nutrient density (per 1000 calories) and supplies a total score plus 12 component scores. These component scores are divided into 2 groups: foods/nutrients to increase (total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood/plant proteins, and ratio of mono/polyunsaturated fatty acids to saturated fatty acids) and foods/nutrients to decrease (refined grains, sodium, and empty calories) (40). Higher scores are indicative of higher diet quality. HEI-2010 scores were calculated from NDSR output based on a previously developed method (60).

Statistical Analysis

Participants who had two documented 24-hour recalls at baseline, 6 months and 18 months, had documented weight change at 18 months, and were randomized to one of the two intervention arms were included in analysis. To answer research question one, we used a logistic regression to compare 6 month HEI-2010 scores and two groups of participants: Those who regained >3% of their 6 month body weight, and those that maintained body weight ± 3% or continued to lose weight. For this question, 6 month HEI-2010 score was the independent variable, and weight maintenance group was the dependent variable. We also analyzed the randomized intervention's effect on weight maintenance. For this question, 6 month HEI-2010 score and randomization group were the independent variables, and odds of maintaining weight was the dependent variable. We used ANOVA to determine if there was a significant difference in HEI-2010 scores between randomization groups at the 18 month timepoint. ANOVA analysis was also used to determine significant differences between HEI-2010 scores at 6 months and HEI-2010 scores at 18 months. Finally, we used a multiple linear regression to analyze the relationship between 6 month HEI-2010 scores and HEI-2010 score change during the weight loss phase to predict 18 month HEI-2010 scores. For this question, 6 month HEI-2010 score and HEI-2010 score change during weight loss were the independent variables, and 18 month HEI-2010 score was the dependent variable. All data were analyzed using SAS University Edition v. 9.4.

Chapter 4. Results

Summary statistics are displayed in Table 1. Mean age was 58.8 years. Average education was 3.3, falling within the “some college” category. Mean BMI at baseline was 34.2 kg/m^2, and mean baseline weight was 91.4 kg.

Table 1. Baseline Descriptive Characteristics

Variable	Mean or N (%)	SD	Range
Age (years)	58.8	± 7.8	36-75
Education level			
High School	29 (22%)		
Some College	49 (37%)		
Bachelors’s degree	30 (23%)		
Master’s degree	23 (17%)		
Doctorate	1 (1%)		
BMI (kg/m^2)	34.2	± 4.5	27.4-44.5
Weight (kg)	91.4	± 13.8	65.2-130.8

Table 2 displays mean HEI-2010 score by component at baseline, the 6 month timepoint, and the 18 month timepoint.

Table 2. Mean HEI-2010 score by component at baseline, 6 months, and 18 months

Component	HEI-2010 @ baseline	HEI-2010 @ 6 mo.	HEI-2010 @ 18 mo.
Total Fruit (5 pt max)	1.8	4.2	3.6
Whole Fruit (5 pt max)	2.3	4.6	4.1
Total Vegetables (5 pt max)	3.0	4.1	3.8
Greens and Beans (5 pt max)	1.0	1.9	1.6
Refined Grains (10 pt max)	6.7	7.1	7.3
Whole Grains (10 pt max)	4.3	3.3	4.2
Dairy (10 pt max)	4.6	7.8	6.1
Total Protein Foods (5 pt max)	4.0	3.4	3.8
Seafood and Plant Proteins (5 pt max)	1.5	1.3	1.7
Fatty Acids (10 pt max)	5.4	4.9	5
Sodium (10 pt max)	3.2	3.9	3.7
Empty Calories (20 pt max)	14.7	17.8	19.6
Total Score (100 pt max)	52.5	64.2	64.6

To examine the relationships between randomization group, weight maintenance, and HEI-2010 scores at six months, a logistic regression was used. Odds ratios, confidence intervals, and p-values comparing weight maintenance groups, HEI-2010 scores at six months, and randomization group are shown in Table 3.

Table 3. Logistic regression between 6 month HEI-2010 score and randomization group (independent variables) to predict odds of being within weight maintenance group
.

Independent variable	Point Estimate	Confidence Interval	SE	p-value
6 month HEI-2010 score	1.03	0.99-1.07	0.03	0.13
Intervention Arm: Hone v. Mail	2.81	1.30-6.05	0.39	0.01

The logistic regression between HEI-2010 scores at the six-month timepoint and weight maintenance at the 18 month timepoint was insignificant (p=0.1331).

The comparison between randomization group and weight maintenance category was significant (p=.01). The odds ratio for this comparison was 2.806, suggesting that participants in the phone randomization group had ~181% greater chance of maintaining their body weight from the end of the 6 month weight loss intervention to the 18 month weight maintenance timepoint. Figure 1 shows the predicted probability of maintaining weight given HEI-2010 scores at 6 months and randomization group.

Figure 1. Predicted probability of maintaining weight adjusting for 6-month HEI-2010 scores and randomization group.

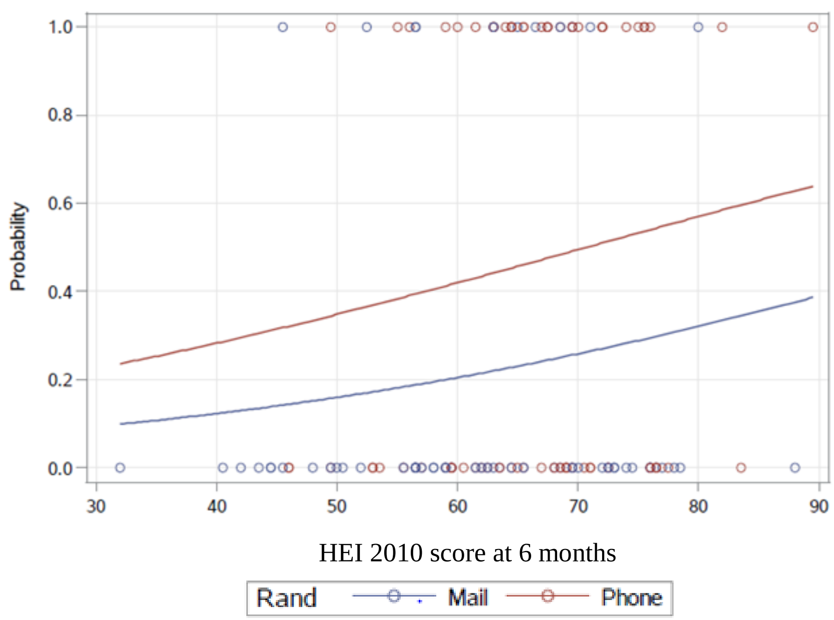


Figure 1 shows that randomization to the phone group resulted in a significant difference in weight maintenance. For example, if a participant had an HEI-2010 score of 60 at the 6 month timepoint, it could be predicted that if that participant was in the phone randomization group, they would have about a 42% chance of maintaining their weight loss, as opposed to a 20% chance in the mail group.

ANOVA analysis was used to examine the differences between randomization groups in regards to their HEI-2010 scores at 18 months. HEI-2010 scores at the 18 month timepoint are shown in Table 4.

Table 4. ANOVA for HEI-2010 scores at 18 months between randomization arms

Randomization Arm	N (%)	HEI-2010 @ 18 months	Difference between groups	p-value
Phone	69 (52.3%)	64.8	0.6	0.72
Mail	63 (47.7%)	64.2		

HEI-2010 score for the phone intervention was 64.8, while the HEI-2010 score for the mail intervention was 64.2. The difference between these scores was insignificant ($p=0.72$), showing no significant difference between randomization groups regarding HEI-2010 scores at the 18 month timepoint.

ANOVA analysis was used to determine if the difference between mean HEI-2010 scores at the 6 month and 18 month timepoints was significant. Results are shown in Table 5.

Table 5. ANOVA for mean HEI-2010 scores at the 6 month and 18 month timepoint

Independent Variable	Mean	SD	Range	Difference between groups	p-value
HEI-2010 @ 6 mo.	64.16	±10.23	32.0-89.5		
HEI-2010 @ 18 mo.	64.52	±9.66	33.0-88.0	0.36	0.69

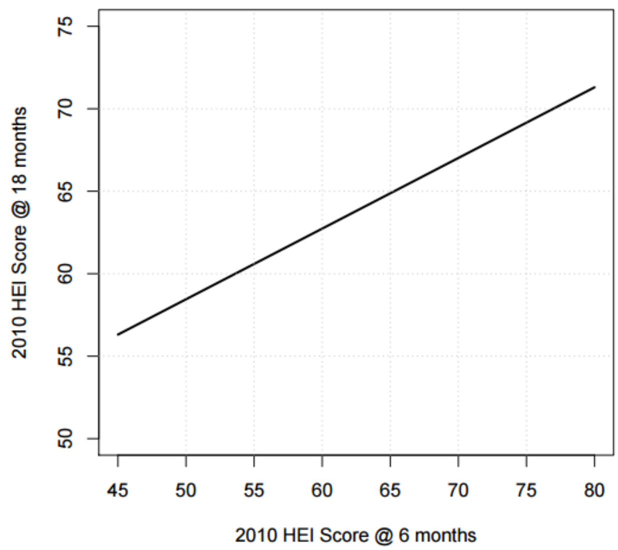
The difference between 6 month mean HEI-2010 score and 18 month mean HEI-2010 score was 0.36, and was not statistically significant (p=0.69).

Table 6 depicts the multiple linear regression between HEI-2010 scores at 6 months, diet quality change during weight loss (measured in change of HEI-2010 scores from baseline to 6 months), and the interaction between these two variables. Figure 3 shows the comparison between 6 month HEI-2010 scores, 18 month HEI-2010 scores, and HEI-2010 score change between baseline and 6 months.

Table 6. Multiple Linear Regression between HEI-2010 Δ at 6 months and HEI-2010 scores at 6 months (independent variables) to predict HEI-2010 scores at 18 months (dependent variable).

Independent Variable	Regression Coefficient	Standard Error	T	p-value
Intercept	25.73	5.77	4.46	<.0001
HEI-2010 score @ at 6 mo.	0.65	0.098	6.63	<.0001
HEI-2010 Δ baseline-6 mo.	0.24	0.27	0.91	0.3624
Interaction of HEI-2010 Δ baseline-6 mo. & HEI-2010 score @ 6 mo.	-0.007	0.004	-1.65	0.1007

Figure 2. Multiple linear regression for HEI-2010 scores at 6 months to predict HEI-2010 scores at 18 months



While the interaction of HEI-2010 Δ from baseline to 6 months & HEI-2010 score at 6 months was not statistically significant (p=0.1), HEI-2010 score at 6 months did have a significant effect on predicting HEI-2010 scores at 18 months (p=<0.0001). The multiple linear regression shows that HEI-2010 scores > 65 at the 6 month timepoint were more difficult to maintain by the 18 month timepoint.

Chapter 5. Discussion

In this study, we demonstrated that HEI-2010 scores at the end of the weight loss intervention did not significantly contribute to weight maintenance at the end of the weight maintenance intervention. However, randomization group did play a significant role in increasing the odds of maintaining weight loss. We also found that HEI-2010 scores at the end of the weight maintenance period were not significantly different between the intervention arms; likewise, mean HEI-2010 scores at the 6 month and 18 month timepoints were not statistically different for the entire group. Finally, we found that HEI-2010 scores at the end of the weight loss intervention had a significant effect on HEI-2010 scores at the end of the weight maintenance intervention.

There are many implications associated with this study. Although there have been mixed results regarding diet quality and recurrence of all cancers (17, 41) and breast cancer (2, 3, 9-13), there have been few studies examining a link between diet quality and weight maintenance in a population of breast cancer survivors. Reduced weight has been linked to recurrence prevention in breast cancer survivors (3), while diet quality indices have been linked to weight reduction and maintenance (18, 63).

In this group of post-menopausal breast cancer survivors, we found no significant difference in HEI-2010 scores between randomization arms at the end of a weight maintenance period. This could be due to the fact that all members of this study completed the same 6-month weight loss intervention, and were able to lose $\geq$5% of their starting body weight. The intensity of the weight loss intervention led to a mean increase of 9.9 in HEI-2010 scores from baseline to 6 months. However, the change in mean 6 month HEI-2010 and mean 18 month HEI-2010 scores was only

0.36, and was insignificant (p=0.69). This demonstrates that regardless of the weight maintenance intervention, mean diet quality improvement in the weight loss period remained steady throughout the weight maintenance period. Randomization to either the phone or mail intervention did not make a significant difference when examining mean HEI-2010 scores at the end of weight maintenance. In this case, it could be assumed that the intensity of the weight loss intervention (phone counseling sessions 1x/week for three months, followed by sessions 2x/month for the next three months) had a greater impact on diet quality throughout the 18-month intervention period than randomization to either the phone or mail groups at the end of the weight loss intervention. From a clinical standpoint, these findings show the importance of intense, personalized counseling during weight loss for the long-term improvement and maintenance of diet quality scores.

Although assignment to randomization group was shown to be statistically insignificant in regards to HEI-2010 score at 18 months, randomization played a major role in improving chances for weight maintenance. Those assigned to the phone intervention had a 181% greater chance of maintaining their weight loss or continuing to lose weight than those participants in the mail intervention. These results demonstrate that intense counseling during a weight maintenance intervention is instrumental in helping participants maintain weight loss long-term. Our findings are consistent with current recommendations for the treatment of obesity, which state that intense counseling is vital for both weight loss and continued maintenance (19).

For our third research question, we attempted to predict HEI-2010 scores at the end of weight maintenance period from diet quality change during the weight loss intervention, HEI-2010 scores at the end of the weight loss intervention, and the interaction of these two variables. Diet quality change during weight loss has been shown to influence dietary quality during weight maintenance (61, 62). Our results demonstrate another important concept behind long term diet quality maintenance: that high diet quality after weight loss may be unsustainable over a long period. This line of thought has influenced government recommendations for weight loss and maintenance (66, 67). Our analysis showed that individuals who had HEI-2010 scores >65 at the end of the weight loss period were predicted to not maintain those scores at the end of the weight maintenance period. This demonstrates the concept that smaller improvements in diet quality are easier to maintain over the long-term.

These findings have important implications in the current weight loss/maintenance environment. As mean HEI score did not change significantly in the entire sample from the 6 month to 18 month timepoints, regardless of randomization group, it can be surmised that the intense counseling during the weight loss phase had lasting effects on diet quality throughout the study duration. HEI-2010 score between randomization groups at the end of weight maintenance was not significant, showing that type of intervention did not influence diet quality. This finding can help direct the course of counseling through both the weight loss and maintenance period. Counseling efforts during the weight loss intervention should focus more on behavior changes related to improving diet quality, while counseling during weight maintenance should focus less on improving diet quality and concentrate on behaviors to help maintain these changes.

There are many strengths to this study. This study was a randomized control trial, thus helping reduce bias. Subjects were recruited from three different geographic areas, thus helping to increase generalizability. The group weight loss/maintenance phone counseling was intensive, with weekly sessions for the first 3 months, followed by bi-weekly sessions for months 4-6, then monthly sessions for months 7-18. There are also several limitations to this study. The average age of subjects in this study was 58.75 years, making results of this study difficult to generalize to both men and pre-menopausal women. Over 97% of subjects were Caucasian, greatly reducing generalizability to other races. All subjects were residents of rural environments, thus making extrapolation to urban populations difficult. All food/liquid intake was self-reported, which can be subject to bias.

In conclusion, this study shows the positive effects of intensive, group-based phone counseling sessions on both diet quality scores and weight maintenance in a population of rural breast cancer survivors. Future studies could expand this treatment model to all obese individuals in rural communities, not limiting the treatment to a particular subset of the population. Befort is currently undertaking such a study, using a similar treatment model with both obese male and female participants throughout 4 Midwestern states in the U.S. (68).

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