METABOLIC SYNDROME, INSULIN RESISTANCE, AND SEDENTARY BEHAVIOR AMONG OVERWEIGHT AND OBESE BREAST CANCER SURVIVORS

By

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ABSTRACT

Introduction: Over half of breast cancer survivors living in the United States are overweight or obese at the time of their diagnosis. Metabolic syndrome (MetS) is a clustering of risk factors linked to insulin resistance that has important long-term health implications for breast cancer survivors. Fasting insulin is associated with breast cancer recurrence and death; however, postprandial measures may be better indicators of insulin resistance among breast cancer survivors. Weight management through diet and physical activity play an important role in improving insulin sensitivity and MetS in the general population, but less is known about these effects among breast cancer survivors. Furthermore, sedentary behavior is a growing problem among the general population and breast cancer survivors alike. Little research has been done to determine effective ways to reduce sedentary behavior and barriers to sitting less are not well understood. The goals of this project were to 1) assess the impact of weight loss and weight loss maintenance on components of MetS among obese and overweight breast cancer survivors, 2) determine relationships between changes in dietary and physical activity variables and changes in the components of MetS, 3) examine changes in fasting and postprandial glucose and insulin, and measures of insulin resistance following the same weight management intervention among breast cancer survivors, 4) determine if change in weight, dietary intake or physical activity are predictors of improvements in insulin sensitivity after a weight management intervention, 5) assess barriers to reduce sedentary behavior within a weight maintenance intervention among breast cancer survivors. **Methods**: Twenty-four obese and overweight women were recruited and enrolled in a 10 month weight management intervention and 22 participants completed the study. Phase one (baseline – 4 months) focused on weight loss through reduced caloric intake

and increased physical activity. Phase two (4 months – 10 months) focused on weight loss maintenance. During phase two, participants were randomized to receive our standard weight loss maintenance program (MAINT) or to the same weight maintenance program with an added intervention aimed to reduce sedentary behavior (MAINT + SED). The MAINT + SED received technology-based tools for tracking weight, diet and physical activity. Assessment visits took place at baseline, 4 months and 10 months. At each time point, anthropometric measurements were completed and fasting blood samples were collected. Participants were fed a standardized meal at each time point and five subsequent blood samples were collected at 30 minutes, 45 minutes, 60 minutes, 90 minutes, and 120 minutes post meal. MetS components (waist circumference, blood pressure, high density lipoprotein cholesterol (HDL-C), triglycerides, fasting glucose), fasting insulin, postprandial insulin as measured by total area under the curve and positive incremental area under the curve (AUC and iAUC), glucose (AUC and iAUC), and two surrogate measures of insulin resistance (HOMA-IR and Matsuda Index) were analyzed and/or calculated at baseline, 4 months and 10 months. Self reported measures of diet (24 hour dietary recalls), moderate to vigorous physical activity (MVPA) (Modifiable Activity Questionnaire) and sedentary time (Multi-context Sitting Time Questionnaire) were assessed at each time point. Qualitative surveys based on the Theory of Planned Behavior were administered to participants in MAINT + SED to assess perceived barriers to reducing sitting time and satisfaction of technology. **Results**: After phase one, participants lost a mean of 10.7% ± 3.9% of their baseline weight and significantly reduced their waist circumference (-7.03 cm), fasting glucose (-7.14 mg/dl), triglycerides (-22.23 mg/dl) and HDL-C (-5.59 mg/dl). From baseline to 4 months, fasting insulin decreased (-5.66 mU/l), postprandial insulin (AUC and iAUC) decreased

by 32% and 28% respectively, and insulin sensitivity significantly improved, as evidenced by a 47% decrease in HOMA-IR and a 44% increase in Matsuda Index. The participants who lost the greatest percent of baseline weight at 4 months had the greatest decreases in waist circumference (*r=0.67*), decreases in percent calories from fat (*r=0.52*) and increases in fruit and vegetable intake(*r=-0.54*). During phase two, participants successfully maintained their weight loss and waist circumference further decreased (-2.76 cm) and HDL-C increased (+11.82 mg/dl). Postprandial insulin (AUC and iAUC), HOMA-IR, and Matsuda Index scores did not significantly change from 4 to 10 months. Dietary changes, MVPA changes and sedentary time changes were not predictive of changes in fasting insulin or changes in insulin sensitivity. Percent weight loss from baseline to 10 months was not significantly related to changes in fasting insulin (r=0.32) or HOMA-IR (r=0.27) from baseline to 10 months. However, changes in Matsuda Index scores were correlated with percent weight loss from baseline to 10 months (r=-0.545). Furthermore, participants in the MAINT + SED arm were not able to successfully reduce their sedentary time during the maintenance phase. Perceived barriers to reducing sitting time included perceived lack of control over changing their sitting behaviors at the workplace.

Conclusion: The 10 month weight management intervention successfully improved components of metabolic syndrome and insulin sensitivity among overweight and obese breast cancer survivors. Reducing sedentary time within a weight maintenance intervention was unsuccessful and the most important perceived barriers were workplace activities. Future interventions should focus on identifying effective lifestyle strategies to alleviate metabolic syndrome and insulin resistance among breast cancer survivors on a larger scale. Feasible strategies to reduce sedentary time should also be identified in this high-risk group.

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CHAPTER ONE

INTRODUCTION

OBESITY AMONG BREAST CANCER SURVIVORS

Breast cancer survivors make up the largest percent (22%) of all cancer survivors in the United States (1). The term cancer survivor is defined by the Centers for Disease Control and Prevention (CDC) as beginning at the time of cancer diagnosis and spanning throughout the entirety of life(1). Cancer survivorship includes the physical, psychosocial, and economic issues of cancer and their impact on the survivor and the family, friends and caregivers of the survivor (2). The number of cancer survivors continues to grow as diagnostic strategies improve and treatments advance. Concurrently, the breadth of survivorship care is expanding and the examination of risk factors for recurrence and other co-morbidities among this high-risk group are mounting areas of research.

In the United States, 20% of cancer mortality among women can be attributed to obesity (3). This is especially problematic for breast cancer survivors, of whom 50% are overweight or obese the time of diagnosis (4, 5). Breast cancer survivors who are obese or overweight at the time of diagnosis have 40% higher risk of recurrence and mortality when compared to normal weight survivors (6, 7). In addition, breast cancer survivors commonly gain weight after diagnosis (8). A weight gain of 6-10 kg is associated with increased risk of cancer recurrence and death from breast cancer (9). Post-diagnosis weight gain is due to a variety of hormonal and lifestyle factors including the effects of chemotherapy, antihormone therapy, increased energy intake, and decreases in physical activity following diagnosis (10). Considerable evidence links both obesity and post-diagnosis weight gain with increased risk of recurrence, death from breast cancer and all-cause mortality (6, 9, 11, 12).

METABOLIC DYSFUNCTION AND BREAST CANCER SURVIVORSHIP

Metabolic syndrome (MetS) is a grouping of risk factors associated with obesity that impacts the health and longevity of breast cancer survivors (13). The concept of MetS was first introduced in 1988 by Dr. Gerald Reaven, an endocrinologist at Stanford University, as a syndrome linking central obesity, elevated circulating free fatty acids, and hypertension to the underlying presence of insulin resistance (14). However, it was not until 1998, that the World Health Organization (WHO) formally defined the syndrome as a clustering of metabolic markers based on insulin resistance (15). Since then, a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity, states the combination of any three or more of the following criteria indicates diagnosis of MetS: elevated fasting glucose (≥ 100 mg/dl) or pharmacologic treatment for hyperglycemia; central adiposity (≥ 88cm for women); elevated serum triglycerides (≥ 150 mg/dl) or pharmacologic treatment for elevated triglycerides; low levels of high density lipoprotein cholesterol (HDL-C) (<50 mg/dl for women) or pharmacologic treatment for elevated HDL-C; and elevated blood pressure (systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg) or antihypertensive drug treatment (16).

A recent meta-analysis of 9 studies determined MetS is associated with 52% increased risk of developing breast cancer in post-menopausal women (17). In each of the studies included in the meta-analysis, the full syndrome explained a greater risk of breast cancer than each of the individual criteria of MetS, suggesting MetS is most predictive of breast cancer when viewed as a whole condition (17). Nonetheless, the individual criteria play an important role in the health

of breast cancer survivors. In one recently published study, 2092 breast cancer survivors were followed for 2.8 years and breast cancer related outcomes and MetS criteria were documented. The authors found that all components of the MetS were individually associated with increased risk of breast cancer events; however, only HDL-C and triglycerides conferred statistically significant risk (18). Women who had MetS were more likely to have a breast cancer recurrence or new primary diagnosis (adjusted OR: 2.17) or breast cancer metastasis (adjusted OR: 2.45) when compared to those who did not have MetS.

The implications of MetS are not only important for prevention of breast cancer recurrence, but are also key in the prevention of other chronic diseases and co-morbidities among breast cancer survivors. Breast cancers survivors with MetS have increased risk of cardiovascular disease, type 2 diabetes and death (19, 20). This is important because MetS confers a fourfold increased risk for type 2 diabetes and a twofold increased risk of cardiovascular disease in the general population (16). Furthermore, older breast cancer survivors diagnosed with early stage breast cancer are more likely to die of cardiovascular disease than breast cancer recurrence (21).

Weight loss through diet and exercise alleviates all components of MetS. The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) recommends Therapeutic Lifestyle Change (TLC) through weight loss and increased physical activity as the first line of treatment for MetS (22). Pharmacologic treatment for individual components of MetS is recommended after 6 weeks of unsuccessful TLC. Cancer specific recommendations from the American Cancer Society and the World Cancer Research Fund are aimed at reducing the risk of recurrence and all-cause mortality, including achieving and maintaining a healthy

weight, eating a diet high in fruits and vegetables and engaging in regular physical activity (23). However, the majority of cancer survivors are not meeting weight, diet or physical activity recommendations (24, 25). For these reason, weight management interventions have been a major focus in survivorship research.

WEIGHT MANAGEMENT AMONG BREAST CANCER SURVIVORS

Several weight management interventions have achieved successful weight loss among breast cancer survivors (26-33); however, very few interventions have examined long-term maintenance of weight loss and its subsequent impact on recurrence. Weight loss has ranged from 3 to 12 kg in interventions lasting 6 months to one year, with the most successful interventions including a comprehensive lifestyle program including a cognitive behavioral approach (28, 33-37). Although long-term successful weight maintenance is crucial to achieve health benefits, very few trials follow-up beyond the intervention phase (38). A recent large-scale review of physical activity and diet intervention trials among breast cancer survivors indicated only 16% of the reviewed trials assessed long term (3-5 year) post-intervention measures and only 6% of reviewed trials indicated successful maintenance of behavioral interventions (39). Befort et al. are currently conducting a long-term maintenance trial (R01 CA155014) designed to assess post intervention maintenance of weight loss in rural breast cancer survivors after a 6-month period of no contact (40). Rock et al. has a similar project underway with goals to examine the effects of long-term post intervention weight maintenance on breast cancer recurrence (41).

Weight regain following a weight loss intervention is an ongoing challenge in commercial, clinical and research settings among the general population. Among the trials examining maintenance of weight loss, 10-30% weight regain was observed over one year (42, 43). In a survey of the National Weight Control Registry, 20% of over 4,000 individuals surveyed were successful maintainers, defined as losing 10% of their initial weight and sustaining the loss for at least one year. The strongest predictor of weight loss maintenance is regular participation in moderate to vigorous physical activity (MVPA) (44, 45). Other predictors of successful maintenance include diet consistency, regular self-monitoring of diet and exercise and breakfast consumption (45). Though the American Cancer Society recommends 150 minutes of MVPA per week for cancer prevention (46), 225-300 minutes of MVPA are required to maintain weight loss (47). The effects of high MVPA recommendations on weight maintenance have not yet been replicated in well-powered trials; however, Donnelly and colleagues have a randomized controlled trial underway to examine the effectiveness of three different levels of MVPA in prevention of regain (48). While MVPA is one of the best predictors of weight regain, increasing MVPA is sometimes compensated for by a simultaneous increase in sitting time (49, 50). Thus, even individuals who participate in planned exercise may compensate by sitting more throughout their day (51).

INSULIN AND BREAST CANCER

Insulin is an anabolic peptide hormone that is secreted by the beta cells of the pancreas and plays an important role in glucose homeostasis and macronutrient metabolism (52). Insulin resistance is a condition in which the body's ability to mediate glucose disposal is attenuated,

resulting in the need for greater levels of insulin production to maintain glucose homeostasis (14). Insulin possesses both metabolic and mitogenic effects that contribute to proliferation of malignant breast cells (53, 54). The mechanisms underlying the connection between breast cancer risk and insulin are not well established, but several are postulated. In vitro studies have demonstrated that insulin stimulates the proliferation of breast cancer cell lines (55, 56). Furthermore, animal models show exogenous insulin can induce mammary tumor growth (57). In humans, chronic hyperinsulinemia is associated with higher levels of ovarian estrogen production and increased circulating estradiol (58). Another potential mechanism involves the subsequent rise in insulin like growth factor-1 (IGF-1), a strong mitogenic signal in normal breast epithelial cells and hyperplasic breast cells (54). In addition, breast cancer cells may overexpress the insulin receptor (59).

Elevated fasting insulin has been associated with increased recurrence and mortality among breast cancer survivors (53, 60-62). Two of three large prospective studies showed an association between increased fasting insulin and greater risk of breast cancer in postmenopausal women (54, 63). However, one study showed no relationship between fasting insulin and risk of breast cancer in premenopausal women (64). This may be related to the fact that in postmenopausal breast cancer, increased levels of bioavailable estrogens are from adipose tissue, whereas the primary source of estrogens in premenopausal women is the ovaries (65).

The connection between obesity, hyperinsulinemia and breast cancer has laid the groundwork for landmark studies targeting insulin modulation through weight loss among overweight and obese breast cancer survivors (66, 67). Several intervention studies among breast cancer survivors show significant decreases in fasting insulin ranging from 17%-26%

following >5% loss of baseline weight (27, 31, 37). A few trials targeting physical activity among breast cancer survivors have observed a subsequent decrease (7-28%) in fasting insulin (68, 69). However, not all trials targeting physical activity alone have observed a significant change in insulin levels in breast cancer survivors (70, 71). The most convincing evidence among this population suggests weight loss through changes in diet and physical activity produces the greatest reductions in insulin.

Significant improvements in insulin resistance as measured by homeostatic model assessment of insulin resistance (HOMA-IR) are evidenced in several weight management studies among breast cancer survivors (27, 31, 72). Improvements in HOMA-IR scores have ranged from 21% - 26% in three 12-month interventions targeting diet and physical activity among overweight and obese breast cancer survivors (27, 31, 72). One study assessing weight loss by way of two different diets (low carbohydrate vs. low fat) found no difference between arms in HOMA-IR scores, but a significant overall difference from baseline to 12 months in both dietary groups was observed after clinically significant weight loss was achieved (27). The Nutrition and Exercise in Women (NEW) study compared the effect of diet only, exercise only, diet and exercise, and a control intervention on weight loss among postmenopausal women. They found the greatest difference in HOMA-IR scores in the diet and exercise group and the diet only group (72). There was no significant change in HOMA-IR scores after one year in the exercise only group. However, the exercise only group did not lose as much weight as the other two groups, suggesting weight loss may have the principal impact on improved insulin sensitivity (72).

MEASURES OF INSULIN RESISTANCE

The gold standard for assessment of whole-body insulin sensitivity is measured through the hyperinsulinemic-euglycemic insulin clamp technique (73). This method uses intravenous insulin to induce hyperinsulinemia and a glucose tracer to quantify site specific insulin resistance and their respective contributions to insulin-mediated glucose disposal (73). The clamp method is time and labor intensive and is rarely used in large epidemiological studies and never used in clinical settings (74). A more common and less invasive assessment of insulin sensitivity and pancreatic beta cell function is a mathematical model utilizing fasting insulin and fasting glucose concentrations to calculate the aforementioned HOMA-IR (75). The HOMA-IR model was originally described in 1985 by Matthews et al. in effort to assess hepatic glucose production and insulin secretion in the basal state (75). HOMA-IR is equal to the product of fasting insulin (mU/l) and fasting glucose (mmol/l), divided by a constant, k, where k=22.5. HOMA-IR is highly correlated with the clamp (r=0.69) and is especially useful in assessing changes in insulin resistance in longitudinal studies (75, 76). However, HOMA-IR is limited to the fasting status of its components and thus cannot distinguish between hepatic and peripheral insulin sensitivity after a meal (77).

Although fasting measures of insulin resistance are clinically convenient, postprandial measures are stronger predictors of cardiovascular disease and all-cause mortality when compared to fasting measures (78-80). Furthermore, oxidative stress is more strongly correlated with glucose excursions after a meal when compared to fasting measures of glycemic control (81). This is likely true because postprandial measures may be more sensitive to abnormalities in glycemic control that are not evident through fasting measures (74, 82). In the fasting state, tight

control is exhibited to maintain equal levels of glucose utilization and endogenous glucose production, namely through increased glucagon secretion and decreased insulin secretion (83). Also during the fasting state, insulin functions to inhibit hepatic glucose production and thereby promote glucose homeostasis. Therefore, fasting measures of glucose and insulin reflect tight homeostatic control in a state of energy conservation (84). After a meal, glucose levels rise and insulin is secreted to coordinate the uptake of glucose by adipose, liver and muscle. It is possible to have apparently normal homeostatic control of fasting glucose and insulin, but dysfunctional regulation of glucose and insulin after a meal. Additionally, the complexity of post meal glycemic control is more than the result of impaired pancreatic beta cells function. Insulin resistance is also a manifestation of altered fat metabolism, incretin deficiency and resistance, increased hepatic sensitivity to glucagon, enhanced renal glucose absorption and impaired insulin utilization by the central nervous system (85).

The Matsuda Index is a mathematical model estimating whole body insulin sensitivity that is highly correlated with the clamp method (r=0.73) (77). This particular index is specifically useful in assessing whole body insulin sensitivity as it takes into account both fasting insulin, fasting glucose, mean postprandial insulin, and mean postprandial glucose (77). The Matsuda Index was first developed as a method of measuring insulin sensitivity following the oral glucose tolerance test (OGTT) and was compared to several other indices of insulin resistance including the HOMA-IR method (77). The Matsuda Index has been strongly correlated with HOMA-IR in individuals with normal glucose tolerance (r=0.935) and individuals with impaired glucose tolerance (r=0.831) (77). The OGTT is used in clinical settings as a diagnostic tool in identifying impaired glucose tolerance and type 2 diabetes (78). While the

OGTT has been widely used in research and clinical settings alike, there have been numerous studies questioning the physiological relevance of a 75 gram glucose load (86-88). Most free-living individuals consume meals containing a mix of protein, fat, and carbohydrate. Although the Matsuda Index was first used with OGTT, Young and colleagues have successfully used the Matsuda Index to determine insulin resistance to a mixed meal (89).

Both HOMA-IR and Matsuda Index will be used in this dissertation as measures of insulin resistance. The HOMA-IR method will use fasting insulin and glucose and the Matsuda Index will use both fasting and postprandial measures to assess insulin resistance. The HOMA-IR method has been used to identify insulin resistance in breast cancer survivors, whereas no published studies have used the Matsuda Index in this population. Postprandial measures are important for this population given the relationship between insulin and breast cancer pathways.

SEDENTARY BEHAVIOR

The term *sedentary* originates from the Latin word *sedere* meaning to sit. Throughout this dissertation the term sedentary behavior will be used to describe any activity that includes sitting, reclining or laying and that requires a low level of energy expenditure, specifically between 1.0-1.5 multiples of the basal metabolic rate (METS) (90) and is distinct from too little exercise (91, 92). Sedentary behaviors encompass all time spent sitting during commutes, sitting throughout the workday, sitting during leisure time (including watching television), and sitting during domestic activities. It is possible for a person to meet physical activity guidelines of 150 minutes per week and still spend the majority of their daily time sedentary (49, 50).

The average American adult spends over half of their daily waking hours in sedentary behaviors (approximately 8 hours per day) as measured by accelerometry data from the National Health and Nutrition Examination Survey (NHANES) (93). The overall increase in sedentary behavior has changed drastically since the 1950's with the decline of work-related activity, transportation-related activity and home-related activity and the increased use of technology (94). Much of the current evidence regarding sedentary behavior of Americans has been focused on television time, especially among children and adolescents (95). However, more recent research has examined the prevalence of workplace sitting and the time spent in front of screens other than televisions (91, 96).

Emerging research indicates the overall increase in sedentary behavior is associated with significant health risks, including obesity (97), cardiovascular disease (98), type 2 diabetes (97, 99), certain cancers (100) and all-cause mortality (101). Katzmarzyk and colleagues observed a dose response between sitting time and death from all causes after adjusting for all potential confounding variables including MVPA, smoking and diet (102). Numerous studies have shown the risk factors associated with sedentary behavior are independent of MVPA, suggesting sitting time may be just as important as MVPA in reducing health risks (103, 104).

SEDENTARY BEHAVIOR AND BREAST CANCER

There is a substantial body of evidence in the form of both epidemiological and intervention studies, linking increased MVPA with reduced risk of breast cancer risk in both pre and post-menopausal women (105, 106). The relationship between sedentary behavior and breast cancer risk was first introduced as a lack of MVPA; however, observational data suggest

there is an independent relationship between sedentary behavior and breast cancer risk (107). These risk factors are important because objectively measured data from the NHANES data shows breast cancer survivors spend 68% of their waking hours sedentary and less than 1% of waking hours doing MVPA (100).

There have been mixed results among the few observational studies examining sedentary behaviors and health related outcomes among breast cancer survivors. A cross sectional study revealed associations between objectively measured MVPA and sedentary behavior with established biomarkers of breast cancer risk, including body mass index (BMI), waist circumference, C-reactive protein, fasting insulin and HOMA-IR. The same study also suggested that light intensity activity might play a protective role in breast cancer risk, independent of MVPA (105). Another cross sectional study indicated high levels of sedentary behavior was positively associated with breast cancer among a survey of 996 breast cancer patients and 1164 controls (odds ratio: 1.81) (107). However, no relationship was observed between light intensity activity and breast cancer.

The research revealing a connection between sedentary behavior and breast cancer risk has been observational in nature. Thus a recent review by Lynch et al. highlights the need for simple and effective interventions to decrease sedentary behavior among breast cancer survivors (100). No published research has attempted to decrease sedentary behavior within a weight management intervention.

INTERVENTIONS TARGETING SEDENTARY BEHAVIOR

Interventions targeting sedentary behavior among adults are limited and it is clear there is an impetus to create effective interventions to decrease sedentary behavior in prospective, long-term studies (108). The field of sedentary behavior research is relatively new, and interventions targeting sedentary behavior in adults are limited. One study by Gardiner et al. examined the feasibility of reducing sedentary time throughout the day and in multiple contexts in older adults through a single face-to-face consultation with study staff and subsequent tailored print materials reviewing each individual's progress (109). Gardiner reported a 3.2% decrease in overall sedentary time, increased breaks in sedentary time and high program satisfaction among participants from baseline to 2 weeks; however no other health outcomes were assessed nor did the study have long term follow up. Another study among adults was successful in reducing overall TV time by use of a system that turned off the television after an allotted amount of time. There was a 61% reduction in TV time among the intervention group, with a 3.8% decrease in overall sedentary time when compared to the control group (110). In addition to the reduction in TV time, the intervention group demonstrated a significant increase in energy expenditure when compared to the control group.

Three interventions have been conducted with the single goal of reducing sedentary behavior in the workplace. They report different effects based on whether sedentary time is measured via self-report or objectively through the use of accelerometers. Objectively measured sitting time was significantly reduced by 11% among overweight men and women in a 12 week internet-based intervention in the workplace (111). Another study using accelerometers also showed a modest but significant reduction (1.6%) in sitting time among Australian office

workers (112). A study assessing both self-reported changes and objective changes in sitting time found a significant 20% reduction in self-reported sitting time (-12.0 hours per week); however, there was no reduction in objectively measured sitting time (113).

A few studies have targeted MVPA and sedentary behavior in the same intervention and have reported a modest reduction in sedentary time (93, 110, 114). Studies that have targeted MVPA only have been less successful in reducing sedentary behavior. In fact, work by Befort et al. reported an increase in MVPA over a 6 month weight management intervention, but no significant differences in sedentary minutes, with a trend toward increasing sedentary time as measured by accelerometry (115). Therefore, it seems there must be interventions targeted specifically at reducing sedentary behavior in order to achieve meaningful changes in the sedentary behaviors of adults.

INSULIN MODULATON AND SEDENTARY BEHAVIOR

Reducing sedentary behavior may improve insulin sensitivity. Observational studies based on NHANES data have revealed a relationship between self-reported time spent sitting while watching television and fasting insulin in a group of over 2,000 adults living in the U.S. (116). Population based studies in the U.S. have shown significant associations between objectively measured sedentary time and waist circumference, insulin, insulin resistance, HDL-C and triglycerides (104, 117). A population based study in Australia showed similar associations between objectively measured sitting time and metabolic risk factors, including triglycerides and waist circumference (117).

The mechanisms explaining the link between sedentary behavior levels and insulin sensitivity may include a combination of genetic and physiologic factors by which the body acclimates to low levels of energy expenditure and promotes energy storage, increased adiposity and decreased muscle mass. Much of the mechanistic understanding of the link between sedentary behavior and insulin resistance has been elucidated by studying the transition from low levels of activity to high levels of activity and vice versa (118). This includes, but is not limited to, decreased energy demands from skeletal muscles, decreased glucose uptake by skeletal muscle through decreased concentration and translocation of GLUT-4 (the primary glucose transporter in skeletal muscle which has high affinity for glucose) to skeletal muscle surface, and decreased levels of lipoprotein lipase (119, 120).

Most of the evidence up to this point has shown significant associations between long periods of uninterrupted sedentary behavior and insulin, insulin sensitivity, and glucose tolerance. One study by Stephens et al observed a 39% reduction in whole body insulin response after a 24-hour period of uninterrupted sitting (121). Research among individuals on bed rest revealed that up to 5 days of continuous bed rest resulted in increased fasting insulin, increased fasting glucose, increased triglycerides, increased LDL cholesterol and reduced insulin sensitivity (122). Similar work examining the effects of uninterrupted sedentary behavior has shown significantly reduced levels of lipoprotein lipase activity in skeletal muscle, an essential enzyme responsible for both metabolism and transport of lipids (92).

Interrupting sitting time can obviate the effects of long bouts of uninterrupted sitting time. Frequent interruptions in sedentary time (the transition from sitting to an active state for approximately 4 minutes) were associated with favorable changes in cardiometabolic risk factors

such as improvements in 2-hour OGTT levels, and plasma triglycerides (120). Similarly, Dustan and colleagues conducted a tightly controlled three-arm crossover trial examining the effects uninterrupted sitting, sitting with 2 minute breaks of light intensity activity (leisure walking) every 20 minutes, or sitting with 2 minute breaks of moderate intensity walking (brisk walking) every 20 minutes on postprandial glucose and insulin levels. They found that interrupting sitting time with light intensity or moderate intensity activity every 20 minutes resulted in significant improvements in postprandial glucose positive incremental area under the curve (iAUC) and postprandial insulin positive iAUC. However, there was no difference between the light intensity and moderate intensity conditions, suggesting light intensity activity breaks are sufficient for producing beneficial changes in glucose and insulin modulation (123).

CONCLUSION

Obesity, metabolic syndrome, insulin resistance and sedentary behavior all appear to play a role in increasing the risk of breast cancer recurrence, co-morbidities, and death among breast cancer survivors. Weight loss through lifestyle interventions improves MetS and insulin resistance in the general population. Some studies among breast cancer survivors also show promising outcomes in components of MetS, fasting measures of insulin and HOMA-IR after a period of weight loss. However, effective long-term weight loss maintenance interventions among this high-risk group are few.

While fasting measures have been useful for assessing health risks in the general population, postprandial measures are more sensitive to detecting true metabolic dysfunction and whole body insulin sensitivity. No published research has assessed the change in postprandial

measures of insulin, glucose or insulin sensitivity throughout a weight loss and weight maintenance intervention among breast cancer survivors. Furthermore, breast cancer survivors spend over 65% of waking time in sedentary behaviors and less than 1% of their waking time in MVPA (100). Changing sedentary time of breast cancer survivors may help to reduce the burden of co-morbidities and improve weight loss maintenance; however, there have been no interventions to date that have attempted to intervene in this manner.

PURPOSE OF DISSERTATION

The goals of this project were to 1) assess the impact of a 10 month weight loss and weight loss maintenance intervention on components of metabolic syndrome (MetS) among obese and overweight breast cancer survivors, 2) determine relationships between changes in dietary and physical activity variables and changes in the components of MetS, 3) examine differences in fasting and postprandial glucose and insulin and measures of insulin sensitivity following the same weight management intervention among breast cancer survivors, 4) determine if change in weight, dietary intake or physical activity were predictors of improvements in insulin sensitivity after a weight management intervention, 5) identify barriers to reduce sedentary behavior within a weight maintenance intervention among breast cancer survivors.

CHAPTER TWO

IMPROVEMENTS IN METABOLIC SYNDROME AFTER A WEIGHT MANAGEMENT INTERVENTION AMONG BREAST CANCER SURVIVORS

Abstract:

Introduction: Metabolic syndrome is a clustering of risk factors that have important prognostic and co-morbid implications for breast cancer survivors. Achieving and maintaining a healthy weight can alleviate the components of MetS in the general population; however less is known about the impact of weight loss and weight loss maintenance on MetS components among breast cancer survivors. The objective of this study was to assess the impact of weight loss and weight loss maintenance on components of MetS among obese and overweight breast cancer survivors and to determine relationships between changes in dietary and physical activity variables and changes in the components of MetS. **Methods:** Breast cancer survivors (n=24; age: 53±8.3 years, BMI; 33.3±3.6 kg/m^2) were enrolled in a 10 month weight management intervention consisting of a 4 month weight loss phase with the goal of losing 10% of their baseline weight, followed by a 6 month weight loss maintenance phase. Anthropometric variables, self-reported physical activity, 24 hour dietary recalls and MetS components were measured at baseline, 4 months and 10 months. **Results:** A total of 22 women completed the study. From baseline to four months, participants lost 10.7% ± 3.9% of their baseline weight and significantly reduced their waist circumference (-7.03 cm), fasting glucose (-7.14 mg/dl), triglycerides (-22.23 mg/dl), and HDL-C (-5.59 mg/dl). Percent weight loss from baseline to 4 months was significantly associated with reductions in waist circumference(r=0.67), decreases in percent calories from fat(r=0.52), and increases in fruit and vegetable intake(r=-0.54). Increases in self-reported physical activity was associated with decreases in fasting glucose, (r=-0.458), but not other MetS components. From 4 to 10 months, weight did not change significantly, but there were additional significant reductions in waist circumference (-2.76 cm) and increases in HDL-C (+11.82 mg/dl). Percent

weight change from 4 to 10 months was significantly associated with further decreases in waist circumference (r=0.88) and increases in HDL-C(r=-0.49). **Conclusions:** Components of MetS were successfully ameliorated after a 4 month weight loss phase and sustained after a 6 month weight loss maintenance phase among breast cancer survivors.

Introduction:

For the 3.1 million breast cancer survivors currently living in the United States, obesity is a mounting threat to their cancer prognosis, overall health and longevity (124, 125). Thus, achieving and maintaining a healthy weight is crucial for this high-risk population. Metabolic syndrome (MetS) is a grouping of risk factors associated with obesity and insulin resistance that has prognostic value for recurrence and death among breast cancer survivors (13, 62). The components of MetS - abdominal obesity, hyperglycemia, hypertension, and dyslipidemia – are independently associated with increased risk of breast cancer recurrence; however, the greatest risk is evident when viewed collectively (17). Furthermore, MetS is a well-known risk factor for cardiovascular disease, the most common cause of death among older, early-stage breast cancer survivors (15, 21, 126).

Effective lifestyle strategies have successfully improved the components of MetS among the general population (127, 128). Adherence to the Mediterranean diet, the Dietary Approach to Stop Hypertension, and low glycemic index diets, have all shown beneficial changes in MetS components with and without calorie restriction (129-133). An increase in aerobic activity without changing diet also results in improvements in all MetS components (134). However, the majority of the lifestyle modification studies reporting improvements in MetS components have also reported clinically meaningful weight loss (-5-10% of baseline weight) (135). Consequently, interventions targeting both diet and physical activity have resulted in enhanced improvement in the components of MetS and the overall prevalence of MetS among the general population (131, 132). A large meta-analysis assessing the effect of lifestyle interventions targeting weight loss through diet and exercise on MetS reported the proportion of resolution of MetS was 1.5 to 2.7

times greater in the lifestyle intervention groups compared to the control groups (education only) (128).

However, few studies have analyzed the effect of weight loss and weight loss maintenance on MetS and its components among breast cancer survivors. One trial examined the effects of a 16-week exercise intervention among breast cancer survivors and reported subsequent significant increases in MetS in participants who adhered to the prescribed exercise (136). Dietary interventions in the context of MetS have shown that adherence to low carbohydrate and low fat diets both equally improve MetS among breast cancer survivors (27). To our knowledge, these are the only published studies that have assessed the impact of diet and exercise on MetS among breast cancer survivors; however, none have assessed MetS in the context of weight loss and weight loss maintenance.

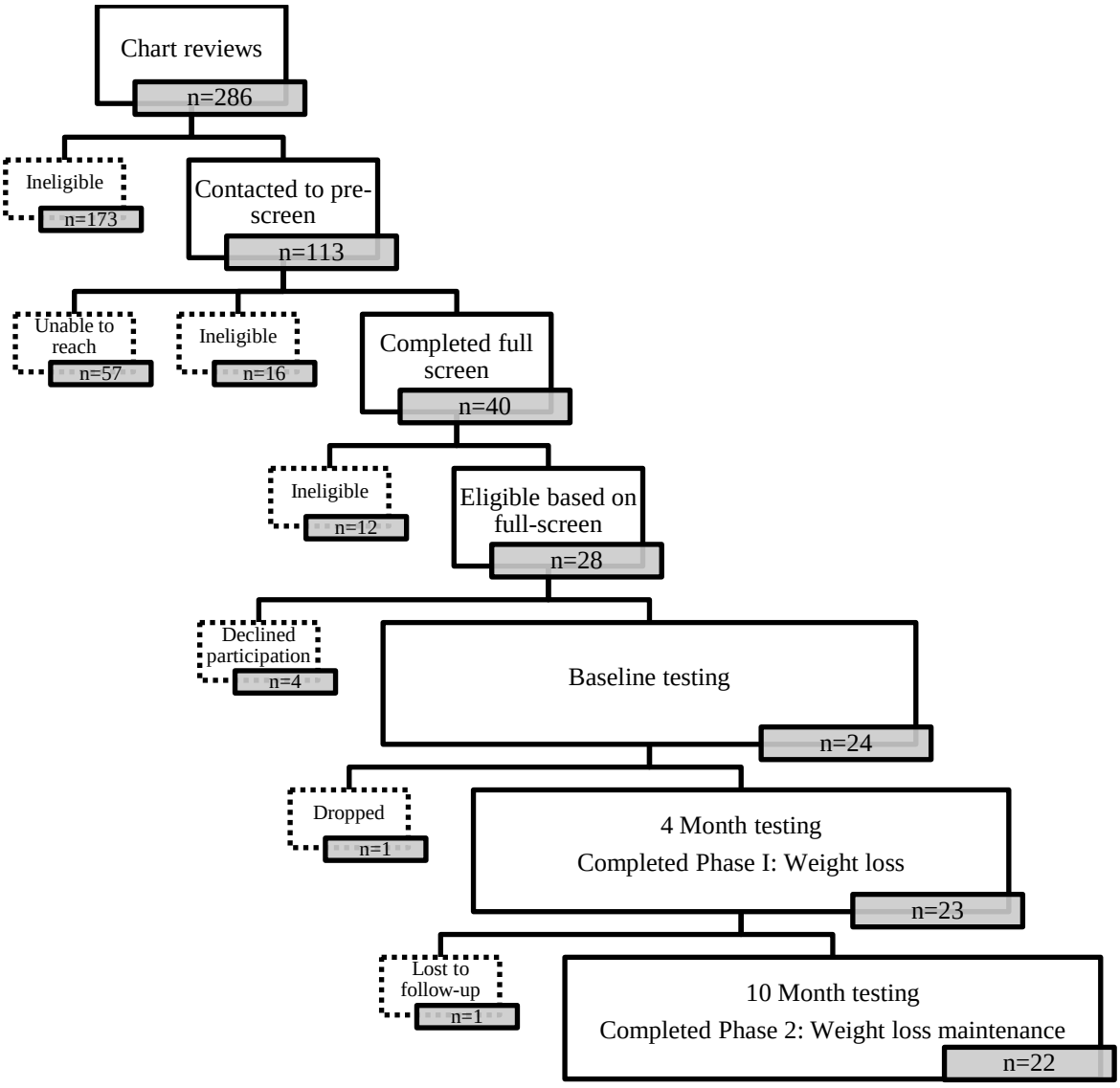
Effective and sustainable lifestyle interventions to alleviate MetS among breast cancer survivors have not been identified. The purpose of this analysis was to examine the effects of weight loss and weight loss maintenance on MetS and its components among overweight and obese breast cancer survivors.

Methods:

Sample

Obese and overweight breast cancer survivors (n=24) were identified through chart reviews from the University of Kansas Cancer Center Registry. Those who were eligible based on chart review (n=113) were contacted to complete a series of screening questionnaires by phone (Figure 2.1).

Figure 2.1. Recruitment and Intervention Consort Diagram



Eligible participants were women < 75 years old with a BMI 27-45 kg/m^2, who were diagnosed with Stage I-IIIc breast cancer within the past 10 years, completed all local and systemic therapy at least 3 months prior to screening, and received clearance from their oncologist or current medical provider to participate in a weight loss study. At baseline, women

had to be currently inactive (< 90 min/week of moderate to vigorous physical activity (MVPA), able to walk briskly, and have access to a phone and computer. Women were excluded if they were current smokers, had prior diagnosis of diabetes or were taking insulin, metformin or sulfonylureas, had another cancer diagnosis in the past 5 years other than non-melanoma skin cancer, had pending joint replacements, a history of bariatric surgery, and those who had participated in a formal weight loss program or used pharmacotherapy for weight loss within 6 months prior to enrollment. Women who screened positive for binge eating disorder, current major depressive disorder or current substance abuse were also excluded. The procedures for this study were approved by the Human Subjects Committee at the University of Kansas Medical Center under protocol #13700 and comply with the Declaration of Helenski.

Intervention

Phase One: Weight loss

During phase one (baseline to 4 months), participants were encouraged to lose 10% of their baseline weight through a combination of decreased caloric intake and increased MVPA. Group meetings were held on a weekly basis via conference call with one in-person meeting per month. The intervention sessions were based on social cognitive theory and led by a trained group facilitator. Weekly sessions included topics on nutrition, physical activity, self-monitoring, and breast cancer survivorship (Appendix II).

During weight loss, participants were instructed to follow a diet containing 1200-1500 calories per day and less than 25% of calories from fat and include at least 5 one-cup servings of fruits and vegetables, two pre-prepared frozen meals and two whey-based protein meal

replacement shakes per day. Participants were asked to purchase pre-prepared frozen meals that contained less than 350 calories and less than 9 grams of fat. In addition, participants were provided with whey-based protein meal replacement shakes (120 kcal and 21grams protein per shake) to ensure they were meeting their protein needs and to aid in satiety. Participants were also encouraged to increase MVPA throughout the program to achieve a goal of 225 minutes per week, most commonly through brisk walking.

Phase 2: Weight loss maintenance intervention

During Phase 2, participants were encouraged to maintain their weight loss and were given a new individualized calorie goal calculated from the Harris-Benedict equation (137). During the maintenance phase, group meetings were held bi-weekly and were focused on relapse prevention using the problem-solving model developed by Perri et al (138). Participants were encouraged to continue to consume at least one pre-prepared frozen meal and one whey based protein shake per day while incorporating one healthy home-prepared meal. They were instructed to maintain 225 minutes of MVPA per week.

Measures

Demographic and breast cancer history information were collected at baseline. Weight, waist circumference, blood pressure, triglycerides, HDL-C, and fasting glucose were examined at baseline, 4 month, and 10 month. Diet and physical activity measures were also measured at each time point.

Anthropometrics

Participants were weighed on a calibrated digital scale (± 0.1 lb; Befour, Inc) in light clothing without shoes. Weight measurements were taken in duplicate. Height was measured

using a portable stadiometer (± 0.1 cm; SECA217) without shoes. Height measurements were taken in duplicate and a third measure was taken if the first two measures differed by 2.0 cm or more. Waist circumference was taken at the narrowest point waist upon participant full exhalation and measured to the nearest 0.1 cm using a tension-loaded tape measure. Waist circumference measures were taken in duplicate and a third measure was taken if the first two differed by 2.0 cm or more. All duplicate and/or triplicate measures were averaged and recorded.

Blood Pressure

A clinical research nurse measured systolic and diastolic blood pressure with an automated oscillometric device after the participant had rested in a seated position for 5 minutes. Two measurements were taken and recorded. If either the systolic or diastolic measurements were greater than 5mm Hg apart, a third measurement was taken after a one-minute break. All duplicate and/or triplicate measures were averaged and recorded.

Blood Collection and Assays

A clinical research nurse placed a small in-line catheter in the antecubital vein and collected fasting blood samples (10 ml) after an overnight fast of 10-12 hours. Participants were asked to refrain from physical activity for 24 hours prior to their blood draw and were instructed to consume a standardized meal consisting of a specific frozen entrée and apple 12 hours before their appointment in order to control for variability due to the macronutrient distribution of meal choices. The blood samples were processed within 30 minutes of collection and centrifuged for 10 minutes at 3500 RPM. Serum was aliquoted into cryo-vials and stored in a -80°C freezer until the end of the 10 month study. Triglycerides, HDL-C and glucose were enzymatically

measured using an ADVIA® 1800 Chemistry systems (Siemens Healthcare Diagnostics Inc; Tarrytown, NY). All samples were analyzed at Physicians Reference Laboratory in Overland Park, Kansas. Samples from all time points were run together to avoid batch variation.

Assessment of MetS

For this study, the definition of MetS in women was based on a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity, which states the combination of any three or more of the following criteria indicates diagnosis of MetS: elevated fasting glucose (≥ 100 mg/dl) or pharmacologic treatment; central adiposity (≥ 88cm waist circumference); elevated serum triglycerides (≥ 150 mg/dl) or pharmacologic treatment for elevated triglycerides; low HDL-C cholesterol (<50 mg/dl) or pharmacologic treatment for elevated HDL-C); and elevated blood pressure (systolic ≥ 130 mm Hg and/or diastolic ≥ 85 mm Hg) or antihypertensive drug treatment(16).

Diet

Dietary intake was assessed by 24-hour diet recalls on 2 non-consecutive days by trained staff. The recalls were taken on one weekday and one weekend day using the USDA multiple-pass approach. The first recall was completed at the in-person baseline orientation visit with 2 and 3 dimensional food models to help participants estimate accurate portion sizes. The second recall was completed over the phone using a food amounts booklet containing food photos and 2 dimensional food models to estimate accurate portion sizes. During the 4 and 10 month assessment visits, both 24-hour dietary recalls were conducted over the phone. The 24-hour

dietary recalls were entered into the Nutrition Data System for Research (NDSR, 2012) software and assessed for energy, macronutrients and food group servings.

Physical Activity

Participants completed the Modifiable Activity Questionnaire, a self-report measure that assesses leisure activities, including both sports and recreational activities over a one-week time frame. Activity levels were scored based on the product of the duration and frequency of the activity and were weighted based on Metabolic Equivalents (MET) values for that particular activity. Data from all activities were summed and presented as MET hours per week (139).

Statistical Analysis

Descriptive data are presented as mean ± standard deviation or frequency %(n) for all participants. A repeated measures ANOVA was conducted among participants who completed through 10 month testing to determine the effect of the intervention on MetS components at three time points (baseline, 4 months, 10 months). Post hoc analyses were conducted using the Bonferroni adjustment and pairwise comparisons were examined. A McNemar chi-square test was used to determine the association between time point and presence of MetS among the sample. Pearson's product moment correlations were conducted to determine correlations between baseline to 4 month changes and 4 month to 10 month changes in weight loss, dietary factors, physical activity and MetS components. For variables that violated the Shapiro-Wilk test for normality, Spearman's rho was conducted. All analyses were completed using IBM SPSS Statistics, Version 22.0; IBM Corporation, Armonk, NY and statistical significance was defined as $p<0.05$.

Results

Baseline Characteristic:

There were 24 participants enrolled in the study and 22 participants who completed all three assessment visits.

Table 2.1. Participant Baseline Characteristics (n=24)

	Mean ± SD or n (%)	Range
Age (years)	53.0 ± 8.3	39.7-65.2
BMI (kg/m^2)	33.3 ± 3.6	27.4-41.2
Weight (kg)	88.9 ± 10.7	70.0 – 108.3
Time since diagnosis (years)	3.9 ± 1.9	1.2-7.3
Cancer stage (AJCC 7th Edition)		
Stage I	14 (58.3%)	
Stage II	10 (41.7%)	
Stage III	0 (0%)	
Current Antihormone Therapy Use	17 (70.8%)	
Estrogen Receptor Status		
Positive	17 (70.8%)	
Negative	7 (29.2%)	
Treatment and Surgical history		
Chemotherapy	15 (62.5%)	
Radiation	14 (58.3%)	
Mastectomy	11 (45.8%)	
Lumpectomy	13 (54.2%)	
Race		
African American	1 (4.2%)	
Native Hawaiian or other Pacific Islander	1 (4.2%)	
White	22 (91.7%)	
Education Status		
Less than high school	1 (4.2%)	
High school/GED	3 (12.5%)	
Some college or associate's degree	9 (37.5%)	
Bachelor's degree	6 (25.5%)	
Graduate level degree	5 (20.8%)	
Employment Status		
Full Time	13 (54.2%)	
Part Time	7 (29.2%)	
Unemployed/Retired	4 (16.7%)	
Marital Status		
Married/Cohabitating	18 (75%)	
Divorced/Separated	3 (12.5%)	
Single/Widowed	3 (12.5%)	

One participant dropped out of the study for personal reasons between baseline and 4 month testing and one participant was lost to follow up between 4 and 10 months (Figure 2.1). Participant baseline characteristics are described in Table 2.1. On average, women were middle-aged, obese, white, and well-educated. At the time enrollment, participants were an average of 3.9 ± 1.9 years out from their breast cancer diagnosis.

Weight Loss Results

After the four-month weight loss phase, participants lost an average of 10.7 ± 3.9% of their baseline weight. Participants significantly reduced total daily caloric intake and percent calories from fat, and increased daily totals of fruit and vegetable servings (all $p<0.01$) after the four month weight loss phase (Table 2.2). Self-reported MVPA increased by 58.57 ± 131.67 minutes per week from baseline to four months. Participants did not increase their physical activity to the recommended 225 minutes per week throughout the intervention; reporting 125.70 ± 110.07 minutes per week at 4 months.

Table 2.2 Changes in Weight, Diet and MVPA

	Baseline n=22 Mean ± SD	4 months n=22 Mean ± SD	10 months n=22[1] Mean ± SD
Weight (kg)	89.5 ± 10.5	79.8 ± 10.1[a]	79.0 ± 11.5 [a]
Calories (kcals per day)	1776.3 ± 435.4	1343.4 ± 249.2 [a]	1367.8 ± 383.6 [a]
Percent calories from fat (% kcal)	35.9% ± 7.7%	22.1% ± 8.3%[a]	29.6% ± 7.2% [a,b]
Percent calories from MUFA (% kcal)	12.4% ± 3.1%	7.3% ± 3.0%[a]	10.1% ± 3.0% [a,b]
Percent calories from PUFA (% kcal)	8.8% ± 3.2%	5.5% ± 2.9%[a]	6.6% ± 2.7% [a]
Percent calories from saturated fat (% kcal)	11.9% ± 2.8%	7.2% ± 3.0%[a]	10.1% ± 3.1% [a]
Percent calories from carbohydrates (% kcal)	44.4% ± 7.9%	53.4% ± 7.8%[a]	49.0% ± 8.2% [a]
Percent calories from protein (% kcal)	17.1% ± 4.1%	23.5% ± 4.9%[a]	20.8% ± 5.3% [a]
Fruit and vegetable intake (servings per day)	4.4 ± 2.6	7.8 ± 3.0[a]	5.7 ± 3.0 [a]
MVPA (min/wk)	60.6 ± 96.9	131.4 ± 109.1[a]	95.7 ± 100.0 [a]
MVPA (METS/wk)	4.2 ± 6.6	8.7 ± 7.9[a]	7.1 ± 8.3[a]

Data presented as mean ± SD. [1]four people could not be reached for 24 hour diet recalls at 10 months; n=18 for dietary data at 10 months; [a]indicates value is significantly different from baseline ($p\leq0.01$); [b]indicates value is significantly different from 4 months ($p\leq0.01$).

The number of participants who met criteria for MetS decreased from 12 participants (54.5%) at baseline to 9 participants (40.9%) at 4 months; however, the relationship between time point and the presence of MetS was not significant (Figure 2.2).

Figure 2.2. Number of MetS Components By Time Point (n=22)

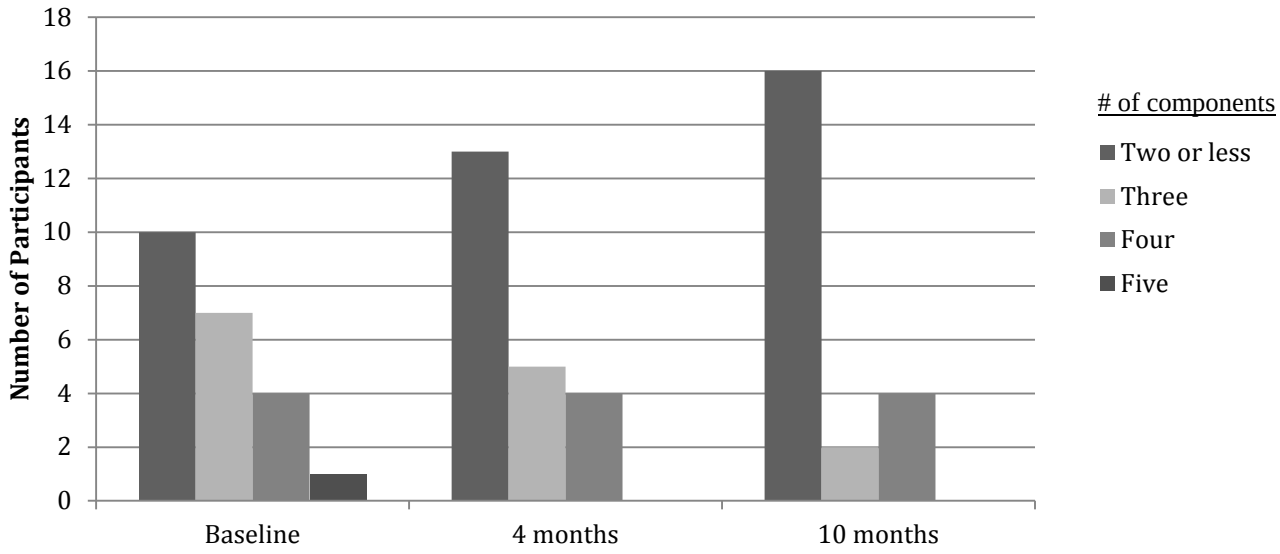


Figure 2.2. The number of MetS components at each time point (baseline, 4 months, 10 months).

Mean values for waist circumference and fasting triglycerides were in high-risk ranges at baseline; whereas; mean blood pressure, triglycerides, and HDL-C did not meet their respective component criteria for MetS at baseline (Figure 2.3). Participants significantly reduced their waist circumference (-7.03 cm; $p \leq 0.01$), fasting glucose (-7.14 mg/dl; $p \leq 0.01$), and triglycerides (-22.23 mg/dl; $p \leq 0.05$), from baseline to four months. The weight loss phase resulted in a statistically significant unfavorable change in HDL-C (-5.59 mg/dl; $p \leq 0.05$).

Figure 2.3 Change in MetS Components over Time (n=22)

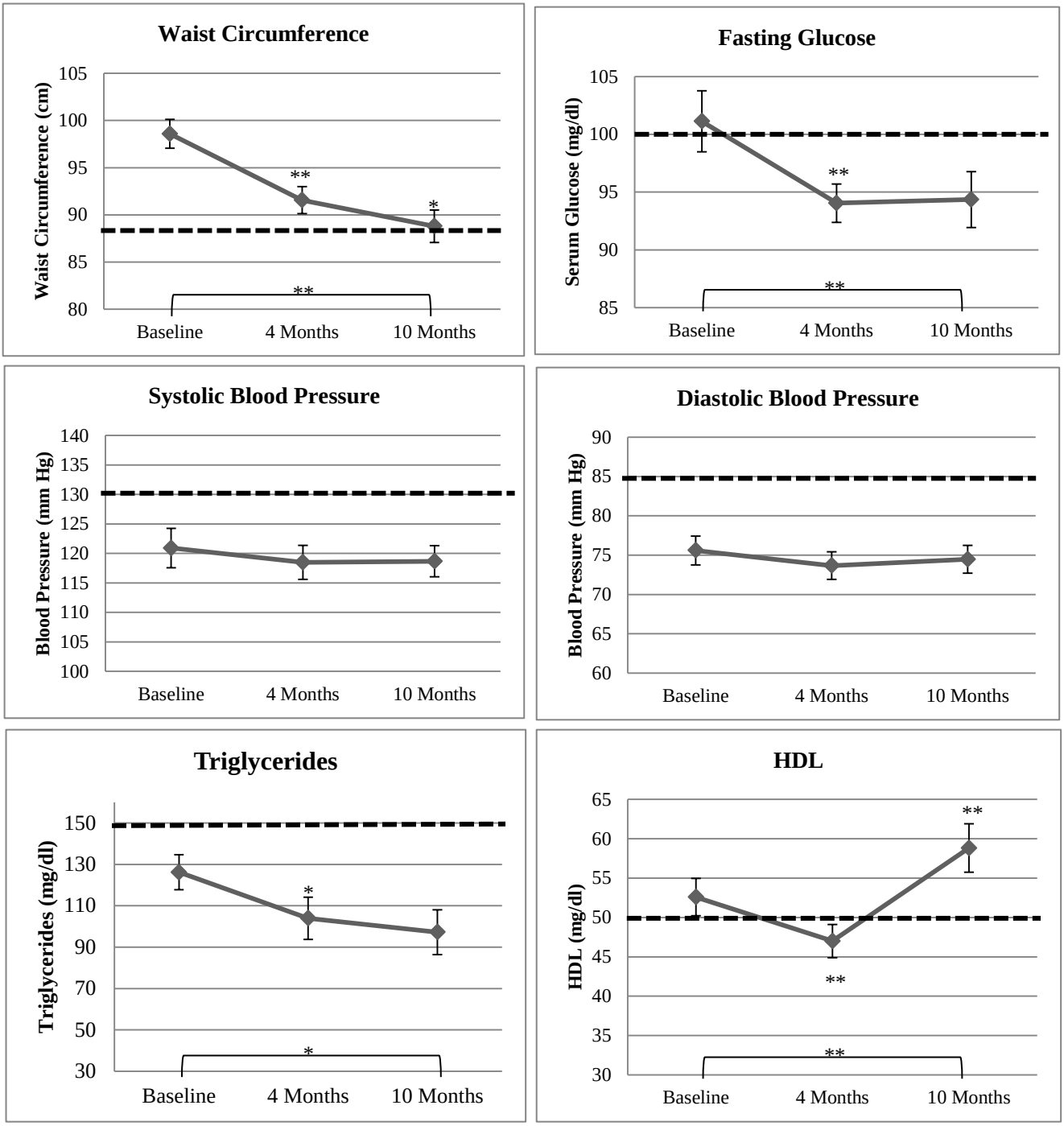


Figure 2.3 The effect of each time point (baseline, 4 months and 10 months) on components of MetS. Data are presented as mean ± SE. *values significant at p≤0.05 for change from previous time point. **values significant at p≤0.01 for change from previous time point. ▬▬ indicates cutoff for MetS ⌜‾‾‾‾⌝ indicates difference between baseline and 10 months.

Scatterplots were examined to determine the relationships between percent weight loss from baseline to 4 months and changes in dietary factors, physical activity, and the components of MetS. There were statistically significant relationships between percent weight loss from baseline to 4 months and change in waist circumference ($r=0.67, p\leq0.01$), change in percent calories from fat ($r=0.52, p\leq0.01$), and change in fruit and vegetable intake ($r=-0.54, p\leq0.01$). In other words, participants with greater percent weight loss had greater decreases in waist circumference, greater decreases in percent calories from fat, and greater increases in fruit and vegetable intake. Additionally, there was a negative association between changes in percent calories from fat and change in total fruit and vegetable intake, such that as participants decreased their percent calories from fat, they increased their fruit and vegetable intake ($r=-0.511, p\leq0.05$). Decreases in percent of calories from fat were also related to favorable changes in serum triglycerides ($r=0.454, p\leq0.05$). Additionally, participants who had favorable changes in triglycerides had unfavorable changes in HDL-C from baseline to 4 months ($r=0.433, p\leq0.05$). Increases in self-reported MVPA from baseline to 4 months were associated with decreases in fasting glucose ($r=-0.458; p\leq0.05$).

Weight Maintenance Results

There was no significant change in body weight during the weight maintenance phase (-0.76 kg ± 3.59 kg). Four participants could not be reached for diet recalls after 10 month testing, thus the dietary data reflects a sample of n=18. From 4 to 10 months, participants did not significantly change their total daily calorie intake or fruit and vegetable intake (Table 2.2). However, participants reported a significant increase in percent calories from fat from 4 to 10

months (+7.92% ± 10.14%, *p≤0.01).* Self-reported MVPA was 95.68 ± 99.99 minutes per week at 10 months, a non-significant change from 4 months (Table 2.2).

The number of people who met criteria for metabolic syndrome decreased from 9 participants (40.9%) at 4 months to 6 participants (27.3%) at 10 months (Figure 2.2). However, this change was not significant. Participants significantly improved their HDL-C levels by 11.82 mg/dl from 4 to 10 months (*p≤0.001*)(Figure 2.3). Participants also continued to reduce their waist circumference from 4-10 months (-2.76 cm; *p≤0.01*). Blood pressure, triglycerides, and fasting glucose did not change significantly from 4 months to 10 months.

The relationship between significant changes in lifestyle factors and metabolic syndrome components from 4 to 10 months was also examined. Percent weight loss from 4 to 10 months was associated with greater changes in waist circumference(*r=0.883, p≤0.001*), greater increases in percent calories from fat (*r=0.572, p≤0.05)* and greater increases in HDL-C *(r=-0.492; p≤0.05*). Favorable changes in waist circumference from 4 to 10 months were associated with greater increases in percent calories from fat (*r=0.572, p≤0.05).* As total daily calorie intake decreased from 4 to 10 months, triglycerides also decreased *(r=0.533; p≤0.05).*

Discussion

Our findings demonstrate several components of MetS can be effectively improved after a weight loss intervention and sustained after a weight loss maintenance intervention among breast cancer survivors. More than half of the women who completed the study presented with MetS at baseline thereby placing them at greater risk for breast cancer recurrence and other related co-morbidities. The prevalence of MetS in our sample is comparable to what others have

observed in larger samples of breast cancer survivors (136, 140). Although, the number of participants who met criteria for MetS did not significantly change throughout our study, our 10 month lifestyle intervention had a positive impact on waist circumference, fasting glucose, triglycerides and HDL-C.

Weight loss consistently results in subsequent improvements in MetS among the general population (15, 128, 141). In our sample, weight loss produced significant improvements in waist circumference, fasting glucose and triglycerides; whereas, HDL-C- decreased significantly throughout the 4 month weight loss intervention. The participants in our sample reported a mean decrease in calories from fat (-13.8% ± 11.57%) and increases in percent calories from carbohydrate and protein (+8.92% ± 12.13%, +6.4% ± 6.80%, respectively) from baseline to four months, suggesting many participants exchanged fat for carbohydrates and protein during the weight loss phase. Furthermore, the type of fat consumed is known to play an important role in the effects on the components of MetS (142). In our sample, the percent of calories consumed from saturated fatty acids, monounsaturated fatty acids (MUFAS) and polyunsaturated fatty acids (PUFAS) significantly decreased by -4.7% ± 4.25%, -5.12 ± 4.40%, and -3.31 ± 4.39% respectively (all $p \leq 0.05$). While the overall decrease in saturated fat intake likely helped to resolve MetS, the simultaneous decrease in MUFAs and PUFAs may have contributed to the overall decrease in HDL-C during the weight loss phase. Furthermore, we observed no changes in blood pressure in our sample. This finding is not in line with previous studies reporting significant weight loss after a lifestyle intervention (128). However, the mean systolic and diastolic blood pressure of the participants in our sample were in the normal range at the start of the study, thus improvements in blood pressure were not required for improvements in MetS.

Weight management interventions are shifting to focus on sustained weight maintenance because weight regain after weight loss is an unresolved obstacle (45). A recent meta-analysis examined the effect of maintenance of weight loss on MetS and concluded that 2-6% weight regain after weight loss is associated with a return to baseline MetS status (127). Furthermore, the same meta-analysis reported weight loss and weight maintenance to have minimal overall impact on HDL-C. However, in our sample, HDL-C increased above baseline levels after the 10 month intervention. Maintaining adequate HDL-C is important for prevention of cardiovascular disease and death – especially among breast cancer survivors. Although there were initial detrimental changes in HDL-C cholesterol after weight loss, the weight maintenance phase showed full recovery in HDL-C levels. One study among healthy obese subjects also reported an increase in HDL-C after a period of weight loss maintenance (143). The authors also reported an increase in MVPA during this phase, which could be a possible explanation for the increase in HDL-C during a period of no weight loss. Furthermore, moderate levels of exercise during weight maintenance have been shown to sustain improvements in MetS after weight loss, even when up to 50% of weight loss is regained (144). This cannot explain the decrease in HDL-C in our sample, as the women did not report increases in MVPA during the maintenance phase. However, in our sample, it is possible the increase in dietary fat intake, specifically MUFAs and PUFAs, during the weight loss maintenance phase may have played a role in the increase in HDL-C (22).

Waist circumference continued to decrease during the weight maintenance phase although there was not a significant change in weight. The change in waist circumference without weight loss has been noted in other studies, particularly when there are decreases in

visceral fat (136, 145). We did not measure visceral fat mass, so it is difficult to know if this effect is true in our sample.

The relationships between MetS components and changes in dietary and physical activity variables from baseline to 4 months confirmed what has been observed in the literature in the general population. While reductions in percent calories from fat was associated with favorable changes in percent weight loss, the opposite was true from 4 months to 10 months. During the weight maintenance phase, participants who continued to lose weight had greater increases in percent calories from fat. Total caloric intake did not change significantly during the weight loss maintenance phase. However, participants who continued to lose weight during the weight loss maintenance phase continued to reduce calories, This is in line with the literature showing caloric restriction is more important than macronutrient distribution for weight management (146). It should be noted that 4 participants could not be reached for dietary recalls at 10 months, thus this relationship is only true of a smaller portion of the sample (n=18).

Given the relationship between breast cancer, heart disease, and MetS, the identification of effective lifestyle strategies to alleviate the burden of MetS is of great value to breast cancer survivors. A large, randomized controlled trial is currently underway to determine the impact of a 6-month aerobic and resistance exercise intervention on MetS components among breast cancer survivors, and will likely contribute to gaps in the literature regarding the mechanism behind MetS and exercise among this high-risk group (147). A recent review by Azard et al. highlighted the importance of establishing effective lifestyle interventions to address MetS among breast cancer survivors (148). The present study is one such example of how a lifestyle intervention can successfully reduce the components of MetS among breast cancer survivors.

A major strength of this study was the presence of distinct weight loss and weight loss mainenance phases and the ability to assess MetS in a high-risk group of breast cancer survivors. Additionally, we followed our participants through a weight loss phase and weight maintenance phase, and were thus able to demonstrate the effects of each on MetS. A limitation of this study was the small sample size and the lack of a control group in which to compare the intervention results. Furthermore, participants did not achieve the recommended physical activity requirements throughout the intervention, making it difficult to interpret the results in the context of exercise. We could not reach four participants at the 10 month time point to collect diet recalls, which limits the interpretability of the dietary changes during the maintenance phase.

In conclusion, components of metabolic syndrome can be successfully ameliorated through weight management lifestyle intervention among breast cancer survivors. Large-scale, randomized controlled trials should be conducted to determine an optimal prescription of weight management, dietary changes and exercise to resolve MetS in the growing population of breast cancer survivors.

CHAPTER THREE

IMPACT OF A WEIGHT MANAGAMENT INTERVENTION ON FASTING AND POSTPRANDIAL MEASURES OF INSULIN AND INSULIN RESISTANCE AMONG BREAST CANCER SURVIVORS

Abstract:

Introduction: Fasting insulin has been associated with breast cancer outcomes; however, postprandial measures may be a more sensitive to impaired insulin resistance with possibly greater prognostic value. Weight management through diet and physical activity are known to play an important role in improving insulin sensitivity, but less is known about these effects among breast cancer survivors. The purpose of this analysis was to assess the impact of weight management intervention on fasting insulin, postprandial insulin and glucose and measures of insulin resistance. **Methods:** Breast cancer survivors (n=22) completed a 4 month weight loss intervention and were randomized to a standard weight maintenance intervention (MAINT) or a maintenance intervention with an added component of reducing sedentary behavior (MAINT + SED). At baseline, 4 months and 10 months fasting blood samples were collected and a standardized meal was provided to each participant. Blood was collected 30 min, 45 min, 60 min, 90 min and 120 min post meal. Changes in fasting insulin and glucose, postprandial insulin and glucose, and two measures of insulin resistance (HOMA-IR and Matsuda Index) were recorded at 4 months and 10 months. **Results:** There was no difference between groups in weight loss or any of the measured glycemic parameters. Fasting glucose (-7.63 mg/dl) and insulin levels (-5.66 mU/l) were significantly reduced in both groups after weight loss and were maintained after weight loss maintenance. Postprandial insulin (AUC and iAUC) significantly decreased from baseline to 4 months and reductions were maintained at 10 months; however there was no change in postprandial glucose (AUC and iAUC) at either time point. HOMA-IR decreased by 49% and Matsuda Index scores increased by 67% from baseline to 10 months. Change in fasting insulin was not associated with change in 10 month percent weight loss,

however changes in Matsuda index score from baseline to 10 months showed a modest by significant association with percent weight loss from baseline to 10 months (r=-0.545).

Conclusions: Insulin sensitivity was significantly improved after a period of weight loss and weight loss maintenance among breast cancer survivors. Measures of insulin resistance, which incorporate postprandial measures, may be more strongly correlated with reductions in weight when compared to fasting measures.

Introduction

Insulin is an anabolic peptide hormone responsible for exhibiting tight control over hepatic glucose production and peripheral glucose utilization (82). Chronically high levels of insulin are pervasive in obesity and result in diminished whole body insulin sensitivity (52). Obesity induced hyperinsulinemia is associated with a two fold increased risk of recurrence and a four-fold increased risk of death among breast cancer survivors (60-62, 149). Furthermore, insulin is well known for its mitogenic properties, which are implicated in breast cancer recurrence and death (54). In addition to breast cancer recurrence and death, insulin resistance is a serious risk factor for heart disease, type 2 diabetes and all cause mortality – all of which are co-morbidities among cancer survivors (38, 126).

While fasting insulin levels have been highly correlated with outcomes among breast cancer survivors (61), postprandial measures of insulin sensitivity may be more indicative of metabolic dysfunction among this high risk group. The gold standard for assessment of whole-body insulin sensitivity is measured through the hyperinsulinemic-euglycemic insulin clamp technique (73). However, the most common assessment of insulin sensitivity and pancreatic beta cell function relies on more simple measures of fasting insulin and fasting glucose to calculate the homeostatic model of assessment (HOMA-IR) (75). HOMA-IR is highly correlated with the clamp method and is specifically useful in longitudinal observational studies because of its ease of use and routine measurement (75, 76). The Matsuda Index is a postprandial measure of insulin sensitivity that is based mathematical model designed to estimate whole body insulin sensitivity. The Matsuda Index shows a slightly stronger correlation (r=0.73) with the clamp method when compared to HOMA-IR (r=0.69) (77). The difference between the strength of the

correlations these correlations are expected to be greater with varying levels of insulin sensitivity. The Matsuda Index was first developed as a method of measuring insulin sensitivity following the oral glucose tolerance test (OGTT), but it has been used to assess insulin sensitivity after a mixed meal (89).

The HOMA-IR method has successfully identified insulin resistance in breast cancer survivors (150). The greatest reductions in HOMA-IR are evidenced in interventions targeting weight loss through both diet and physical activity when compared to targeting diet alone or activity alone (31). However, no published research has examined the changes in postprandial insulin after a period of weight loss and weight loss maintenance among breast cancer survivors. Furthermore, changes in insulin sensitivity as measured by the Matsuda Index after a weight management intervention have not been assessed in breast cancer survivors.

Sedentary behavior may play an important role in the development of insulin resistance (116, 151). Population based studies in the U.S. have shown significant associations between objectively measured sedentary time and both fasting insulin and insulin resistance (104, 117). Inactivity in the form of sedentary behavior is as an important risk factor for breast cancer survivors as well (100). Few interventions have aimed to reduce sedentary time and no published studies have reduced sedentary time within a weight management intervention (109). The degree to which MVPA and sedentary activity are predictive of change in insulin response within a weight loss intervention in the general population is more controversial with some interventions revealing a protective effect of MVPA and insulin resistance (68, 69) and others showing no effect (69, 71).

The purpose of this analysis was to examine changes in fasting insulin and insulin sensitivity throughout a weight management intervention among breast cancer survivors. An additional aim of this study was to examine the relationship between changes in weight, total calorie intake, sedentary behavior and MVPA and changes in fasting insulin and insulin sensitivity throughout this weight management intervention.

Methods

Overview

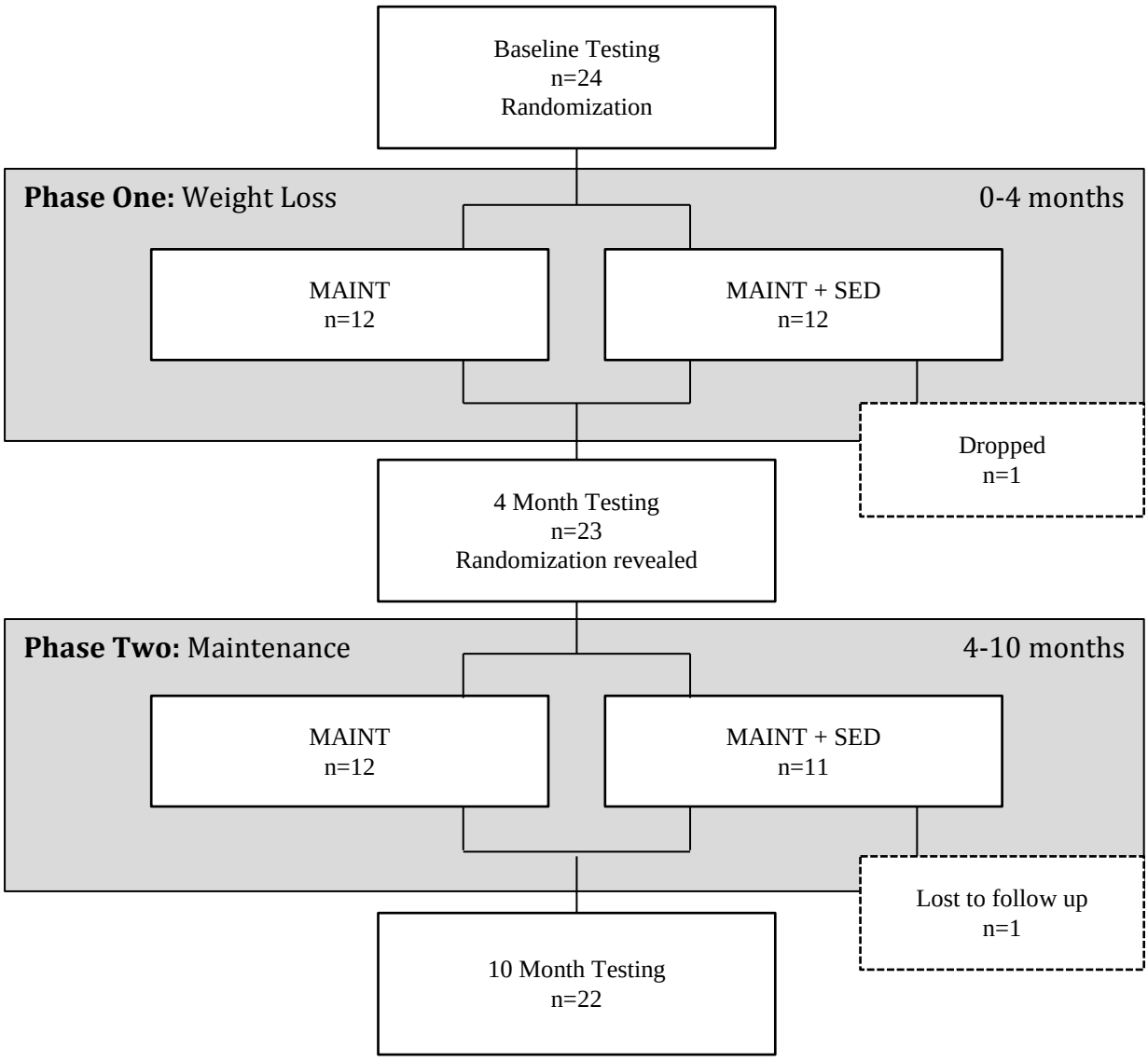
This was a10-month randomized controlled trial examining a novel approach to weight loss maintenance through decreasing sedentary behavior among 24 overweight and obese breast cancer survivors. This pilot study consisted of two main phases: Phase 1 – Weight Loss (0-4 months); Phase 2 – Weight Loss Maintenance (4-10 months)(Figure 3.1). During Phase 1, all participants were encouraged to lose 10% of their baseline weight through a reduced calorie diet and the incorporation of moderate to vigorous physical activity (MVPA). During Phase 2, participants were randomized to either receive our standard maintenance intervention for 6 months (MAINT) (37) or to receive our standard maintenance intervention plus an additional component aimed to decrease sedentary behavior for 6 months (MAINT + SED). Data collection visits took place at baseline, 4 months and 10 months.

Sample

Recruitment and eligibility details can be found in Chapter 2. Briefly, 24 overweight and obese breast cancer survivors were recruited from the University of Kansas Cancer Center

Registry and all participants had physician clearance to participate. The procedures for this study were approved by the Human Subjects Committee at the University of Kansas Medical Center under protocol #13700 and comply with the Declaration of Helenski.

Figure 3.1 Intervention Consort Diagram



Intervention

Phase One: Weight Loss

All participants were encouraged to lose 10% of their baseline weight. They were instructed to consume at least five one-cup servings of fruits and vegetables, two frozen pre-prepared meals and two whey protein shakes per day. Participants were also asked to work up to 225 minutes of MVPA per week, most commonly through brisk walking. For the first four months, participants met weekly via conference call and were led by an experienced group facilitator. Once each month, participants were given the option to come to an in-person meeting. If participants could not attend the in-person meeting, they were still asked to attend the meeting via conference call. The in-person meetings included a weigh-in component and allowed the participants to meet face-to-face with each other and their group leader. Group sessions focused on nutrition, physical activity, self-monitoring and breast cancer survivorship (Appendix II).

Phase Two: Weight Loss Maintenance

After the four-month weight loss phase, participants completed either our standard 6 month maintenance intervention (MAINT) or our standard maintenance intervention with an added component to reduce sedentary behavior (MAINT + SED). Participants in both groups were given a maintenance calorie goal calculated by the Harris Benedict equation(137). They were encouraged to consume at least five one-cup servings of fruits and vegetables, one pre-prepared meal and one whey protein shake per day; however, they were also encouraged to consume one healthy home-prepared meal. Participants remained in the same groups from the weight loss phase to the weight maintenance phase. Group meetings were held via conference

call every other week for six months. During the maintenance phase, the meetings were less didactic and were based on the problem-solving model developed by Perri et al (43).

Participants in the MAINT + SED group also received a Fitbit Zip® activity tracker, a Fitbit Aria Smart Scale® and a Lose It® account to track their calories. In addition to the standard maintenance components, participants were encouraged to reduce their overall sitting time by 1) increasing their light activity by an average of 30 minutes per day, 2) reducing their TV time to less than 90 minutes per day, and 3) reduce their bouts of uninterrupted sitting to no more than 30 minutes in duration.

Measures

Anthropometrics

Anthropometric measurements are detailed in Chapter 2. Briefly, height, weight, and waist circumference were measured and recorded according to our standard protocol.

Activity

All participants completed the Multi-context Sitting Time Questionnaire (MSTQ) and the Modifiable Activity Questionnaire (MAQ) at all time points. The MSTQ is a brief self report measure that assesses usual sitting time across occupational, leisure time and transportation domains on both weekdays and weekend days (152). The MAQ is a self-report measure that assesses leisure activities, including both sports and recreational activities during the past week (139).

Blood Collection

Fasting and postprandial samples were collected by nurses at the University of Kansas Clinical Research Center. Participants were instructed to fast overnight (10-12h) and refrain from MVPA for 24 hours prior to their testing session to minimize the effects of acute physical activity on insulin. Participants were also asked not to consume caffeine or alcohol for 24 hours prior to their assessment. All participants were instructed to eat the same frozen entrée and a similar apple exactly 12 hours before their testing session in order to control for variability due to macronutrient distribution of meal choices. At baseline, entrées and apples were provided to participants at the orientation visit. At 4 and 10 month testing, participants were asked to purchase the entrée and apple to consume 12 hours before their testing session.

Upon completion of anthropomorphic measures, a small in-line catheter was placed in an arm vein, and a baseline blood sample (≤10 ml) was collected. Participants then consumed a standardized meal consisting of ~350 kcal and ~50 g carbohydrates (Table 3.1). Macronutrient distributions were chosen based on other studies using meals to assess postprandial glucose and insulin (153, 154). They were asked to consume the meal within a 10-15 minute period. For the next 2 hours, they were asked to lie still in a reclining chair while nurses collect blood samples (≤ 10 ml) at 30, 45, 60, 90, and 120 minutes post-meal. Serum was processed within 10 minutes of the draw time at 3500 PRM. Serum was aliquoted into cryo-vials and stored in a -80°C freezer until the end of the 10 month study.

Table 3.1 Meal Composition

	Amount	Calories	Fat (g)	CHO (g)	Pro (g)	Fiber (g)
Wheat bread	2 oz	151	2.1	27	6.2	2
Butter	11 g	79	8.9	0	0.1	0
Jam	11g	31	0	7.6	0	0.1
SMART® Smoothie	10 g	34	0.3	1.3	6.7	0.3
Grapes	75 g	52	0.1	13.6	0.5	0.7
Total (grams)		**347**	**11.4**	**49.5**	**13.5**	**3.1**
% of Total			**29%**	**55%**	**16%**	

All insulin samples were run together at a University of Kansas Medical Center laboratory (KIDDRC). Serum insulin was analyzed with a human ELISA kit (Genway #GWB-9BC0DA, 40-521-475037). Serum glucose was analyzed at Physicians Reference Laboratory in Overland Park, KS via the Glucose Oxidase Trinder method (ADVIA® Chemistry Systems. Siemens Healthcare Diagnostics Inc).

Calculations

Total area under the curve (AUC) and positive incremental area under the curve (iAUC) for insulin and glucose were calculated using the trapezoidal method (155). Total AUC includes the entire area under the curve and positive iAUC subtracts baseline (fasting) measures from all subsequent reading and calculates the remaining area under the curve, eliminating all negative values that fall below baseline (fasting). Positive iAUC is criticized for eliminating potential variance added by negative values(156). Total AUC is not dependent on changing baseline values and does not eliminate any values. Both AUC and iAUC were calculated so as to gain perspective from both. Surrogate measures of insulin resistance were calculated using HOMA-IR and Matsuda Index. HOMA-IR was calculated using the following equation, with higher HOMA-IR scores indicating more insulin resistance (75).

$\frac{Fasting\ insulin\left(\frac{mU}{l}\right)\times Fasting\ glucose\left(\frac{mmol}{l}\right)}{22.5}$, where $1\frac{mg}{dl}\ glucose = 0.0555\ \frac{mmol}{l}\ glucose$

Matsuda Index scores were calculated according to the following equation (77), where mean postprandial (PP) glucose and insulin was calculated based on measures from 30 min, 45 min, 60 min, 90 min and 120 min post meal. Higher Matsuda Index scores indicate more insulin sensitivity. $\frac{10000}{\sqrt{Fasting\ glucose\left(\frac{mg}{dl}\right)\times Fasting\ insulin\left(\frac{mU}{l}\right)\times mean\ PP\ glucose\left(\frac{mg}{dl}\right)\times mean\ PP\ insulin\left(\frac{mU}{l}\right)}}$

Statistical Analysis

Participant baseline characteristics by group are described as mean ± standard deviation and range or frequency (Table 3.2). A two-way repeated measures ANOVA was conducted to determine differences between groups at each time point for weight, activity levels, fasting insulin, fasting glucose, postprandial insulin (AUC and iAUC), postprandial glucose (AUC and iAUC), HOMA-IR, and Matsuda Index. Post hoc analyses were conducted using the Bonferroni adjustment and pairwise comparisons were examined. Linear regression was used to determine predictors of improvements in fasting insulin from baseline to 10 months. Fasting insulin was chosen as an outcome variable because it is a simple and common measure implicated in prognosis and health of breast cancer survivors. The same predictors were used in a separate linear regression model to assess the improvements in insulin sensitivity as measured by the Matsuda index from baseline to 10 months. Matsuda Index scores were chosen because of the postprandial nature of the measure of insulin sensitivity which could potentially be a useful prognostic indicator in this population. All analyses were completed using IBM SPSS Statistics, Version 22.0; IBM Corporation, Armonk, NY and statistical significance was defined as $p \leq 0.05$.

Results

Twenty-two participants completed the study: 12 in the MAINT arm and 10 in the MAINT + SED arm (Figure 3.1). Participant baseline characteristics did not differ between groups (Table 3.2). On average, women were obese and had high-risk waist circumference at enrollment. At the start of the study, all women were at least 1 year out for the time of their diagnosis of stage 1 or 2 breast cancer and 70.8% were taking antihormone therapy.

Table 3.2 Participant Characteristics (n=22)

	MAINT (n=12)		**MAINT + SED (n=10)**	
	Mean ± SD or n (%)	Range	Mean ± SD or n (%)	Range
Age (years)	54.7 ± 6.9	43.8-64.0	51.1 ± 8.6	42.3-65.2
BMI (kg/m^2)	33.5 ± 3.7	27.4-38.7	33.3 ± 4.0	28.1-41.2
Weight (kg)	88.3 ± 11.8	70.0-108.3	91.0 ± 9.2	76.3-104.0
Waist circumf. (cm)	99.2 ± 8.0	89.6-112.8	97.8 ± 6.2	83.1-108.3
Time since diagnosis (years)	4.1 ± 1.8	1.5-6.4	3.9 ± 2.2	1.2-7.3
Cancer stage				
Stage I	8 (66.7%)		4 (40.0%)	
Stage II	4 (33.3%)		6 (60.0%)	
Stage III	0 (0%)		0 (0%)	
Current antihormone therapy use (% yes)	10 (83.3%)		5 (50%)	

Weight change did not differ between groups at any time point (Figure 3.2). The MAINT group reported a significantly greater change in MVPA from baseline to 4 months when compared to MAINT+SED ($p \leq 0.05$). Self-reported change in week day and weekend sitting time did not differ by group from baseline to 4 months. However, from 4 to 10 months, the MAINT + SED arm reported significantly less sitting time on weekends (-1.0 ± 2.4 hours per day) when compared to MAINT arm (0.7 ± 1.4 hours per day) ($p \leq 0.05$).

Figure 3.2 Weight and Activity by Group At Baseline, 4 Months, and 10 Months

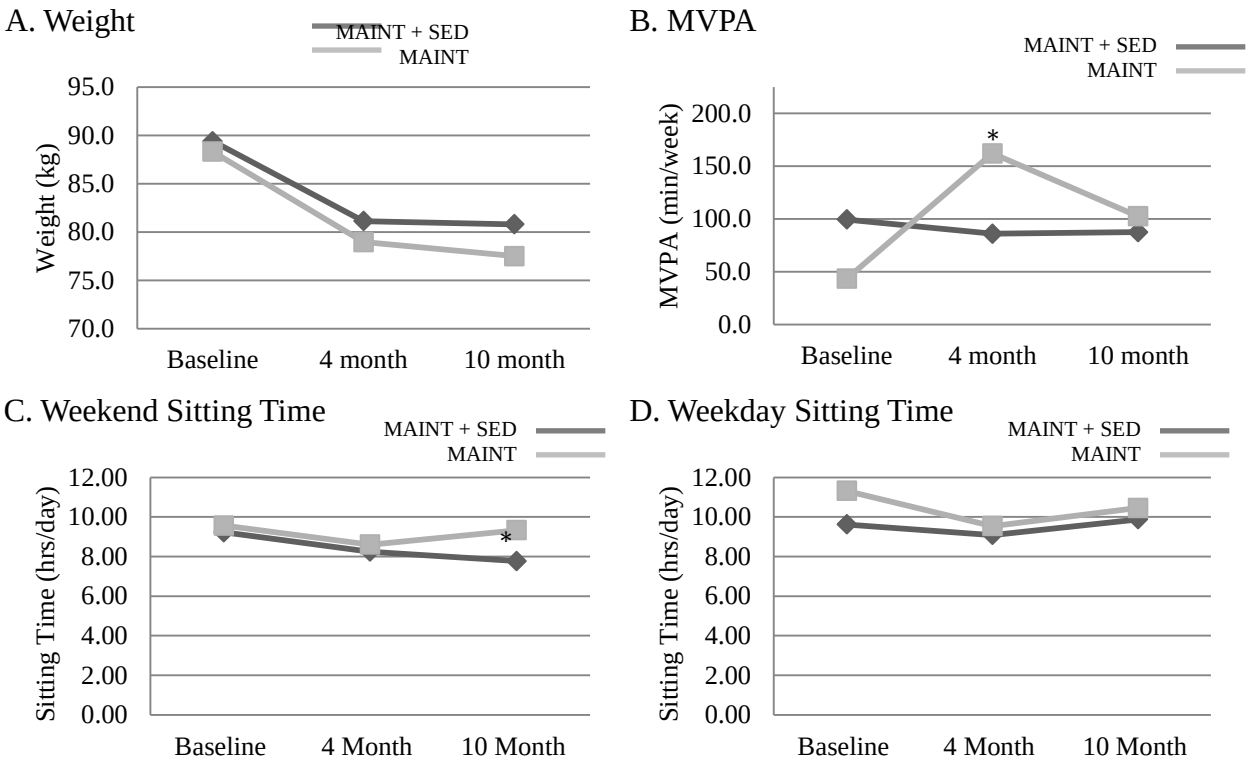


Figure 3.2. The effect of groups (MAINT or MAINT + SED) on weight (A); MVPA (B); non-work day sitting time or weekend sitting time (C); and work day or weekday sitting time (D). Data presented as mean. *indicates between group difference is significant ($p \leq 0.05$).

There was no difference between groups at any time point in fasting insulin, fasting glucose or insulin resistance measures. The repeated measures ANOVA revealed favorable significant changes from baseline to 4 months in fasting insulin (-5.70 ± 1.31), fasting glucose (-7.74 ± 2.27), and HOMA-IR (-1.63 ± 0.39). Matsuda index values significantly increased from baseline to four months (+2.03 ± 0.59) (Table 3.3).

Table 3.3 Fasting Glucose, Insulin and Measures of Insulin Resistance

Measure	Mean ± SE
Fasting glucose (mg/dl)	
Baseline	100.1 ± 2.52
4 months	92.47 ± 1.40[a]
10 months	91.90 ± 2.26[a]
Fasting insulin (mU/L)	
Baseline	13.61 ± 2.01
4 months	7.95 ± 1.16[a]
10 months	7.68 ± 1.29[a]
HOMA-IR	
Baseline	3.42 ± 0.53
4 months	1.81 ± 0.27[a]
10 months	1.75 ± 0.31[a]
Matsuda Index	
Baseline	4.57 ± 0.65
4 months	6.60 ± 0.83[a]
10 months	7.62 ± 0.94[a]

Data are presented as mean ± SE. [a]mean difference between baseline value significantly different ($p \leq 0.01$).

Postprandial measures of insulin AUC and iAUC were significantly different from baseline to 4 months (Figure 3.3). Insulin levels were significantly different between baseline and 10 months for all draw times except 90 minutes. There was no difference in glucose AUC or iAUC from baseline to 4 months. However, fasting glucose was significantly different from baseline to four months and from baseline to 10 months. The 30 minute glucose levels were significantly different from baseline to 10 months, but not baseline to 4 months. There were no statistically significant changes between 4 months and 10 months for any of the examined variables.

Figure 3.3 Postprandial Insulin and Glucose

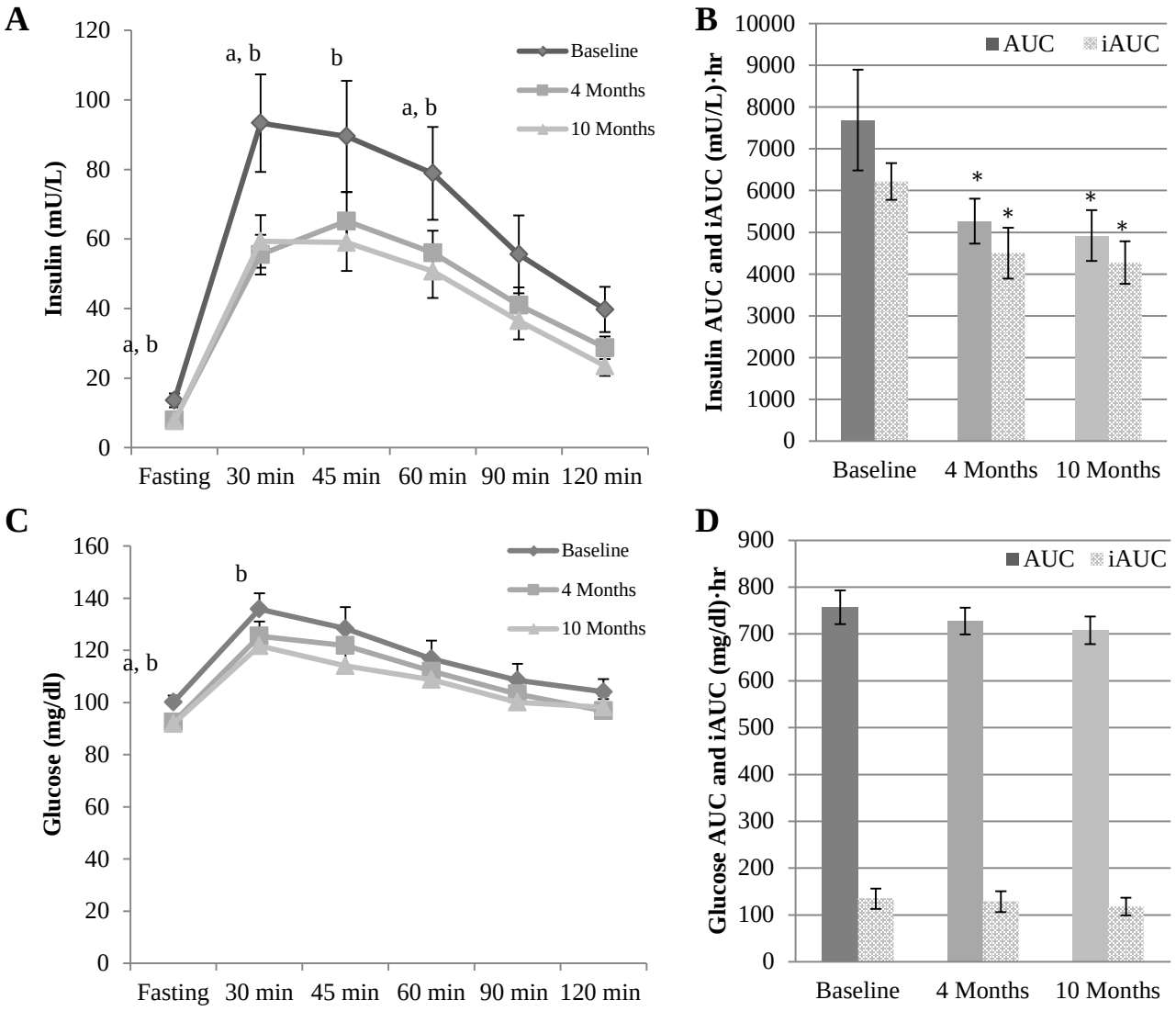


Figure 3.3 The effect of three time points (baseline, 4 months, 10 months) on postprandial insulin levels (A); insulin AUC and positive iAUC (B); postprandial glucose levels (C); and glucose AUC and positive iAUC (D). Data for postprandial insulin and glucose represent mean ± SE. [a]indicates baseline value is significantly different from 4 months ($p \leq 0.01$); [b] indicates baseline value is significantly different from 10 months ($p \leq 0.01$; *indicates value to significantly different from baseline ($p < 0.01$).

The regression models revealed changes in diet and activity variables did not significantly predict changes in fasting insulin or changes in insulin sensitivity. Furthermore, the bivariate correlation between change in fasting insulin from baseline to 10 months and percent weight loss was also non-significant. However, there was a significant negative correlation between percent weight loss from baseline to 10 months and Matsuda Index score (*r=-0.545; p<0.01*) (Figure 3.4).

Figure 3.4 Percent Weight Loss and Change in Insulin Sensitivity

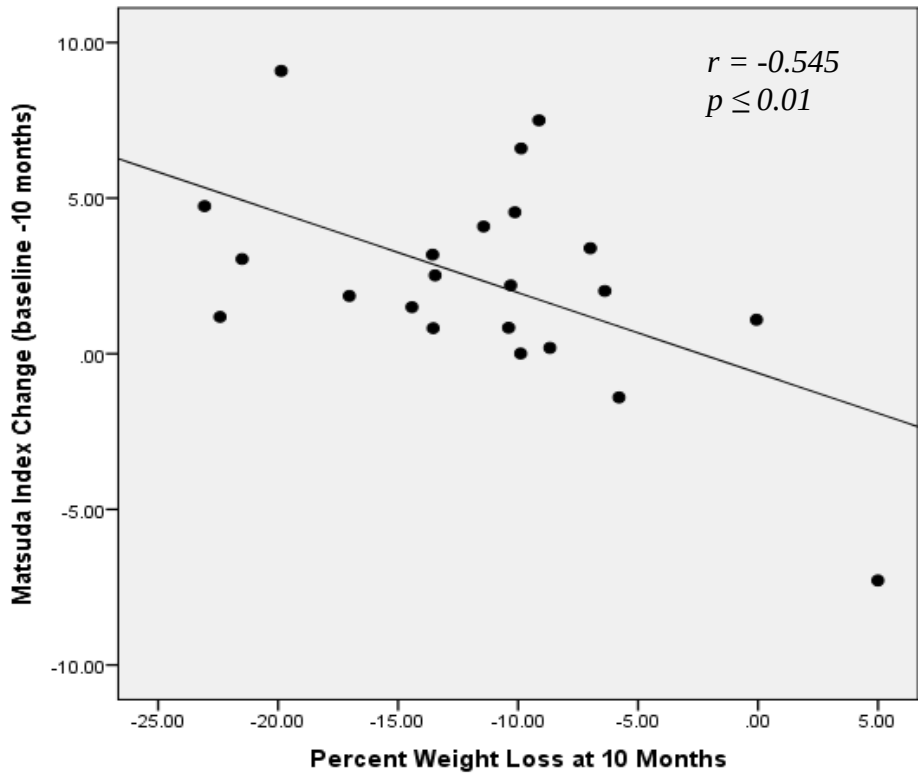


Figure 3.4 The relationship between percent weight loss at 10 months and Matsuda Index change from baseline to 10 months. Data presented as one data point per participant and Pearson correlation coefficient (r), p value, and line of best fit

Discussion

Our findings show fasting insulin and postprandial insulin levels were significantly improved after a weight loss intervention and were sustained during a 6 month period of weight maintenance. Furthermore, insulin sensitivity improved among our sample of breast cancer survivors, evidenced by a 48% reduction in HOMA-IR scores and a 40% increase in Matsuda Index score from baseline to 10 months. This is in line with prior studies examining the effects of weight loss on fasting insulin in obese breast cancer survivors (27, 37, 67) and in obese women without breast cancer (72). In other weight management studies among overweight and obese breast cancer survivors, improvements in HOMA-IR scores have ranged from 17% - 30% (27, 31). In our sample, the mean baseline HOMA-IR was indicative of insulin resistance as evidenced by a HOMA-IR value greater than 2.5, a commonly used cut point for determining insulin resistance (150). However, after the 4 month weight loss phase and the 6 month maintenance phase, mean HOMA-IR values were decreased below the 2.5 cut point, suggesting the women in our sample significantly improved their insulin sensitivity after a period of weight loss and maintenance.

In the pre-diabetic state, an individual can have normal fasting glucose levels, but can present with impaired glucose tolerance following a meal (74). The oral glucose tolerance test (OGTT) has been used clinically to detect impaired insulin sensitivity. However, the OGTT has received much criticism, as a 75-gram glucose dose is not comparable to the macronutrient distribution of a typical meal or the subsequent insulin response (86). Thus in our sample, we analyzed glucose and insulin levels following a meal consisting of 347 calories (55% carbohydrates, 16% protein and 29% fat) with the intention of eliciting a more typical glycemic

response. At baseline, the mean fasting glucose levels in our samples was 100 mg/dl – the cut point indicating impaired fasting glucose. Impaired fasting glucose is clinically interpreted as an intermediate state between healthy glucose homeostasis and overt diabetes. At 4 and 10 months, mean fasting glucose significantly decreased from baseline levels, such that participants transitioned from impaired fasting glucose to normal fasting glucose. This finding alone implies participants improved their overall hepatic insulin sensitivity. At baseline, 4 months and 10 months the two hour post meal mean glucose levels returned to fasting levels, indicating our sample did not present with impaired glucose tolerance at any time point. Furthermore, the area under the curve for glucose did not change significantly over time, providing further evidence that our sample on average did not present with impaired glucose tolerance.

To gain more insight as to how insulin sensitivity changes over time, we analyzed fasting insulin, postprandial insulin and insulin sensitivity indices longitudinally. The total AUC and positive iAUC for insulin decreased significantly from baseline to 4 months and baseline to 10 months. This finding implies a greater release of insulin was required at baseline compared to 4 and 10 months to uptake the same amount of glucose. In other words, participants were able to improve their overall insulin sensitivity after ingesting the same amount and proportion of macronutrients at each time point. Furthermore, HOMA-IR and Matsuda Index scores both significantly improved from baseline to months. HOMA-IR tends to be more indicative of hepatic insulin sensitivity, whereas the Matsuda Index reflects both hepatic and peripheral insulin sensitivity. Therefore it follows that both hepatic and peripheral insulin sensitivity were improved from baseline to 4 months and baseline to 10 months in our sample.

Improved insulin sensitivity is especially important in our sample of breast cancer survivors, given the prognostic value of insulin for breast cancer recurrence, heart disease and type 2 diabetes (53, 60). To this point, a recent review highlighted the importance of addressing the problem of insulin resistance among breast cancer survivors as it may exacerbate co-morbidities (157). The breast cancer survivors in our sample were able to improve their insulin sensitivity through adhering to a weight management intervention targeting diet and exercise. The women in our sample did not achieve the recommended amount of exercise throughout the intervention, however we still observed overall improvements in insulin sensitivity, suggesting weight loss improve insulin sensitivity regardless of changes in MVPA. Furthermore, the women in our sample were not able to successfully reduce sedentary behavior and thus the effect of changing sedentary time could not be assessed in our sample. We believe future research should focus on establishing feasible methods for reducing sedentary time. Qualitative assessments in our sample indicated reducing sedentary time were not perceived as being as important as diet or exercise.

Weight loss and decreased central adiposity as measured by waist circumference were predictive of improved insulin response in prior weight loss studies (32, 68). In our sample, change in weight was not predictive of change in fasting insulin. However, percent weight loss was associated with improved insulin sensitivity as measured by the Matsuda Index. Physical activity levels, sedentary time and change in diet were not predictive of change in fasting insulin or insulin sensitivity in our sample. This finding is not in agreement with other studies that have examined the relationship between physical activity levels and insulin sensitivity (158). Although the women in our sample significant increased their activity throughout the course of

the intervention, they did not increase physical activity to the recommended level and thus the lack of predictive quality of physical activity is not surprising. Furthermore, changes in postprandial glycemic control are affected by short-term changes in activity, as evidenced by a study by Mikus et al. in which apparently healthy individuals wore continuous glucose monitors during three-day periods of high activity and three day periods of low-activity and changes in postprandial glucose were observed between the two conditions (159). Because acute changes in activity result in immediate physiologic changes in postprandial glycemic control, it is possible changes in activity in our sample were missed due to the 6 month time period between postprandial measures. Additionally, changes in total calorie intake throughout the intervention were not predictive of changes in insulin sensitivity in our sample. Chronic energy imbalance, particularly through excessive caloric intake has been linked to insulin resistance through the promotion of hyperinsulinemia and increased production of triglycerides and subsequent fat storage (52). Thus it follows that a decrease in calorie intake may be predictive of improvements in insulin sensitivity; however this relationship was not the case in our small sample.

The most notable strength of our study was the assessment of postprandial glucose and insulin throughout a weight management intervention among a group of overweight and obese breast cancer survivors. The postprandial piece contributes important physiological understanding as to the impact our intervention on glycemic control among breast cancer survivors. A limitation of our study was the small sample size and the limited generalizability of the study findings due to our homogenous sample demographics. Another limitation was the inability to determine if changes in sedentary time is a potential predictor of changes in insulin resistance.

In conclusion, a weight management intervention among breast cancer survivors can successfully reduce fasting insulin, fasting glucose, postprandial insulin and can produce sustainable improvements in insulin sensitivity. Future interventions should include larger sample sizes and aim to assess predictors of improved insulin sensitivity among more diverse populations of overweight and obese cancer survivors.

CHAPTER FOUR

PERCEIVED BARRIERS TO REDUCING SEDENTARY BEHAVIOR WITHIN A WEIGHT MANAGEMENT INTERVENTION

Abstract:

Introduction: Sedentary behavior is an emerging health risk for the general population and may be especially problematic for breast cancer survivors in terms of recurrence and risk of co-morbidities. Interventions to reduce sedentary time among breast cancer survivors have not been conducted and barriers to reducing sitting time are unknown. The purpose of this study was to assess perceived barriers to reducing sitting time among breast cancer survivors enrolled in a weight management intervention. **Methods:** Breast cancer survivors who completed a 4 month weight loss intervention were encouraged to reduce sedentary time during a 6 month weight maintenance phase. Participants were not successful in significantly reducing sedentary time. In order to gain better understanding of perceived barriers to reducing sedentary time the participants were contacted by study staff to complete a 26-question survey based on the Theory of Planned Behavior including assessments of perceived control, perceived importance, and perceived norms and intentions. Experiences with technology were also assessed. Responses were recorded and analyzed to determine frequencies, means and representative comments. **Results:** All participants completed the survey (n=10; age: 51.1±8.6 years; 33.3±4.0 kg/m^2). Only 30% of participants felt it was very important to reduce sedentary time and the majority thought diet and exercise were more important than reducing their sitting time. Although 60% of the women felt they were more aware of the harms of sedentary behavior than the general public, they had low levels of perceived control (7.3 on a 10 point scale) of changing these behaviors. They also did not have strong intentions of changing their sitting time (6.3 on a 10 point scale). Workplace environment was the primary barrier to reducing sedentary time. Overall, participants enjoyed the technology components of the intervention, but it was not enough to

produce significant changes in sitting time. **Conclusion:** Participants' perceived importance, norms, control and intentions did not support their ability to change sedentary behaviors.

Introduction

Emerging research has linked sedentary behavior to a myriad of health risks including obesity, cardiovascular disease, type 2 diabetes, certain types of cancer, and all cause mortality (99, 102). In the U.S., breast cancer survivors spend over 65% of waking time in sedentary behaviors (e.g. sitting, reclining, laying down) and less than 1% of their waking time engaging in moderate to vigorous physical activity (100). Well established data from observational and intervention studies have demonstrated that breast cancer survivors who engage in regular moderate to vigorous activity have reduced risk of recurrence and death when compared to survivors who do not engage in physical activity (12). Although regular exercise may reduce risk, new findings suggest those who engage in regular exercise may compensate by sitting more throughout their day (91). This finding has also been demonstrated in breast cancer survivors (160).

Although many observational studies have indicated an association between sitting time and health risks, few interventions have targeted a reduction in sedentary time among adults. The few interventions that have been conducted have ranged from 6-12 weeks and have shown modest reductions in self-reported and objectively measured sitting time (111-113). No long-term interventions have been conducted to determine if the reduction in sitting time can be maintained over a longer period of time. Furthermore, only one intervention to our knowledge has been conducted outside of the workplace in adults (109). Lastly, no interventions to date have tested the feasibility of reducing sedentary behavior within a weight maintenance intervention.

To address this gap in the literature, we designed an intervention to determine the feasibility of reducing sitting time within a weight maintenance intervention among breast cancer survivors. Although participants lost more than and average of 10% of their baseline weight and maintain that weight loss throughout a 6 month maintenance phase, the added component of reducing sedentary behavior was largely unsuccessful.

The purpose of this secondary analysis was to assess the perceived barriers to reducing sitting time among a group of breast cancer survivors who were enrolled in a weight management intervention. The Theory of Planned Behavior served as the basis for the evaluation of this intervention as it is a widely accepted method for assessing behavior change (161). The Theory of Planned Behavior includes four main domains: importance of the behavior/attitudes toward the behavior, subjective norms, perceived behavioral control and intention to change the behavior.

Methods

Sample

Participants were breast cancer survivors who were enrolled in a 10 month weight management intervention and randomized to receive a maintenance intervention aimed at reducing sedentary behavior (n=10). Intervention components are detailed in Chapter 3. Briefly, participants completed a 4 month weight loss intervention and were then randomized to a 6 month maintenance intervention. After the four month weight loss period, participants randomized to the sedentary behavior intervention received a FitbitZip® activity tracker, an Aria Fitbit Smart Scale® and a Lose It® account to track their diet. Participants met bi-weekly via

group conference call. Participants were given individualized calorie goals to optimize weight maintenance and were encouraged to complete 225 minutes of MVPA per week. Participants were given three main goals to help reduce sedentary behavior: reduce sedentary behavior by replacing sitting activities with light intensity activities; limit television time to less than 90 min/day; and limit uninterrupted sitting bouts lasting 30 minutes or longer. Intervention materials can be found in Appendix III.

The interviews were developed and conducted as a part of a Health of the Public course for 4th year medical students at The University of Kansas Medical Center. Dr. Christie Befort oversaw the project design and development and I served as the site mentor. Together, we developed and conducted a 26-question survey based on the Theory of Planned Behavior. Responses options were based on a four-level Likert scale or a 1-10 level ranking system. Following each close-ended question, we asked open-ended questions (e.g. Why? Explain?) to gain further insight into their response. The survey questions were designed to assess participants' perceived control, behavioral attitudes and subjective norms as they related to changing their sedentary time. In addition, the survey aimed to assess the participants' experiences with the technology components of the intervention. The survey can be found in Appendix II (page 141).

Data collection

Trained students called each participant to complete a telephone interview survey after 16 weeks of participation in 6 month maintenance intervention. Each of the three medical students contacted 3-4 participants. The interviews lasted approximately 20-40 minutes. Responses were recorded in RedCAP, a web-based survey application.

Data analysis

All survey responses were recorded in RedCAP at the time of the interview and exported into Microsoft Excel for data coding and analysis. Responses were coded by two independent sets of trained staff. Qualitative data are reported as mean and standard deviation or frequency of responses. Content analysis was conducted for all open-ended questions. Representative comments were selected for presentation.

Results

All of the 10 participants that completed the sedentary behavior intervention completed the telephone survey. Participant characteristics at enrollment are listed in Table 4.1. Participants lost a mean of 11.3% ± 4.8% of their baseline weight after the weight loss phase and 11.2% ± 7.8% of their baseline weight after the weight maintenance phase. According to self-reported measures, participants did not significantly increase their MVPA from 4 to 10 months. Self reported sitting time did not change significantly from 4 months to 10 months on weekdays or weekend day.

Table 4.1. Participant Characteristics (n=10)

	Mean ± SD or n (%)	Range
Age (years)	51.1 ± 8.6	42.3-65.2
BMI (kg/m^2)	33.3 ± 4.0	28.1-41.2
Weight (kg)	91.0 ± 9.2	76.3-104.0
Waist circumference (cm)	97.8 ± 6.2	83.1-108.3
Time since diagnosis (years)	3.9 ± 2.2	1.2-7.3
Cancer stage		
Stage I	4 (40.0%)	
Stage II	6 (60.0%)	
Stage III	0 (0%)	
Employment Status		
Unemployed/retired	3 (30%)	
Part Time (< 35 hrs/wk)	2 (20%)	
Full Time (>35 hrs/wk)	5 (50%)	

Data are presented as mean ± SD or n(%) and range.

Table 4.2. Weight Loss and Activity Outcomes (n=10)

	4 month	10 month	4-10 month change
	Mean ± SD	Mean ± SD	Mean Δ ± SD
Weight loss (% of baseline)	11.3% ± 4.8%	11.2% ± 7.8%	0.2% ± 3.8%
MVPA (min/week)	94.6 ± 92.4	87.5 ± 96.9	-7.1 ± 78.3
Work day sitting time (hrs/day)	9.6 ± 2.1	9.8 ± 2.3	0.3 ± 2.8
Non work day sitting time	8.8 ± 2.4	7.8 ± 1.8	-1.0 ± 2.4

Data are presented as mean ± SD. No significant differences observed from 4 to 10 months.

Survey Results:

Frequencies or mean ± SD of responses to the survey questions and the specific component of the Theory of Planned Behavior addressed in each question are presented in Table 4.3.

Table 4.3 Sedentary Behavior Survey Responses (n=10)

Component	**Survey Question**	**Responses as n(%) or mean(SD)**			
		Not at all important	*Slightly important*	*Moderately important*	*Very important*
Importance	How important is it to you to reduce the amount of time your spend sitting?	0 (0%)	1 (10%)	6 (60%)	3 (30%)
		Much less	*Somewhat less*	*Somewhat more*	*Much more*
Importance	How much time and effort do you put into exercise compared to reducing sitting time?	2 (20%)	1 (10%)	3 (30%)	4 (40%)
Importance	How much time and effort do you put into your diet compared to reducing your sitting time?	1 (10%)	0 (0%)	3 (30%)	6 (60%)
Norms	Compared to you, how concerned do you think other women your age are about the amount of time they spend sitting?	6 (60%)	2 (20%)	1 (10%)	1 (10%)
Norms	How much time do you believe other women your age spend sitting compared to you?	0 (0%)	2 (20%)	8 (80%)	0 (0%)
		Mean ± SD	*Range*		
Perceived Control	On a scale from 1-10, with 1 being the least and 10 being the most, how confident are you that you can reduce your sitting time over the next two weeks?	7.3 ± 1.6	5-10		
Perceived Control	On a scale from 1-10, with 1 being the least and 10 being the most, how much control do you have over changing the amount of time you spend sitting?	7.3 ± 2.4	5-10		
Intentions	On a scale from 1-10, with 1 being the least and 10 being the most, to what extent do you intend to reduce your sitting time as recommended by the program in the next 2 weeks?	6.3 ± 2.0	2-9		

Attitude Toward Behavior

The telephone survey indicated only 30% of participants thought it was very important to reduce their sitting time. The majority of participants reported that exercise and diet were more important than reducing their sitting time, with 70% of participants

indicating that they put more of their time and effort into exercise and 90% saying they put more time and effort into their diet.

> *"I spend somewhat more time on my diet because it's such a good idea to get in all the vegetables and eat balanced meals. It's important in getting weight down and keeping weight down."*

Subjective Norms

The majority of participants (80%) believed that other women their age were less concerned about sitting. Furthermore, 80% of the women believed that women their age spend more time sitting. Overall they commented that other women tend to be less aware and less educated about the harms of too much sitting.

> *"Most people out there don't have as many issues and they aren't educated on the importance of reducing sitting time, even though it's been shown to be helpful for multiple conditions. Most Americans sit around and are couch potatoes, and aren't aware of the benefits of reducing sitting."*

Perceived Control and Intention

The women were asked to rate their confidence as it regarded to reducing their sitting time over the next two week period on a scale from 1-10, with 1 being the least and 10 being the most confident. Women reported a mean confidence of 7.3 ± 1.6. They also reported a mean of 7.3 ± 2.4 when asked how much control they had over changing their sitting time. However, when women were asked to what extent they intended to change the amount of time they spent sitting, the mean rating was a 6.6 ± 2.0 and ranged from 2.0-9.0. Participants reported they had the most control outside of their workplace and they had least control of their sitting at work or while driving.

> *"I don't have a lot of control at work and I sit a lot there, even though I wants to be on my feet as much as possible."*

"If I am at home, I have 100% control. My job requires a lot of sitting because I am a bus driver, but I get up and move about when I'm not driving."

"I have a new job and to do a good job, I have to email and be online and reporting and that seems impossible if you're standing. Can't work as fast if you're standing up.

Table 4.4 Sedentary Behavior Technology Survey Responses (n=10)

	Phone	*Computer*	*Both*		
How do you access your dashboard or app interface?	4 (40%)	3 (30%)	3 (30%)		
	Weight	*Calories Consumed*	*Steps*	*Very Active Minutes*	*Activity log*
Of the following, which component of the dashboard or app interface do you pay most attention to?	1 (10%)	0 (0%)	8 (80%)	0 (0%)	1 (10%)
Which component of the dashboard or app interface do you pay next most attention to?	0 (0%)	4 (40%)	1 (10%)	3 (30%)	2 (20%)
	Never	*Once per week*	*Several times a week*	*Every day or more*	
How often do you check your lightly active minutes?	3 (30%)	3 (30%)		4 (40%)	
	Yes	*No*			
Do you feel the Fitbit® provides accurate feedback about your light activity?	9 (90%)	1 (10%)			
	Not at all useful	*Slightly useful*	*Moderately useful*	*Very useful*	
How useful was the Fitbit® feedback in increasing your light activity?	1 (10%)		5 (50%)	4 (40%)	
	No affect	*Minor affect*	*Moderate affect*	*Major affect*	
How much did tracking your light activity affect your behavior?	1 (10%)		6 (60%)	3 (30%)	
What affect did tracking your TV time have on decreasing your TV time?	6 (60%)	1 (10%)	2 (20%)	1 (10%)	

	No difference	*Slightly more easy*	*Moderately more easy*	*Much more easy*
How much easier has the Aria® scale made it to track your weight?	0 (0%)	1 (10%)	3 (30%)	6 (60%)
	Much less easy	*Somewhat less easy*	*Somewhat more easy*	*Much more easy*
How easy is it to use the Lose It account compared to paper tracking?	0 (0%)	0 (0%)	1 (10%)	9 (90%)
	Much less time	*Somewhat less time*	*Somewhat more time*	*Much more time*
How much time do you spend using the Lose It® app compared to paper tracking?	2 (20%)	3 (30%)	1 (10%)	4 (40%)

Technology

Participants reported high satisfaction with the technology component of the program. 90% of the women thought the Fitbit Zip® activity trackers were useful in increasing their light activity time and 90% felt the Fitbit was accurate in tracking their activity levels. Additionally, 90% of the women reported the Fitbit Aria Smart Scale® made it easier to track their weight and 100% of the women said their Lose It® account was easier than keeping a paper food diary.

> *"Love the Aria scale! And fitbit! Wifi sync made it easier. Weighing on analog scale didn't sync with app, so couldn't see trends."*

> *"Everything has a barcode you can scan – it's the bomb!"*

Discussion

The Theory of Planned Behavior includes assessment of perceived importance and beliefs, subjective norms, perceived control, and intentions to make the behavior change. The results from our survey indicate participants thought reducing sitting time was of low importance compared to dietary and physical activity goals. Although they felt like they

had more knowledge about the harms of too much sitting and thought that they spent less time sitting than other adults their age, they reported having only a moderate amount of control over the amount of sitting time. Furthermore, participants did not have strong intentions of reducing their sitting time throughout the intervention.

The most commonly reported barrier to reducing sitting time was workplace activities. Seven of the ten women had full time or part time jobs and three of the women were retired or unemployed. Of the women who were employed, 90% reported work related activities as the largest barrier to reducing their sitting time and specifically cited computer time, meetings, work environment, confinement to cubicle or desk as barriers while at work. Many of the participants also reported traveling time as a significant barrier to reducing their sitting time. One participant who was a bus driver was unable to move around for a substantial part of each work day as she was driving a school bus. Other reported barriers included inclement weather and sitting hobbies (e.g. sewing, scrapbooking, reading). The three women who were not employed most commonly cited computer time at home as an important barrier to reducing sitting time. One participant spent most of her time quilting and sewing – both of which she felt she could not do while standing.

Although participants overwhelmingly enjoyed of the technology components of the intervention, it did not appear to enhance their ability to reduce their sitting time. The Fitbit® and Lose It® technology components were given to the participants after a 4 month weight loss intervention in which they tracked their diet and physical activity manually on paper. Most participants reported the technology made it much easier to track their

weight, diet and physical activity throughout the maintenance phase. However, some participants reported they thought it would have been helpful to have more time to acclimate to the devices before the maintenance phase began. Although participants were instructed to look at their apps or check the website every day to assess activity, only 40% of participants reported doing so. In fact, two of the women reported never checking their lightly active time because they could not access the information easily from their mobile phone.

The biggest strength of this secondary analysis is the insight gained into the perceptions and feelings of women participating in an intervention that attempted to reduce sedentary behavior. Several limitations were present in the analysis. The interviews were conducted four months into the intervention, instead of at the end of the intervention and only captured the participants' opinions at one point in time. Furthermore, the interviews were conducted over the phone, which may have limited the interpretability of certain responses.

In conclusion, reducing sedentary behavior was not as important to participants as other components of the weight management program. Furthermore, participants did not feel they had control over their sitting time and their intentions of reducing sedentary time were not strong. In the future, interventions should focus on sedentary time alone without the introduction of other lifestyle behaviors. Furthermore, initiatives are needed to make light activity more conducive in the workplace. Finally, usability of technology should be improved to provide participants with easy access to activity data.

CHAPTER FIVE

DISCUSSION AND CONCLUSION

Summary of Findings

The studies presented in this dissertation aimed to 1) assess the impact of weight loss and weight loss maintenance on components of MetS among obese and overweight breast cancer survivors, 2) determine relationships between changes in dietary and activity variables and changes in the components of MetS, 3) examine differences in fasting and postprandial glucose and insulin and measures of insulin sensitivity following the same weight management intervention among breast cancer survivors, 4) determine if change in weight, diet or activity were predictors of improvements in insulin sensitivity after a weight management intervention, 5) assess barriers to reducing sedentary behavior within a weight maintenance intervention among breast cancer survivors.

Overall, the 10 month weight management intervention resulted in marked improvements in the components of MetS (except blood pressure) and measures of insulin sensitivity among breast cancer survivors. Associations between changes in dietary and physical activity components confirmed what is congruent with the literature regarding weight loss through lifestyle changes and MetS. Furthermore, participants were unable to successfully reduce their sitting time throughout the intervention. Low levels of perceived control and little intention of changing behaviors were likely the cause of the unchanged sitting time.

Improvements in Metabolic Syndrome After a Weight Management Intervention Among Breast Cancer Survivors

The effects of a 4 month weight loss intervention and a 6 month weight maintenance intervention on changes in components of MetS among overweight and obese breast cancer

survivors were examined. Participants who met criteria for MetS decreased throughout the intervention, with 12 (54%) participants meeting criteria at baseline, 9 (41%) participants at 4 months and 6 (27%) participants at 10 months. However the change in number of participants who met criteria from baseline to 10 months was not significant in this small study. Participants lost a mean of 10.7 ± 3.9% of baseline weight after the 4 month weight loss intervention and achieved significant improvements in waist circumference (-7.03 cm), fasting glucose (-7.14 mg/dl), and triglycerides (-22.23 mg/dl). However, there was significant decrease in HDL-C after the 4 month weight loss period (-5.59 mg/dl). The participants who lost the greatest percent of baseline weight also exhibited the greatest decreases in waist circumference (*r=0.67*), decreases in percent calories from fat (*r=0.52*), and increases in fruit and vegetable intake(*r=-0.54*). Furthermore, decreases in percent calories from fat were associated with decreases in serum triglycerides (*r=0.454*). Additionally, decreases in fasting glucose were associated with increases in MVPA *(r=-0.458).*

The 6 month weight maintenance intervention was successful (i.e. they did not regain their weight), as participants maintained their 4 month weight loss within a mean of -0.76 kg ± 3.59 kg. Our weight loss maintenance results are impressive in light of the literature in this area commonly reporting regain after a period of weight loss(45, 162). Although participants did not continue to lose significant amounts of weight, they continued to reduce their waist circumference throughout the 6 month maintenance phase (-2.76 cm). HDL-C significantly increased (+11.82 mg/dl) during the maintenance phase. Percent weight loss from 4 to 10 months was associated with continued decreases in waist circumference *(r=0.883*). Increases in percent

fat intake from 4 months to 10 months were associated with greater reductions in percent weight loss (*r=0.572)* and waist circumference (*r=0.572).*

Impact of a Weight Management Intervention on Fasting and Postprandial Measures of Insulin and Insulin Resistance Among Breast Cancer Survivors

Our results show that a 4 month weight loss intervention successfully reduced both fasting insulin (-5.72 mU/l) and fasting glucose (-7.63 mg/dl) among a group of overweight and obese breast cancer survivors. Furthermore, 4 month values for postprandial insulin (AUC and iAUC) were significantly reduced by 31.5% and 27.5% respectively and this reduction was sustained for the subsequent 6 months of weight maintenance. However, there was no change in postprandial glucose at any time point. Measures of insulin resistance were also significantly improved after weight loss and sustained after weight maintenance, as evidenced by marked improvements in HOMA-IR (-49%) and Matsuda index scores (+67%) from baseline to 10 months.

Changes in dietary and activity factors did not predict changes in insulin sensitivity. Percent weight loss was not associated with change in fasting insulin levels. However, improvements in Matsuda Index scores were significantly associated with percent weight loss from baseline to 10 months (r=-0.545), whereas changes in fasting insulin (r=0.32) and HOMA-IR scores (r=0.32) were not significantly association with percent weight loss.

Perceived Barriers to Reducing Sedentary Behavior Within a Weight Management Intervention

We found no evidence no difference between the sedentary behavior group and the standard weight maintenance group in their ability to maintain weight loss. In order to better understand the perceived barriers to reducing sedentary time among breast cancer survivors, we conducted phone interviews based on the Theory of Planned Behavior. The results for these interviews suggested participants felt reducing sedentary time was not as important as diet and exercise. Relative to peers outside the study, they felt they had more knowledge about the health impact of too much sedentary behavior and felt they were more active. Participants reported little control of their sedentary time. Using the Theory of Planned Behavior as our framework, our interviews identified workplace environment as the major barrier to reducing sedentary behavior. Participants also reported sitting hobbies like sewing and scrapbooking as significant barriers. Furthermore, they did not have strong intentions of reducing their sedentary time.

We also assessed experiences with the technology components of the intervention and found that participants were highly satisfied with the Fitbit® activity tracker, Aria® smart scale and their Lose It® accounts. While they reported that these tools made them more aware of their behaviors, it was not enough to significantly change sedentary behaviors.

Clinical Significance

As science progresses and treatments for breast cancer are optimized, the number of long term survivors of breast cancer increases (124). Obesity will continue to be a threat to breast cancer survivors. Breast cancer survivors have a unique set of health risks following treatment,

of which obesity plays an important role (163). Metabolic syndrome and insulin resistance are both condition that underlie obesity and must be closely monitored after breast cancer treatment because a significant amount of evidence suggests they play an important role in the health and longevity of these women. The results of the research presented in this dissertation, suggest weight loss through diet and exercise results in improvements in components of MetS and insulin resistance and these improvements can be effectively sustained after a period of weight maintenance. This is important for breast cancer survivors who are especially vulnerable to obesity and cardiovascular disease.

The clinical utility of MetS in the general population has been criticized for a number of practical reasons. First, there are at least sixteen different cutoffs and/or combinations of diagnostic criteria used to define MetS (15). Although efforts have been made to harmonize the definition of MetS, there still remains some controversy in literature regarding appropriate cutoffs for specific demographic and ethnic groups. There is not one unifying mechanism that can describe the interplay between the components of MetS. Furthermore, there is no single drug that can adequately address all of the components of MetS at the same time, and physicians are left to treat all components of MetS on an individual level. All of these factors have resulted in frustration for physicians and a consequent lack of diagnosis of MetS in the clinic (164).

Regardless of which cutoffs are used, the only successful treatment of MetS as a whole is achieving and maintaining healthy weight through lifestyle changes in diet and exercise. Although the National Cholesterol Education program recommends Therapeutic Lifestyle Change (TLC) as the first treatment for MetS, physicians are more often prescribing drugs than lifestyle (22, 165). I would argue that MetS can and should be utilized as a teachable moment in

the clinic in which the promotion of healthy lifestyle can play a central role. Instead of reviewing individual components and prescribing specific medications for each component, physicians could instead have a more general conversation with their patients about the benefits of healthy lifestyle.

Furthermore, MetS may have particular importance for the clinical implications of breast cancer survivors in terms of both breast cancer recurrence and risk of comorbidities (13, 166). A combination of adjuvant breast cancer treatment (167), weight gain after treatment (168), and obesity (65) all contribute to the higher prevalence of MetS in breast cancer survivors when compared to non-cancer survivors. We found that successful weight loss and weight maintenance effectively reduces components of MetS among breast cancer survivors. However, lifestyle change is rarely a part of the conversation between oncologists and their patients (169, 170). Survivorship care plans are now becoming a standard of care in cancer centers across the nation; however, more research is needed to determine the proper time and delivery of lifestyle recommendations for cancer survivors (171).

Identifying insulin resistance is a valuable extension of metabolic syndrome that also deserves clinical attention. The Center for Disease Control (CDC) estimates from 2009-2012, 12.3% of adults age 20 and older had diabetes and 37% had prediabetes – that is nearly half of the US population who likely had some degree of impaired insulin sensitivity (172). Hemoglobin A1C is the most commonly used diagnostic criteria for diabetes and prediabetes, with values between 5.7% and 6.4% indicating prediabetes and values greater than or equal to 6.5% indicating diabetes (173). This measurement does not allow clinicians to make any definitive diagnosis of insulin resistance. Furthermore, there is not a universally accepted

measure or cutoff for insulin resistance. Simple mathematical calculations, like HOMA-IR and Matsuda Index should be further developed and studied in larger populations so that they can be viably used in clinical settings. This would allow physicians to have a more complete understanding of their patients' physiology and prescribe proper treatment regimens (like lifestyle adjustments).

Changing sedentary behavior remains a major obstacle among breast cancer survivors. Since increased sitting time has been linked to risk of cancer, MetS, and insulin resistance – it is in the best interest of clinicians to encourage people to move more and sit less. The best way to deliver this message is yet to be determined. One strategy could be to harness the universal dependence on technology. While the increased time spent in front of screens has led to an overwhelming amount of sedentary time (174), we could alternatively use technology to help promote active lifestyle through activity trackers like the Fitbit® with added features built-in to prompt movement after long periods of uninterrupted sitting. Our research found changing sitting behaviors among breast cancer survivors is difficult because people tend to believe they have little control over changing these behaviors. Furthermore, they believe that other lifestyle pursuits like weight loss, dietary changes and exercise are more important than reducing sitting time. When in actuality all of these components play important independent roles in overall health.

Limitations

The small sample size is an obvious limitation of the presented research. As with any pilot study, statistical analyses are limited when sample sizes are small. Specifically, predictive models are difficult in small samples, as the general rule of thumb states one predictor should be added to the model per 10 participants. However, effect sizes are robust with a small sample sizes. A larger sample size would have increased the power to detect meaningful differences and may have provided more insight into the effects of the intervention.

The inherent issues with self-reported physical activity and dietary data are another limitation of the presented research (175). For this study we used self reported data to report changes in MVPA, siting time and diet. Actigraph accelerometers were used at each time point, but there were several issues with the functionality of the accelerometer itself and thus could not derive meaningful data from the whole sample. At baseline, 2 participants did not register valid wear time and one accelerometer chip was broken. At 4 months, two participants did not register valid wear time, one participant did not return her accelerometer, and one accelerometer chip was broken. At 10 months, one participant did not have valid wear time. Of the total sample only 15 participants had valid accelerometer data for all three time points (n=6 for MAINT + SED and n=9 for MAINT). Furthermore, we observed a higher than expected amount of MVPA at baseline (>30min/day) as measured by accelerometry. This could have been the case for a few reasons. First, there was up to 30 days between their screening date and their baseline testing session. After screening, participants may have been motivated to make changes in their activity or diet so as to get a "jump start" on their weight loss before the program started. Second, the accelerometers were distributed after their baseline testing visit and worn for 8 consecutive days.

Although participants were instructed not to change their activity while wearing the accelerometer, the Hawthorne Effect may have played a role in the amount of MVPA observed at baseline, such that the act of knowing their activity was being monitored impacted their activity levels. A combination of the lapse in time between screening and enrollment and the act of wearing the device could have contributed to the high levels of MVPA at baseline. Despite all of this, there was no difference between groups at any time point in accelerometer derived sedentary time, light activity or MVPA in the valid sample (n=15) (Figure 5.1)

Lastly, the generalizability of this pilot study is limited as the recruitment base for the breast cancer survivors took place at one clinic in Kansas City. Most participants were white, married and well educated – therefore our findings may not be generalizable to all survivors.

Figure 5.1 Accelerometer Derived Activity By Timepoint and Group (n=15)

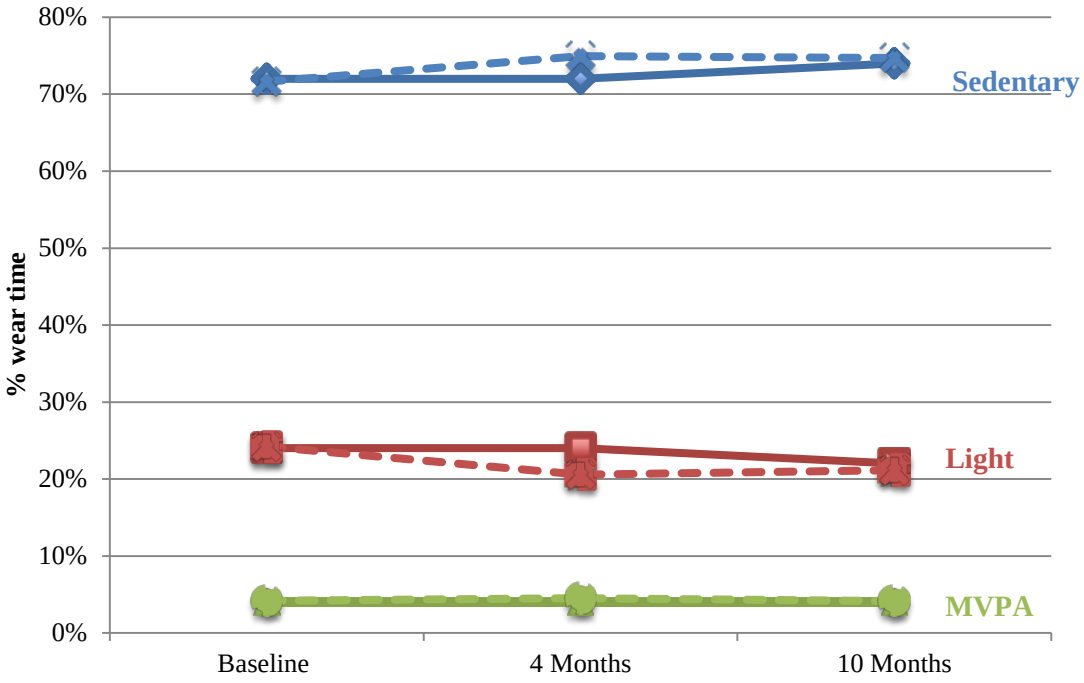


Figure 5.1 Data presented as mean percent of wear time for each level of activity for each group. Dotted lines represent MAINT ONLY (n=9). Solid lines represent MAINT + SED (n=6). Sedentary minutes defined as <100 counts per minute, light activity defined as 100-1951 counts per minute and MVPA defined as ≥ 1952 counts per minute

Future Directions

Future research should focus on determining dietary strategies and activity levels required to promote optimal metabolic health for breast cancer survivors. Large-scale longitudinal trials are needed to determine the proper amount of calorie reduction and physical activity to improve components of MetS and insulin resistance in the long term. Although this research is necessary in the general population, it is specifically needed among breast cancer survivors.

In addition, future interventions and public health efforts should be aimed at determining feasible ways to reduce sedentary time. The message to reduce sedentary time may have been diluted by dietary and MVPA recommendations in our intervention. One strategy may be to focus solely on reducing sedentary time for a 4-8 week period before the introduction of weight loss. Participants in our sample reported that they spent more of their time and energy focused on diet and physical activity when compared to reducing sedentary time because they viewed diet and exercise as more important strategies for weight loss and weight maintenance. They were right to do so, as the evidence suggests diet and exercise are the key components of successful lifestyle-based weight loss. Therefore, participants could be given a period of time before the intervention began to focus on becoming more aware of sedentary time and then setting individualized goals to reduce their sedentary time. After successful reduction of sitting time, the participants could start a weight loss phase, in which they begin to focus on diet and exercise while carrying over reduced levels of sedentary time.

Future interventions should use recurrence, co-morbidities and death as primary endpoints in long-term lifestyle-based weight management programs. Disentangling the individual and combined effects of diet and activity on the metabolic health of survivors is necessary and requires randomized controlled trials. Dissemination research is also necessary to determine ways to best translate these findings to the general public.

Conclusions

The work presented in this dissertation suggests a lifestyle-based weight loss and weight loss maintenance intervention results in successful improvements of components of metabolic syndrome and insulin sensitivity among overweight and obese breast cancer survivors. Reducing sedentary behavior remains an unconquered challenge. Workplace interventions to reduce sedentary time may be an important focus for breast cancer survivors. Most importantly, future endeavors should focus on empowering breast cancer survivors to lead healthy lives.

CHAPTER 6

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APPENDIX I

HSC APPROVAL AND CONSENT FORM

Women Standing for Better Health

You are being asked to take part in this research study because you are a female breast cancer survivor and you are currently in an unhealthy weight category (body mass index, BMI>26.9). This study will take place through the University of Kansas Medical Center (KUMC) in Kansas City, KS, with Dr. Christie Befort as the primary researcher. Two groups of about 15 women will be in the study.

You can choose whether or not to join, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at the University of Kansas Medical Center (KUMC).

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to before making your decision. If you decide to participate, you can continue to ask questions anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating.

BACKGROUND

Two-thirds of women in the United States are overweight (BMI 25-29.9 kg/m^2) or obese (BMI > 30 kg/m^2). Breast cancer survivors who are overweight or obese have a higher risk of cancer returning, along with shorter overall survival after diagnosis. Physical inactivity and sedentary behavior, or too much sitting time, is associated with obesity, heart disease and multiple cancers.

PURPOSE

Many diet and exercise programs focus on eating a healthy diet and increasing moderate intensity exercise in order to lose weight and maintain that weight loss. This study will help us learn if reducing sitting time has a positive effect on maintaining weight loss long-term. The results may be useful for improving and increasing the success of future weight management programs.

PROCEDURES

Months 1-4: Weight Loss Intervention

For the first 4 months, you will complete a weight loss program where you will have group meetings with a group leader and about 12-15 other breast cancer survivors once per week. The meetings last around 60 minutes. Group meetings are conducted by phone, and are set up as a conference call that you will join by calling a toll free number. Once per month, group meetings will be held in person. You may still call in if you are unable to attend in person.

During the meetings, you will learn about the diet and will receive education on nutrition and physical activity. You will also learn ways to change your habits related to diet and exercise, and you will have the chance to share with other women in the group and to ask questions and problem-solve about how to lose weight and overcome barriers. You will also learn about how diet and physical activity impacts breast cancer risk and have the opportunity to ask questions and share experiences related to being a breast cancer survivor. You will be asked to weigh yourself weekly and to keep track of your diet and exercise using a self-monitoring log. You will report this information to your group leader twice per week

by email or by phone. Group meetings will be recorded in order to evaluate how the program is working. These audio-recordings will be kept confidential and will be destroyed after 5 years.

Diet. The diet recommendations will be a 1200 to 1500 calorie/day diet consisting of 2 meal replacement shakes, 2 entrées available in grocery stores, and 5 one cup servings of fruits and vegetables (F/V) per day. During the first 4 months, you will receive the shakes free of charge. The shakes are made by Complete Nutrition LLC, a commercial vendor. Entrees, fruits, and vegetables will not be provided, and you will need to purchase them from the grocery store. A list of acceptable entrees will be provided to you at the beginning of the study. You will also learn about dietary guidelines for weight loss to assist you with modifying home-prepared meals to be lower in calories.

The shakes you will be using will be shipped directly to your home by Complete Nutrition, LLC. We will share your name, shipping address, and phone number with Complete Nutrition, LLC to allow them to ship the shakes directly to you. The only reason Complete Nutrition, LLC will have your name and address is to keep track of orders through their online shipping system. Complete Nutrition, LLC will be aware that you are in this study but will have no other information about you. They will not contact you or use your name for marketing purposes.

Physical Activity. You will work toward a goal of 225 minutes per week of moderate intensity exercise, such as brisk walking. You will work up to this goal slowly, beginning with 15 minutes per day, 3 days per week. You will be given a physical activity kit to assist you in increasing your weekly exercise minutes. Items in this kit include exercise DVDs to assist with aerobic exercise, and a pedometer for you to track physical activity levels daily.

Months 4 – 10: Weight Loss Maintenance Intervention

For months 4-10, you will be assigned to a treatment group by a process called randomization (like flipping a coin). What happens to you during this part of study will depend on which group you are assigned to. You will have an equal chance of being assigned to either group. You will find out at 4 months which group you have been assigned to.

If you are assigned to receive the weight loss maintenance intervention you will have group phone meetings every other week for 6 months with the same group of women as the first 4 months. In-person meetings will take place once every 2 months. These meetings will last about 60 minutes. During the meetings, you will learn to solve problems related to maintaining lifestyle changes and will review nutrition and physical activity information. You will be given a daily calorie goal based on your estimated caloric needs to maintain your weight loss, and you will be encouraged to continue to consume 2 shakes and/or entrees per day. You will also continue with physical activity with a goal of 225 minutes per week of moderate intensity exercise. You will continue to weigh yourself weekly and keep track of your diet and exercise. You will report this information to your phone counselor once per week by email or by phone. Group meetings will be recorded in order to evaluate how the program is working. These audio-recordings will be kept confidential and will be destroyed after 5 years.

If you are assigned to receive the weight loss maintenance plus sedentary behavior intervention you will also follow the guidelines of the weight loss maintenance intervention, however your bi-weekly meetings will include an additional sedentary behavior component. For months 4-10, you will set additional goals to decrease your television time, overall sitting time, and to increase your light intensity activity throughout the day. You will receive a Fitbit Zip activity monitor and a Fitbit Aria Wi-Fi Smart Scale to help track your weight and sedentary time. You will receive thorough instructions from your leader as to how to use these devices after your 4 month visit. During the 6 month maintenance phase,

you will be asked to sync your Fitbit Zip at least once daily and to weigh yourself on the Fitbit Aria Scale at least once weekly. You will self monitor your sedentary time based on the information provided through your Fitbit account. In addition, your group leader will provide feedback based on your Fitbit account and help you to create goals aimed at decreasing your sedentary time. In addition to monitoring your activity, you will be asked to use a diet tracking website to log your daily food intake.

The following data collection visits apply to all participants:

Data Collection Visits

You will meet in-person with research staff persons 3 different times for data collection. Before beginning the weight loss program, you will attend your first in-person data collection visit (called the baseline visit). You will then start the weight loss program. At 4 months, you will attend the second in-person data collection visit. The last visit will be at 10 months. These will be private meetings between you and the research staff, and will take place in the morning at the University of Kansas Medical Center Clinical and Translational Research Unit located in Fairway, KS.

At these visits, the following tests will be completed:

- Your height, weight, waist circumference, and blood pressure will be measured.
- You will complete a survey that asks questions about your background, health, diet and physical activity behaviors and beliefs, and quality of life.
- You will be asked questions about your food intake, specifically what your ate and drank during the previous day.
- You will be asked to come to the appointment following an overnight (10-12 hour) fast. Upon your arrival, a small catheter will be placed in your arm by a trained nurse, and a blood sample (≤ 3 teaspoons) will be collected. You will then be asked to consume a breakfast meal consisting of approximately 350 calories and 50 g carbohydrates. For the next 2 hours, you will be asked to lie still on a bed while we will collect a small blood sample (1-2 tablespoons) at 30, 45, 60, 90, and 120 minutes after you finish the meal.
- You will be given an accelerometer (looks like a pager), which you will wear around a belt for 7 days and return to us by mail in a pre-stamped envelope. Accelerometers will measure how much exercise you are doing each day.

In addition to the above tests, at the baseline visit we will collect demographic and medical history information and take a picture of you that will be included on the roster given to your group leader.

The in-person data collection visits will last about 3 hours each. Following each in-person visit, a research staff person will call you two times to ask questions about your food intake and to clarify any questions about your medical history or survey responses. These phone calls will take about 20-30 minutes. Finally, at month 5 and 8 you will be interviewed by one of the researchers to ask about your feedback on the program, including what you liked and did not like. This interview will last approximately 15 minutes. In addition, you may be contacted by the research staff for up to one year after the study to clarify your information or discuss future research projects.

RISKS

You may feel some tiredness during your exercise, and your heart rate and blood pressure will increase. Under extreme conditions, this can lead to a serious cardiac event, such as a heart attack. The possibility of experiencing a serious cardiac event has been estimated to be less than 1 per 20,000 in

adults who exercise. There is also a risk for physical activity related injury, such as a sprained ankle. Because of the risks related to starting and participating in a regular exercise program, you have to get approval from your physician before starting the study.

If you have had lymph node removal, you are at risk for lymphedema, which is the chronic swelling and tightness in the arm or hand due to an accumulation of lymphatic fluid in the soft tissue of the arm. It is important to monitor this carefully and, before beginning a strength training program, speak to your doctor about any weight limits you might have.

Some pain, swelling, bruising, and bleeding may occur at the site of blood sampling. There is also a possibility of infection resulting from the blood draw. You may experience a vasovagal response which can include lightheadedness, dizziness, sweating, sudden warmth or coldness, nausea and/or vomiting, very rarely visual disturbances or passing out. If this happens we will position your body appropriately, and hydrate you with oral fluids. Rarely, thrombosis of the vein may occur resulting in thrombophlebitis (swelling of a vein caused by a blood clot). Treatment for thrombophlebitis will mostly consist of applying warm pads and supportive care.

Another risk is that you may feel uncomfortable when talking about weight or breast cancer issues. Because names are used and audio recorded, there is a risk your confidentiality may be breached.

There may be other risks of the study that are not yet known. You understand that your participation in this study is voluntary, and you can choose to end your participation at any time.

NEW FINDINGS STATEMENT

You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS

You may benefit by losing weight and maintaining that weight loss. The information gained in this study will help determine decreasing sedentary behavior will help to maintain weight loss.

ALTERNATIVES

You may choose not to participate in this research study. Some of the other options instead of participating include joining a commercially available weight loss program (e.g. Weight Watchers, TOPS, etc), using online resources (www.ediets.com, Weight Watchers online, etc), and/or following recommendations from the United States Department of Agriculture's food guide pyramid. Participation is voluntary. Deciding not to participate will have no effect on the care or services you receive at the University of Kansas Medical Center.

PAYMENT AND COSTS

You will be need to purchase your own pre-packaged entrees (two per day), available at the grocery store in the frozen food section. The cost for these entrees varies greatly, but is estimated at $5.00 per day. You will also need to purchase enough fruits and vegetables to eat five one-cup servings per day. The intervention sessions, materials, physical activity kits, and the shakes from Complete Nutrition are provided at no cost to you.

For data collection visits at baseline and 4 months, you will receive a Target gift card in the amount of $50 per visit, and at the 10 month visit, you will receive a $75 Target gift card in return for the time required. For all three visits you will receive a total of $175 in gift cards. If you withdraw from the study,

you will be paid for the completed visits. Your name and other identifying information, as well as the title of this study will be used by offices at KUMC that process payments to research subjects.

IN THE EVENT OF INJURY

If you have a serious side effect or other problem during this study, you should seek appropriate medical care. If it is an emergency, call 911. You should also contact Dr. Christie Befort at (913) 588-3338. The research team will decide what modifications to the study intervention, if any, is best for you at that time.

INSTITUTIONAL DISCLAIMER STATEMENT

If you think you have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KUMC.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

The researchers will protect your information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. Your health information is protected by a federal privacy law called HIPAA. By signing this consent form, you are giving permission for KUMC to use and share your health information. If you decide not to sign the form, you cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study activities and from your medical record. You may be identified by information such as name, address, phone, date of birth, social security number, or other identifiers. Your health information will be used at KUMC by Dr. Befort, members of the research team, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

By signing this form, you are giving Dr. Befort and the research team permission to share information about you with persons or groups outside KUMC. Your information will be shared with representatives of Complete Nutrition, LLC to allow them to ship the shakes directly to you. Your information may also be shared with U.S. agencies that oversee human research (if a study audit is performed) who may make copies of study records for audit purposes. The purpose for using and sharing your information is to make sure the study is done properly and to evaluate the safety and effectiveness of the weight loss intervention.

The HIPAA privacy law may not apply to everyone who receives your health information. Your information might not be protected by HIPAA if persons outside KUMC disclose it. In some cases, there may be other laws that protect your information from improper use.

Your permission to use and share your health information will not expire unless you cancel it. The study records kept only by the researcher may not be available to you until the end of the study. The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study. Finally, you understand that the investigator is not prevented from taking steps, including reporting to the proper authorities, to prevent serious harm to yourself or others.

You have the right to cancel this authorization at any time. Your cancellation must be in writing addressed to Dr. Christie Befort, 3901 Rainbow Blvd, MS 1008, Kansas City, KS 66160. You are aware that even if you cancel this authorization and withdraw from the study, researchers may continue to use and disclose information that was gathered before they received your cancellation.

QUESTIONS

You have read the information in this form, this study has been explained to you by one of the study staff, and your questions have been answered. If you have any more questions, you may contact Dr. Christie Befort at 913-588-3338. If you have any questions about your rights as a research subject, you may call 913-588-1240 or write the Human Subjects Committee, University of Kansas Medical Center, 5012 Wescoe, 3901 Rainbow Blvd, Kansas City, Kansas 66160-7700.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

You may stop being in the study at any time. Your decision to stop will not prevent you from getting treatment or services at KUMC or the medical center where you receive your cancer care. The entire study may be discontinued for any reason without your consent by the investigator conducting the study.

CONSENT

Dr. Befort or the other research team has given you information about what will be done in this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study. You are aware that you may refuse to answer any questions or you may stop participating in the study at any time. Your participation will have no effect upon the medical care or treatment you receive in the future from your health clinic. You may have this form read to you if it would help your understanding of this study. By signing this form, you say that you freely and voluntarily consent to participate in this research study. You will be given a signed copy of the consent form to keep for your records.

_____
Print Participant's Name

_____ _____ _____
Signature of Participant Time Date

_____
Print Name of Person Obtaining Consent

_____ _____ _____
Signature of Person Obtaining Consent Time Date

Permission to Contact for Future Research

Please check only **one** of the two boxes below

In the future, Dr. Befort and researchers at KUMC will be conducting additional studies which may apply to you. A separate consent would be obtained at the time of your participation in any additional studies. Please check one of the two boxes below to indicate whether or not you are willing to have us contact you when such future studies come up.

☐ Yes, I am willing to be contacted about future studies for which I might be eligible.

☐ No, I do not want to be contacted about future studies for which I might be eligible.

_____ _____

Participant's Signature Date

Use of Data and/or Blood Samples for Future Research

Please check only **one** of the two boxes below

☐ I agree to allow the use of my data and/or blood samples collected during this study to be used for future research that is unrelated to this study. Specifically, the data will be kept for 25 years and will be de-identified to prevent any identification back to you. The blood samples will be stored for 10 years. These samples will likely be used for future analysis of weight loss and breast cancer biomarkers that have not yet been identified or are currently unable to be measured. The use and disclosures of personal information listed in the consent form also apply to the saved data and/or blood samples. However, at any time, I can request that the data and/or blood samples be destroyed if I change our mind. If this occurs, I will provide a written request to Dr. Befort at the address listed below. Lastly, I understand that Dr. Befort can use and share information that was gathered before this request was received.

Christe Befort, PhD
University of Kansas Medical Center, MS 1008
3901 Rainbow Blvd
Kansas City, KS 66160

☐ I request my data and/or blood samples collected during this study to NOT be used for any future research that is unrelated to this study. I understand that I can still participate in this study if I refuse to have the data and/or blood samples retained.

_____ _____

Participant's Signature Date

APPENDIX II

SCREENING FORMS AND ASSESSMENT SURVEYS

Chart Screen

Contact Information

First Name _____

Last Name _____

Primary Phone Number _____

Other Phone Number _____

Email Address _____

Chart Screen Criteria

BrCa Stage (TNM) _____

Eligible based on staging?
☐ Yes
☐ No
(Stage I-III)

Date of last treatment _____

Eligible based on date of last treatment?
☐ Yes
☐ No
(greater/equal to 3 mo since last treatment)

Date of qualifying diganosis (most recent)? _____

Eligible based on date of diagnosis?
☐ Yes
☐ No
(3 mo - 10 years)

Chart Weight _____
(lbs)

Chart Height _____
(inches)

Chart BMI _____

Eligible based on chart BMI?
☐ Yes
☐ No
(25-46)

Chart states use of metformin, glipizides, or insulin?
☐ Yes
☐ No

List drug used: _____

Diagnosis of type 1, type 2 or prediabetes?
☐ Yes
☐ No

List diganosis: _____

Eligible based on use of medications/diagnosis of diabetes?
☐ Yes
☐ No

Chart smoking history

- ☐ Past smoker
- ☐ Current smoker
- ☐ Never smoked

List other major medical conditions potentially preventing eligibility (i.e. lung disease, diagnosis of heart disease or other co-morbidities) _____

Addtional Comments: _____

Eligible based on chart screen?

- ☐ Yes
- ☐ No

Pre Screen

Today's Date _____

Date of Birth _____

Age _____

Eligible based on age?
☐ Yes
☐ No
(< 75)

Weight - Self Report _____
(lbs)

Height - self report _____
(inches)

BMI - Self Report _____

Eligible based on BMI?
☐ Yes
☐ No
(27-45)

Have you gained more than 10 lb in the last 3 months?
☐ Yes
☐ No

Comments _____

Have you lost more than 10 lbs in the past 3 months?
☐ Yes
☐ No

Comments _____

Eligible based on gain/loss?
☐ Yes
☐ No

The following questions ask you to think about the activities you have done on a typical week during the past month and the average time per week you spent doing each activity. If you participate in any of the activities less than once per week, your response should be no.

In a typical week in the past month, did you spend time walking for exercise?
☐ Yes
☐ No

If yes, how many minutes did you spend per week?
☐ 1-15
☐ 16-30
☐ 31-45
☐ 46-60
☐ 61-75
☐ 76-90
☐ >90

In a typical week in the past month, did you spend time jogging (slower than 10 minutes/mile)?
☐ Yes
☐ No

If yes, how many minutes did you spend per week?
☐ 1-15
☐ 16-30
☐ 31-45
☐ 46-60
☐ 61-75
☐ 76-90
☐ >90

In a typical week in the past month, did you spend time running (10 minutes/mile or faster)?
☐ Yes
☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time playing tennis, squash, racquetball?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time bicycling (including stationary machine)?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time lap swimming?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time doing other aerobic exercise (aerobic dance, ski or stair machine, ect)?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time doing other vigorous activities?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time doing weight training or resistance exercises?

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

In a typical week in the past month, did you spend time doing low intensity exercise (yoga, stretching, toning)

- ☐ Yes
- ☐ No

If yes, how many minutes did you spend per week?

- ☐ 1-15
- ☐ 16-30
- ☐ 31-45
- ☐ 46-60
- ☐ 61-75
- ☐ 76-90
- ☐ >90

Total time spent active per week (excluding low intensity exercise): _____

Comments _____

Eligible based on time spent active?

- ☐ Yes
- ☐ No

(< 90 min/wk)

Can you currently walk briskly unassisted for at least 10 minutes, for example, can you walk six blocks briskly without stopping?

- ☐ Yes
- ☐ No

Comments _____

Eligible based on ability to walk?

- ☐ Yes
- ☐ No

Eligible based on pre-screen?

- ☐ Yes
- ☐ No

Full Screen

Weight/Diet History

Are you currently participating in any other weight loss treatment?
- ☐ Yes and willing to discontinue current treatment
- ☐ Yes and not willing to discontinue current treatment
- ☐ No

Comments _____

Eligible based on participation in weight loss treatment?
- ☐ Yes
- ☐ No

Over the past 6 months, have you taken any weight loss medications, or other medications that affect metabolism (ex. phentermine, steroids, ect)?
- ☐ Yes and willing to stop using this medication
- ☐ Yes and not willing to stop using this medication
- ☐ No

Comments _____

Eligible based on use of metabolism altering medications?
- ☐ Yes
- ☐ No

Do you have food allergies or intolerances, or are you currently on any special diet regimens (taking metabolic altering products such as Metabolife, macrobiotic or vegetarian diets, ect)?
- ☐ Yes
- ☐ No

Comments _____

Eligible based on diet regualtions?
- ☐ Yes
- ☐ No

Medical History

Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
- ☐ Yes
- ☐ No

Comments _____

Do you have any pending joint replacements?
- ☐ Yes
- ☐ No

Comments _____

Eligible based on joint health?
- ☐ Yes
- ☐ No

Do you have congestive heart failure or other cardiac conditions?
- ☐ Yes
- ☐ No

If yes, describe: _____

Do you feel pain in your chest when you do physical activity?
- ☐ Yes
- ☐ No

If yes, describe: _____

In the past month, have you had chest pain when you were not doing physical activity?
- ☐ Yes
- ☐ No

If yes, describe: _____

Do you lose your balance because of dizziness or do you ever lose consciousness?
☐ Yes
☐ No

If yes, describe: _____

Eligible based on cardiac history?
☐ Yes
☐ No

Have you been diagnosed with any other cancer (other than non-melanoma skin cancer) within the past five years?
☐ Yes
☐ No

If yes, describe: _____

Eligible based on diganosis of other cancers?
☐ Yes
☐ No

Do you have any lung diseases?
☐ Yes
☐ No

If yes, describe: _____

Eligible based on pulmonary history?
☐ Yes
☐ No

Have you ever had bariatric surgery (gastric bypass, banding or "stomach stapling")?
☐ Yes
☐ No

Comments _____

Eligible based on bariatric surgery history?
☐ Yes
☐ No

Please list any other diganosed medical conditions/events including any medications taken for these conditions. _____

Comments _____

Eligible based on other major medical events?
☐ Yes
☐ No

Have you ever been diagnosed with type 1, or type 2, or pre-diabetes?
☐ Yes
☐ No

Comments _____

Do you currently take insulin, metformin or glipizides?
☐ Yes
☐ No

Comments _____

Eligible based on diagnosis of diabetes or use of medications for diabetes?
☐ Yes
☐ No

Do you currently smoke, or do you have a history of smoking in the past?
☐ Never smoked
☐ Past smoker
☐ Current smoker

Comments (If you are a past smoker, is this a good time for you to participate in a weight management study?) _____

Eligible based on smoking history?
☐ Yes
☐ No

Health Screening Questions

In the past year, have you ever drunk or used drugs more than you meant to?
☐ Yes
☐ No

Comments _____

Have you felt you wanted or needed to cut down on your drinking or drug use in the past year?
☐ Yes
☐ No

Comments _____

Eligible based on substance abuse?
☐ Yes
☐ No

Have you been treated for a psychological disorder or substance abuse in the past 6 months?
☐ Yes
☐ No

If yes, describe: _____

Did you receive a diagnosis?
☐ Yes
☐ No

If yes, what was your diagnosis? _____

Eligible based on psych history?
☐ Yes
☐ No

Do you often feel you can't control how much you eat?
☐ Yes
☐ No

Comments _____

Do you often eat, within any 2 hour period, what most people would regard as an unusually large amount of food (if yes, refer to unusually large amount of food)?
☐ Yes
☐ No

Comments _____

Eligible based on binge eating?
☐ Yes
☐ No

Availability

Do you plan to spend frequent time out of town during the next 10 months?
☐ Yes
☐ No

Comments _____

Will you have a working home phone or cell phone and computer continually for the next 10 months?
☐ Yes
☐ No

Comments _____

Eligible based on availability?
☐ Yes
☐ No

Final Eligibility

Eligible based on BrCa history form?
☐ Yes
☐ No

Comments _____

Screened positive for depression using PHQ-9?
☐ Yes
☐ No

Comments _____

Eligible based on PHQ-9
☐ Yes
☐ No

Comments _____

Physician Consent received?
☐ Yes
☐ No

Comments _____

Consent form signed?
☐ Yes
☐ No

Comments _____

Completed orientation visit?
☐ Yes
☐ No

Comments _____

Completed baseline testing and randomized?
☐ Yes
☐ No

Comments _____

Lost after initially eligible?
☐ Yes
☐ No

Check applicable reason:
☐ No reason givien/lost contact
☐ Could not attend orientation
☐ Too busy
☐ Not interested in food plan
☐ Scheduling conflicts
☐ Not interested in group calls
☐ "Personal reasons"
☐ Too much travel

Breast Cancer History

Date of most recent breast cancer dianogisis

_____
(Month/Year)

Breast

☐ Left
☐ Right
☐ Both

Stage of most recent breast cancer at diagnosis:

_____
(TNM and/or Anatomical Stage (0-IIIc))

Original breast cancer ER+?

☐ Yes
☐ No

Currently using antihormone therapy?

☐ Yes
☐ No

Current antihormone therapy type:

_____

Past use of anti hormone therapy?

☐ Yes
☐ No

Past antihormone type:

_____

Stop date:

_____
(Month/Year)

Radiation therapy

☐ Yes
☐ No

Stop date:

_____
(Month/Year)

Chemotherapy

☐ Yes
☐ No

Chemotherapy type(s):

_____

Stop date:

_____
(Month/Year)

Surgery history (check all that apply)

☐ Lumpectomy
☐ Mastectomy
☐ None
☐ Unknown

Lumpectomy date:

_____
(Month/Year)

Mastectomy date:

_____
(Month/Year)

Demographics

Please complete the survey below.

Thank you!

1) Screening ID _____

2) Highest education level completed
- ☐ Less than high school
- ☐ high school/GED
- ☐ Some college or associate's degree
- ☐ Bachelor's degree
- ☐ Master's degree
- ☐ Doctoral level degree

3) Ethnicity
- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino
- ☐ Unknown

4) Race
- ☐ African American
- ☐ American Indian or Alaskan Native
- ☐ Asian
- ☐ Native Hawaiian or other Pacific Islander
- ☐ White
- ☐ Unknown

5) Marital Status
- ☐ Married
- ☐ Co-habitating
- ☐ Divorced or separated
- ☐ Single
- ☐ Widowed

6) Are you currently employed?
- ☐ Yes, full time (35 hours per week or more)
- ☐ Yes, part time (less than 35 hours per week)
- ☐ No

7) What is your occupation? _____

Sedentary Behavior and Weight Loss Maintenance for Breast Cancer Survivors
PROTOCOL # 0192

	Time of Draw/Meal	Blood draw completed?	Initial
Fasting Draw	Time Due: Actual Time:	□ Yes □ No If no; explain:	
Meal Consumed (should take 10 minutes)	Time to Start Meal: Actual Time Started Meal:	Comments:	
30 Minutes Post-Meal	Time Due: Actual Time:	□ Yes □ No If no; explain:	
45 Minutes Post-Meal	Time Due: Actual Time:	□ Yes □ No If no; explain:	
60 Minutes Post-Meal	Time Due: Actual Time:	□ Yes □ No If no; explain:	
90 Minutes Post-Meal	Time Due: Actual Time:	□ Yes □ No If no; explain:	
120 Minutes Post-Meal	Time Due: Actual Time:	□ Yes □ No If no; explain:	

Nurse's Signature: _____ **Date** _____

Anthropormorphics

Date of last food ingestion: _____

Time of last food ingestion: _____

Comments: _____

Have you consumed caffeine or coffee within the last 12 hours?
☐ Yes
☐ No

Comments: _____

Have you exercised within the past 24 hours?
☐ Yes
☐ No

Comments: _____

Weight

Fasting Weight 1 _____
(lbs (###.#))

Fasting Weight 2 _____
(lbs (###.#))

Height (Criteria: Measure height twice; must be < 2 cm difference. Take 3rd height measurement if first 2 do not meet criteria. Do not delete any measurements.)

Height 1 _____
(cm (###.#))

Height 2 _____
(cm (###.#))

Height 3 _____
(cm (###.#))

Waist Circumference (Criteria: < 2 cm; 3 measurements)

Waist Circumference 1 _____
(cm (###.#))

Waist Circumference 2 _____
(cm (###.#))

Waist Circumference 3 _____
(cm (###.#))

Resting Blood Pressure

****Must be taken in supine position at rest for 5 minutes prior**

(Criteria: Take 2 BP; SBP < 5 mmHg difference and DBP < 5 mmHg difference. Take a 3rd BP if first two do not meet criteria. Do not cross out any of the 3 BPs.)

Resting Blood Pressure 1: Systolic
_____
(mm Hg)

Resting Blood Pressure 1: Diastolic
_____

Resting Blood Pressure 2: Systolic
_____
(mm Hg)

Resting Blood Pressure 2: Diastolic
_____

Resting Blood Pressure 3: Systolic
_____
(mmHg)

Resting Blood Pressure 3: Diastolic
_____

Systolic higher than 140?
☐ Yes
☐ No
(If over 140 have ppt sit for 5 minutes before taking next reading. Instruct ppt to follow up with PCP regarding high BP.)

Diastolic higher than 80?
☐ Yes
☐ No
(If over 80 have ppt sit for 5 minutes before taking next reading. Instruct ppt to follow up with PCP regarding high BP.)

If higher than 140/80, did you instruct participant to follow up with PCP?
☐ yes
☐ no
☐ N/A

If blood pressure is 160/80 and not currently treated, alert study staff before beginning draw.
Comments:
_____

Did participant take usual blood pressure medications?
☐ Yes
☐ No
☐ Not on meds

Select cuff size used
☐ Small adult
☐ Adult
☐ Large adult
☐ Thigh

General Medical History

Have you ever been diagnosed with any cancers other than breast cancer?
☐ Yes
☐ No

Description _____

Date Diagnosed: _____
((month/year))

Date Treatment Completed: _____
((month/year))

Do you have immediate family members who are blood relatives, including parents, sibling, children, who have been diagnosed with any cancers (including breast and ovarian cancer)?
☐ Yes
☐ No

Family Members and Type: _____

Age of diagnosis: _____

Additional Comments _____

Have you ever been told by a doctor that you have high blood pressure?
☐ Yes
☐ No

Start Date: _____
((month/year))

End Date (if applicable): _____
((month/year))

Are you currently taking medications for high blood pressure?
☐ Yes
☐ No

When was the last time your blood pressure was checked by a health professional? _____

Was it elevated?
☐ Yes
☐ No
☐ Don't Know

What level was it at that time? _____

Additional Comments: _____

Has your doctor ever told you that you have any cardiovascular diseases or disorders? (i.e. heart attack, heart surgery, heart murmur, angioplasty, pacemaker, arrythmias, stroke, heart valve disease, lower limb edema, etc.)
☐ Yes
☐ No

Description: _____

Start Date: _____
((month/year))

End date (if applicable): _____

When was the last time your cholesterol was checked by a health professional? _____

Was it elevated?
☐ Yes
☐ No
☐ Don't know

What level was it at that time? _____

Have you had any close blood relatives who had a heart attack or heart surgery before age 55 (father or brother) or age 65 (mother or sister)?
☐ Yes
☐ No

Family members and type: _____

Age of diagnosis: _____

Additional comments: _____

Has your doctor ever told you that you have any lung diseases or disorders? (i.e. dyspnea/shortness of breath, asthma, pneumonia, bronchitis, etc.)?
☐ Yes
☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional comments: _____

Has your doctor ever told you that you have any diseases or disorders related to the liver, bile ducts, gallbladder, or pancreas? (i.e. cirrhosis, hepatitis, pancreatitis, gall stones, etc.)
☐ Yes
☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional Comments: _____

Has your doctor ever told you that you have any gastrointestinal diseases or disorders? (i.e. irritable bowel syndrome, diverticular disease, colitis, etc.)
☐ Yes
☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional Comments: _____

Has your doctor ever told you that you have any diseases or disorders related to the thyroid (i.e. hyperthyroid, hypothyroid, goiter, etc.)?
☐ Yes
☐ No

Description: _____

Start date: _____

End date (if applicable): _____

Additional Comments: _____

Has your doctor ever told you that you have diabetes or pre-diabetes?
☐ Yes
☐ No
☐ Pre-diabetes

Start Date: _____

When was the last time your fasting blood sugar was checked by a health professional? _____

Was it elevated?
- ☐ Yes
- ☐ No
- ☐ Don't know

What was the level at that time? _____

On average, how often do you monitor your blood glucose?
- ☐ Several times per day
- ☐ Once per day
- ☐ At least once per week
- ☐ At least once per month
- ☐ Only when I go to the doctor
- ☐ Never
- ☐ I have never been diagnosed with diabetes or pre-diabetes

Additional Comments: _____

Has your doctor ever told you that you have any other endocrine or metabolic diseases/disorders? (i.e. osteoporosis, hypoglycemia, etc.)?
- ☐ Yes
- ☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional Comments: _____

Has your doctor ever told you that you have arthritis, or do you experience pain in one or more of your joints (arthralgia)?
- ☐ Yes
- ☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional Comments: _____

Have you ever been treated for any mood disorders (i.e. depression, anxiety, etc.)?
- ☐ Yes
- ☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Additional Comments: _____

Do you currently smoke, or do you have a history of smoking?
- ☐ Current smoker
- ☐ Past smoker
- ☐ Never smoked

Start date: _____

End date (if applicable): _____

How many cigarettes do you smoke now, or did you smoke in the past? _____
((number per day/week/month/year))

Years smoked: _____

Additional Comments: _____

Do you ever drink alcoholic beverages?
- ☐ Yes
- ☐ No

If yes, how often do you drink?
- ☐ Daily or almost every day
- ☐ At least once per week
- ☐ At least once per month
- ☐ Once or twice per year

If daily, how many drinks do you have per day? _____

If weekly, how many drinks do you have per week? _____

Additional Comments: _____

Have you ever been told by a doctor that you have any other medical diseases or disorders that we have not already covered?
- ☐ Yes
- ☐ No

Description: _____

Start Date: _____

End date (if applicable): _____

Have you ever been diagnosed with lymphedema?
- ☐ Yes
- ☐ No

Additional Comments: _____

If no, have you ever noticed that one hand, lower arm, or upper arm was larger than the other? _____

If yes, have you ever received treatment? Describe: _____

Medication Record

Medication Name ______________________

Amount Taken ______________________

Reason Taken ______________________

Frequency ______________________
(times per day/week/month/year)

Start Date ______________________
((Month/Year))

Medication Name ______________________

Amount Taken ______________________

Reason Taken ______________________

Frequency ______________________
(times per day/week/month/year)

Start Date ______________________
((Month/Year))

Medication Name ______________________

Amount Taken ______________________

Reason Taken ______________________

Frequency ______________________
(times per day/week/month/year)

Start Date ______________________
((Month/Year))

Medication Name ______________________

Amount Taken ______________________

Reason Taken ______________________

Frequency ______________________
(times per day/week/month/year)

Start Date ______________________
((Month/Year))

Medication Name ______________________

Amount Taken ______________________

Reason Taken ______________________

Frequency ______________________
(times per day/week/month/year)

Start Date ______________________
((Month/Year))

Medication Name ______________________

Amount Taken ______________________

Modifiable Activity Questionnaire

Please complete the survey below.

Thank you!

Please the box of all activities that you have done during the past 7 days.

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Aerobics Dance/Step Aerobics	☐	☐	☐	☐	☐	☐	☐
Badminton	☐	☐	☐	☐	☐	☐	☐
Basketball	☐	☐	☐	☐	☐	☐	☐
Bicycling (indoor/outdoor)	☐	☐	☐	☐	☐	☐	☐
Bowling	☐	☐	☐	☐	☐	☐	☐
Calisthenics/Toning Exercises	☐	☐	☐	☐	☐	☐	☐
Canoeing/Rowing/Kayaking	☐	☐	☐	☐	☐	☐	☐
Dancing (square, line, ballroom)	☐	☐	☐	☐	☐	☐	☐
Elliptical trainer	☐	☐	☐	☐	☐	☐	☐
Fencing	☐	☐	☐	☐	☐	☐	☐
Fishing	☐	☐	☐	☐	☐	☐	☐
Football/Soccer	☐	☐	☐	☐	☐	☐	☐
Gardening/yardwork	☐	☐	☐	☐	☐	☐	☐
Golf	☐	☐	☐	☐	☐	☐	☐
Hiking	☐	☐	☐	☐	☐	☐	☐
Horseback riding	☐	☐	☐	☐	☐	☐	☐
Hunting	☐	☐	☐	☐	☐	☐	☐
Jogging (outdoor, indoor)	☐	☐	☐	☐	☐	☐	☐
Jumping Rope	☐	☐	☐	☐	☐	☐	☐
Martial Arts (karate, judo)	☐	☐	☐	☐	☐	☐	☐
Pilates	☐	☐	☐	☐	☐	☐	☐
Raquetball/Handball/Squash	☐	☐	☐	☐	☐	☐	☐
Rock climbing	☐	☐	☐	☐	☐	☐	☐
Scuba Diving	☐	☐	☐	☐	☐	☐	☐
Skating (roller, ice, blading)	☐	☐	☐	☐	☐	☐	☐
Snow Shoeing	☐	☐	☐	☐	☐	☐	☐
Snow skiing (downhill)	☐	☐	☐	☐	☐	☐	☐
Snow skiing (cross country, Nordic Track)	☐	☐	☐	☐	☐	☐	☐
Softball/Baseball	☐	☐	☐	☐	☐	☐	☐

Stairmaster	☐	☐	☐	☐	☐	☐	☐
Strength/Weight Training	☐	☐	☐	☐	☐	☐	☐
Swimming (laps, snorkeling)	☐	☐	☐	☐	☐	☐	☐
Tai Chi	☐	☐	☐	☐	☐	☐	☐
Tennis	☐	☐	☐	☐	☐	☐	☐
Volleyball	☐	☐	☐	☐	☐	☐	☐
Walking for Exercise (outdoor, indoor, treadmill)	☐	☐	☐	☐	☐	☐	☐
Water Aerobics	☐	☐	☐	☐	☐	☐	☐
Yoga	☐	☐	☐	☐	☐	☐	☐
Other	☐	☐	☐	☐	☐	☐	☐

Enter the total number of minutes that you spent doing aerobic dance/step aerobics each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing badminton each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing basketball each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing bicycling (indoor,outdoor) each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent bowling each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing calisthenics/toning exercises each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent canoeing/rowing/kayaking each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent dancing (square, line, ballroom) each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing the elliptical trainer each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent fencing each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent fishing each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing football/soccer each day that you checked above.
_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing gardening or yardwork each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent golfing each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent hiking each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent horseback riding each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent hunting each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent jogging (outdoor,indoor) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent jumping rope each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing martial arts (Karate, Judo) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing pilates each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing raquetball, handball or squash each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent rock climbing each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent scuba diving each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent skating (roller, ice, blading) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent snow shoeing each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent snow skiing (downhill) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent snow skiing (cross country, Nordic Track) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing softball/baseball each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing the stairmaster each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing strength/weight training each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent swimming (laps, snorkeling) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you did Tai Chi each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing tennis each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing volleyball each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent walking for exercise (outdoor, indoor, treadmill) each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing water aerobics each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing yoga each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Enter the total number of minutes that you spent doing other activity each day that you checked above.

_____
(Example: (Monday - 30 minutes, Wednesday - 30 minutes))

Name: _____ Time Point: _____

Think about a usual week. In the table below, please indicate the total number of hours and minutes per day you spend doing each of the activities listed. There is space to answer for a typical work day and non-work day. Please try to remember as specifically as possible. Please do not record time twice in different categories: for example, if you were reading while watching TV, only report that time under one category.

	Work day	Non-work day
Sleeping/trying to sleep	___ hr ___min	___ hr ___min
Sitting while working	___ hr ___min	___ hr ___min
Sitting while using a computer (not at work) or video game	___ hr ___min	___ hr ___min
Sitting while watching TV or movies	___ hr ___min	___ hr ___min
Sitting during transportation (not including bicycles)	___ hr ___min	___ hr ___min
Sitting while talking, texting, or other socializing	___ hr ___min	___ hr ___min
Sitting while reading, sewing, or doing other activities/hobbiesDescribe: _____	___ hr ___min	___ hr ___min

Technology Survey

Do you use a smartphone on a daily basis (i.e.android, iphone, blackberry)?

- ☐ Yes
- ☐ No

Check all methods that you use to track your weekly data and/or food diaries.

- ☐ Desktop Computer
- ☐ Laptop Computer
- ☐ Tablet (i-pad, Kindle Fire, Nook, ect)
- ☐ Smartphone
- ☐ Pen and paper
- ☐ Other

If other, please type the method you use: _____

Check all websites/applications you use to help track your weekly data and/or food diaries.

- ☐ Lose it!
- ☐ My Fitness Pal
- ☐ Calorie King
- ☐ Fitday.com
- ☐ Myplate.com
- ☐ Sparkpeople.com
- ☐ Myfatsecret.com
- ☐ Other
- ☐ I do not use websites or applications.

If other, please type the website or application you use: _____

Phone Survey

Record ID _____

How important is it to you to reduce the amount of time you spend sitting?
- ☐ Not at all important
- ☐ Slightly important
- ☐ Moderately important
- ☐ Very important

Explain. _____

How much time and effort do you put into exercise compared to reducing sitting time?
- ☐ Much less
- ☐ Somewhat less
- ☐ Somewhat more
- ☐ Much more

Why? _____

How much time and effort do you put into your diet compared to reducing sitting time?
- ☐ Much less
- ☐ Somewhat less
- ☐ Somewhat more
- ☐ Much more

Why? _____

Compared to you, how concerned do you think other women your age are about the amount of time they spend sitting?
- ☐ Much less concerned
- ☐ Slightly less concerned
- ☐ Slightly more concerned
- ☐ Much more concerned

Explain. _____

How much time do you believe other women your age spend sitting compared to you?
- ☐ Much less
- ☐ Somewhat less
- ☐ Somewhat more
- ☐ Much more

Explain _____

On a scale from 1-10, with 1 being the least and 10 being the most, how confident are you that you can reduce your sitting time over the next two weeks? _____

Explain. _____

On a scale from 1-10, with 1 being the least and 10 being the most, how much control do you have over changing the amount of time you spend sitting? _____

Explain. _____

In which area of your life do you feel you have the most control over changing the amount of time you sit? (For example: at work, computer or video game, TV or movies, transportation, socializing- talking, texting, hobbies, other). _____

Explain. _____

In which area of your life do you feel you have the least control over changing the amount of time you sit? _____

Explain _____

What would make it easier for you to spend less time sitting?

_____

Explain.

_____

What would make it difficult or prevent you from reducing the amount of time you spend sitting?

_____

Explain.

_____

On a scale from 1-10, with 1 being the least and 10 being the most, to what extent do you intend to reduce your sitting time as recommended by the program in the next 2 weeks?

_____

Explain.

_____

How do you access your dashboard or app interface?

- ☐ Phone
- ☐ Computer
- ☐ Both

Explain.

_____

Which component of the dashboard or app interface do you pay most attention to?

_____

Of the following, which component of the dashboard or app interface do you pay most attention to?

- ☐ Weight
- ☐ Calories consumed
- ☐ Steps
- ☐ Very active minutes
- ☐ Activity graph

Explain.

_____

Which component of the dashboard or app interface do you pay next most attention to?

- ☐ Weight
- ☐ Calories consumed
- ☐ Steps
- ☐ Very active minutes
- ☐ Activity log

Explain.

_____

How often do you check your lightly active minutes?

- ☐ Never
- ☐ Once a week
- ☐ Several times a week
- ☐ Every day or more

Explain

_____

Do you feel the fitbit provides accurate feedback about your light activity?

- ☐ Yes
- ☐ No

Explain.

_____

How useful was the fitbit feedback in increasing your light activity?

- ☐ Not at all useful
- ☐ Slightly useful
- ☐ Moderately useful
- ☐ Very useful

Explain.

_____

How much did tracking your light activity affect your behavior?

- ☐ No affect
- ☐ Minor affect
- ☐ Moderate affect
- ☐ Major affect

Explain.

_____

What affect does tracking your TV time have on decreasing your TV time?

- ☐ No affect
- ☐ Minor affect
- ☐ Moderate affect
- ☐ Major affect

Explain. _____

How much easier has the Aria scale made it to track your weight?

- ☐ No difference
- ☐ Slightly more easy
- ☐ Moderately more easy
- ☐ Much more easy

Explain. _____

How easy is it to use the LoseIt account compared to paper tracking?

- ☐ Much less easy
- ☐ Somewhat less easy
- ☐ Somewhat more easy
- ☐ Much more easy

Explain. _____

How much time do you spend using the LoseIt app compared to paper tracking?

- ☐ Much less time
- ☐ Somewhat less time
- ☐ Somewhat more time
- ☐ Much more time

Explain. _____

What changes, if any, would you make to the technology provided? _____

What changes, if any, would you make to the feedback provided in the bi-weekly reports Danielle gives you? _____

APPENDIX III

INTERVENTION SESSION SCHEDULES

AND MAINTENANCE INTERVENTION MATERIALS

Weekly Schedule

Weight Loss Phase

Session	Week of:	Topic
1	6/17/13	Getting Started
2	6/24/13	Self-Monitoring and Goal Setting
3	7/1/13	Get Moving to Better Health
4	7/8/13	Getting the Social Support You Need
5	7/15/13	Physical Activity and Breast Cancer
6	7/22/13	Fruits and Veggies: More Matters
7	7/29/13	Food Labels
8	8/5/13	Taking Charge of What's Around You
9	8/12/13	Nutrition and Breast Cancer
10	8/19/13	Eating More for Less
11	8/26/13	How Do You See Yourself?
12	9/2/13	Pick up the Pace
13	9/9/13	Smart Shopping & Portion Control
14	9/16/13	Managing Stress
15	9/23/13	Eating on the Go
16	9/30/13	My Plan for Maintenance

Phone Group –Four Month Program

Phone Meeting Day/Time

All meetings are held by conference call on your assigned evening from 5:30 p.m. to 6:30 p.m. Please call 5-10 minutes early.
After the first meeting (60-75 minutes), sessions will last about 60 minutes.

Accountability

You will send in food and exercise reports in the middle and at the end of each week.

- Reports for _____ through _____ are due on _____ by 10 a.m.
- Reports for _____ through _____ are due on _____ by 10 a.m.

Counselor Contact Information

Send Reports To: Danielle Christifano
Phone: (913) 945-7890
Email: **dchristifano@kumc.edu**

Every meeting will begin with an opportunity to review diet and exercise behaviors, and to discuss challenges and successes since the last session. Your counselor will then lead the group in a discussion covering the main lesson for the week. You are always encouraged to participate, to ask questions, and to provide support to your group members.

Joining Your Group Meeting

You will be able to call in from any phone.

1. Call this number: **1-800-977-8002**
   Because this is an 800 number, you will not have to pay any long distance charges.

2. After you hear the ring, you will hear a recording. When the recording asks for a PIN number, enter 2154448#. Do not share this number with anyone outside of the group.

3. After entering your PIN number, you will hear a beep. When you hear this beep, you know you have joined the call. Your counselor will hear the beep as well, and will welcome you to the group.

*If you join before your counselor, you will be put on hold until she dials in.
*DO NOT call in while driving.

Weekly Schedule

Weight Maintenance Phase

Session	Date	Objective	Topic
1 In Person	10/8/13	Nutrition News	My Plate and Meal Planning
2	10/22/13	Life Lessons	Power of Problem Solving
3	11/5/13	Fitness Flash	Interpreting Accelerometer Data
4 In Person	11/19/13	Nutrition News	Holiday Planning
5	12/3/13	Planning and Prevention	Acceptance and Commitment (Guest Speaker)
6 In Person	12/17/13	Life Lessons	Making Peace with the Scale
7	12/30/13 (Monday)	Fitness Flash	Commit to Staying Active
8 In Person	1/14/14	Life Lessons	Mindful Eating (Guest Speaker)
9	1/28/14	Planning and Prevention	Eating Out and Regain
10 In Person	2/11/14	Fitness Flash	Fitness and Your Health (Guest Speaker)
11	2/25/14	Nutrition News	Decisions, Decisions
12 In Person	3/11/14	Nutrition News	Keeping Nutrition Information in Perspective (Guest Speaker)
13	3/25/14	Planning and Prevention	Planning for the Future
10 month testing sessions will be Tuesday, April 1st – Friday, April 4th			

Weekly Schedule

Weight Maintenance Phase

Session	Date	Objective	Maintenance Topic
1 In Person	10/10/13	Introduction	Intro to Standing for Better Health
2	10/24/13	Nutrition News	Lightly Active Time & Meal Planning
3	11/7/13	Fitness Flash	TV Time & Accelerometer Data
4 In Person	11/21/13	Nutrition News	Uninterrupted Sitting & Holiday Planning
5	12/5/13	Life Lessons	Power of Problem Solving
6 In Person	12/19/13	Planning and Prevention	Acceptance and Commitment (Guest Speaker)
7	1/2/14	Life Lessons	Making Peace with the Scale
8 In Person	1/16/14	Life Lessons	Mindful Eating (Guest Speaker)
9	1/30/14	Planning and Prevention	Eating Out and Regain
10 In Person	2/13/14	Fitness Flash	Commit to Being Fit (Guest Speaker)
11	2/27/14	Nutrition News	Decisions, Decisions
12 In Person	3/13/14	Nutrition News	Keeping Nutrition Information in Perspective (Guest Speaker)
13	3/27/14	Planning and Prevention	Planning for the Future
10 month testing sessions will be Tuesday, April 1st – Friday, April 4th			

Phase 2: Stand UP!

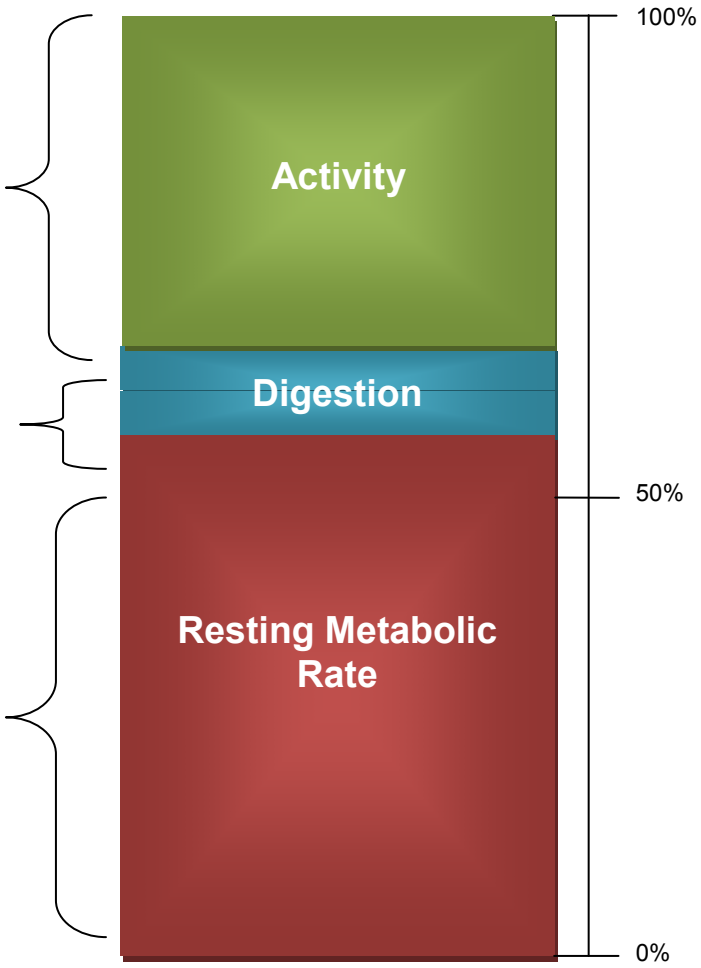
What is sedentary behavior?

Sedentary behavior is simply the time you spend sitting or reclining throughout your day. These activities require little or no energy to do (remember, energy = calories). We have talked a lot about calories in foods during phase 1, but we will now focus on calories in a new way. Below is a graph that shows you how your body uses calories on a daily basis.

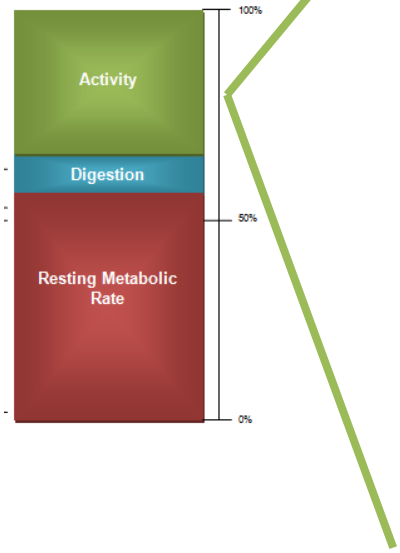
This is the energy you use for all of your daily activity– this includes your planned physical activity and light, lifestyle activity like sitting while talking or watching television. **You have the most control over this portion of your daily energy!**

This is the energy you use for digestion.

Your Resting Metabolic Rate (RMR) is the energy your body needs when it is at rest. An estimate of RMR can be calculated based on your age, sex, weight and height. This is what we use to calculate the base for your maintenance calorie goals.



Most Americans spend the majority of their "activity" section doing only things that involve sitting. Let's take a closer look at calories burned during activities of daily life.



Home & Daily Life Activities	Calories burned per 30 min	
	155 lb person	185 lb person
Sleeping	23	28
Watching TV	28	33
Reading: sitting	42	50
Standing in line	47	56
Computer Work	51	61
Light Office Work	56	67
Sitting in Meetings	60	72
Desk Work	65	78
Cooking	93	111
Food Shopping: with cart	130	155
Moving: unpacking	130	155
Playing w/kids: moderate effort	149	178
Heavy Cleaning: wash car, windows	167	200
Leisurely walking	130	155
Brisk walking	149	178
Swimming	223	266
Jogging (5 mph – 12 min/mile)	298	355

During this phase of the program you will try to maintain physical activity at 225 minutes per week, while replacing sitting time with light activity.

Why?

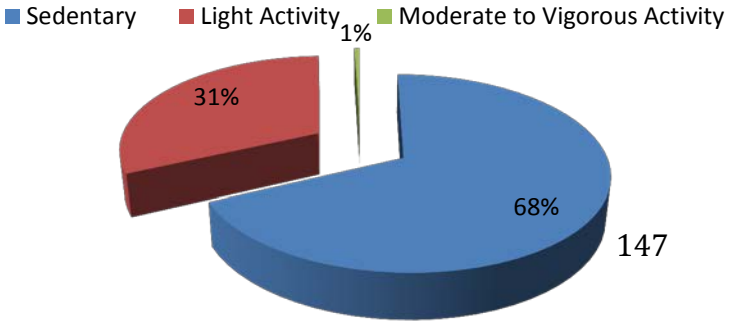
Replacing sitting time with other light activities will help you burn extra calories throughout your day. It can also help to improve circulation, prevent swollen ankles or feet and help relieve aches and pains.

What else?
Reducing sitting time has been shown to reduce the risk of heart disease, diabetes, cancer, and death.

Did you know??

The average American spends over 50% of their waking hours sitting and the average breast cancer survivor and older adult spends approximately 68% of their waking hours sitting.

Breast Cancer Survivors in the US



What are some common activities that involve sitting for a long period of time?

_____ _____

_____ _____

_____ _____

How often do you sit?

1. Are you sitting more now than you did when you were a child?
2. Are you sitting more now than you did before your breast cancer diagnosis?
3. Are you sitting more than your parents did at your same age?

Now think about yesterday – List your daily activities on the schedule below:

6:00 am		3:00 pm	
7:00 am		4:00 pm	
8:00 am		5:00 pm	
9:00 am		6:00 pm	
10:00 am		7:00 pm	
11:00 am		8:00 pm	
12:00 pm		9:00 pm	
1:00 pm		10:00 pm	
2:00 pm		11:00 pm	

Place a star next to all of the activities that involve sitting

STRATEGIES TO REDUCE SEDENATARY BEHAVIOR

The following goals will help you to be more active throughout the entire day, not just during your planned exercise minutes. We will discuss each of these three goals in more detail throughout the next three sessions.

1. Increase light activity time
2. Decrease TV time
3. Limit uninterrupted bouts of sitting to less than 30 minutes

What is new?

During the next 6 months, we will focus on weight loss maintenance and decreasing sitting time. Much of what you have done in the first 4 months will remain the same, however there will be a few new and exciting elements to add! Your Fitbit Zip is designed to help you to monitor your sitting time. New technology will be introduced during this phase because it will help you to be more aware and becoming more aware will help you to change your habits!

Your group leader will help you set up your accounts and provide you with a password.

Fitbit Zip

Your Fitbit Zip will be your new pedometer for phase 2. You will also use your Fitbit account online to determine when you spend the most time sitting each day of the week. We will review how to do this during the meeting.

Aria Smart Scale

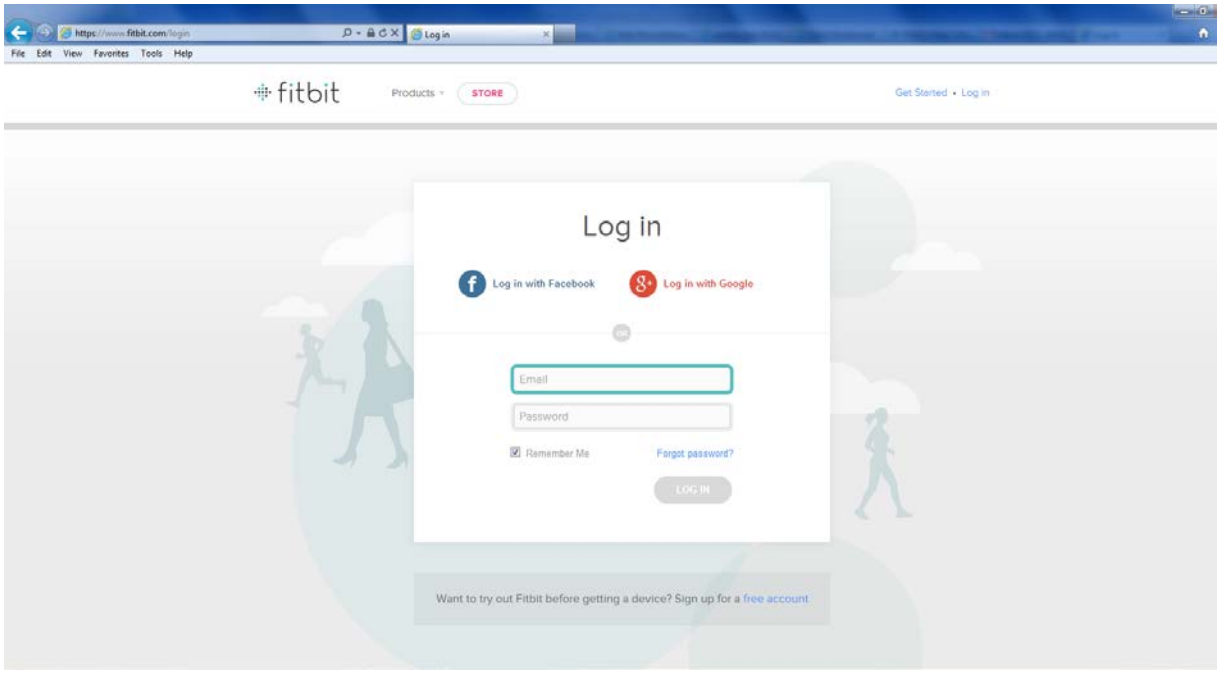
Your Aria Smart Scale will be the scale you weigh on during phase 2. The scale will sync wirelessly with your Fitbit account.

Lose It! Account

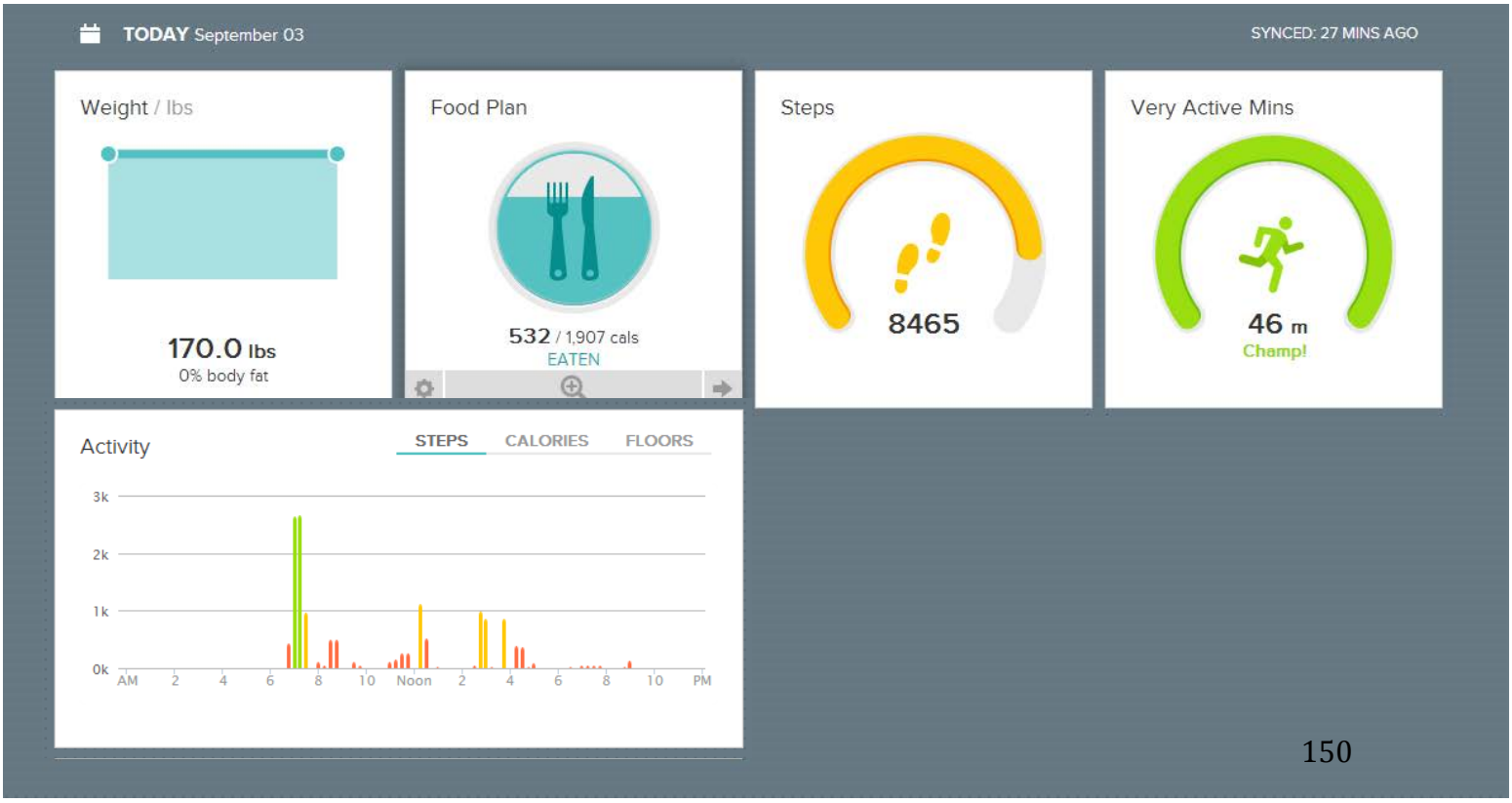
Lose It!

Instead of keeping monthly food diaries on paper, you will now log your food through your Lose It account. Your daily calories will also sync with your Fitbit account – this means your weight, daily calorie intake, steps, and physical activity will all be visible in one place!

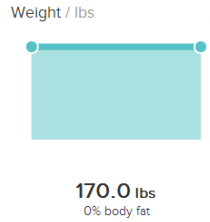
HOW TO LOG IN: You will sign into www.fitbit.com/login and enter the login information given to you by your group leader.



WHAT YOU WILL SEE: When you log in to your Fitbit account you will see your dashboard. Your dashboard has been set up specifically for you. Below is an example.



WEIGHT:

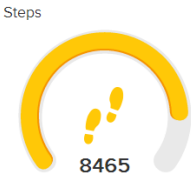


Here you will see the weight from your Aria Smart Scale. This weight will wirelessly sync with your account – all you need to do is step on the scale!

FOOD PLAN:

Here you will see how many calories you have consumed, compared to how many calories you should eat to meet your weight goal. This will sync automatically from your lose it account.

STEPS:



Here you will see your daily step total.

VERY ACTIVE MINUTES:

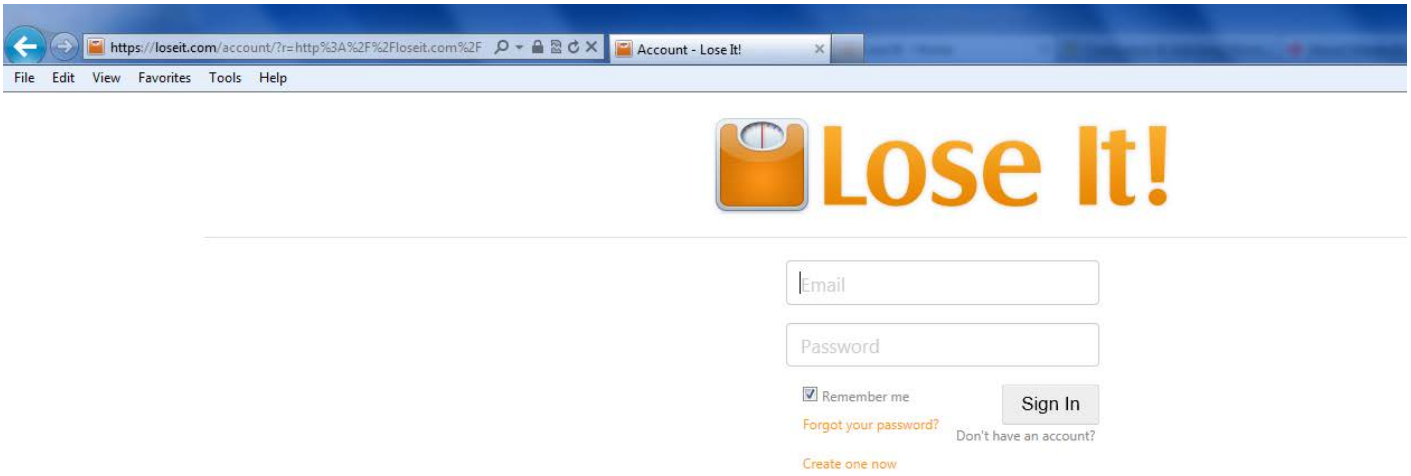
Here you will see your daily moderate-vigorous intensity physical activity minutes.

ACTIVITY:

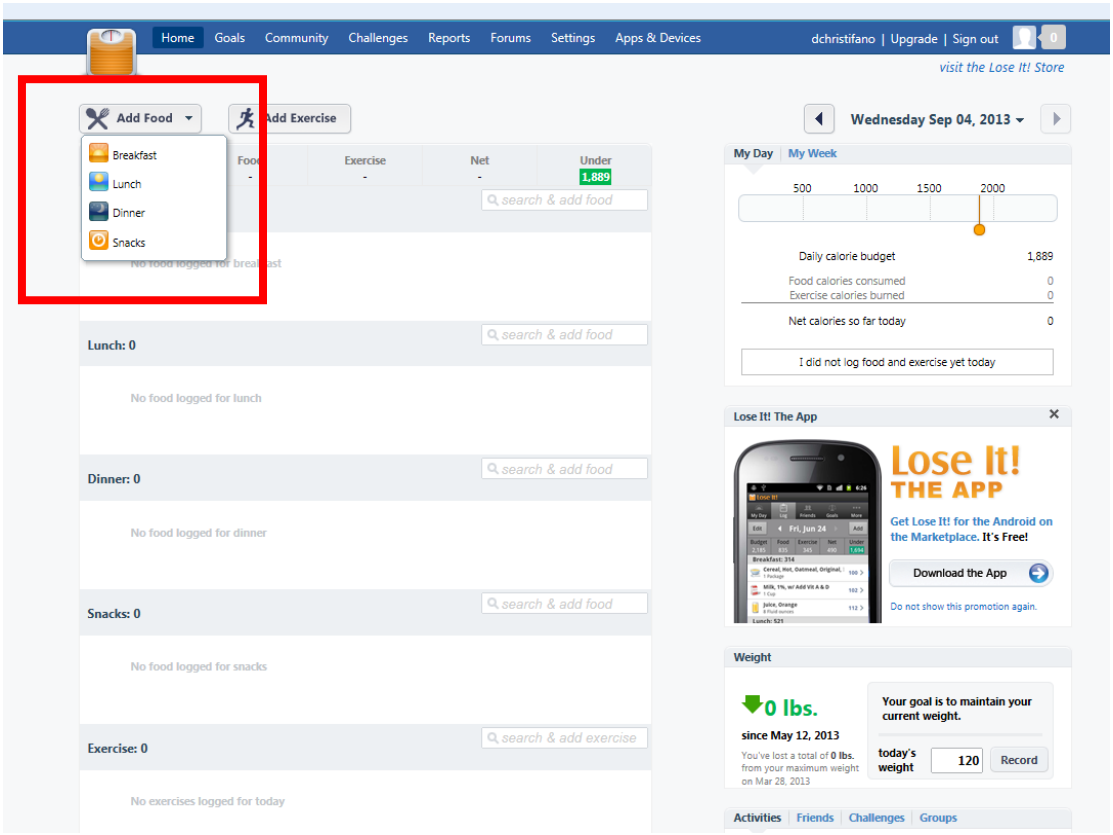
You will also see a graph that charts your step activity throughout the day. This is the chart you will use to determine what times throughout the day you are sitting the most.

HOW TO USE LOSE IT!

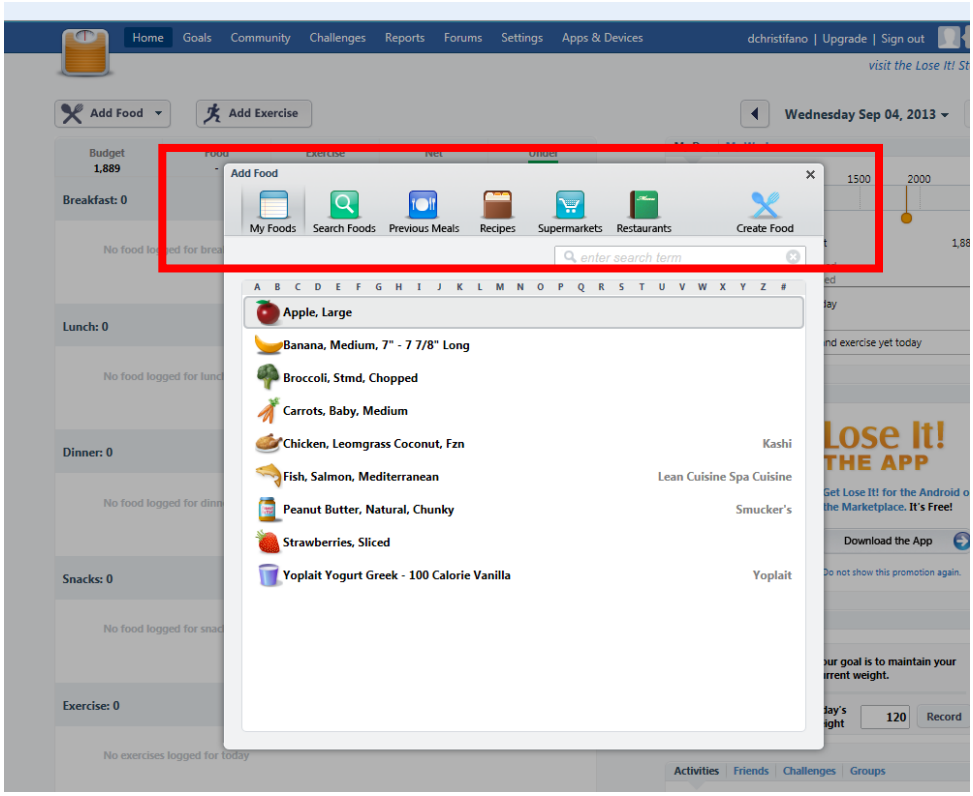
STEP ONE: Go to **https://wsbh.loseit.com/**. You will enter your email and the password assigned to you by your group leader.



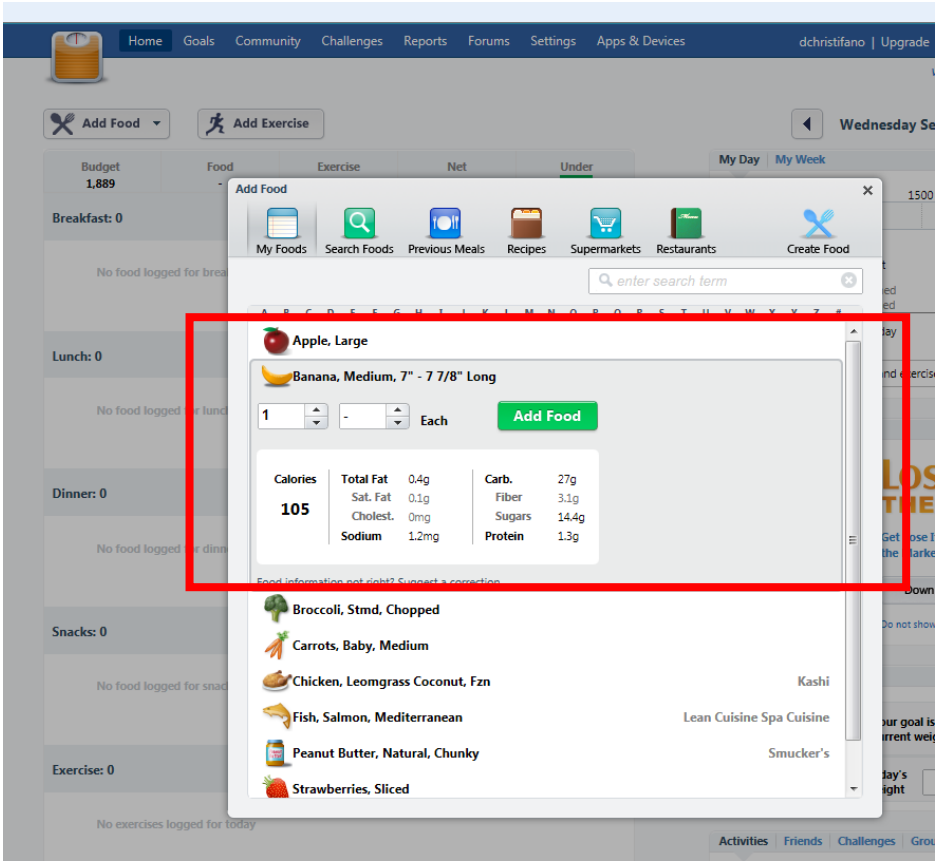
STEP TWO: You will see your home screen immediately after you log in. You will click on "Add Food" in the upper left hand corner and click the meal you plan to enter.



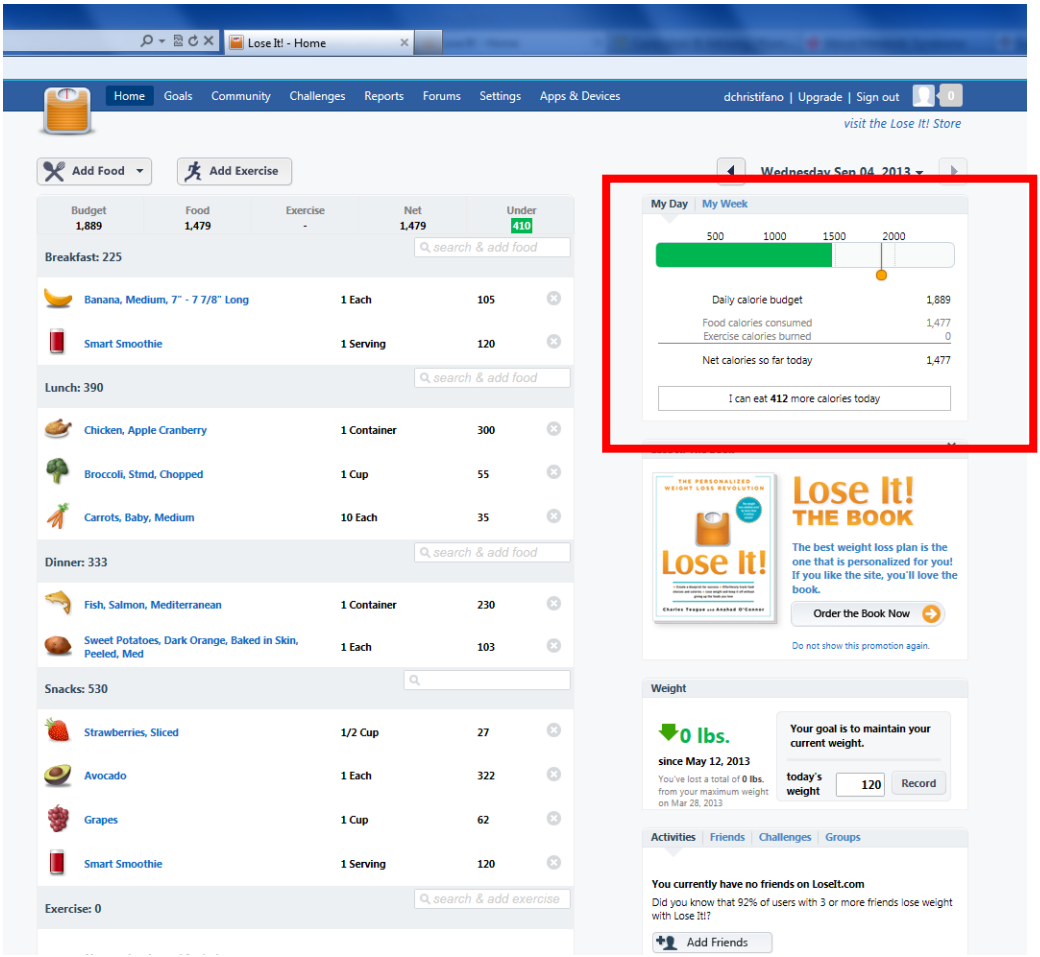
STEP THREE: Choose from the following options: add an item from your food list, search for a new food, add or create a recipe, search for a supermarket food, or search for a restaurant food.



STEP FOUR: Enter the serving size of the food.



STEP FIVE: Repeat steps 2-4 until you have added all of your daily intake. The green bar will show you your total calorie intake for the day.



LET'S PRACTICE!

Your food tracking information will only be visible to you and your group leader. Your daily intake will sync automatically with your Fitbit account.

What should I do to succeed at maintenance?

1. **Attend Meetings:** Successful weight managers attend sessions. Motivation can easily slide when you do not attend the phone sessions or in-person meetings.
2. **Be Physically Active:** Exercise is essential for long-term weight management.
3. **Monitor Your Food, Exercise, Sitting Time:** Self-monitoring makes you aware of your eating and exercise habits, allows you to evaluate areas of success and failure, and keeps you accountable.
4. **Control Your Portions:** Oversized portions are everywhere, from restaurants to supermarkets to vending machines. One of the keys to maintaining a healthy weight is to control portion sizes.
5. **Eat Fruits and Vegetables:** Fruits and vegetables are low in calories, help to fill you up fast, and are full of nutrients. They work to crowd out other higher calorie foods in your diet.
6. **Change Your Environment:** You will need to continue to change things in your life in order to make your new behaviors lifelong habits.

What are the diet, exercise and sitting time recommendations?

Each day we recommend the following:

- At least two of your meals are pre-packaged meals (shakes and/or entrees)
- At least 5 one-cup servings of fruits and veggies
- Snacks should consist of only fruits and veggies.
- Condiments less than 15 calories per tablespoon

Note about Calcium – Remember that the Institute of Medicine recommends that women age 51 and older get 1200 mg of calcium per day. If you choose to incorporate low-fat dairy products into your diet, you may be able to reduce your calcium supplementation to 500-600 mg per day.

Self-Monitoring: You will continue to send in your weekly data form once per week. You will keep a food diary via your Lose It account every day.

Exercise: The exercise goal is still 225 minutes of aerobic activity each week or more.

Sitting Time: We will focus on a new goal to reduce sitting time for the next three sessions.

Increase Light Activity Time

Now that you have had a chance to use your new devices, we will focus on how you will use your Fitbit to set goals to reduce your sitting time. The next three sessions will each focus on a new goal. Today we will focus on the first goal – increase light activity time!

1. Increase light activity time
2. Reduce TV time
3. Limit uninterrupted bouts of sitting to less than 30 minutes

Goal One: Increase light activity by an average of 30 minutes per day after the first two weeks. If you meet your goal for a two week period, you will increase your average lightly active minutes by an average of 15 minutes per day for the next two weeks. If you do not meet your goal, you can keep the same goal for the next two weeks. Your group leader will help you determine your goals each two week period.

Why bother??

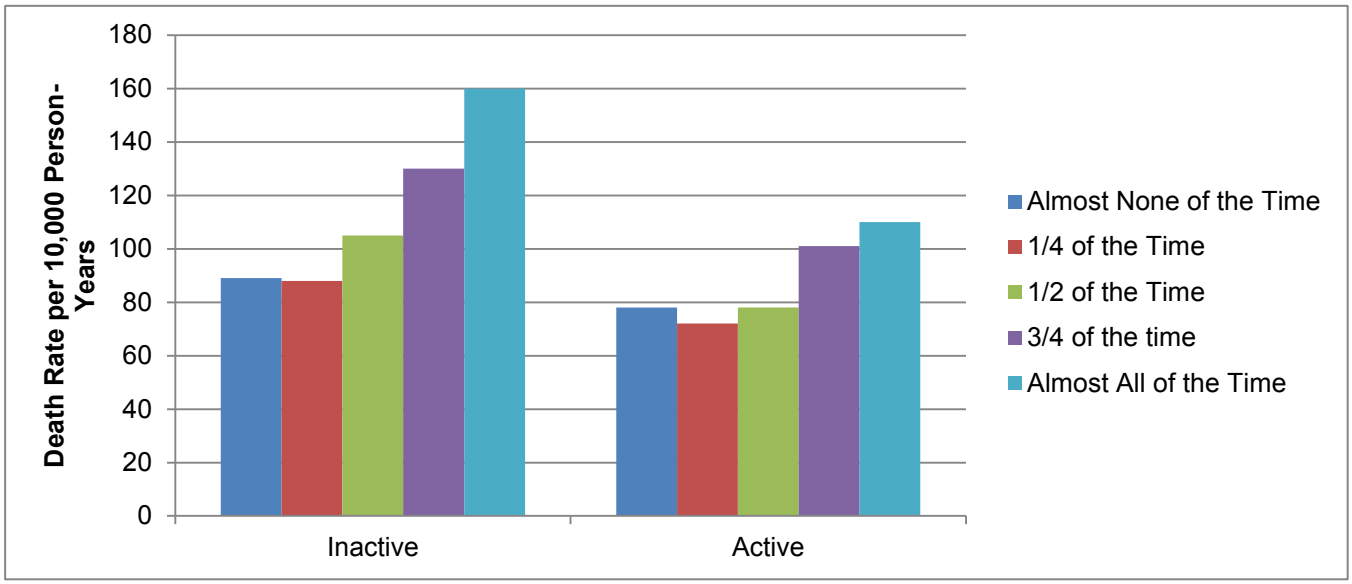
The act of standing up requires your large muscles to engage, specifically your quadriceps and core muscles. Muscle engagement requires calories, so the more standing you do, the more calories you burn. On the flip side, sitting for too long causes your muscles to enter a sort of hibernation mode. Your muscles stop using calories and stop producing key enzymes used to regulate metabolism. Bottom line is sitting too long and too often can be detrimental to your health.

In fact, recent research from dozens of studies suggests the more time you spend sitting, the higher your risk for:

- Obesity
- Type 2 diabetes
- Heart disease
- Metabolic syndrome
- Cancer
- Mortality

Interestingly, these relationships hold true even for those people who exercise on a regular basis. Through our own research among breast cancer survivors, we found women tend to increase their physical activity minutes while simultaneously increasing their sitting time. Have you ever finished a work out and thought, “Great! I completed my exercise for the day – now it’s time to sit down and relax” ?? This is not the case! Standing up and moving around throughout the day may be just as important as exercise.

Look at the graph below. The “Inactive” bars are those people who exercise less than 150 minutes per week and the “Active” bars are those people who exercise at least 150 minutes per week. The vertical axis represents death rates. Each color indicates varying levels of sitting time. You will notice the rate of death increases as sedentary time increases for both people meeting exercise recommendations of 150 minutes per week and people who are not.



Katzmarzyk PT, Church TS, Craig CL, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. Medicine and science in sports and exercise 2009;41(5):998-1005. doi: 10.1249/MSS.0b013e3181930355.

Self Monitor

Every two weeks you will get a report from your group leader stating your activity averages over the past two weeks – including your minutes sedentary and your minutes lightly active. On your activity report, you will also see a graph of your activity averages over the past 4 weeks. This will help you to gauge your own progress. Lastly, you will see your goal for lightly active minutes for the next two weeks.

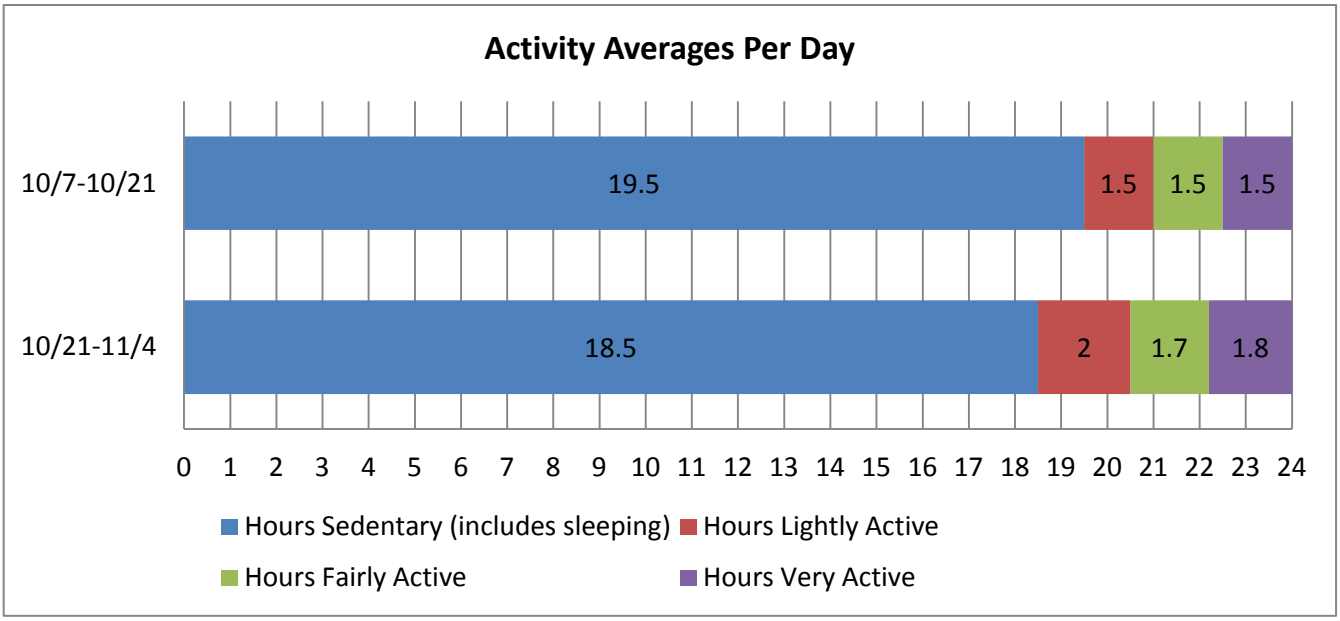
On your activity worksheet you will see a summary of your minutes sedentary (including sleeping), minutes lightly active, minutes fairly active and minutes very active. Let’s review what counts toward each activity level. Keep in mind this will vary slightly based on the individual.

Activity Level	Examples
Sedentary	Sitting, reclining, laying down, sleeping
Lightly Active	Walking at a leisurely pace (e.g. light house work: dusting, sweeping, dishes, cooking)
Fairly Active	Walking at a quicker pace (e.g. mowing the lawn, moderate house work: mopping, vacuuming, scrubbing floors)
Very Active	Any activity that causes you to break a sweat (e.g. brisk walking, jogging, running)

Activity Report

EXAMPLE

Date	Day	Weight	Steps	Minutes Sedentary (includes sleeping)	Minutes Lightly Active	Minutes Fairly Active	Minutes Very Active
10/7/2013	Mon	180.00	12,890	1,202	68	35	135
10/8/2013	Tues	180.20	10,108	1,312	78	10	40
10/9/2013	Wed	180.10	2,919	1,100	162	30	148
10/10/2013	Thurs	179.80	4,155	1,235	80	85	40
10/11/2013	Fri	179.90	6,836	1,255	97	48	40
10/12/2013	Sat	179.50	10,304	989	225	185	41
10/13/2013	Sun	179.80	14,903	1,002	70	152	216
10/14/2013	Mon	180.00	12890	1,080	200	80	80
10/15/2013	Tues	180.20	10,108	1,100	120	180	40
10/16/2013	Wed	180.10	2,919	1,240	65	95	40
10/17/2013	Thurs	179.80	4,155	956	180	125	179
10/18/2013	Fri	179.90	6,836	1,069	150	200	21
10/19/2013	Sat	179.50	10,304	989	102	115	234
10/20/2013	Sun	179.80	14,903	1,020	60	80	280
Average			**8,874**	**1,111**	**118**	**101**	**110**
				18.5 hrs	**2.0 hrs**	**1.7 hrs**	**1.8 hrs**



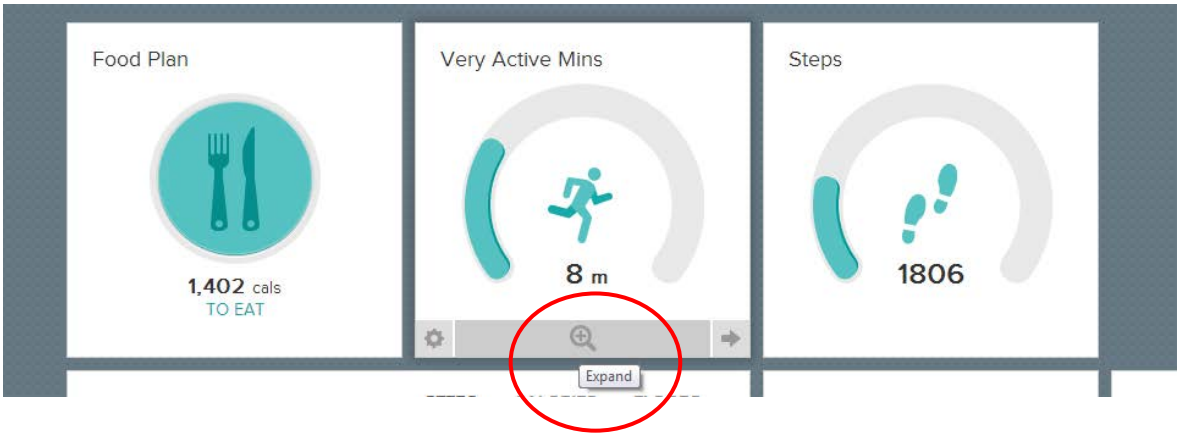
Example Goal for 11/4 – 11/18

Average <u>2 hours 30 minutes</u> (150 minutes) of lightly active minutes per day

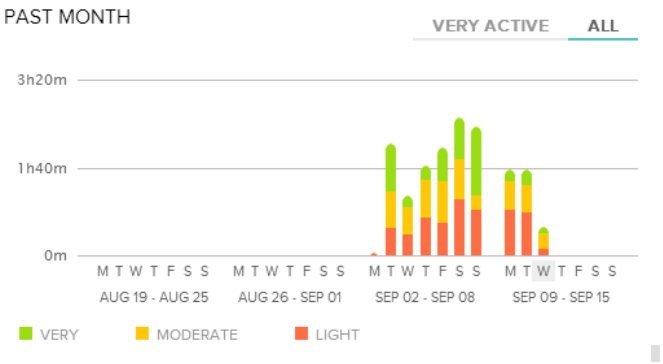
Monitoring your Daily Lightly Active Time:

Step One: Log in to your Fitbit account.

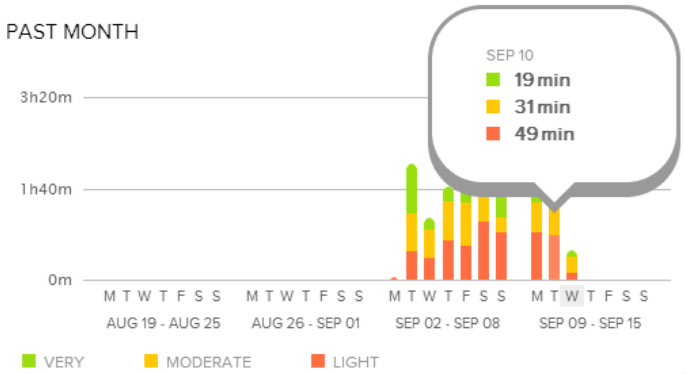
Step Two: Click on the "Expand" magnifying glass on the "Very Active Minutes" Tile of your dashboard.



Step Three: Your activity over the past month will appear. Click on the "All" option on the upper right.



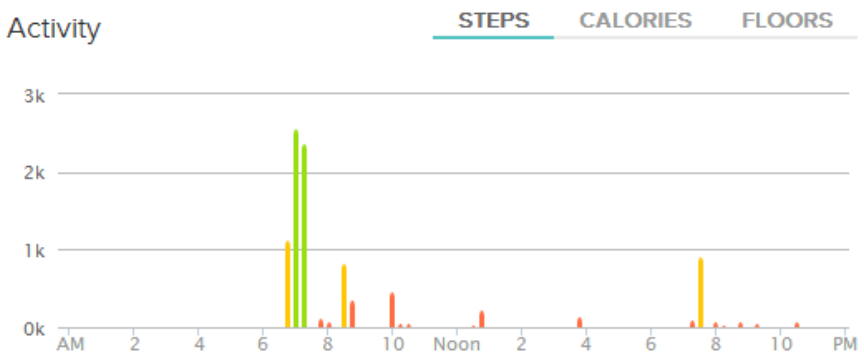
Step Four: Hover your mouse over the day that you will like to see. And write down the minutes in red – these are your lightly active minutes.



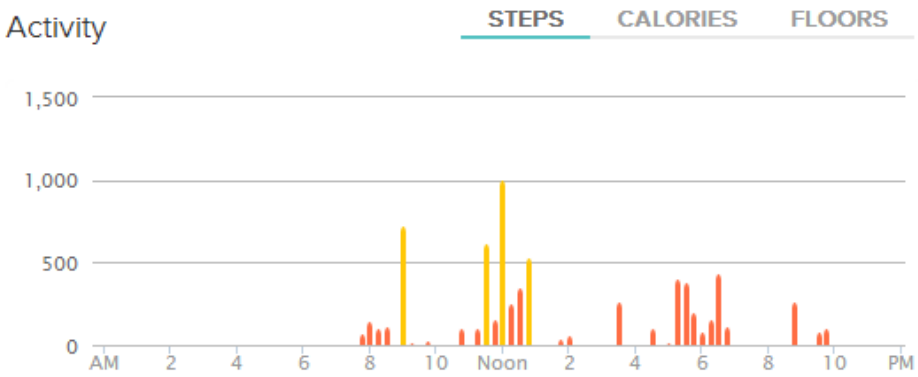
When do you Sit?

Take a look at your "Activity" tile on your Fitbit dashboard. Below you will see an example of Sally's Activity Tiles from a work day and non-work day. Notice how her work day included exercise in the morning, but the remainder of her day was spent sitting. On her non-work day, Sally was much more active throughout the day with fewer bouts of sitting.

Example Work Day



Example Non-Work Day



When are you sitting the most on work and non-work days?

Work Days	Non-Work Days

How do you unwind?

In Phase 1 we discussed the role stress plays in your weight management journey and how it is important to find positive ways to cope and reduce stress levels. Taking time to unwind is one such technique that is very important for stress management. Often times people associate their relaxation or enjoyment time with sitting time. **First think of a few of your major stressors and ask yourself, could I do a standing activity to help reduce this stress?** If not, that's okay! We do not want you to cut your relaxation time you cherish the most, but the goal is to determine which activities are worth it and which could be spent in other ways. **List a few of the activities you look forward to most in your day that help you unwind. Then list the average time you spend doing each activity, and ask yourself is it worth it?**

Activity	Average time spent	Is it worth it?

Strategies to Increase Light Activity

Let's review a few strategies to help you meet your light activity goals! Below are a few examples and space for you to add your own ideas.

1. **Replace sitting activities with light activities.**

- Fold laundry while standing
- Stand up while reading rather than sitting down
- Shop at stores rather than shopping online
- Stand up and walk around when talking on the phone at home or when socializing at social gatherings
- Stand up while doing arts and crafts such as sewing or quilting
- Stand up while doing crossword puzzles or other games
- Take a shower instead of a bath
- _____
- _____
- _____

2. **Add new hobbies and chores to your daily routine that are more active**
    - Walk with friends or a pet
    - Walk to the park with your kids or grandkids
    - Play with pets – either your own, others' pets, or at a pet store
    - Ride your bike for short trips to the grocery store
    - Dance
    - Work in the garden
    - Complete home improvement projects you've been wanting to do
    - Rake leaves or shovel snow
    - Cook or bake healthy recipes
    - Deliver notes or meals to neighbors by walking to their homes
    - Volunteer at a local charity
    - _____
    - _____
    - _____

3. **Add more standing into your work day routine**
    - Hold walking or standing meetings
    - Move your computer to a higher surface so you can stand and type
    - Stand when you are on the phone
    - Drink more water so you have to walk to the restroom more often
    - Drink from a smaller glass so you have to refill it more often
    - Instead of sending an email or calling your co-workers, walk to their office
    - _____
    - _____
    - _____

4. **General suggestions to increase light activity**
    - When you have to recycle an item, walk to your garage to throw the item away
    - Walk outside to retrieve the mail instead of driving
    - Drive less and participate in more carpools
    - Go for more walks – for both transportation and recreation purposes
    - Take the stairs instead of the elevator
    - Park further away from your destination
    - Walk to any of your errands that are only a short distance away (e.g. grocery store, pharmacy, bank)
    - _____
    - _____
    - _____

Reduce TV Time

1. Increase light activity time
2. Reduce TV time
3. Limit uninterrupted bouts of sitting to less than 30 minutes

Goal TWO: Reduce TV time to less than 90 minutes per day and replace TV time with light activity.

Using a TV log will be helpful in counting your TV time. You can leave a copy of this log next to your couch or TV for the next week. Every time you sit down to watch to TV, you should write the start time and the stop time. You should also rate your enjoyment from 1-10 (1 = no enjoyment and 10 = maximum enjoyment). Each week, you will fill in your daily TV time goal and track your actual TV time on your weekly data form. There are more copies of this log in the back of your binder.

Day	Programs Watched	Were you Sitting?	Start Time	Stop Time	Total TV Time	Rate Enjoyment (1-10)
Example	Good Morning America Jeopardy	No Yes	6:30am 5:00 pm	7:15am 6:00 pm	45 minutes 60 minutes	4 8
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						
Saturday						
Sunday						

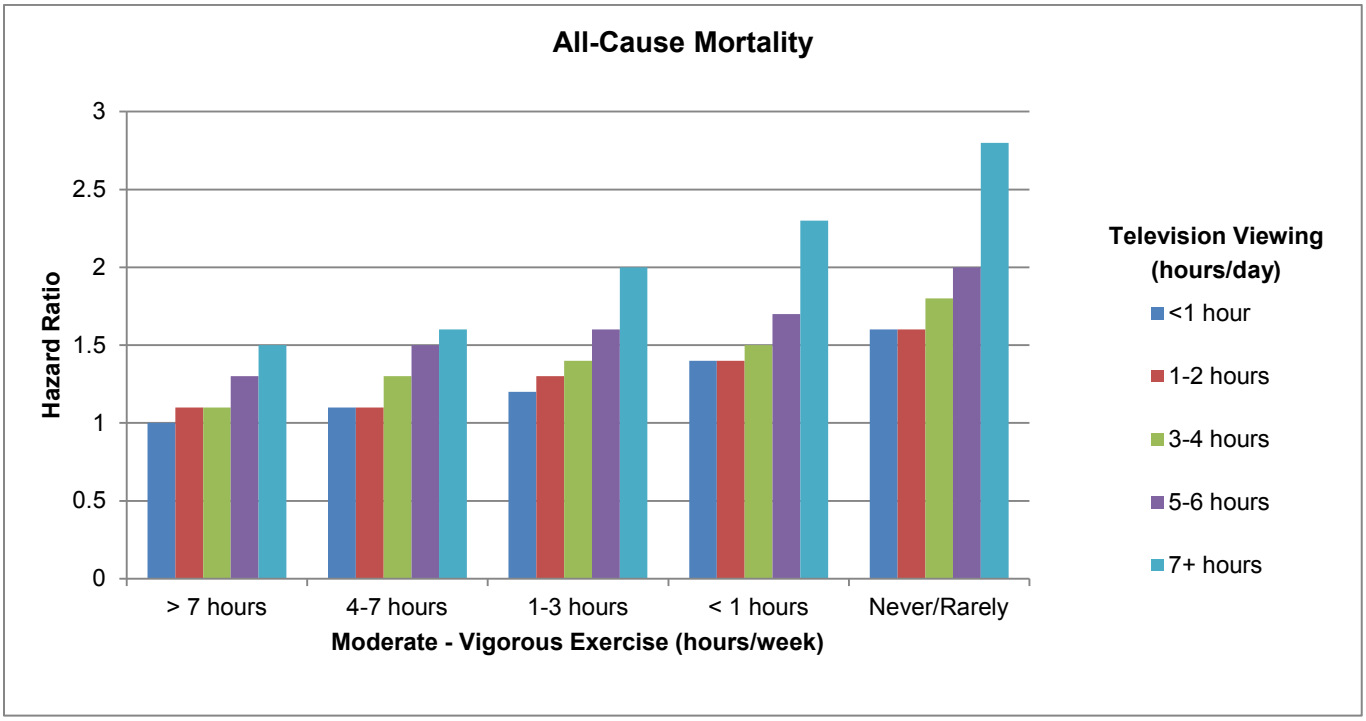
Trouble With TV

Did you know that the average American spends over 2 hours per day watching television? In fact, after work and sleep, TV time is the most commonly reported activity among Americans. There is substantial evidence that all of this TV time is not helping America's waist line. Several reasons for the link between TV time and obesity are listed below:

- TV time encourages more sitting and results in less calories burned throughout the day.
- TV time promotes more unhealthy snacking and mindless eating.
- TV time leaves less time for exercise and light activities.

Let's take a look at the research…

In a study reporting TV time and mortality rates among over 200,000 Americans, the people who reported the most television viewing (more than 7 hours per day) were at the greater risk for heart disease, cancer and death when compared to those people who watched less than one hour per day of television. The graph below shows the relative risk of dying based on hours of TV watched per day. Watching more television was associated with greater likelihood of death for all groups, including those who exercise a lot and those who do not exercise.



Matthews CE, George SM, Moore SC, et al. Amount of time spent in sedentary behaviors and cause-specific mortality in US adults. The American journal of clinical nutrition 2012;95(2):437-45. doi: 10.3945/ajcn.111.019620.

TV Watching Habits

What kind of TV watcher are you?

A. Channel Surfer
B. Weekends only
C. Morning news
D. Background
E. DVR only
F. Other

Where do you watch the most TV?

A. In the family room/living room
B. In the bedroom/in bed
C. In the kitchen
D. Other

What is your favorite show? _____

Do you crave certain foods when you watch TV? _____

Strategies to Reduce TV Time

- Be more selective about what to watch
- Rather than channel surfing, turn the TV on only for specific programs
- Make some days of the week TV-free days
- Cancel your cable subscription, or reduce the number of channels you receive
- Stop watching TV at dinner and other meal times
- Have only one TV in the house, or have only one designated room in the house for television watching even if there are other TVs around
- If you can, record the show and fast-forward through commercials
- Keep a timer near your TV and turn the television off when the timer goes off
- Keep a log near the television and document how much time is spent watching television
- _____
- _____
- _____
- _____

Reduce Uninterrupted Sitting Time

1. Increase light activity time
2. Reduce TV time
3. Limit uninterrupted bouts of sitting to less than 30 minutes

Now that you have had practice reducing your overall sitting time, we will focus on identifying the time periods each day when you sit the longest without getting up at all. You will only be asked to monitor your uninterrupted sitting time a few times throughout phase two.

Goal 2: Stand up and move after 30 minutes of uninterrupted sitting.

You will use your activity summaries from your Fitbit dashboard to determine when you do the most uninterrupted sitting. You should sign into your Fitbit account at the end of each day this week and view the "Activity" tile on your dashboard. You will identify all of the "blank" periods of time (the periods of time with no bars) throughout your day lasting longer than 30 minutes. Think about what activities you were doing during each 30 minute period of uninterrupted sitting.

For example, in the graph below, this person was sitting from 10am -11am, 1pm – 2:30pm, 5pm-6:30pm, and from 8pm-9pm.

Why bother??

Think about your day. Chances are it probably includes several, if not all of the items listed to the right. Our days revolve around sitting. In fact, most Americans spend over half of their waking hours sitting. (I bet you are sitting as we review this session!)

Breaking up your sitting time with short bouts of standing has been shown to improve the body's ability to regulate blood sugar and insulin levels. Controlled studies have examined the effects of breaking up prolonged sitting time every 20 minutes with leisurely or brisk walking over a 4 hour period. The groups that got up every 20 minutes after a meal had lower glucose and insulin levels than the group that sat the entire time. This is very important for breast cancer survivors given the association between insulin and recurrence.

Taking a "standing break" can also help to improve blood circulation, prevent swollen ankles and feet, and assist in the management of muscle aches and pain.

Take a look at your "Activity" tile on your Fitbit Dashboard. When are you sitting uninterrupted the most?

_____

_____

_____

_____

What do you need to focus on during long uninterrupted bouts of sitting?

_____

_____

_____

_____

How can you interrupt your sitting time while still being able to sustain needed attention? How can you set up your own reminder system?

_____

_____

_____

_____

Strategies to Reduce Long Sitting Bouts

Common activities	Strategies
Watching TV	• Stand up and do something different during advertisements • Put the remote control by the TV • _____
Reading	• Get up and walk between chapters • Organize a desk drawer or closet or (un)pack a box in between chapters • Stand while reading for every other chapter • _____
Computer Use (at home)	• Listen to music and stand up after each song • Stand up after each e-mail you send • Stand up and walk around after each game you play • _____
Computer Use (at work)	• Set an alarm on your computer to remind you to stand every 30 minutes • Use an app like Fitbolt.com or Workrave.com to remind you to get up and move. • _____
Socializing	• Offer to get other family members food/refreshments • _____ • _____
Hobbies	• Listen to music and stand up after each song • _____ • _____
Driving	• Start a car pool for your children so you can spend less time driving. • Rearrange driving schedule to drive less • _____
	• _____ • _____
	• _____ • _____

Sitting Bouts Log

Day	Time Frame	Sitting Activity	Strategy to Change
Example	10am-11am 1pm-2:30pm 5pm-6pm 8pm-9:30pm	Working at computer Eating lunch/socializing Eating dinner/family time Watching TV	Set alarm for 30 minutes After eating, stand up to socialize After eating, suggest a family walk Stand up during commercial breaks
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

NAME:

Weekly Reports

Dates:	My Goal	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Fruits	/day							
Veggies	/day							
Shakes	/day							
Entrées	/day							
Meals Out								
Unplanned Snacks								
Exercise Min	_____min _____ times per week							
Lightly Active Min	Weekdays:							
	Weekends:							
TV Time Min	Weekdays:							
	Weekends:							

Did you meet your diet goal?	**Yes / No**
Did you meet your exercise minutes goal?	**Yes / No**
Did you meet your lightly active minutes goal?	**Yes / No**
Did you meet your TV time minutes goal?	**Yes / No**

What barriers did you encounter while trying to meet you goals?

Were your goals too high?

What will you change for next week?

Have you had any changes to your health or medications?