Lifestyle Interventions For Endometrial Cancer Survivors: Feasibility and Efficacy of a Novel Mindfulness and Dietary Counseling Program

Dissertation

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By

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Abstract

Introduction: Endometrial cancer (EnCa) is currently the most common form of gynecological cancer affecting women in the United States. In 2014 there was an estimated 56,230 new cases and 8,590 deaths as a result of the disease. Type I endometrioid cancers, the most common form, are primarily driven by hyperestrogenism linked to excess adiposity and obesity. Despite the prognosis for this form of the disease being good, EnCa survivors are at higher than normal risk of developing chronic diseases associated with lifestyle such as type II diabetes mellitus and cardiovascular disease. Finding ways to improve the long-term health of this population of cancer survivors is therefore an important goal. Methods: The current study aimed to i) explore the correlates of physical activity (PA), Diet and quality of life in EnCa survivors and ii) determine the feasibility and preliminary efficacy of a novel mindfulness-based intervention coupled with dietary counseling (MIM+Diet) to the same population. Results: In the cross sectional survey 71 type II EnCa survivors reported extremely low levels of physical activity and poor dietary habits, however mean levels of self-reported, health related quality of life (HRQL) were not compromised as compared with US based norms. Findings from the MIM+Diet intervention study revealed improvements in aspects of HRQL (PSQI, FACT-En and RAND SF-36 MHS) but not diet and physical
activity (Cohen’s $d$). Aspects of physical functioning showed improvement as measured by the short physical performance battery (SPPB). **Discussion:** Future studies need to target the most at risk survivors, as soon after diagnosis as possible to improve long term quality of life and a disease prognosis. Recruitment of EnCa survivors to interventions is a challenge that requires novel approaches that can be tailored on an individual basis. Mindfulness may be one avenue that shows promise in this regard.
Dedication

I would like to dedicate the following dissertation to my wonderfully supportive and loving wife Sarah.
Acknowledgments

I would like to take this opportunity to recognize the part that has been played by so many people along this journey.

Firstly I would like to thank my advisor Dr. Brian Focht for all the guidance and support you have provided me with over the course of the recent years I have spent in your lab. You are always available to offer advice and to lend an ear. Thank you also for being a mentor that I truly respect and appreciate for all the opportunities you have provided me with. I look forward to continuing our work together in the future.

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Chapter 1: Introduction

The purpose of the current study was threefold. First, given the growing prevalence of overweight and obesity in endometrial cancer (EnCa) survivors it is important to determine the relationship between theory-driven correlates of lifestyle behaviors, quality of life, and health risk factors within a specific population of type I EnCa survivors who are at disproportionate risk for future cancer recurrence and chronic disease onset. The second purpose was to determine the feasibility and preliminary efficacy of implementing a novel lifestyle intervention to the population EnCa survivors identified in part I. Finally, a comprehensive evaluation of the challenges and approaches taken in conducting parts I and II was conducted in order to improve the quality of future investigations of this nature.

Cancer is currently the second highest cause of death in the United States after Cardiovascular Diseases (CVD). Increasingly incident cancer and cancer death is linked to lifestyle factors, including poor diet and physical inactivity among others. Indirectly both of these aspects of lifestyle are associated with increased body weight and obesity. For many cancer patients the improved medical treatments and technologies available mean greater odds of survivorship. However, this inadvertently places these survivors at greater risk for further diseases of lifestyle including cardiovascular disease and type II diabetes.
It serves to reason then, that in addition to the treatments for primary disease processes such as cancer, that health care providers need to address secondary (in some cases primary) lifestyle related risk factors with the aims of avoiding future chronic disease as well as improving quality of life. Diet and physical activity (PA) are two obvious aspects of lifestyle and behavior. Diet can improve health in a number of ways. According to the widely accepted energy balance hypothesis, diets high in fat and sugar provide an excess of “empty” calories, which leads to energy imbalance (more calorie consumed vs. expended) and development overweight and obesity. Most efforts to improve diet advocate for reduction of fat and sugar with an increase in consumption of foods such as whole grains, fruits and vegetables. Physical activity (PA) involving bodily movement requires energy supplied through the metabolic assimilation of food. By regularly engaging in PA, individuals are more easily able to manage energy balance (calories expended). In addition to improved energy balance, increased cardiovascular and muscular fitness leads to better control of homeostasis including blood pressure, lipid profiles and insulin regulation.

Current Approaches to Standard of Care Practice in EnCa

In current best practice approaches to treatment of EnCa—post-surgery—patients are offered information or education regarding the importance of eating healthy diets and engaging in physical activity in order to improve health. However, research has shown that education alone is ineffective as a moderator of change in behavior. Furthermore in terms of treatment for chronic disease associated with lifestyle, physical activity and diet alone have both shown efficacy but a combination of the two simultaneously offers more
impact. The ideal goal then for many patients is to begin to eat more healthily and do more physical activity in their daily lives.

A further aspect of health care—which is becoming better understood within the context of supportive care—is stress management. Many cancer patients and survivors are dealing with a multitude of stressful life events over and above the profound diagnosis, treatment and survivorship experience. Stress has powerful and well-understood impacts on the functioning of the immune system as well as on the mental health of individuals. For this reason, many cancer patients are attracted to and increasingly report using Complimentary Alternative Modalities or CAM for the treatment of stress and or conditions peripheral to primary disease processes. Modalities that fall under this description include activities such as yoga and meditation among many others. While there are growing bodies of research examining the efficacy of these approaches, the quality and objectivity is often lacking. It is therefore important to be able to advise cancer survivors of actual benefits they can expect from alternative modes of lifestyle treatment such as yoga, mindfulness and meditation and how they may be incorporated into lifestyle approaches to offer a balanced approach to health management. A further aspect of interest for the investigators in the current study was for the usefulness of a novel lifestyle change intervention such as gentle yoga based movement to act as a stepping stone to more comprehensive behavior change. In other words could survivors who had no previous experience or capacity to engage in a lifestyle change that included adding physical activity and dietary modification do so more easily after an 8-week program to develop mindful awareness. Mindfulness in
Motion (MIM) is a mindfulness based stress reduction technique with a foundation in yoga that may be useful in this regard.

Etiology of EnCa: The Importance of Lifestyle Behaviors

Specifically, endometrial cancer (EnCa) is the most common female gynecological cancer and in 2014 there was an estimated 56,230 new cases and 8,590 deaths in the US as a result of the disease (Siegel, Ma, Zou, & Jemal, 2014). There are two broad pathological subtypes of EnCa, hypothesized to develop due to different etiological processes. The majority of EnCa diagnoses are of type I endometrioid endometrial cancer (80%). In this first pathogenic subtype of endometrial cancer, women typically exhibit a high prevalence of obesity, hyperlipidemia and signs associated with hyperestrogenism while the second subtype in contrast is typified by an absence of the characteristics of the first subtype or poorly defined characteristics. A growing body of research has linked the characteristics of the typical Type I endometrial cancer patient such as overweight and obesity as well as the metabolic syndrome, with a high risk for disease onset, recurrence if treated and for further chronic disease onset. These patients most often do not engage in physical activity and are prime candidates for lifestyle and behavioral modification.

In order to better understand the correlates and/or factors associated with lifestyle behaviors for the typical type I endometrial cancer patient and how these factors may influence change in relevant health related outcomes, the current project had a multi-stage/study approach. In stage I it was deemed necessary to firstly identify and then understand the relationships between lifestyle behaviors, specifically diet and PA and health outcomes from a sound theoretical perspective. This resulted in an observational
cross sectional study of theory-based correlates of lifestyle behaviors and quality of life among Type I EnCa patients. In addition to dietary and PA behaviors we assessed health outcomes associated with lifestyle such as physical function (PF), quality of life (QOL), depression and mindfulness. Based on both previous research and the findings from the Stage I investigation we then designed a lifestyle intervention to target areas of interest.

Given the nature of this preliminary efficacy and feasibility study one of the primary endpoints of interest was to simply engage a population of EnCa survivors in a lifestyle intervention given the higher than normal health risks these individuals face when compared with age matched controls. The lifestyle study (stage II) was developed to take information gleaned from previous research and study I about the needs of EnCa survivors and use this to deliver a lifestyle intervention that incorporated both aspects of physical activity and dietary guidance with the end goal of improving functional outcomes, and quality of life. Furthermore there was a specific effort to use an alternative mode of exercise, namely gentle yoga as an intermediate form of gentle PA and lifestyle modification. This approach may help to bridge the gap between an inactive and low functional capacity (EnCa Survivor) and a level of exercise at or near the current recommended guidelines of 150 minutes of moderate to vigorous PA most if not all days of the week.

Another important aspect of the gentle yoga program was a focus on developing a mindful state of awareness or increased mindfulness. Mindfulness is a skill that may be developed through various methods most notably meditation practices. These practices bring attention to bodily sensations, the breath or on thoughts and feelings as they enter the consciousness. The ability to bring attention in a nonjudgmental way to the everyday
experience is seen as a way to dampen the stress response. This mindfulness was hypothesized to aid in the assimilation of the experience of healthy lifestyle and health education such that it would become more likely to translate into home based practice post intervention and even further moving the survivor closer to other lifestyle changes such as incorporating adequate daily PA. This approach was rooted in the idea that for an unfit overweight low functioning individual, the recommendations to be physically active at the level of the current guidelines would be discouraging. Another important goal of the gentle yoga program was to aid the survivor in dealing with daily life stress. As well as the impacts that stress may have physiologically—such as reduced immune function—it also impacts upon unhealthy behaviors such as poor eating. Therefore, a positive experience of gentle movement in a group based setting such as that provided by mindfulness based yoga would be a stepping stone to more comprehensive behavior change.

Finally, nested within the two separate, but temporally related studies is an assessment of the challenges of implementing the two stage approach to first examine cross-sectional relationships and subsequently design and deliver a lifestyle intervention targeting this understudied population of EnCa survivors. The recruitment rates and viability of engaging EnCa survivors to both the survey and lifestyle intervention was conducted. The reasons for this are to i) improve the design and implementation of future studies, ii) aid in future recruitment efforts to lifestyle type interventions by iii) identifying the most successful recruitment strategies given the current age and demographics of typical EnCa survivors.
Potential Limitations in Current Standard of Care Approaches

It is well accepted that a lifestyle change to include a healthy diet and physical activity is beneficial to the average individual. However, it may be especially so for cancer patients and survivors. Despite this knowledge being readily accessible and freely dispersed, the incredible multitude of challenges faced by the person experiencing the diagnosis and impact of Cancer means it is often overlooked in the hierarchy of treatment “must do’s”. In fact it would seem that although primary care physicians and treating oncologists are aware of the need for lifestyle change and may advise patients that they should make such changes, they are not adequately trained to deliver advice to patients on how to begin this process. In this regard there are many lessons to be learned from the attempts made within the field of cardiac rehabilitation, where a systematic and clinical evidence based approach to exercise and lifestyle change has been made in the treatment of cardiac patients. Despite the knowledge that accurately prescribed exercise is a necessary part of patient recovery, so much so it is now reimbursed through health insurance, many patients do not start or complete this therapy. In a similar fashion, awareness of the need for and benefits from lifestyle interventions that include physical activity and dietary change within cancer treatments continues to grow. For this increased awareness and growth to flourish requires the knowledge of very the specific impacts that physical activity, diet and stress reduction may have on the biological systems of the body and also including tumor biology itself. Additionally, how the environmental and genetic templates of each individual determine the responses to lifestyle change must be examined and understood. Finally and perhaps as, if not more importantly we need to understand the factors that determine which survivors under what circumstances are more
likely to “buy in” to the process of lifestyle change. It may be that for certain individuals
the effort and energy required to change a lifestyle pattern may be better served in
application to other ends. However from a humanistic point of view it may be seen that as
the effectiveness of modern scientific and medical approaches to cancer treatment
improve, it is imperative that it is realized that the individual patient’s quality of life and
not only the quantity of life, is appreciated. As drugs and therapies more effectively
improve the longevity of the biological organism we must still pay attention to the notion
that in the words of Abraham Lincoln “in the end, it’s not the years in your life that
count. It’s the life in your years.”

Given the growing prevalence of obesity, which may increase risk of cancer
recurrence as well for chronic disease that accompanies it, the primary purpose of the
present studies were 1) to examine lifestyle behaviors in Type I, early stage (I&II) EnCa
survivors, 2) to determine the feasibility and preliminary efficacy of a novel lifestyle
intervention in the same population and 3) to report on the recruitment and logistical
aspects of developing a lifestyle intervention for EnCa survivors.

**Definition of Terms**

*Type I Endometrial Cancer (EnCa):* This form of the disease is distinct from the
serous type II form of the disease based on a number of identifying criteria. The
differential etiology is a major classifying characteristic of the disease subtype and is
what has lead researchers and clinicians to identify this form of the disease as a target for
lifestyle intervention. Overweight, Obesity and the metabolic syndrome as well as
physical inactivity lead to a milieu of physiological changes that promote a state of
hyperestrogenemia, leading to increased disease risk. Despite successful treatment
techniques for Type I EnCa many of the risk factors that predispose to the development
of EnCa continue to exist post treatment, placing survivors at disproportionate risk for
recurrence and chronic diseases of lifestyle such as CVD and T2D.

**Lifestyle Behaviors/ Health related Habits (HrH):** Lifestyle behaviors or Health
related Habits are constructs that are used to conceptually describe aspects of individuals’
typical habitual behaviors and include many aspects. These behaviors include diet and or
exercise behaviors, sleep, stress and or coping, substance use and others. Lifestyle
interventions will refer to experimental and research related approaches to changing diet
and or physical activity behavior. In this work we will use lifestyle behaviors to refer
specifically to dietary and physical activity/exercise, however a more in-depth discussion
of these concepts will follow.

**Diet:** Refers to the composition of food in the form of different combinations of
essential and non essential nutrients such as carbohydrates, protein, fats, vitamins and
minerals. The different food types supply a mix of these nutrients in forms that are
necessary for the sustaining of life from a metabolic standpoint. The growth, repair and
function of the brain, skeletal muscles and organs in sustaining life all use energy
produced by the breakdown and assimilation of foods that can be broadly be considered
the “diet”. A healthy diet is one that is determined to be adequate for sustaining optimal
functioning whereas an unhealthy diet will result in deficits in functioning and health.

**Physical Activity:** A broad term that encompasses the varying levels of metabolic
activity that result from the action or lack of action of the skeletal muscle complex. On
the low end of the physical activity spectrum is physical inactivity or sedentary behavior.
On the other end of the spectrum would be exercise that is structured physical activity to enhance some aspect of health or performance. While athletes may use different modes of exercise to improve their performance at specific events, patients with chronic disease may use exercise to improve cardiometabolic or skeletal muscle function leading to improved health outcomes. Physical activity in the context of this work will refer to any muscular activity that requires the metabolic breakdown of nutrient substrates supplied via the “diet”. While exercise is a form of physical activity not all physical activity is exercise. Indeed for low fit individuals the mere act of ambulation in order to get from point A to point B may serve as healthful physical activity.

**Overweight and Obesity:** These terms are used to describe the body composition (BC) of an individual. While there are different components of BC such as muscle mass, bone mass or bone mineral density, the aspect of BC that is deemed most important to metabolic health is body fat percent. The categorization of persons into differing levels of body fat % determines their level of normal weight, overweight or obese. Traditionally there are a number of criteria used to make this categorization depending on whether the evaluation is epidemiological, clinical or empirical. Overweight by the most commonly used criteria of Body mass index or BMI is 25 kg/m\(^2\) − 29.9 kg/m\(^2\). Obese level I is 30-34.9kg/m\(^2\) and Obese level II and level III is 35 – 39.9kg/m\(^2\) and >40kg/m\(^2\) respectively.

**Metabolic Syndrome:** The metabolic syndrome originally called “syndrome X” and described as an aggregation of coronary heart disease risk factors in the same individual (Reaven, 1988) is now more broadly accepted as collection of individual cardiometabolic risk factors that are strongly linked to the development of cardiovascular disease, and Type II Diabetes Mellitus. While different classification systems use slightly
different criteria the most generally accepted are obesity, insulin resistance, hypertension, and dyslipidemia. (Roberts, Hevener, & Barnard, 2013). Many of the outcomes of lifestyle behaviors are related to the onset or development of one or many of the criteria that make up the metabolic syndrome.

**Physical Function/ Functional status:** This is a concept or construct that has been developed out of the work of scientists evaluating disability and independence with aging. Nagi (Nagi, 1965) and then Verbrugge and Jette in some of the earliest work describing the disablement process (Verbrugge & Jette, 1994) refer to functional limitations as the loss of the capacity to perform tasks of daily living at a level that is deemed adequate to maintain independence and quality of life for one’s age and sex. More recent evaluations have had broad interpretations of functional status as is measured by multiple outcomes such as self reported disability or performance on tasks that tap into functional capacity such as a 400 m walk mobility and fitness test or a stair climb test. Many interventions aim to improve functional limitations in order to improve health outcomes or rather aim to prevent declines in function that will lead to disability.

**Yoga:** is an ancient practice that originates in the present day India. Yoga as is known in the West is a combination of physical postures (asanas) that can improve overall strength and flexibility. They are practiced in conjunction with breath control (pranayama) and sometimes meditation. Originally yoga, which means to yoke in sanscrit, was a way of life or living that had as its primary goal, a spiritual path to enlightenment. In past and recent times the medical and health community has begun to examine the mechanisms behind the purported health benefits of the practice.
**Mindfulness:** Is operationalized in slightly different ways but is described by Jon Kabat-Zinn as “paying attention in a particular way: on purpose, in the present moment, and non-judgmentally” (Kabat-Zinn, 1994). Mindfulness is a skill that may be developed through various methods most notably meditation practices that have their origin in Buddhism and eastern religions. Practices may bring attention to bodily sensations, the breath or on thoughts and feelings as they enter the consciousness. The ability to bring attention in a nonjudgmental way to the everyday experience is seen as a way to dampen the stress response. By removing the emotional assessment individuals give to occurrences as they arise, reactivity is reduced. Physiologically the stress response is linked to the up-regulation of the sympathetic nervous system and the hypothalamic-adrenal axis (HPA). In the West there have been attempts to develop mindfulness in ways separate from the religious context. Most well known is the method developed by Jon Kabat-Zinn called Mindfulness Based Stress Reduction (MBSR). This is a combination of meditative practices, hatha yoga postures and didactic learning.

**Quality of Life (QOL) and health related quality of life (HRQL):** These are terms that are used often in the literature of psychology, behavioral, medical and related disciplines. The view of mainstream psychology is one of QOL reflecting an overall life satisfaction (Diener, 2000; Focht et al., 2012; Rejeski & Mihalko, 2001) or satisfaction with one’s life in a global sense, while the term HRQL is more related to the medical fields use of and conceptualization of QOL, which is one of a measure of “health” status. In this operationalization, HRQL is an umbrella term that encompasses the functioning of an individual in related but distinct functional domains, such as physical function, psychological well-being and social relationships. Measures such as the medical
outcomes -Short form 36 are a measure of HRQL and aim to quantify subdomains of functioning such as mental and physical functioning. When using measures of QOL it is important to approach the questions being asked from a theoretically sound perspective.

**Social Cognitive Theory (SCT):** Is a theory of behavior posited by Albert Bandura in his book “Social foundations of thought and action: A social cognitive theory” (Bandura, 1986). The SCT posits that a core set of determinants, the mechanisms through which they work and the most effective ways of translating this knowledge into behavior determines the control with which an individual can successfully govern their behavior. For example knowledge about the health risks of lifestyle choices and the, self-efficacy (SE) or the perceived capacity of an individual to change these behaviors and whether the cost vs. the benefit of changing those behaviors (outcome expectancy) will all determine whether an individual attempts to change their behavior. There are four major sources of SE information; a) performance accomplishments, b) vicarious experience c) verbal persuasion and d) interpretation of physiological and psychological arousal. Furthermore, person’s goals can govern their behavior by allowing them to generate plans and strategies to achieve an outcome. This may be additionally supported or thwarted by barriers such as a lack of time to exercise or facilitators such as social support existent in the environment in which the behavior will take place. SCT posits that there is a triadic reciprocal determinism between the behavior of the individual (physical activity), the environment in which the person is acting and the personal expectations and values of that activity to the person. This interrelationship is in constant effect.

**Self Determination Theory (SDT):** is a theory of motivation developed by Edward Deci and Richard Ryan (Deci & Ryan, 2008). It is a broad conceptual model that
aims to define and explain intrinsic and extrinsic sources of motivation and the roles that these varied forms of motivation play in the social and cognitive development of the individual. The theory also aims to take into account how social and cultural factors support or undermine individuals’ efforts to be successful in their performances. It is hypothesized that the degree to which a person is able to act with a sense of **Autonomy**, **Competence and Relatedness** determines the quality of their engagement in a given task. In the context of this study the tasks relate to physical activity and diet as lifestyle behaviors.

**Biomarkers:** A biomarker is defined as a “characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention”, as defined by the Biomarkers Definitions Working Group. (Biomarkers Definitions Working, 2001)

**Hypothesis and goals**

**Objectives**

Endometrial cancer is normally discovered in a relatively early stage (I&II). Initial treatment involves surgery to excise malignant tumors and affected tissues. Due to this successful strategy the majority of patients become cancer survivors at 5 years post diagnosis (80%). One downside of this situation is that for the most part EnCa is not seen as a major target for intervention development or as a malignancy requiring extensive funding comparable with other tumor sites. However, the emerging obesity epidemic—as evidenced by the increasing prevalence of diabetes, polycystic ovarian syndrome (PCOS) and metabolic syndrome in younger and younger women—is substantial cause for
concern that can have considerable public health impact. Specifically, the number of new patients and survivors living with EnCa will only continue to grow. Discovering the most effective means of nullifying the long-term impacts of this disease through lifestyle modification is an overarching goal of this line of research. In the context of the current study, identifying theory-based behavioral strategies to help women diagnosed with EnCa make positive lifestyle changes is a key early step for designing future large scale randomized controlled trials (RCTs) to improve long term clinically relevant treatment strategies.

Accordingly, the present studies had multiple objectives. 1) The purpose of the observational cross sectional study was to determine correlates of lifestyle behaviors (Physical Activity & Diet (D)) and both disease specific health related quality of life (HRQL) and broad quality of life outcomes. The hypotheses were that higher levels of PA and better dietary habits would be associated with better quality of life. We also hypothesized that psychosocial theory variables would mediate this relationship. 2) The primary purpose of study II was to determine the feasibility and preliminary efficacy of developing and delivering the MIM+D intervention to endometrial cancer survivors. Our hypothesis was that the lifestyle intervention would be safe and tolerable for EnCa survivors and that an 8-week program of MIM is an achievable time commitment. Furthermore, a second hypothesis is that for woman who are overweight/obese with low levels of physical fitness and physical function who adhere to the 8-week mindfulness intervention, we will see improvements in self reported QOL and objectively measured physical functioning (PF).
3) The purpose of the final part of the study was to evaluate the logistical aspects of recruitment to each phase of the study. The goal of this process was to inform the future approach to such studies by identifying weaknesses and strengths with some suggested conclusions.

The secondary aim of this study is to determine whether a yoga based Mindfulness intervention for EnCa survivors results in meaningful improvements in quality of life and PF outcomes for a low fit and sedentary population. Our hypothesis is that for woman who are overweight/obese with low levels of physical fitness and physical function who adhere to the 8-week mindfulness intervention, we will see improvements in self reported QOL and objectively measured PF.

Finally, an ancillary exploratory aim is to conduct a comprehensive evaluation of the process of recruiting EnCa survivors into a lifestyle intervention. The logistics of recruiting a sample of EnCa survivors to a lifestyle intervention that involves a novel approach to lifestyle change, namely yoga and mindfulness are unique and require a multi strategy approach. This documentation is aimed at improving future recruitment efforts for larger trials in the same population.

**Innovation**

There are several features of the present studies that make them unique from existing lifestyle research targeting EnCa survivors. Endometrial cancer patients are an understudied population of survivors who are at disproportionate risk of disease recurrence and future morbidity directly related to lifestyle. Engaging in a lifestyle that includes physical activity and healthy dietary practices has been shown to be efficacious
in modifying facets of risk profiles such as body weight and cardiovascular fitness. The modification of both diet and exercise in the context of lifestyle behaviors has yet to be evaluated in this population of cancer survivors.

In addition to traditional forms of PA such as aerobic walking, alternative exercise modalities such as yoga are commonly available and increasingly tailored to special needs populations (Kiecolt-Glaser et al., 2014). For a low functioning, overweight and obese population of EnCa survivors this alternative exercise may offer comparable benefits for improving function and quality of life outcomes, and more importantly may serve as a more navigable entry into the lifestyle change landscape.

Importantly this study would be the first to directly evaluate the efficacy of lifestyle change in EnCa survivors in the context of an intervention (objective 1) and to further examine the effects of a novel approach to behavior change in EnCa survivors such as fostered by using a mindfulness based approach (objective 2).

**Significance and background of Endometrial Cancer**

**Project Overview**

Endometrial cancer (EnCa) is one of the most common forms of malignancy affecting women over the age of 55. In 2012 there was an estimated 47,000 new cases of EnCa diagnosed in the U.S and an estimated 8,000 deaths (Siegel, Naishadham, & Jemal, 2012). Endometrial adenocarcinomas tend to be diagnosed early (stage I, II) which leads to successful intervention strategies. The initial treatment of EnCa usually involves surgery to remove and stage the tumor, followed by either radiation therapy and or adjuvant chemotherapy. Due to the effectiveness of these strategies, typically stage I and
II EnCa cancer patients have a high 5-year survival rate (>96%) (Jemal, Siegel, Xu, & Ward, 2010). Associated with this longer life expectancy however is a significantly higher risk for developing co-morbidities such as cardiovascular disease (CVD), diabetes and functional decline (Fader, Arriba, Frasure, & von Gruenigen, 2009). Increasingly, evidence for the higher mortality rates associated with secondary diseases of lifestyle in this population is starting to surface. Pre diagnosis obesity is a significant predictor of all cause mortality in EnCa survivors, (Chia, Newcomb, Trentham-Dietz, & Hampton, 2007). Additionally, recent findings demonstrate that the majority of EnCa survivors fail to obtain recommended PA and dietary recommendations. Consequently, it is becoming increasingly evident that EnCa survivors are at a disproportionately high risk for obesity and chronic disease and they could particularly benefit from lifestyle interventions involving the modification of diet and exercise.

In a population-based study, Irwin and Mayne (2008) examined whether mortality after endometrial cancer diagnosis was affected by pre-diagnosis obesity, diabetes, smoking, oral contraceptive use, parity, or postmenopausal hormone (PMH) use. Eligible women, aged 40-79 years, diagnosed from 1991-1994 with incident invasive endometrial cancer and identified through the Wisconsin statewide mandatory cancer registry were invited to participate. Of 745 eligible cases, 166 women were deceased after 9.3 years of follow-up, with 43 attributable to endometrial cancer, based upon vital records linkage. Hazard rate ratios (HRR) and 95% confidence intervals were adjusted for age at diagnosis, menopausal status, stage of disease, and other exposures of interest. Obese women (body mass index [BMI] ≥30 kg/m(2)) prior to endometrial cancer diagnosis had an increased risk of both all-cause (HRR=1.6, 95% CI 1.0-2.5) and endometrial
cancer (HRR=2.0, 95% CI 0.8-5.1) mortality, compared with non overweight women (BMI<25 kg/m(2)). Endometrial cancer cases with diabetes also had an increased risk of all-cause mortality compared with non diabetic women (HRR=1.7, 95% CI 1.1-2.5), although there was no association with endometrial cancer mortality. There were no associations between PMH use, oral contraceptive use, parity, or smoking and mortality from any cause. The results suggest that history of obesity and diabetes may increase risk of mortality after endometrial cancer diagnosis; modification of these characteristics may improve survival after endometrial cancer diagnosis (Irwin & Mayne, 2008).

The biological mechanisms underlying the association of obesity with many cancers are both complex and differential depending on disease stage, however they are becoming increasingly well understood (Lynch, 2010) (Schmandt, Iglesias, Co, & Lu, 2011). In a study by Renehan et al. (2008) it was shown that the risk of developing EnCa increased by 60% with each 5kg/m2 increase in BMI (RR = 1.6). In addition to the association shown between excess body weight and EnCa, type II diabetes mellitus is independently associated with EnCa risk (RR = 2.1) (2007). EnCa is a sex hormone responsive form of carcinoma and therefore estrogen levels across the cancer continuum from pre-diagnosis to survivorship, may be related differentially to a) increased risk for EnCa, b) severity of EnCa, c) recurrence and to d) unfavorable treatment outcome. PA and diet are powerful behavioral tools that may reduce risk, buffer against treatment side effects and improve treatment outcomes for EnCa survivors (Basen-Engquist et al., 2009) (Courneya et al., 2005). Furthermore, obesity as a condition is associated with a high level of systemic inflammation as indicated by the presence of C-reactive protein (CRP), IL-6, TNF-α and other inflammatory markers, which serve to exacerbate many chronic
disease processes as well as the risk for further development of the cancer in question (Wang et al., 2011). Dietary and PA interventions can individually and in conjunction attenuate this inflammatory response (Michigan, Johnson, & Master, 2011). In addition to the biomedical effects of lifestyle on EnCa risk and progression, it is also important to consider the psychosocial factors that may play a role in the disease management. High levels of perceived stress, anxiety, and depression have all been linked to lowered immune function (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002), which can be particularly important for cancer patients, as response to treatment and positive treatment outcomes are significantly improved when patients are healthy. For clinicians, understanding the most effective approach to augment current treatment options is a priority for this understudied cancer survivorship population.

Previous research has provided strong evidence for the effectiveness of diet and exercise for improving physical function (Messier, 2010), reducing cardiovascular disease risk, reducing risk of type two diabetes (Laaksonen et al., 2005) and improving quality of life in a variety of chronic disease populations (Rejeski, Brawley, & Shumaker, 1996). Nonetheless, to date, this approach has not been systematically evaluated among overweight or obese EnCa survivors who could benefit significantly from behavioral weight management interventions. Consequently, the present study will be one of the first to examine the feasibility and preliminary efficacy of implementing a lifestyle intervention combining yoga and diet as a support care approach in the treatment of EnCa survivors.
Innovation

Background and Rationale

It is well established that physical activity (PA) results in significant improvements in physical fitness, physical function and quality of life (QOL) outcomes for cancer patients and survivors. Furthermore PA forms an important cornerstone of weight management efforts. Given that over 50% of EnCa survivors are overweight or obese, they are at disproportionate risk for chronic disease such as type II diabetes and CVD. This underserved survivorship population could uniquely benefit from lifestyle interventions targeting change in lifestyle behaviors. While PA alone is not associated with significant weight loss, PA in conjunction with dietary adjustment is superior to diet alone for weight management and or weight loss (Wing, 1999). Foster-Schubert et al., (Foster-Schubert et al., 2012) randomized 439 postmenopausal women (mean age = 58) into 1 of four comparison groups; i) diet, ii) exercise, iii) diet and exercise or iv) control group, to determine the comparable efficacy of lifestyle change interventions for achieving weight loss and body composition change. The target weight loss of 10% body weight while being a small amount in absolute terms is associated with significant chronic disease risk reduction as demonstrated by the findings of the diabetes prevention program DPP (Knowler et al., 2002).

Despite the promising findings, evidence from well-controlled randomized trials for the efficacy of PA for producing meaningful improvements in health and quality of life outcomes in overweight and obese EnCa survivors remains surprisingly limited. A small scale RCT based in the UK demonstrated the preliminary efficacy of PA behavior change interventions in sample of 33 gynecological cancer patients and survivors (12
ovarian, 11 endometrial) (Donnelly et al., 2011). Patients randomized into the PA intervention had significantly improved fatigue at 12 weeks and 6 months post intervention. However, to our knowledge there has been only one RCT that has targeted weight loss in EnCa survivors through counseling on diet and exercise behaviors. This study randomized 75 early stage EnCa patients into a 6-month lifestyle counseling intervention (including Diet and PA) with follow-up at 6 and 12 months. Significant differences existed between the diet and exercise counseled group compared with usual care controls in kilograms of weight lost (p<0.001), minutes of self reported physical activity (p<0.038 and p<0.02) and servings of fruits and vegetables (p<0.001) (von Gruenigen et al., 2012).

Exercise/PA is an integral component of behavioral weight management interventions. However, it is well–established that the demands of traditional exercise programs often lead to high dropout rates, and are often daunting for persons with no previous exercise experience. This situation highlights the need to explore alternative modes of PA for EnCa survivors.

Yoga is one possible unique exercise modality that has gained popularity in recent decades. It has been investigated in regards to its effects on a number of chronic health conditions, including among others, hypertension (Cohen et al., 2009), arthritis (Bosch, Traustadottir, Howard, & Matt, 2009) and cancer (Coker, 1999) as well as improving the functional capacity of older adults as they age (Brown, Koziol, & Lotz, 2008) (Chen et al., 2010). There are therefore multiple aspects of this form of activity that may be beneficial to EnCa survivors. Specifically, the use of breath control, posture and attentional focus can have significant affects on flexibility, strength and cardiovascular
function. Notably yoga can be designed to target the specific needs of EnCa survivors. Gentle muscle toning and flexibility in conjunction with breath control, can bring a person to movement and bodily awareness in a gradual manner. Importantly, these alternative forms of exercise may be more palatable and more encouraging of an attempt at lifestyle change than traditional exercise interventions focusing on walking programs or strength training only.

Yoga has been found to have significant effects on aspects of bodily functioning related to quality of life such as immune function and stress relief. This may provide an important opportunity for those prescribing exercise as well as a window of opportunity through which to begin counseling of EnCa patients regarding lifestyle change.

We began this process with a theory-driven cross-sectional examination of lifestyle behaviors in EnCa in order to better delineate target areas for the proposed intervention in this population of survivors. The survey includes measures of typical levels of physical activity, composition of diet, quality of life (sleep, depression, stress) and other psychosocial variables related to motivation and perceived ability to engage in lifestyle change. This preliminary data will be an important guide as to the focus of our theory driven lifestyle intervention. Given that many cancer patients are inundated with multiple treatments and after care requirements, one goal of this study included identifying possible theory-based mediators of behavior change. This will allow better use of resources to keep participant burden at a minimum during the intervention.

Overweight and/or obese EnCa survivors could significantly benefit from lifestyle interventions promoting change in physical activity and dietary behavior. Unfortunately, knowledge of the factors associated with physical activity and dietary behaviors of EnCa
survivors remains limited. Furthermore, the feasibility and efficacy of delivering a lifestyle intervention combining exercise and dietary behavior change has yet to be systematically evaluated. Consequently, the purpose of the observational cross sectional study was to determine correlates of lifestyle behaviors (PA & D) and both disease specific health related quality of life (HRQL) and broad quality of life outcomes. The primary purpose of study II was to determine the feasibility and preliminary efficacy of developing and delivering the MIM+D intervention to endometrial cancer survivors. Finally we aimed to evaluate the logistical aspects of recruitment to each phase of the study. The goal of this process was to inform the future approach to such studies by identifying weaknesses and strengths with some suggested conclusions.
Chapter 2: Literature Review

**Epidemiology of Endometrial Cancer**

There will be an estimated 49,500 new cases of endometrial cancer in 2013, making it the most common form of female gynecological malignancy in the U.S. (Siegel, Naishadham, & Jemal, 2013). Furthermore there will be an expected 8,000 deaths attributable to this form of gynecologic malignancy. The possible options for treatment and prevention of this chronic disease are varied and determined by the biological roots of the specific subtype of tumor. Typically, surgical intervention without additional adjuvant radiotherapy and chemotherapy is sufficient for type I tumors, and results in favorable outcomes (> 95%, 5-year survival) (Siegel et al., 2012). In a smaller group of patients the treatment is more intensive, as the tumors are more aggressive, less differentiated more likely to spread resulting in less positive outcomes for these patients (± 50%, 5-year survival).

The majority of endometrial cancers are considered to be endometrioid endometrial adenocarcinomas (>80%). The classification of endometrial cancers into subtypes is based on the etiology of the tumor, its behavior and the subsequent disease profile. In a seminal paper by Bokhman (Bokhman, 1983), the classification of tumors into two broad subtypes was made after 366 patients were prospectively studied for a period of 20 years.
In the first pathogenic subtype of endometrial cancer, women typically exhibit a high prevalence of obesity, hyperlipidemia and signs associated with hyperestrogenism; such as anovulatory bleeding, infertility, late onset of menopause, and hyperplasia of the stroma of the ovaries and endometrium. These characteristics lead to highly and moderately differentiated tumors that do not invade the deep tissues of the uterus and have a low rate of spread to nearby lymph nodes. These tumors are responsive to treatment with progesterone and the prognosis is good.

The second subtype is in contrast typified by an absence of the characteristics of the first subtype or poorly defined characteristics. Therefore there are no salient endocrine and metabolic disturbances, invasion of tumors into the myometrium is deep, tumors are poorly differentiated, often metastasize and they do not respond to progesterone. This leads to poor outcomes for treatment when compared with type I tumors.

It is interesting to note that the symptoms for the first type of tumor tend to exist for prolonged periods of time, and when patients do seek help they can have positive outcomes. In contrast the symptoms associated with the second subtype do not last long and therefore many patients may only be aware of a problem when the tumor has already developed past a point where treatments are effective. So it would seem that while in many cases the factors associated with the development of type I tumors are also responsible for the high degree of differentiation of tumor cells after onset, which allows them to behave more like normal cells than the less well differentiated, invasive tissues associated with a lack of hormonal stimulus, i.e. estrogen, in type II tumors.
Interestingly data from the 2009 AICR cancer risk awareness show that only 51% of the US population believe there to be any link between obesity and risk of cancer. In terms of the role of obesity in the etiology of all cancers, the relationship is strongest for endometrial cancer. It has also been shown that as well as the high incidence rate, increased rates of death are also a function of adiposity. A study by Reeves and colleagues (2007) conducted with the Million Women cohort, showed that for a 10 unit increase in BMI the statistically significant increase in relative risk was 2.89 (95% CI, 2.62 – 3.18). In another recent study, the already known association between endometrial cancer mortality and obesity was highlighted by the fact that for women in the highest category of BMI (>40kg/m²), the risk of death was nearly 525% higher than for that of the normal weight patients (RR 6.25; 95% CI, 3.75 – 10.42) (Calle, Rodriguez, Walker-Thurmond, & Thun, 2003). What is interesting to note with these observations, is that despite the fact that a large number of women who developed endometrial cancer and were morbidly obese, which would have protected them if they had the type I subtype of tumor, the death rate was still excessive. This may point to the fact that even though well-differentiated tumors associated with metabolic conditions (high unopposed estrogen levels) are less deadly, the high prevalence still means a high mortality rate. This points to the significance of the changes in population trends from the time of Bokhman’s observations (±1960-1980), to the present time (2000’s). The Russian sample of women in Bokhman’s study were roughly split at 65% type I and 35% type II tumors whereas the prevalence in the U.S. currently is closer to 70%- 90% type I and roughly 10% type II tumors (Fader et al., 2009; von Gruenigen, Gil, Frasure, Jenison, & Hopkins, 2005). Finally in a world wide report started in 2007 and published in 2013 it is estimated that 3
out of 5 endometrial cancers are preventable (Research, 2007). This has massive implications for the prevention and additionally treatment through survivorship given that the majority of EnCa survivors do not change their lifestyles or risk factors associated therewith.

A recent examination of the cohort from the nurses health study, where 71570 women were followed from their initial assessment in 1986 and then every 2-4 years until 2008, provided information regarding level of PA and incident endometrial adenocarcinoma (Du et al., 2013). During the course of follow-up there were 777 cases of invasive endometrial cancer. In comparing those who achieved <3METhrs per week (<1 hr per week of walking) to women who were engaged in moderate PA (9-<18METhrs/wk), the relate risk was reduced by 39% (RR=0.61, 95% CI:0.48-0.78) and reduced by 27% for high PA , (>/= 27METhrs/wk, RR=0.73, 95% CI:0.58-0.92). Interestingly, recent PA was associated with risk reduction but past PA was not. Furthermore when BMI was taken into account the significance of the risk reduction due to level of PA became non significant. This led the authors to suggest that PA was related to risk for EnCa but not independently of the influence of BMI.

The impacts that a high level of obesity in the population has had on endometrial cancer have allowed for detailed observations about the specific mechanisms involved in tumor development. Additionally through elucidation of these pathways, it is possible to map out strategies for prevention and treatment on both a person-based and at a more broad population based level.
Etiology of Endometrial Cancer

Estrogen is responsible for the growth of the endometrium (hyperplasia) in preparation for the implantation of the ovum after a successful fertilization. Should this not be the case the natural cycle of menstruation ensues and the thickened endometrial lining is shed. This process may become imbalanced depending on the state of the tissues in the body producing both increased amounts of available estrogen and not enough progesterone.

In premenopausal women the main source of estrogen is the stromal cells of the ovaries but in post menopause this function is shifted to peripheral tissues including adipose tissue. Another enzyme produced by specialized cells in adipose tissue is the enzyme aromatase. Aromatase functions to convert the androgens (estrogen and testosterone) into estrone and estradiol in adipose tissues. With an increase in age and adiposity there is an increase in the activity of aromatase in the body with Cauley et al, (Cauley, Gutai, Kuller, LeDonne, & Powell, 1989), reporting a >40% increase in estrone and estradiol in obese (>30kg/m^2) vs. normal weight (<27kg/m^2) postmenopausal women. Another important factor is that Sex hormone-binding globulin (SHBG) responsible for removing free sex hormones from the serum, is decreased with increased adiposity.

Estrogen also has a significant effect, through its up-regulations of kinase pathways on cell growth and tumor progression. In Figure 1, increased, unopposed estrogen results in higher levels of estradiol and estrone. Estradiol leads to activation of phosphoinositol 3-kinase (PI3K) and mitogen-activated protein kinase (MAPK) pathways further leading to proliferation of cells. Other conditions such as polycystic
ovarian syndrome (PCOS) in premenopausal women can also lead to an increase in the conditions favorable to the development of endometrial hyperplasia and finally endometrial cancer. In this condition we also see the prevalence of insulin resistance, again a factor worsened by obesity. An Australian study showed that for women with PCOS, there was a fourfold increase in the risk for developing EnCa (OR 4.0, 95% CI 1.7-9.3) however this was attenuated when controlling for BMI (OR 2.2, 95% CI 0.9-5.7) (Fearnley et al., 2010).

Figure 1 Obesity Related Etiology of Endometrial Cancers (type I) (Reproduced with permission from (Fader et al., 2009)
Obesity is associated with a state of hyperinsulinemia in the tissues of body, and while some studies have shown an association between high levels of insulin and EnCa risk this relationship alone does not account for the increased risks due to obesity. Related but different is the state of insulin resistance, whereby there are high levels of circulating insulin, but this has no effect of the muscle and liver which usually act to then remove glucose from the blood stream. Adiponectin is a specialized adipokine (chemicals produced in adipose tissue) that is a marker for insulin resistance. This inverse relationship seen with insulin resistance and low levels of adiponectin is strongly associated with EnCa risk independent of BMI.

Insulin like growth factors IGF’s are also affected by obesity, with sustained hyperinsulinemia resulting in decreased levels of the IGF binding proteins. Specifically IGFBP1 is most highly expressed in human endometrium, so obesity contributes to the net increase in IGF-1.

IGF and insulin use similar pathways leading to the activation of the same PI3K pathway for cellular proliferation, the MAPK pathway as well as the mammalian target of rapamycin (mTOR) promoting cell survival (AKT) and proliferation. This pathway is frequently seen in EnCa. Additional compounds such as the phosphatase and tensin homolog (PTEN) impact this pathway by normally acting as an antagonist to PI3K and as a tumor suppression gene. Its down regulation therefore allows this pathway to stay activated. Adenosine monophosphate-activated protein kinase (AMPK) inhibits the above-mentioned PI3K/AKT/mTOR pathway, however AMPK inactivation is often seen in obese individuals with insulin resistance.
Adipokines produced by adipose tissue such as tumor necrosis factor alpha (TNFα) and other pro inflammatory cytokines such as leptin, interleukin-6 (IL-6) and resistin, contribute to a general state of inflammation in the body. This inflammation is linked to the metabolic syndrome, type II diabetes and insulin resistance, further exacerbating this “perfect storm” whereby conditions are ideal for the uncontrolled proliferation of estrogen sensitive endometrial tumors as is seen in type I EnCa (Modugno, Ness, Chen, & Weiss, 2005). See Figure 2 and Table 1 for a summary of factors both contributing to EnCa.

There has been a significant increase in the rate of obesity in the U.S. and developed western nations as reflected by high levels of chronic diseases of lifestyle such as CVD, Type II Diabetes Mellitus (CDC, 2008) and increasingly specific cancers (Reeves et al., 2007). These diseases are largely preventable, but will remain a significant challenge for health care providers into the future. Already ⅔ of currently obese children in the U.S. are predicted to obese as an adult and this is associated with higher rates of premature death, despite increasing life expectancy (Franks et al., 2010).
Figure 2 Influence of Lifestyle Related Factors on Inflammation and Endometrial Carcinogenesis. Reproduced with permission from (Modugno et al., 2005)

Table 1
Factors Contributing to Endometrial Cancer (Type I) in Obesity

<table>
<thead>
<tr>
<th>Factor</th>
<th>Action</th>
<th>State of Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI3K/AKT/mTOR</td>
<td>Cellular proliferation</td>
<td>Up regulated</td>
</tr>
<tr>
<td>MAPK</td>
<td>Cellular proliferation</td>
<td>Up regulated</td>
</tr>
<tr>
<td>IGF</td>
<td>Cellular proliferation</td>
<td>Unopposed</td>
</tr>
<tr>
<td>IRS-1</td>
<td>Activates PI3K etc.</td>
<td>Activated</td>
</tr>
<tr>
<td>TNFα</td>
<td>Inflammation/ Insulin resistance</td>
<td>Up regulated</td>
</tr>
<tr>
<td>AMPK</td>
<td>Inhibits signaling – PI3K…</td>
<td>Inactivated</td>
</tr>
<tr>
<td>PTEN</td>
<td>PI3K antagonist/ Suppressor gene</td>
<td>Inactivated</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>Marker of insulin resistance</td>
<td>Lowered</td>
</tr>
</tbody>
</table>
**Diagnosis of Endometrial Cancer**

Since 1988, endometrial carcinoma has been surgically staged according to the FIGO staging systems; last revised in 2009. FIGO stage is the single strongest prognostic factor, with a significant reduction in disease-specific survival with higher stages: 96% 5-year survival is reported for patients with localized disease, 67% with regional disease, and 17% with distant metastasis. (Jemal et al., 2010)

In one of the only prospective cohort studies to evaluate the relationship of Body mass (BMI) and moderate to vigorous physical activity (MVPA), 983 postmenopausal women who were diagnosed with endometrial cancer in the Women’s Health Initiative Observational Study were followed for a median of 5.2 years. The main outcome of interest was death from endometrial cancer (EnCa) (Arem, Chlebowski, et al., 2013). There were 193 deaths over follow up of which 66 were attributed to EnCa, resulting in an all cause mortality hazard ratio of 1.85 for women with a BMI >35 when compared with those with a BMI of <25. (HR = 1.85, 95% CI 1.19–2.88). Interestingly the HR for some MVPA vs none at baseline suggested a reduction in risk for death from EnCa, however this became non-significant when adjusting for BMI. This finding seems to point to the relative importance of body composition over activity level in terms of risk for EnCa death.

**Outcomes of Endometrial Cancer**

Unfortunately there is evidence to suggest that a large number of woman are unaware of the risks of developing endometrial cancer associated with obesity (Soliman et al., 2008). Furthermore, many of the women who are obese and who will develop endometrial cancer will also likely suffer from one or more of the following chronic
diseases, hypertension, TTDM, CVD among others. This places them at increased rates of death above those attributed to Cancer alone. Recent evidence suggests that the primary cause of death for endometrial cancer survivors who were diagnosed with low grade localized cancer is cardiovascular disease (Ward et al., 2012). Women who are successfully treated for their primary cancers will also have a high chance of developing recurrent EnCa and so the need for interventions addressing these lifestyle factors, that predispose to future risk of comorbidity, are essential.

Most of the spending within the health care system is targeted at the diseases that result in the highest rates of death such as CVD and the most prevalent cancers; breast cancer in women and prostate cancer in men. It seems there is less concern for conditions such as endometrial cancer, which by and large are viewed as a problem solved. This is evidenced by the amount of NIH dollars spent on studies of EnCa. This may be related to the fact that there is a high 5-year survival for the majority of patients treated with highly efficacious surgical and adjuvant therapies.

This situation however does provide opportunities for researchers and indeed the primary care physicians treating patients living with this condition. With the increase in the incidence and prevalence of heart disease, there was an intense research effort to better treat and prevent future burden. In a similar sense there are more patients now with EnCa who will need treatment into the future. By learning more about the evolving epidemiology of the disease we may better treat the EnCa patients of the future, ideally with a combination of lifestyle modifications and medical care to improve prevention and positive outcomes.
EnCa is strongly associated with obesity which in turn is associated with multiple chronic disease processes including Hypertension, Type II diabetes, CVD, osteoarthritis, chronic low grade inflammation and in terms of psychosocial functioning a reduction in health related quality of Life (HRQL) and physical functioning.

**Treatment options for Endometrial Cancer**

Primary treatment for EnCa involves hysterectomy and is typically a Salpingo-oophorectomy procedure. It can include pelvic lymph node dissection and laproscopic lymph node sampling. Depending on the FIGO staging of the tumor patients may additionally receive radiation therapy, chemotherapy and or hormone therapy with Progesterone or Tamoxifen. This treatment regimen determines the degree and type of side effects a patient may experience. Many patients experience a reduction in quality of life and physical functioning as a result of this treatment. These side effects further warrant treatment that includes psychosocial counseling.

Recently there have been efforts to develop a panel of biomarkers that can aid in the early detection of EnCa risk. One such attempt includes a 5 panel assay to measure prolactin, GH, Eotaxin, E-selectin, and TSH (Yurkovetsky et al., 2007). Results from this study were able to detect differences between EnCa, breast cancer and ovarian cancer with high specificity and sensitivity. This approach has many strengths and in addition to indication of early risk may also be able to detect changes in risk factors as a result of lifestyle changes or alternative interventions such as bariatric surgery.

Whilst bariatric surgery is an expensive and more extreme option that may be used to both prevent and treat endometrial cancer patients, it is highly effective with regards to changing the biomarkers associated with EnCa and alleviating the mechanisms
that are related to high levels of adipose tissues. This option has been growing in interest for many obese EnCa survivors as well as for their treating oncologists as the evidence for the efficacy of weight loss interventions has shown that most subjects regain lost weight within a relatively short period of time.

Increasingly, the role that lifestyle behaviors have across the continuum of the cancer experience (reference) is recognized and valued. Unfortunately for many individuals the first encounter with a need for change in behavior will be as a survivor of cancer. Years of poor eating habits, lack of physical activity and perhaps high stress living and working conditions will result in an environment which may encourage the development of the disease. For those who have a genetic basis to their cancer, further insults to health will only foster a faster development of cancer, and if successful treatment results in remission then cancer patients are at greater risk of chronic disease such as T2D and CVD.

Endometrial cancer survivors are perhaps at an even greater disadvantage with regards to the risk of developing chronic disease as much of the development of the initial tumor process is related to obesity, inactivity and poor lifestyle habits.

Another aspect of lifestyle habits related to quality of life is the ability to cope with stress. As such many persons faced with stress tend to make questionable health choices. In a recent study by Parelkar and colleagues (2013) (Parelkar, Thompson, Kaw, Miner, & Stein, 2013) it was found that cancer patients from a national registry who had made active efforts to control their stress were more likely to make health choices to improve physical, psychosocial and preventive health measures than did cancer survivors who had not.
There is an accepted need for the counseling of cancer survivors to adjust their lifestyle behaviors by those who are treating them in oncology. In a recent survey of providers of care for gynecological cancer survivors and patients, 240 respondents to an online survey (30%) detailed that they felt it was important to approach the subject of obesity with their patients, and that these conversations would not affect the quality of their relationships with their patients (Jernigan, Tergas, Satin, & Fader, 2013). Of interest was that while oncology providers believed it was their responsibility to initiate the counseling on issues related to obesity, they also felt the majority of care should be passed on to other specialists working within obesity interventions.

Efforts to provide EnCa patients with interventions to address weight loss have been limited. Von Gruenigen and colleagues (von Gruenigen et al., 2008) assessed the feasibility of a lifestyle intervention to promote weight loss and change eating habits and increase levels of PA in a sample of EnCa survivors. 45 early stage survivors were randomized into a 6 month lifestyle intervention or usual care. The intervention group received both group and individual counseling for 6 months with the primary outcome being weight change. The active intervention group achieved a 3.5 kg weight loss compared to a 1.4 kg weight gain in the control group leading the authors to conclude that a 12 month weight loss and lifestyle change intervention was a feasible approach in this group of survivors.

**Connection to Obesity**

Since type I EnCa is undoubtedly linked to obesity and associated mechanisms, one of the most important goals for both the prevention and treatment of this form of
carcinoma is efforts to educate younger woman about the risks of weight gain on their future health. For older woman who are already diagnosed and treated for their disease being provided with options that will allow them to engage in healthy lifestyle related habits are associated with risk for disease recurrence and future comorbidity such as CVD, TTDM and metabolic syndrome.

**Age**

Endometrial cancer patients are normally over the age of 45 and the disease progression is associated with the onset of menopause and the change in hormonal balance in the female body at this time. Exceptions are for younger women who are diagnosed with PCOS, a condition that may also cause an imbalance of reproductive hormones.

**BMI**

During and following menopause the female body shifts the primary production of estrogen from the ovaries to peripheral adipose tissue. As such an increase in or high level of Adipose tissue up-regulates the production of estrogen, a factor known to stimulate endometriosis, which is a precursor to type I endometrioid endometrial cancer.

**Sedentary Behavior**

Low levels of physical activity are typically associated with low levels of cardiovascular fitness, increased body weight and low levels of physical function. Aerobic fitness measured with objective laboratory tests is the gold standard of cardiovascular health. VO2 max or the maximal amount of oxygen the working muscles and metabolically active tissues can consume during exercise is the strongest predictor of
mortality in humans (Kodama et al., 2009). Increased body weight is indicative of energy imbalance and is associated with multiple aspects of health.

**Diet**

Diet is an important aspect of any attempts to maintain energy balance. Increasing the intake of fruits and vegetables while lowering the intake of refined carbohydrates such as white bread and white rice whilst avoiding saturated animal fats is ideal. A combination of both dietary modification and physical activity is known to result in the most meaningful changes in body weight. It is therefore essential that lifestyle interventions take both aspects of behavior change into account.

**Obesity and Overweight**

There are a number of criteria for characterizing or diagnosing someone as being overweight (OW) and or suffering from obesity. The most commonly used epidemiological measures for overweight (OW) and obesity are the a) Body Mass Index (BMI) b) Waist Hip Ratio (WHR) and c) Waist Circumference (WC) with more precise objective measures of OW and obesity being d) Underwater weighing (UWW), e) BodPod f) skinfolds and g) IDXA (dual X-ray absorptiometry). Essentially the purpose of these measures is to categorize an individual into meaningful levels of body fat and lean tissue mass. The 3 primarily epidemiological measures are easily calculated from self-report of known height and weight (BMI), waist circumference (WC) and ratio of waist to hip circumference (WHR) and are closely correlated with body composition. One of the downsides of self-report data is they are subject to reporting bias.
The clinical measures (d - g) are more accurate depending on technician skill and additionally offer the benefit of being able to compartmentalize the different components of body mass i.e. fat mass, lean body mass and % body fat with the IDXA being able to determine bone density too. This means being able to more accurately disassociate the healthy tissue mass of skeletal muscle and bone with disease outcomes such as is not possible with a heavy and muscularly athletic individual reporting a high BMI.

Another more important distinction in the description of body composition is the distribution of body fat. Visceral fat or intra abdominal fat also known as organ fat have been linked to cardiovascular disease risk and cancer risk (Britton et al., 2013). More recently General Electric has developed software for the IDXA (CoreScan) has that aims to evaluate the visceral adipose tissue volume. There have been limited published works that have reported on the usefulness of the technology for evaluating the response to change or intervention longitudinally, however it has been reported as a precise measure (Rothney et al., 2013).

Recently the American Medical Association (AMA) declared that obesity was a disease. This determination of the condition of having excess body fat as a disease has many implications for patients and their treatment and in the wider public health and policy domain. Allison et al. (2008) (Allison et al., 2008) make the case for the designation of obesity as a disease by evaluating the process by which such decisions are made. In their paper they suggest that the definition of obesity by simple BMI criteria whilst a useful clinical and operational definition has significant flaws. Simply being classified as Obese for having a BMI >30kg/M2 does not provide any information on the functioning of adipose tissue. The specific adipokines and paracrines that are associated
with excessive adipose tissue cell size and number result in challenges to good health. The level at which those factors produce negative effects on health may therefore be varied among individuals.

**Epidemiology of Obesity**

The prevalence of overweight and obesity in the U.S. has continued to increase since the early 1980’s. Data from NHANES showed that from the period of 1976-1980 (NHANES II) to the period 1988-1994 (NHANES III), the prevalence of obesity increased by 8% from 14.5% to 22.5% (Flegal, Carroll, Kuczmarski, & Johnson, 1998). Furthermore the increase in the prevalence was statistically significant for all sex and age groups. Interestingly, while the prevalence of overweight remained relatively stable at 30-32% the prevalence of obesity has increased steadily. More recently in the period of 2007-2008 it was found that the prevalence of age-adjusted obesity was 33.8%, with 32.2% and 35.5% for men and women respectively. The estimated prevalence of overweight and obesity combined (BMI>25) were for the same segments 68%, 72.3% and 64.1% (Flegal, Carroll, Ogden, & Curtin, 2010). This places a large number of individuals at risk for future disease risk. As the prevalence of obesity continues to be a problem with younger age groups this is not seen as a problem that will be going away any time soon.

As previously stated, the prevalence of overweight and obesity within endometrial cancer survivors is extremely high. In a meta-analysis of 19 prospective studies it was found that for each 5kg/m2 increase in BMI the risk of developing EnCa was significantly raised (RR 1.59, 95% CI 1.50-1.68) (Renehan et al., 2008). Further in a recent analysis Arem and colleagues (Arem, Park, et al., 2013) examined the influence of
BMI on all cause and disease specific mortality in woman with a diagnosis of endometrial cancer. Compared to women who had a BMI of between 18.5 and 24.9, the 5-year all cause mortality hazard ratio (HR) was 1.74 (95% CI = 1.13 to 2.66) for BMI 25-29.9, 1.84 (95% CI = 1.17 to 2.88) for BMI 30-34.9 and 2.35 (95% CI = 1.48 to 3.73) for BMI greater than or equal to 35kg/m(2) (P trend < .001). In a disease specific analysis Higher BMI was associated with endometrial cancer specific mortality at 5 years but not cardiovascular disease related 5-year mortality, however by 10 years cardiovascular disease was significantly associated with BMI. The effect of greater levels of physical activity was to reduce risk of death at 5-years however this was attenuated by BMI.

**Etiology of Obesity**

The dominant position on obesity is that the development of adipose tissue hyperplasia and adipocyte hypertrophy is the result of energy imbalance. That is an excess of calories consumed and an under expenditure of calories through daily living and physical activity. Currently, the debate as to the cause of the growing obesity epidemic continues. Some have postulated that the reduction in work and daily life activity has resulted less caloric expenditure leading to slow and steady weight gain (Church et al., 2011). Others have said the increase in availability of dietary calories either from fat or carbohydrates (refined sugars) or simply total calories are responsible (Swinburn et al., 2011). One form of evidence provided for this is the increase in rates of obesity in third world countries that are now dependent on westernized diets as well as a concomitant reduction in everyday activity. Finally there is the theory of genetic susceptibility, which poses that some individuals have a predisposition to gain weight,
perhaps a result of historical lack (thrifty genes), or random variation over time (Speakman, 2013).

In a more specific context the actual source of calories may be more important than total per se. In a recent paper looking at the changes in fat and high fat content of the diet in comparison to the national guidelines, a subset of the Framingham heart study subjects were examined over 20 years (Vadiveloo, Scott, Quatromoni, Jacques, & Parekh, 2013). Fat from all sources increased from 27.3% to 29.8% as a percentage of calories. Protein increased from 16.8 to 18.0% of energy and carbohydrate derived energy decreased from 51.0 to 46.8% of calories. Trends were found to be similar for both men and women, however there was a greater increase in the proportion of calories from saturated fat in women and less reduction in energy from transfats. Trends were also similar across BMI categories. This is an interesting finding as despite the increase in calories consumed as fat, this amount is still less than the national guidelines of 35%.

Carbohydrates also contribute to overall calories in the diet and more importantly can influence the mechanisms of metabolism and energy balance. Furthermore it is increasingly being proposed that certain forms of carbohydrates, such as highly refined sugars are powerful drivers of the metabolic process and can lead to increased rates of CVD, TTDM and inflammation. In a test of the effects of a high carb diet compared with a low carb high-fat diet in a number of individuals with artherogenic dyslipidemia, Volek and colleagues (2009) found that after 12 weeks, subjects on the low carb diet had reduced glucose and insulin concentrations, improved insulin sensitivity, reduced body weight and adiposity (-12%, -50%, -55%, -10%, -14% respectively). Despite a 3-fold higher intake of dietary saturated fat in the carb-restricted diet, markers of endogenous
lipogenesis were significantly reduced. These findings lead the authors to conclude there
is a link between dietary carbohydrate and markers of the metabolic syndrome.

Adipose tissue has in recent times become recognized as an endocrine tissue and
as such it is therefore understood to influence more than just the storage of adipocytes.
The white adipose tissue is responsible for regulation of energy balance, glucose
homeostasis, blood pressure and inflammation (Trayhurn, 2007). Within obesity affected
persons, altered endocrine function may lead to an increased release of pro-inflammatory
cytokines and decreased levels of adiponectin which can result in dyslipidemia,
hypertension, insulin resistance and type II diabetes mellitus (Yusuf et al., 2005). As
mentioned in Section I, many of these same mechanisms can also result in endometrial
hyperplasia. It is therefore a double insult to the metabolic health of a post-menopausal
female with a diagnosis of EnCa. On top of the cancer diagnosis there is an increased risk
of cardiovascular injury, type II diabetes and metabolic syndrome. A further observation
that has been made regarding the increase in adiposity with obesity is the specific
location of the fat cell deposition. It is thought that visceral adipose tissue associated with
an android (apple) rather than a gynoid (pear) shape is more closely associated with the
production of inflammatory cytokines, down regulation of adiponectin and therefore the
onset of metabolic syndrome and associated diseases (Trayhurn, 2007).

Speaker and colleagues (Speaker & Fleshner, 2012) examined the potential
influence of a repeated stress response on the deposition of adipose tissue into visceral
rather than subcutaneous stores. Using a rat model the authors found that Interleukin-1B
released due to a repeat stressor may be responsible for decreased ability of subcutaneous
fat stores to uptake excess energy substrates leaving them in circulation and resulting in
subsequent visceral storage. This in turn may be related to above-mentioned processes whereby even in the absence of obesity, metabolic dysfunction may lead to onset of disease states such as hypertension, dyslipidemia and type II diabetes. This may further highlight the need to investigate more fully the influence of stress on the metabolic health of individuals, including those with a diagnosis of Endometrial Cancer.

It is therefore likely that multiple sources of risk for developing obesity exist and that for many women the combination of excess dietary calories, probably in the form of refined energy dense carbohydrates as well as reduced levels of daily and leisure time PA, possibly on top of genetic susceptibility may lead to obesity and related disease processes. The outcome of endometrial cancer however has the strongest link of any cancer with levels of obesity.

**Outcomes of Obesity**

**Mortality**

Body composition has increasingly been associated with disease outcomes in the past few decades, leading to a so called “war on fat”. The associations of BMI with all cause mortality have been previously reported (Manson et al., 1995). In the examination of 115 195 U.S. women over a period of 16 years in the Nurses Health Study, it was found that the relative risk of death was 1.3 in those with a BMI of 25.0-26.9, 1.6 in those with a BMI 27.0-28.9 and was doubled (2.1) for those with a BMI of 29.0-31.9. For women with a BMI above 32 the risk of death from cardiovascular disease was 4.1 and from cancer was 2.1. Furthermore a weight gain of 22lb or more since the age of 18 was associated with mortality in middle age. These are strong associations and the support for
weight loss of even modest amounts is unquestionable. What is not clear is how much weight loss over what period of time is the minimum necessary to improve health outcomes and protect from mortality.

**Type II Diabetes Mellitus**

Body composition and the mechanisms behind increases in levels of body fat are strongly linked to the development of metabolic conditions such as type II diabetes mellitus (TTDM). One position is that central adiposity leads to the increased delivery of fatty acids via the portal vein to the liver. This results in hepatic insulin resistance and reduced insulin clearance (Lewis, Carpentier, Adeli, & Giacca, 2002). Colditz et al., (1995) also studied women from the Nurses Health Study and followed 114,281 women prospectively between 1976 and 1990. It was found that after controlling for age, BMI was the dominant risk factor for TTDM. Furthermore, after controlling for age and BMI at 18 years of age, compared with those whose weight was stable, a gain of 5.0-7.9 kg was associated with a risk of developing TTDM of 1.9 (95% CI, 1.5 to 2.3). For women who gained between 8.0 and 10.9 kg the risk was 2.7 (CI, 2.1 to 3.3). Importantly for women who lost more than 5 kg the risk was reduced by more than 50%. Again highlighting the substantial health related outcomes associated with weight loss, despite the negative consequences of weight gain initially. Further evidence from prospective trials involving lifestyle modification has shown that even an average weight loss of 7 kg over a 6-month period is associated with a 58% cumulative reduction in diabetes incidence, despite some regain of weight accounted for (Knowler et al., 2002; Tuomilehto et al., 2001).
**Dyslipidemia**

The mechanism behind the association of obesity with dyslipidemia is not fully understood, however is thought to be the result of hyperinsulinemia and insulin resistance stimulating hepatic fatty acid production from a larger free fatty acid pool (Lewis et al., 2002). This process in turn leads to post-prandial LDL and HDL production. Weight loss due to physical activity and dietary modification are thought to aid in the reduction of high circulation of free fatty acids, however after returning to a stable diet and maintenance of weight thereafter the cholesterol concentrations can return to pre weight loss levels. The standard of treatment currently for high levels of cholesterol are statin drugs.

**Hypertension**

Like dyslipidemia the mechanisms linking obesity and hypertension are not well understood however they are thought to be related to increased renal sodium reabsorption, increased sympathetic nervous system activation throughout the renin-angiotensin complex and increased physical pressure on the kidneys from visceral deposition of fat (Hall et al., 2003). While there are undoubtedly improvements in hypertension due to the improved lifestyle choices including physical activity and diets reduced in sodium, for most established hypertension cases concurrent pharmacological treatment is also necessary.

**Cardiovascular disease**

An increase in obesity results from an increase in both fat and lean tissues, both of which require an oxygen supply. The increased workload on the heart via a need for
increased ventricular capacity can lead to hypertrophy of the left ventricle. This physical change in conjunction with the systemic hypertension can lead to a further concentric hypertrophy (reducing filling space) leading to systolic and diastolic heart failure. Frequently this process is coupled with coronary heart disease whereby the blood supply to the tissues of the heart is compromised. Increased obesity is positively correlated with high circulation of inflammatory cytokines such as CRP, compounds known to further degrade the endothelial lining of the blood vessels and contribute to poor outcomes in cardiovascular diseased patients. A 26-year follow up of persons from the Framingham Heart Study showed that coronary artery disease was two fold more likely in the obese (Hubert, Feinleib, McNamara, & Castelli, 1983). Physical activity and diet are powerful tools for treatment of cardiovascular disease, however one question being asked with greater frequency is whether these lifestyle changes are enough even in the absence of weight loss (Gaesser, Angadi, & Sawyer, 2011).

**Obstructive Sleep Apnea (OSA)**

Increased deposition of fat in the chest wall and abdomen may adjust the breathing mechanics of obese individuals. Increases in side of the pharyngeal fat pad and the reaction of airway space especially in the prone position can lead to a mismatch in the ventilation perfusion ratio resulting in arterial oxygen desaturation (Koenig, 2001). This can occur in as many as 50% of obese subject and is often undiagnosed. Poor sleep quality leads to increased feelings of tiredness and fatigue, reduced quality of life, hypertension, increased risk of stroke, and reduced life expectancy. Weight loss can improve the condition markedly and in the case of bariatric surgery it can subside altogether (Dhabuwala, Cannan, & Stubbs, 2000).
Fatty Liver

A number of obese subjects particularly those with central or visceral adiposity may present with non alcoholic fatty liver disease (Lawrence & Kopelman, 2004). A proposed mechanism is that hyperinsulinemia blocks hepatic fatty acid oxidation and leads to an accrual of intracellular fatty acid levels. This can cause toxic oxidative stress. In itself this form of fatty liver disease seems to be benign however the liver may be susceptible to hepatotoxic agents. There is limited evidence that weight loss can improve the condition and further slow gradual weight loss may be preferential to rapid weight loss (Lawrence & Kopelman, 2004).

Polycystic Ovarian Syndrome (PCOS)

PCOS is an endocrine abnormality, which is classified clinically by the presence of hyperandrogenic features, oligomeorrhea/amenorrhea and infertility (Lawrence & Kopelman, 2004). Approximately 50% of patients with PCOS have obesity and the severity, degree to which the condition is treated, and resulting insulin resistance are all related to the degree of obesity. The presence of multiple ovarian cysts, increased levels of circulating androstenedione and testosterone, reduced levels of sex hormone binding globulin (SHBG) and androgen secreting tumors are possible. There is a hypothesis that in amenorrheic obese women that overstimulation of the endometrium may lead to endometrial carcinoma. Trials of diet and lifestyle interventions have shown amelioration of clinical and chemical markers of the disease even with as little as 5% weight loss (Pasquali, Casimirri, & Vicennati, 1997).
Cancer

Obesity is associated with the formation of a number of neoplasms due to variable endocrine and metabolic factors and their influence on the growth, maintenance and apoptosis of cellular tissues. In a 2002 report from the International Agency for Research on Cancer (IARC), the link between obesity and cancer was brought to wider attention. It published that sufficient evidence existed for the link between colon cancer, post-menopausal breast cancer, endometrial cancer, renal cell cancer and adenocarcinoma of the esophagus (Vainio, Kaaks, & Bianchini, 2002). Further studies have elucidated that of all the cancers endometrial cancer has the highest association with obesity (RR 2.89, 95% CI 2.62 to 3.18) (Reeves et al., 2007). But associations have also been found between leukemia, multiple myeloma, pancreatic cancer and non-Hodgkins lymphoma. The impact of lifestyle interventions and weight loss on cancer risk and mortality are ongoing (Morey et al., 2009). In order to better understand the way that biologic mechanisms may be altered with weight loss, serum samples from 89 class II and Class III obese patients were taken from a subset of persons from the RENEW trial and compared with controls (Linkov et al., 2012). The results showing that VEGF, GH, adiponectin, IL-6 and IL-7, and IGFBP-1 significantly varied with time in the trial and with weight loss. This highlighted the fact that biomarkers may vary and change with weight loss and are possible targets with intervention. More specifically with a large proportion of endometrial cancer patients suffering with morbid obesity (30-40%), however, the most promising treatment of obesity and its effects may be bariatric surgery. A small subset of patients also from the RENEW study were provided with this option.
**Treatment Options for Obesity**

A recent panel at the ACSM’s national conference addressed the subject of whether weight-loss or fitness was a healthier and or a more achievable goal for persons with obesity. Given the recent declaration of obesity as a disease by the AMA, the question is of significant import. Furthermore, this is directly related to the debate on what is more critical for the obese patient; namely fitness or fatness. Proponents of fitness put forth that despite the best efforts of mainstream medicine (and the fitness industry) most conventional attempts at weight loss result in failure and more detrimentally a yo yo effect or weight cycling whereby the weight lost is replaced in a relatively short time. There is some conflicting evidence as to the extent that body weight cycling is detrimental to health, with recent reviews of the literature not finding excessive risk (Muls, Kempen, Vansant, & Saris, 1995; "Weight cycling. National Task Force on the Prevention and Treatment of Obesity," 1994). However some more recent evidence suggests that weight cycling has a stronger association with metabolic damage (Lawrence & Kopelman, 2004), hypertension and artherosclerosis (Weyer, Hanson, Bogardus, & Pratley, 2000) than obesity alone per se. This position is based on the idea that the majority of obese patients will have been through periods of weight loss and regain throughout their lives. The question then is instead of having a short term goal of extreme weight loss “should patients be trying to improve their cardiometabolic fitness?”, which can lead to enhanced cardiovascular function, insulin metabolism, muscle strengthening among other beneficial physiological changes. If this fitness is maintained over time weight loss may occur as a part of the process. More tradition approaches to the problem
of obesity have been predominantly dietary and more recently exercise or exercise and diet related.

**Diet**

Manipulation of diet has been the corner stone of weight loss efforts for much of the recent past. While a number of dietary approaches to weight loss have been tried and studied over time there is still no consensus as to the best method for all. Generally, caloric restriction is seen as the underlying mechanism supporting the efficacy of the energy balance approach. Other methods include the low-carb or ketogenic diet popularly known as “The Adkins Diet”. Low fat diet, changing to primarily vegetarian or plant based foods, and even raw foods only.

In the 1980’s and 1990’s a plethora of “fat free” and “low-fat” foods were popularized as the solution to CVD. “Fat-free” was and still is to some degree a form of health food and reducing fat in the diet a goal for most individuals. However, simple sugars such as high fructose corn syrup typically took the place of fat in “fat free” foods in order to maintain the palatability and taste of the food. Simple sugars stimulate the release of insulin by the pancreas shortly after ingestion and long term this mechanism is linked to the development of T2D. According to the energy balance theory, irregardless of the source of calories overeating without physical activity to balance the excess, will lead to weight gain. Furthermore simple sugars provide a short pronounced spike in the blood glucose response leaving a person with a low blood sugar, low energy level and hungry in a relatively short time thereafter. Ideally sugars should be consumed in the form of more complex carbohydrates that have a high fibrous content that can prolong the glycemic response. This high fiber whole grain and legume approach to carbohydrate can
also reduce markers of inflammation in obese and overweight subjects (Neuhouser et al., 2012).

Typical dietary restriction for purposes of weight loss aims to decrease daily caloric intake by up to 500 Kcal usually from a reduction in fat calories, but also simple sugars and carbohydrates. Studies that have used this approach will aim for a 10% weight loss goal, however many report closer to 8.5% weight loss (Foster-Schubert et al., 2012).

The American Institute for Cancer Research (AICR) provides recommendations for healthy eating in order to prevent cancer, treat cancer and for maintained health into survival. The New American Plate is the basis for guiding the macronutrient composition of dietary intake. This approach moves away from the food pyramid and puts focus on portion size rather than caloric content. It guides that a plate should consist of 2/3 or more of vegetables, fruit and whole grains and 1/3 or less of meat or animal protein. In their report *Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective*, the AICR states that after a review of over 7000 studies that a predominantly plant based diet, similar to that of the New American Plate may reduce risk of cancer (Research, 2007). In addition to the health benefit of plant based whole foods, higher fiber and water content make this dietary approach beneficial for weight loss purposes.

A recent study investigated whether adherence to the World Cancer Research Fund/American Cancer Institute, diet and physical activity guidelines was associated with improved HRQL outcomes among older female cancer survivors (Inoue-Choi, Lazovich, Prizment, & Robien, 2013). In this study a total of 2193 women in the Iowa Women’s Health Study were assessed for their compliance to the 7 guidelines and assigned a score of 1-7. Physical and mental component scores from the SF-36 were found to be
associated with the body weight, and dietary recommendations. However, the higher MCS were associated with adherence to dietary guidelines but not body weight, while adherence to body weight was associated with higher PHS scores and lower MHS. Adherence to the physical activity guidelines were associated with higher scores in both the Mental Health Summary Scores (MHS) and the Physical Health Summary Scores (PHS) even after adjusting for confounders.

**Physical Activity**

The question of whether exercise alone can be a successful approach for weight loss attempts has been asked many times. A recent paper makes the case that it is the ease with which high calorie dense foods are available and not low levels of PA that have resulted in the obesity epidemic (Luke & Cooper, 2013). The authors do clarify that they believe moderate to vigorous cardiovascular exercise plays an important role in health status, but that such a small proportion of US individuals achieve the recommended guidelines that it cannot be a significant factor in the control or cause of weight loss. Much of the argument put forth is based on the use of modern techniques such as isotope measurement to determine typical caloric expenditures in populations free living conditions. The comparison is made between developing and developed nations. The findings indicating that there are no real differences in the caloric expenditures of low body weight active individuals compared with their obese low active counterparts. The view of mainstream western medicine and sports science however is that physical activity has a major part to play in the control of body weight and whilst it may not be the ideal sole treatment option for the majority of individuals it is perhaps better used in conjunction with dietary restriction of energy dense foods. Furthermore In a response to
the above study Blair and Colleagues (Blair, Archer, & Hand, 2013) state that a separate study that examined occupational PA from the past 50 years a reduction in 120Kcal and 140 Kcal per day for men and women respectively can be shown to predict the increases in BMI from NHANES data over the same period. The response goes on to cite numerous sources of evidence that support the role of PA in the prevention and management of the obesity epidemic. In the context of disease risk it is arguably of more importance that when dietary restriction is compared to combination diet and exercise interventions, it is shown that exercise allows the maintenance of lean body mass compared to severe caloric restriction. Lean body mass is an important metabolic tissue that impacts the risk of conditions like the metabolic syndrome and type II diabetes.

**Combination/Lifestyle**

The evidence seems to be more clear that the most comprehensive and successful lifestyle modifications in the context of interventions for the purpose of inducing healthy weight loss are those that include both and physical activity and a dietary program. In a previously mentioned study the evidence for compared approaches (diet alone, exercise alone or diet and exercise) showed that diet alone lead to a weight loss of 8.5%, physical activity a weight loss of 2.4% and the combined program 10.8% (Foster-Schubert et al., 2012).

Despite the evidence that has been regularly provided for the efficacy of diet, exercise and combination approaches, there are some researchers who question the utility and long term effectiveness of this approach. A review of the historical evidence from trials using weight loss interventions in obese patients (Miller, 1999), examined whether long term outcomes (3-5 years) actually support the notion that this approach is
warranted. In the review, the dietary restriction methods of the past 40 years show that the most popular ones tend to cycle in and out of favor. Many of these practices are known to be detrimental to health. The typical data supports a 15 week diet or diet plus exercise program and results in an 11kg weight loss with a 60-80% maintenance after year 1. Despite a lack of long term data the indication is that by 3-5 years most individuals have relapsed. Furthermore the lack of evidence for long term success of weight loss interventions is itself worrying and the profitability of the weight loss industry may be one such reason. This perhaps further supports the notion that the focus for obese individuals should be one of a healthy lifestyle change and not weight loss only in and of itself. Still more drastic approaches exist for weight loss and are usually reserved for the morbidly obese (BMI >40) patient who is at significant risk of disease and death.

**Bariatric Surgery**

Bariatric surgery has increasingly become the treatment option of choice for obese individuals who cannot afford to continue to live with obesity. There are a number of different methods of surgical intervention in order to effect weight loss. The most common being the *Laparoscopic roux-en-y gastric bypass (LRYGB)* which is also the most studied procedure. The mechanism of action is both restrictive and malabsorptive. Restrictive in that it limits the size of the stomach and malabsorptive because it reroutes the nutrients to only pass through a shorter section of the intestine. Results of the LRYGB have been excess weight loss as much as 60-70% being maintained at 5 years post surgery. In addition to weight loss there has also been a reported remission rate for diabetes of up to 42% in a group treated with surgery compared with an intensive medical
therapy group (Schauer et al., 2012). Another method of surgical treatment is
*Laparoscopic adjustable gastric band* (LAGB), a method more commonly performed in
Europe and which uses only a restrictive mechanism. A band is placed around part of the
stomach and slowly inflated over a period of 6-8 weeks in order to form a gastric pouch.
This is the least complicated of the measures to perform. Efficacy is shown to be in the
region of 45-48% excess weight loss by 5 years (Franco, Ruiz, Palermo, & Gagner,
2011). LAGB has also been shown to positively influence diabetes remission despite
being less successful at causing weight loss than other methods. *Laparoscopic sleeve
gastrectomy (LSG)* was originally used as an early stage for other procedures (staged
LRYGB) but has since become a stand alone procedure (Franco et al., 2011). This is an
irreversible procedure where the stomach is resected to form a small tubular shape to the
stomach along the lesser curve of roughly 60-80 ml in size. A number of studies have
reported a wide range in excess weight loss of between 47-66% and LSG has also been
shown to be successful in the remission of type II diabetes (Gill, Birch, Shi, Sharma, &
Karmali, 2010). *Biliopancreatic diversion and duodenal switch (BPD-DS)* is the least
common bariatric procedure. It has both a restrictive and malabsorptive mechanism
however the procedure has been modified from its original method due to complications
associated with ulceration and dumping. Of the four mentioned techniques it shows
impressive efficacy for excess weight loss (70.1%). In addition the BPD-DS is very
effective at inducing remission of TIIDM, Buchwald et al.,(Buchwald et al., 2004)
reporting a 98% remission rate which is a full 15% higher than any other procedure.
Unfortunately the downside is that the mortality rate of the procedure is also the highest
reported at 1.1% and reported complications in the first 30 days after surgery 14.4% and 24% for subjects <50 and >50 BMI respectively.

In one of the first prospective studies of a bariatric surgery intervention on the incidence of cancer in a Swedish cohort, 2010 obese individuals who received surgery were compared to matched controls (Sjostrom et al., 2009). While the main outcome of the Swedish Obese Subjects study (SOS) study was mortality, the current examination looked at incidence of cancer. Bariatric surgery in this trial resulted in a mean weight loss of 19.9 kg (43.78lbs) over 10 years while controls increased their weight over the same period by 1.3kg (2.86lbs). Furthermore it was found that there was a lower number of first time cancers in the surgery group compared with the control group, however this was only significant when looking at the interaction of sex and surgery with women having lower rates with surgery but no difference for men. One of the downsides of this form of treatment is the high cost and also the fact that with this intervention there is also a high rate of weight gain post surgery. This has lead to primary treatment being lifestyle management that focuses on dietary modification with added physical activity prescription.

**Physical Activity for Cancer Survivors**

Casperson and colleagues (1985) wrote a paper with the goal of defining the differences among physical fitness, physical activity and exercise. Firstly recognizing that these terms are not one and the same thing, they defined physical activity (PA) as “any bodily movement produced by skeletal muscles that results in energy expenditure. The energy expenditure can be measured in kilocalories.” Furthermore that “Exercise is a
subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.” In the context of a low fit population such as endometrial cancer survivors, we recognize the value of physical activity for health benefits, especially as for many low fit individuals non-structured physical activity in the form of daily activities (ambulation stair climbing etc) may offer a more reasonable goal or mechanism through which to increase daily energy expenditure and improve health. It is also feasible that by aiming to increase PA through this means initially may be a step in the right direction towards more structured exercise.

Given that the understanding of what it means to be physically active has in recent time again undergone somewhat of a shift, it seems prudent to define and explain the concept of physical activity and that of physical inactivity. These two “states” are not simply the opposite of each other especially with regard to the metabolic impacts on healthy tissues. Hamilton and colleagues have shown that the change in cellular activity of Lipoprotein lipase (LPL) is markedly different in the sedentary vs. the active state (Hamilton, Hamilton, & Zderic, 2004). While many individuals are active while they engage in a bout of exercise, they may spend the rest of their waking hours in a sedentary or inactive state, changing their physiology and therefore health outcomes as a result. Many of the positive effects of exercise may easily be undone by the usually much longer periods of inactivity.

Sedentary behaviors are typically described as sitting time, either during work at a desk or at home during leisure time. Television watching or TV time and now more broadly screen time are still other operationalizations of sedentary time. Owen and
colleagues (Owen, Healy, Matthews, & Dunstan, 2010) report on the findings of the Australian Diabetes Study where TV time was examined for its relationship with biomarkers of cardiometabolic risk factors in 11,000 Australian adults. It was found that when categorizing TV time into reference groups that for those who watched more than 4 hours of TV per day there was an association with undiagnosed abnormal glucose metabolism and metabolic syndrome (Dunstan et al., 2005). Furthermore when TV time was examined as a continuous variable it showed a dose response relationship with 2-h plasma glucose (Dunstan et al., 2007) and fasting insulin. Most significant was that these relationships persisted even when self-reported leisure time physical activity was taken into account as a covariate.

For endometrial cancer survivors and for cancer survivors of many diagnoses it may be very important to consider lowering sedentary time as opposed to trying to increase physical activity to the levels of the current guidelines, a goal that may be seen as daunting. However, it is still vitally important to determine the beneficial effects that structured physical activity or exercise may have for cancer survivors and patients who are undergoing treatment.

In a paper describing the past, present and future of exercise oncology Jones and Alfano (2013) (Jones & Alfano, 2013) describe one of the first trials to utilize aerobic interval training as a treatment for patients of operable breast cancer. The trial at the Ohio State University (MacVicar, Winningham, & Nickel, 1989; Winningham, MacVicar, Bondoc, Anderson, & Minton, 1989), was conducted by Drs. Winningham and MacVicar, two oncology nurses. The outcomes of interest included functional capacity, body composition and patient reported nausea. This trial was certainly
ahead of its time as in the 1980’s exercise would be considered extreme for cancer patients. The findings of the trial however suggested that exercise was not only safe and feasible but improved aerobic capacity, body composition and patient reported nausea (Winningham & MacVicar, 1988).

A paper published in psycho-oncology in 2009 reported on the increase in articles that had PA and or exercise as part of the title since its inception (Courneya, 2009). The first paper published appeared in 1999 which was 7 years after the inception of the journal. In 2008 there was, including a special issue on the topic, a total of 37 articles published over the last decade. With 18 in the 2007 - 2009 period alone. This shift highlights the increasingly recognized benefits that may be achievable for cancer patients and may also be related to the demands of cancer patients themselves for therapies that are considered as complimentary and alternative methodologies (CAM). While exercise or PA is well accepted in the treatment of cardiovascular disease, it has lacked supporting evidence within the field of supportive oncology.

Since that time, Courneya and Friedenreich (Courneya & Friedenreich, 2001) have proposed the framework PEACE or Physical Exercise Across the Cancer Experience, within which to examine the effects and role that physical activity can play across the cancer continuum. This framework breaks up the cancer experience into 6 time periods. There are 2 pre diagnosis (prescreening and screening/diagnosis) and four post diagnosis (I.e. Pretreatment, treatment, post treatment and resumption).

The framework allows a focus on the specific challenges to health and functioning that a cancer patient or survivor may face as they move through treatment into survivorship. Furthermore understanding the specific challenges depending on disease
type and stage means clinicians, patients and researchers can use, benefit and target treatments for maximum efficacy and efficiency. To date the majority of research is conducted with cancer survivors. Because lifestyle interventions that involve a form of physical activity are a relatively new approach to treating cancer related symptoms there has been a cautious approach to working within a population that has historically been faced with significant pain, fatigue and reductions in physical function and HRQL. Like cardiac medicine before it, oncology as been slow to accept the role that increased levels of physical activity can play in the treatment of various cancers. It is the responsibility however of exercise physiologists and health behaviorists to examine exercise and physical activity within a controlled and measured approach using the best science to apply what is known about the correct dose and timing of activity so as to allow patients to benefit rather than be placed at risk.

**Aerobic Exercise**

Aerobic or cardiorespiratory exercise is known to be a significantly important form of activity for cardiovascular health of individuals. Cardiorespiratory fitness is engendered by activities such as walking, running, swimming and cycling, with more recent evidence also being provided for high intensity interval (HIIT) training. More specifically any activity that requires repetitive muscular contraction by the slow twitch or oxygen consuming muscle fibers will provide a stimulus for improved aerobic fitness. Regular aerobic exercise produces changes in the capillary density and mitochondrial density within oxygen consuming muscles cells. The primary measure of cardiorespiratory fitness is VO2 peak or the maximum volume of oxygen the working muscles can extract from the blood during exercise. For both athletes and healthy
individuals this measure is an important indicator of health, being the strongest predictor of all cause mortality. It is argued this may be even more important a measure for the health of cancer patients. Jones et al put forth a concept known as the multiple hit hypothesis (Jones, Haykowsky, Swartz, Douglas, & Mackey, 2007). Although this was proposed as a series of mechanisms affecting the long term cardiovascular health of breast cancer patients receiving adjuvant chemotherapy, many of the same mechanisms exist for endometrial cancer patients.

Endometrial cancer survivors like many breast cancer survivors are typically overweight/obese and or physically inactive. This combination of risk factors places EnCa survivors at increased risk for future incidence of CVD related mortality. It has been found that pre diagnosis obesity and type II diabetes both place survivors at increased risk of death independent of EnCa mortality (Chia et al., 2007). Due to the fact that aerobic exercise has been shown to be efficacious at reducing CVD risk and attenuating or reversing the impact of TIIDM (Knowler et al., 2002; Lindstrom et al., 2003) as part of lifestyle interventions, it should form part of standard treatment for EnCa survivors.

To date there have not been many prospective trials that have specifically included aerobic exercise as part of the intervention in EnCa patients, or survivorship. In one study (von Gruenigen et al., 2008), the primary lifestyle intervention used behavioral counseling to target weight loss, nutrient intake and increased PA in 23 endometrial cancer survivors randomized to treatment vs 22 control subjects. Subjects were encouraged to increase PA to a frequency of 5 days per week for 45 minutes per session. Patients were provided with accelerometers to help with self monitoring, however
objective PA was not an outcome measure in this study. PA was assessed at baseline, 3 months and 12 months with the leisure score index (LSI) of the Godin Leisure time exercise questionnaire (GTEQ). At 3 months, there was a significant increase in LSI in the intervention group (17.0 to 37.9) compared to control group (18.9 to 19.7) which on further analysis of the data was shown to be an increase in moderate activity (1.3 to 3.5 hours per week x 5 METS) and a slight increase in mild activity (3.3 to 4.3 hours per week X 3 METS). By 6 months and 12 months there were no further changes in LSI between groups however the LSI was still higher than baseline (17.0 to 33.7 and 32.8) respectively.

The RENEW study examined biomarkers associated with weight loss through a lifestyle intervention and included measures of inflammation, hormonal balance and cancer antigen expression (Linkov et al., 2012). 89 class II and III obese woman underwent a weight loss intervention and were compared with 43 non-obese subjects over 6 and 12 months. Significant differences were found by time point using a mixed effects models for mean levels of VEGF, soluble E-selectin, GH, adiponectin, IL-6, IL-7 CA-125 and IGFBP-1. Furthermore decreasing BMI was significantly associated with lower levels of biomarkers. Within this study exercise was prescribed in a way to progressively increase time spent in moderate levels of activity such as is similar to brisk walking for 60 minutes per day for 5 days per week (Goodpaster et al., 2010). The authors concluded that a lifestyle intervention that included PA and dietary restriction could successfully lower levels of biomarkers that are associated with Cancer incidence.
**Strength/Resistance Training**

Resistance training has been shown to impart an improvement on muscular strength, hypertrophy and endurance (Kraemer & Ratamess, 2004). In addition to the muscular fitness of healthy individuals who embark on regular resistance training, there have been improvements in chronic disease related outcomes for patients with osteoarthritis, T2D and CVD. In addition to these chronic conditions the metabolic processes associated with a variety tumor types makes resistance training an important consideration for cancer survivors, both in treatment and survivorship.

With increased age there are known decrements in muscle volume and strength that can lead to reduced physical functioning and ultimately loss of independence (Lang et al., 2009). This process of age related decline is known as sarcopenia. This term also encompasses the cellular processes that result in a degradation of muscle fibre cross sectional area as well as reduced innervation. Resistance training can lead to increased muscular volume and strength, which have been shown to add to metabolically active process and may therefore serve a purpose in weight management efforts. In sedentary aging adults the loss in muscle mass is associated with a decreased basal metabolic rate. As caloric intakes usually do not match this decline in BMR this is an important influence on energy balance in the aging.

In adult men the most prevalent form of cancer is carcinoma of the prostate gland. Primary treatment includes prostatectomy and depending on stage and grade chemo and radio therapy. In addition long term treatment involves androgen deprivation therapy (ADT). This leads to reduced testosterone production which has significant effects on the maintenance of muscle and bone tissues. Prostate cancer survivors are therefore one
group of patients for whom there is much interest regarding the potential benefits of resistance exercise. Due to the impacts that adjuvant hormonal treatment can have on the loss of skeletal muscle mass and onset of body fat accumulation, finding ways to counteract these side effects is paramount. A recent review of the evidence regarding the possible expected benefits of resistance training for prostate cancer survivors examined within the framework PEACE was conducted by Focht and colleagues (Focht; 2014).

There have been a number of studies that have examined the efficacy of RT in in Breast cancer patients, who share many similarities and challenges to EnCa patients pre-diagnosis and in survivorship, however they do receive as standard more intensive active adjuvant treatments in the form of chemo and radiotherapy than EnCa patients. In a landmark study Schmitz et al, (Schmitz et al., 2010) showed that resistance training was a safe form of PA for female breast cancer patients who were at risk for developing upper limb lymph edema. Furthermore other trials have been conducted to assess the value of resistance training for reversing the declines in both muscle volume and strength as well as loss of bone mineral density in female cancer patients who have undergone adjuvant therapies (Winters-Stone, Laudermilk, Woo, Brown, & Schmitz, 2014). Findings suggesting that weight training may no be able to affect the rate of BMD, however in a comparison with controls at 12 months, women who had been in the resistance training group had maintained bone health whilst the control group had become osteopenic. The authors concluded that it is as of yet not possible to conclude that rigorous training can improve BMD.

To date there have been no trials that have looked explicitly at the benefits of resistance training for endometrial cancer patients, however there are certainly aspects of
this form of physical activity that would be of physiological and functional benefit for the group of cancer survivors. There has been one case study in which an octogenarian patient underwent rehabilitation prior to robotic surgery for endometrial cancer (Carli, Brown, & Kennepohl, 2012). The patient underwent evaluation and then began a home-based program that included strength and endurance exercises in conjunction with nutritional optimization. Following 8 weeks improvements were seems in 6 minute walk time, and overall functional capacity as measured by the SF-36.

Other than broad aerobic forms of exercise and resistance training there are a number of alternative activities that may incorporate aspects of both as well as offer further health benefits. Some of these activities include Dance, Zumba, tai chi and yoga. As yoga is an increasingly popular form of activity with a growing body of empirical evidence to support its use with health challenged persons it is a primary activity of interest for this study.

Yoga

Yoga has increasingly become mainstream in the western context of health and fitness. While the true practice of yoga in the sense of a spiritual 8-fold path is engaged by some individuals in the West, the primary aspect of yoga that is practiced in the popular studios around the country focus on the strength and flexibility that is engendered through regular practice. One of the less understood benefits of this form of physical activity is the calming effect it has on the nervous system, specifically the parasympathetic tone that allows the relaxation response (Benson & Klipper, 1976).
Due to the many proposed benefits of yoga practice on multiple health outcomes, it has garnered interest among researchers for its usefulness as a modality of treatment for chronic diseases including hypertension and low back pain among others (Raub, 2002).

There are currently many forms of yoga practiced in the West including Ashtanga, Ayengar, Hatha, Kundalini to name a few. Each form of the practice emphasizes different aspects of physical function and emotional well being through a combination of postures (asana), breathing (pranayama), meditation, and relaxation. This broad description of a practice makes its study more difficult especially when aiming to determine what benefits can be expected by which patients or persons under what conditions. Hatha yoga is one of the most common forms and is the foundation for many newer more fitness related aspects of the activity. Furthermore of increasing interest within a population of physically challenged survivors there are benefits of yoga such as reduced physiological and psychological stress responses. A recent study conducted at The Ohio State University examining biomarkers of inflammation, mood and fatigue within a population of breast cancer survivors (Kiecolt-Glaser et al., 2014). The authors concluding that yoga could have beneficial effects on physical function and fatigue leading to improvements in health.

A review on yoga for treatment of survivors of cancer (Bower, Woolery, Sternlieb, & Garet, 2005) and comprehensive review by Raub (Raub, 2002) of the psychophysiology effects of hatha yoga for healthy individuals and those challenged by cardiopulmonary variables documents the increased interest in yoga as a modality of treatment for chronic disease. One of the first examinations of a form of tibetan yoga with an emphasis on breath control aimed to improve quality of life and stress reduction in
lymphoma patients (Cohen, Warneke, Fouladi, Rodriguez, & Chaoul-Reich, 2004). 39 patients who had been undergoing treatment or treated within a year previously were randomized to tibetan yoga treatment group or a wait list control group. Yoga was practiced weekly for a period of 7 weeks with the control group offered the intervention following the 3 month follow up. Patients in the yoga group reported lower sleep disturbances at follow-up compared with control ($P<0.0004$), including better subjective sleep and longer sleep duration ($p<0.03$).

Another interesting aspect of yoga practice is that is can be adjusted to account for the specific needs of practitioners. For example as mentioned the physical poses may be one aspect of yoga practice that leads to improvements in functioning but that aspects of breath control and meditative exercises leading to mindfulness and psychological benefits as well. It is the mindfulness and psychological mechanisms that will be a focus of the current examination.

**Measurement of Physical Activity**

Measurement of PA has taken numerous forms over the past decades. Beginning with some of the earliest epidemiological studies such as the Harvard men’s study, the nurses health study (NHS) self report of exercise was based on single items such as do you exercise regularly? The understanding of the complexity of accurate measurement of physical activity has grown which has led to more in depth and determined attempts to quantify the type, amount intensity and duration of a variety of activity whether it be leisure time pursuits such as exercise for the enhancement of fitness or simply a daily activity of life that may also contribute to the health of the individual.
Yoga and Mindfulness

Yoga is an ancient Indian and Tibetan tradition with origins in some of the earliest writings known to man. Katanjali’s yoga sutras are some of the earliest texts describing a way of life set out by the first sages. The word yoga is derived from “yug” in Sanskrit, meaning to “yoke” and refers to the union of body and mind through a combination of physical postures, meditation, breath control and diet. In many ways yogic practices are also considered a lifestyle or behavior. In recent years yoga has gained popularity in the West, specifically the U.S. (Saper, Eisenberg, Davis, Culpepper, & Phillips, 2004). While traditionally yoga as a practice involves the step wise combination of 8 limbs or aspects of lifestyle, in the West the most practiced of these include breath control (pranayama) and postures (asana’s) and to a lesser extent meditation, diet and spiritual development. In modern times there have been a number of variations of basic practices. Whilst some of these practices emphasize the flexibility and strengthening aspects of yoga (Asana), still others have been developed for use with specific populations for improvement of medical conditions (La Forge, 1997). There are however other important aspects of yoga as a healthful exercise or practice, namely meditation or mindful awareness which aims to achieve a state of relaxed awareness. This “mindful awareness” has been used in other programs to elicit healthful outcomes related to what is sometimes called the relaxation response (Shapiro, Oman, Thoresen, Plante, & Flinders, 2008).

Whilst there have been many attempts to scientifically quantify the numerous health benefits offered by the practice of meditation specifically (Ospina et al., 2007), as well as yoga, many of these studies have lacked the rigorous methodological systems of
analysis which may better explain the underlying mechanisms. Further whilst it could be argued that all forms of exercise training or practice require and or enhance multiple aspects of health including the improvement of cognitive function (Kramer et al., 2003) and mental health, in response to both acute and chronic bouts of exercise (Hillman, Weiss, Hagberg, & Hatfield, 2002). These forms of exercise do not focus specifically on mindfulness development.

Through the adoption and practice of yoga individuals may be able to gain positive experience of both physical activity as well as developing a sense of mindfulness, which could further mediate healthful lifestyle choices. A recent review of mindfulness based physical interventions in breast cancer survivors examined the state of research relating to four activities that have what is considered to be both a mindfulness component as well as a physical activity component. Yoga, Tai Chi Chuan, Pilates and Qigong were the focus of the review as the four most studied and well known of these activities. Yoga is however studied more often than the others with better methodology but there is no standard protocol. However, there has been links to numerous positive outcomes including improved fatigue, sleep, anxiety and depression (Stan, Collins, Olsen, Croghan, & Pruthi, 2012).

**Meditation and Mindfulness**

Eastern meditation practices are varied and have their roots in the many religious and philosophical traditions of the region such as the hindu vedas, Yoga Sutra’s, Tibetan Buddhism and Japanese or Zen Buddhism. Mindfulness meditation is one specific type of meditative practice (*vipassana or insight meditation*) associated with eastern Buddhism in which the practitioner is encouraged to cultivate of nonjudgmental, moment-to-
moment awareness both during the formal mediation practice and in everyday life (Kabat-Zinn, 1991).

One of the primary goals of a comprehensive operationalization of mindfulness is that it will help with an accurate assessment of the construct. This assessment in the context of treatment or intervention can then be used as support for the efficacy of such efforts towards mindfulness but also as a means of assessing a patient’s or person’s need for such tools in the first place. It would seem that through variety of cognitive and lifestyle related practices that some individuals naturally espouse mindful awareness in their daily life.

“Mindfulness” is a construct that in many ways is a Western attempt to define psychological processes that are espoused in the Eastern context of spiritual development. As such there are a number of different definitions and operationalizations that have been proposed. Mindfulness has been described in a modern, Western context by Jon Kabat-Zinn as “paying attention in a particular way: on purpose, in the present moment, and non-judgmentally” (Kabat-Zinn, 1994). Bishop and colleagues (Bishop et al., 2004) proposed a two component model of mindfulness. The first component involves the maintaining of attention on the immediate experience, which allows for recognition of mental events in the present moment. The second component involves adopting an orientation of curiosity, openness and acceptance.

With regard to the first component, self-regulation of attention, it is here that most efforts into developing mindfulness begin. Simply observing as thoughts, feelings and sensations arise allows the individual to be alert to their current experience. One popular method involves bringing attention to the breath and then allowing thoughts to be
noticed. This requires some skill in the practitioner with regard to sustained attention. Furthermore the ability to *switch* attention is another skill necessary to maintaining a mindful awareness of the present moment. *Switching* (Posner, 1980) is having the flexibility to switch attention back to the breath, for example once a thought or sensation has been acknowledged. Furthermore by maintaining a present moment focus of attention a practitioner is able to avoid ruminative thought patterns or in other words the tendency to over elaborate as to the meaning of events or thoughts and the possible outcomes and implications therein (Teasdale, Segal, & Williams, 1995).

There are a number of different techniques that involve bringing a mindful awareness to the present through some form of meditation practice but generally they involve the same process or set of processes. A meditative practice begins by bringing oneself to a comfortable sitting position. In the East this would have been a position on the ground but this is not accessible to most people in the West and it is important that there is not undue physical discomfort in the chosen position as this will distract from the exercise of mindfulness. Next the practitioner brings attention to the present by focusing usually on the breath, and perhaps noticing any other physical sensations in the body. It is normal during this time to have distracting thoughts arise in the mind. Importantly an attempt is made to just be aware of the thought but not to judge any meaning therein, but to then bring the attention back to the breath. The purpose of the structured approach to this practice is that over time a person will be able to shift to this state more easily during the day or when stress producing thoughts arise in response to some stimuli in the environment. By quietening the reactive emotional responses associated with rumination and negative cognitive processes a person can dampen the physiological stress response.
Once this approach of nonjudgmental awareness of the present is developed it allows the practitioner to observe the thoughts, feelings and sensations associated therein with a sense of non-attachment. In other words there is a tendency to realize that thoughts are just that, thoughts, and not necessarily facts. Openness to the experience of observing these thoughts can lead to a less affective response to private experience. Bishop et al (Bishop et al., 2004), therefore define mindfulness as “a process of regulating attention in order to bring a quality of non-elaborative awareness to current experience and a quality of relating to one’s experience within an orientation of curiosity, experiential openness, and acceptance”.

Another of the points made by Bishop and colleagues in their discussion and operationalization of mindfulness was that it is important to understand mindfulness as a psychological process that is a distinct construct. Within the literature of psychology there are a number of constructs which are similar to mindfulness (introspection, observing self and reflective functioning) but also others that may be more related to the outcome of practicing mindfulness such as self knowledge, insight and self awareness (Bishop et al., 2004). Therefore accurately assessing the impacts that mindfulness training can have on the individual within the context of an intervention is important. By delineating the specific mechanisms through which mindfulness can lead to improved psychological functioning, clinicians and researchers can more effectively target treatment to a patients needs. This more clinical focus has led to alternative means of evaluating mindfulness as a construct.

Moreover, with this empirical nature of Western medicine there is an interest in being able to reduce and understand the processes and mechanisms that explain how
“mindfulness” is able to improve mental health of individuals through a stress reduction process. Advances in Neuroscience have allowed scientists to image the brain and neural networks during active phases of meditation and associated practices to visualize how the brain responds. Vargo and Colleagues (Vago & Silbersweig, 2012) postulate what they call the S-ART or Self awareness, Regulation and Transcendence model of mindfulness. This approach is described a systems based neurobiological model that explains mechanisms by which mindfulness can allow the maintenance of a healthy mind. This is a very complex assessment and deconstruction of the mindfulness practices that are proposed to lead to the development of the skill itself. It aims to serve as a framework within which to allow future understanding to develop such that the specific aspects of mindfulness may be applied in a medical context and for the treatment of psychological disorders. This approach is deemed to be a goal for where the field may go in the future and by current understanding does not serve as a useful model by which to measure and assess mindfulness.

Fletcher et al (Fletcher, Schoendorff, & Hayes, 2010) in a manner similar to Bishop believe in the importance of evaluating mindfulness within the context of accepted and tested psychological theory. In this regard the authors propose the framework of the Approach and Commitment Therapy (ACT) which in turn is a part of the wider Relational Frame Theory (RFT), a behavioral theory of cognition. ACT sees the mindfulness process as being a central tenant of psychological well being and is an approach that targets psychological flexibility. This is ability to respond flexibility in a variety of situations and to ones history in terms of thoughts, feelings and sensations whilst still in accord with ones values. Furthermore the view of the authors is that
developments in neuroscience can offer important insight into the biological and neural functioning at the level of the brain in relation to the mindfulness process. It is however important to do so while simultaneously understanding the psychological processes that foster behavioral responses to one’s environment. The four main psychological processes as described by Fletcher and Hayes (Fletcher & Hayes, 2005) within ACT are Acceptance, Defusion, Present-moment awareness and the Observer self. These processes are thought to underly the way in which mindfulness allows persons to change their approach to cognitive action and are therefore the targets of ACT.

Operationalizing of mindfulness allows for more concise attempts towards its measurement—one approach has been to determine the underlying structure of the construct through factor analysis. By analyzing the results of multiple self-report instruments (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; R. A. Baer et al., 2008; Bishop et al., 2004), the factors or latent variables within a construct are then tested for their content, criterion and discriminant validity with other well understood constructs for example psychological well-being (PWB) and profile of mood states (POMS). Another approach is to measure neural activation of specific brain areas with fMRI—shown to be associated with differential aspects of mindfulness as quantified with a self-report measure (FFMQ) (Paul, Stanton, Greeson, Smoski, & Wang, 2013). Importantly, while operationalization of mindfulness in the current work recognizes that there may be complex neurological mechanisms driven by psychological processes—we also concede that measuring them in the context of the current study is not possible. Our approach is to use two separate self-report measures, shown through multiple studies to be associated with change in mindfulness over the course of training therein. One of the most well–
studied, mindfulness based approaches for treatment of psychosocial, physiological and emotional symptoms is mindfulness based stress reduction (MBSR).

**Mindfulness Bases Stress Reduction (MBSR)**

Jon Kabat-Zinn (1982) (Kabat-Zinn, 1982) first described the use of mindfulness meditation (MM) as an intervention in 1982. The MM was delivered as a stress reduction and relaxation program (SR&RP) through the outpatient service of an academic medical center. The aim was to test the clinical effectiveness of meditation for the treatment of chronic pain in patients who would not respond to traditional methods of medical treatment. A very specific aspect of this program was that all meditation techniques were taught in the absence of religious or cultural practices from which these methods came. MM was delivered over a 10 week period and targeted the self regulation skills of patients experiencing a wide variety of pain symptoms. Specifically, meditation was used to develop a detached observation of proprioceptive phenomena (pain). By decoupling the sensation of pain from the affective reaction to the pain, the suffering of the patients could be reduced. Following the 10 week program 65% of the patients treated reported up to a 33% reduction in pain symptoms. The self report measure used was the Melzack pain rating index. The findings of this important study paved the way for the development of the mindfulness based stress reduction (MBSR) program and led the author to conclude that meditation and its outcomes can be used as the basis for a behavioral program of self regulation.

In a more recent study, Dobkin (2008) (Dobkin, 2008) examined the underlying mechanisms associated with reported improvements in symptoms following an MBSR intervention for breast cancer survivors. The author used a mixed methods approach to
both qualitatively and quantitatively explore the relationships between self reported outcomes of interest and information gleaned from personal and group interviews such that they may elucidate the mechanisms at work. The author reported that the mindfulness attention awareness scale (MAAS) was a useful process measure for capturing any changes in mindfulness that may occur as a result of the intervention. Another self report measure, the coping with health injuries and problems questionnaire was useful for documenting changes in self care practices. Finally the sense of coherence (SOC) questionnaire seemed to indicate that women found life more meaningful post intervention. These findings lead the author to support the view of Shapiro et al, (Shapiro, Carlson, Astin, & Freedman, 2006) and conclude that following MBSR participants tended to re-perceive their daily experiences. This is a process by which changes in intention, attention and attitude of the patient lead to reductions in symptoms.

**Mindfulness Based Interventions (MBI)**

There have been many iterations of mindfulness based interventions (MBI) for the treatment of chronic disease and chronic disease related behavioral, psychological and physiological health—some of which have directly stemmed from the initial MBSR—for example the fairly well known mindfulness based cognitive therapy (MBCT). Another program, initially called mindfulness based stress reduction-low dose (MBSR-ld), now Mindfulness in Motion (MIM) to better reflect its focus on yoga—uses similar approaches to mindfulness training as the father program, however low dose because the time commitment deemed necessary to elicit the benefits of training are significant.

Many attempts at behavioral change, including those that target diet and physical activity—cite the most commonly faced barrier to adherence as being time constraints in
subjects’ lives. MBSR-lld, was a 6-week program requiring 1 hour per week—in addition
to home based practice of 10–20 minutes per day. This lower time commitment program,
while still offering the process of mindfulness development was first examined in a
sample of faculty and staff at The Ohio State University (Klatt, Buckworth, & Malarkey,
2009). In this study, investigators used self report of perceived stress, sleep quality, and
mindfulness (MAAS). A biomarker of stress; salivary cortisol was also assessed on a
weekly basis. Improvements were found in both mindfulness and perceived stress. Since
the initial study the MIM program has increased to 8 weeks in length and has been
investigated with a larger sample of adults—faculty and staff working at a large state
university (Malarkey, Jarjoura, & Klatt, 2013). In this study 186 adults were selected for
inclusion based on high levels of C-reactive protein (CRP)—a biomarker of
inflammatory stress in the body. The program was found to significantly increase
mindfulness; a finding that was maintained up to 12 months later. There were however no
significant differences between the intervention and control group on measures of
inflammation, however this seemed to be moderated by BMI, with persons <30kg/m2
having significant improvements in CRP levels.

MBI’s use variations of a structured approach to mindfulness training with an aim
of improved psychological functioning—these skills can lead to increased resiliency for
patients. Ultimately these tools provide them with the ability to manage their response to
challenges through their treatment and recovery. By more reflectively and less reactively
responding to stressful conditions patients can avoid activation of the hormones and
mechanisms of the sympathetic nervous system—the flight or fight response. This
heightened state of physiological stresses often maintained by ruminative thoughts—
many of which are inappropriate. Over time this process places persons at increased risk of chronic disease and reduced rates of immune functioning (Kiecolt-Glaser et al., 2002). One group of patients in particular who are at risk for high stress and psychological disturbance are cancer patients—some estimates of major depression ranging from 10-25% (Pirl, 2004). Understandably, these patients are challenged enough by the primary treatments for their disease and risk for comorbidity should be reduced as much as possible. There have been multiple examinations of MBSR for a wide variety of cancer survivors and patients. Increasingly the role that stress reduction can play in the supportive oncology context is being recognized.

A recent review of mindfulness based interventions that also included a physical activity component (Yoga, Tai Chi, Pilates and Qigong) in breast cancer survivors (Stan et al., 2012) reported that Yoga was the most commonly studied modality. Studies that included yoga were the strongest methodologically and reported a number of outcomes associated with the interventions. Yoga was found to have a positive impact on fatigue, as well as sleep, anxiety, quality of life and post chemotherapy nausea and vomiting. The authors also concluded that at the current time the evidence supporting the other modalities was not sufficient to support their use in a clinical setting.

In another very comprehensive systematic review of mindfulness based interventions for cancer care—Shennan et al, (2011) (Shennan, Payne, & Fenlon, 2011) searched multiple databases, including PubMed, Medline, as well as Web of Science for unpublished abstracts and conference proceedings. Following exclusion, 13 papers were examined for the final review process. The studies included, consisted of mindfulness-based interventions specifically—any papers that also included yoga and other related
activities were excluded. The majority of studies examined the MBSR program with two others focusing on MBCT. Of the 13 included studies—3 were randomized controlled trials, 2 non-randomized trials, 5 pre–post test and 2 qualitative designs. Significant improvements were reported for anxiety, depression, stress, sexual function and immune function. The authors identified inconsistencies in study design as a limitation—however there seemed to be enough evidence of benefits across the cancer trajectory to warrant future trials.

In a novel intervention, mindfulness based art therapy (MBAT) was delivered over a period of 8 weeks to 191 women with breast cancer, who were experiencing high levels of stress (Monti et al., 2013). Women were stratified by stress level and then randomized into the treatment group (MBAT) or into a breast cancer educational support group of equal time and duration. Results showed that while both groups showed significant improvements in psychosocial health and quality of life immediately post intervention—only women in the MBAT who had high baseline stress—showed improvements in all measures of psychosocial stress at 6-months post intervention. Also included in the analyses was a comparison of persons of color and white participants; despite higher reported levels of education and marital status for white women there were no differences in how they benefitted from the program.

**Outcomes of Mindfulness**

One of the most commonly targeted outcomes of interest for those studying mindfulness is that of stress reduction. Psychological stress is related to multiple domains of well-being and quality of life and as such many of the associated outcomes of decreased stress fall under the umbrella of quality of life (QOL) and more specifically
health related quality of life (HRQL). For the current study we will use both broad and disease specific measures to assess the initial deficits in—and potential improvements in QOL following intervention.

In an important evaluation of the effects of mindfulness—defined and operationalized in a previous section as a two component model (Bishop et al., 2004)—Branstrom et al., (2010) conducted a randomized control trial with a variety of cancer survivors (Branstrom, Kvillemo, Brandberg, & Moskowitz, 2010). The study used the MBSR program to examine whether mindfulness improved perceived stress and psychological well-being. Furthermore the study aimed to test whether mindfulness was a mediator of change in outcomes of interest. Participants in the intervention group had significantly lower perceived stress and post-traumatic avoidance symptoms as well as increased positive states of mind. Mindfulness as measured with the FFMQ was higher in the intervention participants compared with controls and additionally FFMQ scores were found to mediate the effects of the intervention on perceived stress, post traumatic avoidance and positive states of mind. This approach is an important step towards understanding the mechanism through which MBI’s can impact psychological well-being. Furthermore when researchers examine behavior within the context of theory they aim to target mediating variables—a practice that can improve the quantitative design quality of studies.

Theories of Behavior Change in Endometrial Cancer Survivors

Theories are in their simplest form models that allow us to represent either graphically or conceptually the relationships between constructs or hypothetical phenomena. We can have notions about the existence of certain aspects of behavior but
theory is what allows the attempt to link these abstract ideas—and measure them. In psychology and behavioral research, having a theory of the way certain facets of a persons’ biology, environment and behavior interact and under which particular conditions, allows us to a) measure, explain and predict future behavior under similar conditions and b) gives us a way of manipulating key variables in order to effect some change in a behavior. For example in Figure 4, we could hypothesize that female breast cancer survivors (FCS) will engage in leisure time physical activity (B) on their own terms under certain conditions A and C, which will lead to improved physical function (PF) and increased quality of life (QOL). By testing and evaluating this theory or model to both understand and then targeting conditions A, B and C—we can possibly improve physical fitness and quality of life of these women. Furthermore, having a measure of the expected benefits and under which conditions survivors may improve we can better allocate resources within the clinical setting. For example if we find that cancer survivors who are undergoing chemotherapy—and experiencing pain—cannot feasibly engage in meaningful PA, then asking them to do so is not a good use of their time. Theories provide a framework, which can be adjusted overtime, based on empirical evidence. This process can also aid others engaging in the examination of novel study populations by suggesting what does and does not work. Two well known theories of behavior that have been studied in the literature of physical activity and lifestyle are the social cognitive theory (SCT) put forward by Ablbert Bandura (Bandura, 1986), and the self determination theory of Edward Deci and Richard Ryan (Deci & Ryan, 1985).
Self Determination Theory

Self Determination Theory (SDT) is a macro theory of motivation. The research informing the development of this theory was conducted in the 1970’s and has continued to evolve as the scope of behavioral research using the theory has expanded. In their book “Intrinsic Motivation and Self-Determination in Human Behavior” (Deci & Ryan, 1985) describing the SDT the authors set forth the basic tenants of the theory.

The SDT is composed of five related sub-theories. Cognitive evaluation theory is the evaluation of the importance of the social environment and how it affects motivation to engage in certain behaviors. Organismic integration theory evaluates the impact of extrinsic motivation in behavioral decisions and how this process may become internalized. Causality orientations theory relates to the variability with which individuals are motivated to engage in autonomous behaviors, in addition this sub-theory describes how persons with different dispositions adapt in different environments. The basic needs theory, which is an underlying aspect of the previous theories, posits that in order for an individual to achieve growth there are basic psychological needs that must be met, namely Autonomy, Competence and Relatedness. A fifth sub-theory of SDT is the goal contents theory—an examination of the contrast between goals that grow out of extrinsic vs. intrinsic motivations. For example it is thought that goals related to desire for wealth, popularity and fame, might be associated with ill health and well-being when compared with those motivated by a sense of community, well-being and personal growth. In Summary SDT has as its goal the examination of people’s inherent growth tendencies and innate psychological needs that form the basis of motivation as well as the conditions that foster the above mentioned processes (Ryan & Deci, 2000).
In addition to the five sub theories of SDT, Deci and Ryan also value *Mindfulness* as a process through which behavior is modulated. In their view mindfulness may be a foundation of autonomous regulation of motivation. One of the commonly used self report measures developed by Brown and Ryan (Brown & Ryan, 2003) is the Mindfulness Attention Awareness Scale or the MAAS. This is a one-dimensional evaluation of the degree of mindfulness with which an individual approaches certain situations and daily life. In a recent review of the role of SDT and mindfulness—and how it may be understood within the context of stress incursion and response—Weinstein and Ryan (Weinstein & Ryan, 2011), suggest that less stress incursion and a more adequate response to life events are associated with more autonomous functioning, higher levels of mindfulness, a greater focus on intrinsic vs. extrinsic goals.

Motivation within the context of SDT is not seen as a singular construct—rather it lies on a continuum. It has on one end non self-determined amotivation, which is by its nature unregulated. This is an unhealthy form of motivation and will not foster efforts into personal growth. Extrinsic motivations are those that have the effects of driving behavior but like amotivation, extrinsic motivation is not seen as the kind that fosters personal growth and long-term attempts at behavior change. It is externally regulated and often driven by things such as rewards and or threats. As external forms of motivation becomes more internally regulated and autonomous it moves towards more intrinsic forms of motivation. Intrinsic motivation is characterized by interest, enjoyment and inherent satisfaction. It is this second tier or sub-theory known as organismic integration theory (OIT) or the self-regulatory facilitators that allow a person to move along the continuum towards self-determination.
Figure 3 Self-Determination Theory (SDT)

With this background in mind it is therefore seen as important to understand the mediators of health behavior change. For many health care researchers the process of change is seen as being externally motivated. Patients are driven by either a reward of health in the future or by a fear of continued ill health in the present. For patients to exercise control over their behaviors they need to internalize and integrate their motivation, therefore they need to value personally the prescribed actions and outcomes of their behavior in order that it is a lasting and committed effort. For example, it is common for endometrial cancer patients and survivors to be prompted to change their dietary behaviors and increase their exercise—due to the high levels of obesity within this patient population—however the actual levels of these behaviors has been shown to be extremely low (Modesitt, Geffel, Via, & A, 2012; von Gruenigen et al., 2011).

A number of interventions have sought to foster the conditions necessary for successful behavior changes within the context of improved health by using the structure and framework of the SDT (Ryan, Patrick, Deci, & Williams, 2008). Through developing a sense of *autonomy* and of *competence* individuals are most able to internalize and
integrate their motivation—leading to efforts at behavior change that are maintained in the long term. Furthermore, persons are more likely to adopt the lifestyles and behaviors promoted to them if they feel a sense of relatedness or connection to those promoting them. A test of the SDT relating to exercise—conducted by Edmunds et al., (2006) examined persons who participated in group exercise classes—found that fulfillment of the 3 basic psychological needs was related to self-determined motivational regulations. Furthermore, identified and introjected regulatory styles were associated with both strenuous and overall exercise levels.

Whether this would also apply to endometrial cancer survivors is unclear. It is possible that the knowledge that the primary disease process is related to lifestyle factors—poor diet and low levels of physical activity—would cause survivors to be either amotivated or extrinsically and externally motivated. “My doctor says I need to change for my health’s sake” rather than “I walk or exercise and eat a healthy diet because I would like to be healthier”. While it is likely that the starting point for any behavior change needs or will be externally motivated, SDT posits that unless the individual internalizes the reasons for behavior change then the behavior will not be long lasting. Indeed it is well known that lifestyle interventions are effective at changing behavior during the active engagement process, but that over time the benefits gained through the intervention are lost as adherence declines over time. This loss of benefit has prompted researchers to enhance the behavioral component of interventions to provide people with tools to maintain their good behaviors over time (Focht et al., 2012).

SDT was used as the framework within which to examine the hypothesis that patients in a weight loss program would be more adherent and therefore lose more
weight. The finding that more autonomous individuals and those that perceived the health care environment as supportive—leading to greater attendance and weight loss—supported this hypothesis (Williams, Grow, Freedman, Ryan, & Deci, 1996). The autonomous motivation level of patients was also found to be predictive of long-term maintenance of weight loss. This examination of a proposed model to determine whether the components of the SDT—showed that both the degree to which patients felt supported and whether their motivations were internalized offer support for the idea that interventions that foster this environment could be more successful than those not designed based on theory. This may further provide support for a mindfulness-based intervention that could serve to foster autonomy, within a group based setting.

SDT theory has not to my knowledge been studied extensively within endometrial cancer survivors, however Milne et al, (2008) conducted a study in breast cancer survivors (Milne, Wallman, Guilfoyle, Gordon, & Corneya, 2008). 558 breast cancer survivors answered questionnaires to measure their perceived autonomy support, motivational disposition and their competence to engage in physical activity. Survivors who achieved PA at the level recommended by the current guidelines—150 minutes/week—had higher levels of intrinsic motivation, perceived competence, autonomy support and a more identified regulatory style. Regression analysis further revealed that SDT constructs explained roughly 20% of the variance in PA behavior. These findings lead the researchers to suggest that this may be a useful model for understanding the way breast cancer survivors engage in physical activity. Because there are many characteristics of breast cancer survivors that are shared with endometrial
cancer survivors it was decided this may be a useful model for the design of lifestyle interventions in the future.

However, there are a number of other theories that have also been used to examine the health behaviors of individuals. One of the most often used—albeit in an incomplete or inappropriately reported manner—is Bandura’s social cognitive theory (SCT). In addition to the main theory, one of the sub-theories of SCT is also a target of many lifestyle or behavioral examinations; namely self-efficacy (SE).

**Social Cognitive Theory**

Albert Bandura developed the social cognitive theory (SCT) (Bandura, 1986), in which he described a complex theory or human behavior. The social cognitive approach posits that there is a reciprocal determinism in action, whereby the person (beliefs, expectations and attitudes), environment (social and physical) and behaviors themselves interact to shape a person’s motivation to act in a certain way. Social cognitive approaches to exercise and wellness are based on the idea that a person’s goals, expectations, beliefs and attitudes as well their interaction with external or environmental factors will impact their motivations to behave in a healthful way.

One of the primary sub theories of SCT is self-efficacy theory. Self-efficacy has become a well-established construct within the exercise psychology landscape. Self-efficacy deals with an individual’s situation specific confidence in their ability to complete a task that will then lead to an expected outcome. This theory deals with the extent to which a person believes they will be successful given their current skill set. Hence self-efficacy is very task specific and situation specific. A person will tend to have greater confidence in their ability to complete a task when they have prior successful
experience of that task. Alternatively if the task is novel to them they can still have a high self-efficacy if they can witness a model whom they deem to be similar in skill level to themselves.

![Social Cognitive Theory (SCT)](image)

Figure 4 Social Cognitive Theory (SCT)

Self-efficacy and the larger SCT have garnered a large amount of interest among physical activity and exercise researchers. In a study of efficacy beliefs and their relationship with QOL in an older sample of adults—McAuley et al, (McAuley et al., 2006) tested multiple hypotheses regarding influence of self-efficacy on health status and global quality of life. The authors examined baseline data from a sample of 249 older individuals (Mage=68.12) using a structural equation modeling approach. This analysis can measure a “goodness of fit” of a proposed theory to the data. It was hypothesized that the relationships between SE, exercise and physical activity—measured with multiple
self-report tools—and health status and QOL were all indirect—in fitting with the pathways proposed by SCT. It was in fact found that the influence of PA on QOL was mediated through more proximal aspects of SE and health status—offering support for the proposed model. The goodness of fit indices were as follows for their main model; $X^2= 114.06$, df=52, SRMR= 0.04, CFI= 0.96. This further substantiates the use of more complex statistical methods to evaluate the intricate relationships between persons, their environment and their behavior—which is further influenced by personal goals, expectations and beliefs.

One weakness of SE—due to the increased lay knowledge of the construct—is that it is often cited as an important theoretical construct without having being hypothesized to influence a relationship a priori. In other words—post primary analysis—it is determined to be a major correlate of the primary outcomes to better explain findings. Furthermore, as Bandura himself felt, many other theories of behavior include self-efficacy, however they call the construct by different names. One such example may be perceived competence from the SDT.

The population of cancer survivors is increasing all the time as a result of improved medical screening and treatment regimens. Many of these cancer survivors are faced with a multitude of challenges to their health and well-being. Using a Social cognitive perspective, Hoffman and colleagues, (Hoffman, Lent, & Raque-Bogdan, 2012) reviewed the literature for evidence of the ways in which cancer survivors cope with the changes and life adjustments they must face following a diagnosis and treatment for cancer. They cite the use of the SCT approach as a comprehensive and complete way to address the impacts that the environmental support structures, personality traits and
coping mechanisms can have on a cancer patients return to a state of well-being. The goal of their review of the literature was to better inform counseling psychologists of the needs of cancer survivors but also to highlight the role that counseling psychologists can play in this process of attaining well-being as a cancer survivor. Further suggestions offered are; more comprehensive use of theory when designing studies—in order to assess the multiple impacts that aspects of environment, behavior, personal motivations and expectations can have on patient’s recovery. Another suggestions is that by using multiple time points of measurement we can more accurately assess the temporal changes in recovery of well being—by having baseline data on well being of patients a more accurate and realistic goal for recovery may be set. Finally by accepting that even though we study and make conclusions about specific groups of cancer patients i.e. Breast cancer survivors—there may be within group differences that require further investigation—not all patients respond to treatments.

Von Gruenigen et al, (von Gruenigen et al., 2009) conducted a trial in which they examined the behavioral mediators of QOL outcomes in a population of EnCa patients. Their findings explored the role of self-efficacy (SE) mechanisms related to successful weight loss efforts. The findings suggested that morbidly obese subjects had significantly lower self-efficacy especially when experiencing physical discomfort. For those individuals who were randomized into the 6-month lifestyle intervention, there were significant increases in SE for social pressure (p=0.03) and restraint (p=0.02). Furthermore they found there to be significant differences in several self-efficacy and quality of life outcomes for women who lost weight compared to those who did not. Specifically differences existed for emotional well-being (p=0.02), self-efficacy
related to negative emotions (p=<0.01), food availability (p=0.03) and physical
discomfort (p=0.01). This reported relationship between different forms of SE—given
that it is theoretically situation specific—highlight a number of targets for interventions
aimed at improving quality of life for patients with obesity as a comorbidity.

In a more recent trial social cognitive theory variables were found to predict
exercise behavior in 100 post-treatment EnCa patients (Basen-Engquist et al., 2013).
Basen-enquist and colleagues provided the 100 subjects with a home based exercise
intervention and collected ecological momentary assessment (EMA) using hand held
computers for 10-12 day periods every two months for the 6 months of the trial. Patients
reported their self-efficacy and expected outcomes. Additionally participants wore
accelerometers. It was found that morning self-efficacy significantly predicted afternoon
minutes of exercise (p=<0.01). Morning positive outcome expectancies were also
associated with exercise—however not after controlling for self-efficacy in the model.
This system of analysis unfortunately does not allow the same level of exploration as
structural equation modeling, although the relative importance of a theoretical construct
to behaviors can be indicated.

One of the primary tenants of SCT theory driven interventions is that they provide
the subject with the opportunity to increase self-efficacy for the behavior that is valued—
increased physical activity or improved diet. A supportive environment where group-
based interventions can be successful, may lead to increased self-efficacy for exercise
and PA. High SE can in turn result in better adherence to the intervention—enhancing
health related outcomes. McAuley and colleagues examined how SE cognitions—
perceptions of self-efficacy for exercise—were related to the adoption and maintenance
phases of exercise adherence in older adults (McAuley, 1992). Interestingly while there was support for this relationship, previous experience of exercise was the most important factor in their model. In a further study the same group evaluated the role that SE played in the long–term maintenance of exercise behavior in older adults (McAuley, 1993). The findings of multiple correlation and regression analysis were that self-efficacy strongly predicted exercise behavior following the intervention; $R^2=.301$, $F(4,54)=6.04,(p<.001)$, after controlling for aerobic capacity and program attendance. Using an ongoing measure of self-efficacy during an intervention may therefore offer a means of measuring as to whether the intervention is likely to have lasting effects on its participants.

Program adherence has been a key concern of trials aiming to improve health outcomes. Whether interventions use physical activity, lifestyle change or drug regimens as the mechanism for improving outcomes—better adherence leads to greater response to treatment. One of the increasingly targeted peripheral outcomes of interest to many researchers and clinicians is health related quality of life (HRQL) and quality of life (QOL).

**Quality of Life**

Quality of life (QOL) and health related quality of life (HRQL) are terms that are used often in the literature of psychology, behavioral, medical and related disciplines. The view of mainstream psychology is one of QOL reflecting an overall life satisfaction (Diener, 2000) (Rejeski & Mihalko, 2001) or satisfaction with ones life in a global sense, while the term HRQL is more related to the medical fields use of and conceptualization of QOL—a measure of “health” status. In this operationalization, HRQL is an umbrella term that encompasses the functioning of an individual in related but distinct functional
domains, such as physical function, psychological well-being and social relationships. This structure seems to show some evidence of being hierarchically organized whereby more proximal discreet aspects of functioning (HRQL) are related to more distal global aspects of well-being and satisfaction with life (SWL). It is therefore often a challenge to draw conclusions from the QOL research—different fields and researchers operationalize this construct in different ways. There has been a number of attempts or at least suggestions regarding the importance of unifying these concepts so that one set of constructs that is measured and understood in the same way by different researchers may be applied to various fields.

There are specific measures to tap into these aspects of both QOL and HRQL, however measures should be used in a valid and reliable way so as not to confuse the constructs being examined. For example a measure such as the Medical Outcomes Study Short Form-36 (SF-36) is a generic measure of aspects of HRQL. Underlying subdomains being measured include both mental and physical aspects of HRQL. This should not be used to make conclusions about overall well-being or satisfaction with life. A person with knee arthritis may experience significant daily pain and this will be reflected in a measure specific to physical functioning and pain such as the Western Ontario McMaster Arthritis Scale (WOMAC), an arthritis specific measure of HRQL but this does not mean the person will experience low or poor life satisfaction. There is some indication that the value a person places on a specific domain of HRQL may determine the impact that it has on more distal measures of QOL or life satisfaction. Again in regard to a person who has been able to be physically active their whole lives, experiencing declines in physical function may impact heavily on global satisfaction with life.
Physical activity and more specifically structured exercise has been evaluated extensively for its efficacy in improving HRQL but also more globally QOL. Due to the impact that exercise can have on outcomes associated with cardiovascular health and muscle strengthening, it is particularly valuable for correcting impairments that may develop as a result of chronic disease or simply as a means of halting the normal aging process. In this sense it is a powerful tool, and some of the specific contexts in which it have been used are discussed in more detail.

Obesity and overweight have been consistently linked with chronic disease outcomes as well as overall mortality. It is therefore not surprising that self reported aspects of HRQL, QOL and different levels of body composition are frequently assessed (Katz, McHorney, & Atkinson, 2000). (Larsson, Karlsson, & Sullivan, 2002)

**QOL and Obesity**

Due the significant increase in the incidence and prevalence of obesity in the U.S. and the burdens of chronic disease conditions affecting those who are obese, exercise is an important treatment consideration. The chronic disease conditions include all of those mentioned above as well as general symptoms of pain, fatigue and declines in functional capacity. One of the primary goals of exercise is to help with the maintenance of weight or body composition and is most effective when used in conjunction with dietary adjustments (Wing, 1999). Other goals are the control of blood sugar profile and improving insulin sensitivity for diabetics and pre-diabetic patients—most of whom are overweight. Exercise is also reported to increase HRQL independently of these changes in objective measures of function, with overweight and obese adults who attained recommended guidelines reporting significantly higher HRQL than sedentary same
weight counterparts (Heath & Brown, 2009). Despite the number of studies of the effects of exercise on weight loss there is a lack of empirical evidence of the specific types of exercise and what benefits in specific aspects of HRQL they may result in. Many studies that include measures of HRQL in a behavioral sense are multicomponent interventions, making the effects of exercise alone difficult to quantify. Some literature from the studies of weight loss in diabetic patients has shown an association between higher body mass and generic physical component scores of the SF-36 (Ryan et al., 2003). An interesting finding for this study was the interaction between obesity category and MET capacity, with higher BMI associated with lower HRQL seen in individuals of low MET capacity, however this was not the case for obese individuals who had maintained a higher MET capacity. The same trial also confirmed findings in other populations, whereby the persons with the lowest levels of HRQL at Baseline saw the largest improvements. There may be a ceiling effect and that people who are high in an overall satisfaction with life (QOL) might more favorably report on more proximal measures of HRQL. This further highlights the need for researchers to target specific aspects of function depending on the population in question and identifying what may be of most importance to them in their daily lives. Another consideration is that different diseases related to obesity may moderate HRQL outcomes of exercise. Obese cardiac patients may value and respond to different aspects of exercise than obese cancer patients or obese osteoarthritis patients.

**QOL and Cancer**

Many aspects of cancer diagnosis, treatment and survival are associated with declines in physical, mental and emotional well-being. Some of the most significant side effects of adjuvant therapies include pain, fatigue, changes in body composition and
reduced physical functioning. Exercise has been identified as having an important role to play in managing both the short and long term health of cancer survivors of whom there are more every year. In the short term—during treatment with chemo and radio therapeutic agents—damage to the heart and organs are common. Exercise may help to protect this cardiovascular function by offsetting declines in aerobic capacity (Jones, Eves, Haykowsky, Freedland, & Mackey, 2009). In the longer term survival is associated with increased rates of chronic disease such as heart disease, diabetes and osteoporosis. The majority of exercise interventions in cancer patients have examined populations of breast cancer survivors, however this has now spread to prostate cancer patients, colon cancer patients and hematological cancers among others. Evidence has shown that disease specific, generic indices and global satisfaction with life have all been assessed in cancer survivors in relation to exercise. Results have been positive with consistent clinically meaningful improvements in multiple HRQL outcomes, such as pain and fatigue on a proximal level and more broadly global satisfaction with life. The Supervised Trial of Aerobic and Resistance Training (START) trial was a multicenter study conducted in breast cancer patients undergoing chemotherapy that utilized both aerobic and resistance exercise programs (Courneya et al., 2007). Both forms of exercise were related to improvements in aspects of HRQL (FACT-Anemia), however the benefits of each form of exercise were slightly different. This highlights the need for an understanding of which factors determine (moderate) the forms of exercise that will be most beneficial to specific individuals or groups of individuals. For example in the FAST study, women who were randomized in to the resistance training arm reported the most change in a cancer specific measure of HRQL. Another factor that may moderate the
effects of exercise is the stage of the disease within which the patient is living. For example exercise may need to be tailored specifically depending on whether the person is newly diagnosed, within treatment or 5 years into survivorship. The cancer continuum is a model that offers much promise for the guidance of exercise based interventions to target specific aspects of HRQL in cancer survivors and patients (Courneya & Friedenreich, 2001).

In a novel approach to assessing the non-cancer related health status of survivors, (Cho, Mariotto, Mann, Klabunde, & Feuer, 2013) examined the Surveillance, Epidemiology and End Results (SEER 2000-2006). By linking the surveillance results to medicare claims they were able to quantify comorbidity prevalence. For early stage breast and prostate cancer patients survival from non-cancer related comorbidity was higher compared with the US population, however for lung cancer patients had worse comorbidity than other cancer patients. This paper is a first attempt to use a larger national database to understand the landscape that is comorbidity—by cancer site—and may provide the basis for patient care through survivorship. Health status, which can otherwise be seen as HRQL in terms of the medical fields assessment, may increasingly point clinicians towards areas of concern and therefore optimize prevention of cancer related comorbidity and ultimately quality of life in a broad sense.

Some of the most salient aspects of HRQL known to have an impact on general wellbeing are sleep quality and psychological and social stress. Sleep quality is important to assess as many self reported aspects of HRQL may in fact be linked to poor quality of sleep.
Sleep Quality for Cancer Survivors

From among 823 patients receiving chemotherapy—mean age of 58 years—as many as 30-90% reported impaired sleep quality post chemotherapy treatment (Palesh et al., 2010) and as such there have been attempts to improve this aspect of HRQL. In a study designed to explore the efficacy of a yoga program to improve sleep in 410 survivors suffering from sleep disturbances. Mustian et al., (2013) used a specifically designed YOga for CAncer Survivors or the YOCAS intervention. Participants met 2 x weekly for a period of 4 weeks where they learnt breathing techniques, gentle restorative asanas or poses and meditation. In this study participants who were receiving either chemotherapy or radiotherapy were randomly assigned to stander care or standard care plus 4 weeks of yoga therapy. 96% of the final sample randomized, were female, while 75% of the subject were also breast cancer survivors. The results showed that on multiple measures of sleep quality the intervention group was significantly beneficial compared with the standard of care ($p < 0.05$).

Another broad area of interest for those studying comorbidity and HRQL in cancer survivors is the degree of stress experienced in relation to receiving a cancer diagnosis and how it may affect the patient’s recovery. One of the ways in which the impacts of stress can be ameliorated is through resilience.

QOL and Resilience

Increasingly it is recognized that the cancer patient is subject to distress when evaluated across the cancer continuum. In a recent review (Carlson, Waller, & Mitchell, 2012) examined the current practice of screening for distress among cancer patients. In their view the quality of measures for assessment are at a reliable and valid level.
Furthermore by accurately screening for distress—placing persons identified into programs to help with this aspect of their care—future quality of life may be improved. However at the time of the review there was not conclusive evidence regarding the direct effects of screening on long term QOL. Of interest in this context is the degree of resistance or the ability to deal with distress—also termed resilience.

Resilience has been defined as a set of characteristics or traits that predispose or protect against the perception of stress. It has also been defined as the ability to negotiate, manage and adapt to significant sources of stress (Windle, Bennett, & Noyes, 2011). Any factors that allow an individual to adapt can facilitate the ability to be resilient. Resilience building within persons who are placed under undue stress—as during the cancer diagnosis and experience—are becoming more common place. (Leppin et al., 2014) et al, recently published a protocol describing a systematic review of resilience training programs and how they may impact QOL outcomes. The authors plan to examine randomized controlled trials designed to enhance resilience. The study will identify characteristics of study populations, and compare all primary outcomes reported—Resilience, self-efficacy and QOL. Secondary outcomes will be any findings of interest with a relationship to the primary outcomes. This study is an attempt to assimilate some of the work being done on resilience given that inter nationally there is an interest in the modifiable factors socially and environmentally that can foster resilience in patients. In the current proposal the authors stipulate that the focus of the program will not solely focus on stress reactivity as is sometimes the case with MBSR, yoga and or meditation. However a program that included these activities could still be included.
Measurement of Quality of Life

Quality of life (QOL) is usually measured with a self-report tool. There are different levels of measurement depending on the context in which the researcher wishes to evaluate QOL. There are measures designed to determine the broad aspect of a person's satisfaction with life and more disease specific measures that aim to quantify the domains of life satisfaction that are most challenged by a diagnosis and illness whether short or long term. While there are broad operationalizations of HRQL and QOL for the current study, physical function—the 400m walk test, the stair climb test and the lift and carry—will be thought of as an aspect of a patient's HRQL. Self-report measures of factors that may directly affect this functional capacity as well as related aspects of proximal HRQL will be assessed with self-report measures such as the Functional Assessment of Cancer Therapy Endometrial (FACT-En). Further generic measures such as the medical outcomes study short form -36 (SF-36) will be used in conjunction. Distal well-being and quality of life will be examined with the satisfaction of life scale.

Designing and Conducting Lifestyle Interventions within an Endometrial Cancer Survivor Population

Research at the most basic and reductionist point of view must examine—in a completely controlled environment—the direct effects of the independent variable/s on targeted outcome/s of interest. How a substance/material/chemical can act through a specific mechanism (mediation) to effect an outcome of interest is of utmost importance. Once these mechanisms are understood, the goal is to translate its action into a
meaningful effect in the real world setting. Each and every place along the continuum has its positives and also its negatives.

Within the behavioral sciences—which arguably research into exercise and dietary should be classified—it is important to be informed by the entire spectrum of research. Understanding the mechanisms through which behaviors—physical activity or dietary practice—can influence health outcomes as well as what outcomes we can expect is vitally important. Furthermore specific “doses” of behaviors can effect the salient outcomes depending on disease stage or starting point. This has implications for recruiting subjects to studies based on criteria that will give us the most power to find relationships between variables of interest (Linden & Satin, 2007). At the opposite end of the spectrum we must understand how and if these processes/behaviors are feasible in the real world. To ask whether a specific amount of physical activity, say a regimen of 3 hours of running a week at a 70% of peak volume of oxygen consumption will improve cardiovascular fitness of endometrial cancer survivors is a different question to “can endometrial cancer survivors achieve such a regimen.

In this light the current dissertation was approached from the methodological standpoint that would allude to some of the behavioral mechanisms impacting on quality of life in endometrial cancer survivors. Initially we wanted to verify the typical activity levels and dietary practices of endometrial cancer survivors and then to understand whether it was possible to deliver an intervention to target some of the identified processes.

The first approach was conducting a cross sectional survey study of EnCa survivors—by using a novel online software program to deliver a survey to patients
during their regular clinic visits. There have been previous attempts by researchers to improve the likelihood that patients visiting their oncologist will have their psychosocial concerns addressed (Boyes, Newell, Girgis, McElduff, & Sanson-Fisher, 2006). In order to facilitate the process patients were randomized into either direct feedback or control. Patients in the direct feedback condition would complete questionnaires on a computer while waiting for the oncologist visit. Their questionnaires would then be scored immediately and the results placed in their patient file. This direct feedback was found to result in a lower likelihood of patients reporting concerns at subsequent follow up visits. In a similar fashion the current study aimed to take advantage of having patients who would be waiting for their doctor—take questionnaires as to their quality of life and typical lifestyle behaviors. This was also hoped to be a method that would aid in efforts to recruit patients to a lifestyle behaviors trial in the future.

The current study was designed with the use of REDCap in mind. REDCap (Research Electronic Data Capture) is a secure web application for the development and management of online surveys and databases (Harris et al., 2009). This type of software solution is in part the response to a need for a fast and secure means of gathering and accessing data. The National Center for Research Resources has previously stated that the future will involve the collaboration of many scientists from a variety of locations and will require high speed computer networks in order that data may be collected, shared and managed.

**Recruitment**

One of the most commonly reported barriers to successful completion of randomized controlled trials (RCT’s) is the failure to reach proposed recruitment targets.
within and allocated timeframe (Campbell et al., 2007). The implications of this smaller than targeted sample size are that statistical power to detect treatment or intervention effects are limited. Another aspect of this inability to recruit participants to trials is that it means future proposals for funding may be viewed less favorably leading to a reduced likelihood of the same (perhaps meaningful) examination being attempted again. Determining the barriers to successful completion of randomized or in fact simply efficacy trials is therefore of great importance.

In one of the few intervention studies that aimed to provide a lifestyle change opportunity to early stage EnCa patients; recruitment efforts were 29% to the study with a 73% adherence rate for the active group. Furthermore 84% of subjects completed follow-up assessments at 12 months (von Gruenigen et al., 2008). Another study by Courneya and colleagues (Courneya et al., 2005) in Alberta, Canada that consisted entirely of mailed out surveys achieved a response rate of 50%. Subjects were identified from the Alberta cancer registry. Patients diagnosed with endometrial cancer between 1994 and 2003 were mailed and invite to the survey. The researchers used a slightly modified version of the Total Design Method, which consists of the the first mailing followed by a post card reminder two weeks later and a final mailout 4 weeks after that. Other techniques that were employed included a personalized letter, color printed questionnaires, original signatures, assurances of confidentiality and institution sponsorship. 248 oncologists were contacted for permission to approach their 1549 endometrial cancer survivors. 198 responses from oncologists (79.8%) resulted in mail outs to 879 patients—just over 55%. A final response was received from 386 patients.
In a previous RCT von Gruenigen and colleagues (von Gruenigen et al., 2008) compared a lifestyle intervention with a usual care control group for EnCa patients identified through the Irish Cancer Center Registry. The primary objective of the study was to assess the feasibility and efficacy of a lifestyle intervention for promoting weight loss, improving eating habits and increasing PA in at risk EnCa patients. Patients were followed prospectively for a 1-year period. The results of the trial indicated that after the completion of the 12 month study period there was a loss of on average 3.5kg of weight in the intervention group compared with a 1.5 kg gain in the control group. This is one of very few trials that have attempted a lifestyle intervention within this population.

From an initial mailout to 156 patients in the registry diagnosed from 2001-2004 there were a final 45 subjects randomized to either of the two groups. This is a recruitment rate of 28%. Of the initial 45 randomized subjects there was a completion rate of 79% and 90% of the lifestyle intervention and usual care control group respectively.

These examples of recruitment rates within populations of cancer survivors indicate that in order for representative samples to be included in trials examining lifestyle factors, a large number of patients should be targeted. Targeting of sample sizes adequate to determine efficacy of interventions—and their ability to effect changes in primary outcomes—will require substantial resources.
Chapter 3: Methods

Overview

The purpose of the observational cross sectional study (study I) was to determine correlates of lifestyle behaviors (PA & D) and both disease specific health related quality of life (HRQL) and broad quality of life outcomes. The hypotheses were that higher levels of PA and better dietary habits would be associated with greater quality of life. We also hypothesized that psychosocial theory variables would mediate this relationship. 2) The primary purpose of study II was to determine the feasibility and preliminary efficacy of developing and delivering the MIM+D intervention to endometrial cancer survivors. Our hypothesis was that the lifestyle intervention would be safe and tolerable for EnCa survivors and that an 8-week program of MIM is an achievable time commitment. Furthermore, a second hypothesis is that for woman who are overweight/obese with low levels of physical fitness and physical function who adhere to the 8-week mindfulness intervention, we will see improvements in self reported QOL and objectively measured PF. 3) The purpose of the final part of the study was to evaluate the logistical aspects of recruitment to each phase of the study. The goal of this process was to inform the future approach to such studies by identifying weaknesses and strengths with some suggested conclusions.
Study I: Survey of Lifestyle Behaviors in Endometrial Cancer Survivors

The study approach involved making use of online data management and survey software in attempt to facilitate an optimal response rate. At the time of development, The Ohio State University had increasingly used the REDcap system to collect real time data from a variety of settings. The hypothesis was; by offering patients who are attending their oncological clinic visits the opportunity to take the survey on an iPad or similar electronic device that responses would be improved over methods such as mail-outs. While survivors were also offered the paper version of the test it was quickly determined that the age cohort of subjects being targeted were not comfortable with technology of the kind proposed for this study.

Study II: Lifestyle Intervention to Improve the Quality of Life and Physical Function in Endometrial Cancer Survivors. The Role of a Gentle Yoga and Mindfulness Based Intervention

The second study within the dissertation was originally designed to compare the effectiveness of a traditional aerobic walking coupled with dietary counseling with a gentle yoga (Mindfulness in Motion) and dietary counseling intervention with the design of the intervention to be guided by the findings from the correlational findings from study I. However, due to a slower rate of recruitment and smaller available participant pool than originally anticipated, the study focused upon determining the feasibility and preliminary efficacy of delivering the MIM + Diet intervention to overweight and/or obese EnCa survivors.

A final objective of the project was to conduct a comprehensive evaluation of the recruitment process that was used for both study I and study II. An in depth description of
this process was conducted in order to inform the design and delivery of future lifestyle intervention research targeting EnCa patients and survivors.

**Cross Sectional Survey (Study I)**

**Study Design and Overview**

This study was designed as a cross sectional analysis of lifestyle behaviors in a target sample of 150 - 200 surgically staged (I&II) and treated, type I endometrial cancer survivors. Subjects who were in remission and currently being treated for their history of endometrial cancer in the division of gynecologic oncology at Ohio State University were the primary recruitment targets of this survey.

**Objective 1:** The primary aim of this study was to determine the relationship between lifestyle behaviors including physical activity (PA)/diet and quality of life in 200 endometrial cancer (EnCa) survivors. Knowledge of these relationships would inform the design and delivery of a lifestyle intervention intended to improve quality of life and reduce risk of disease in EnCa survivors. The present study will provide some of the first empirical data exploring if lifestyle PA and dietary behaviors are directly associated with QOL or indirectly linked to QOL through select social cognitive and self-determination theory constructs.

**Hypothesis 1 & 2:** Our hypothesis was that higher levels of PA and better dietary practices would be associated with higher self reported QOL. Secondary hypotheses were that psychosocial variables would mediate this relationship.

**Objective 2:** The secondary aim of the study was to examine the extent to which select social cognitive theory (SCT) and self-determination theory (SDT) variables
predict participation in PA and dietary behavior in EnCa survivors. No extant studies have examined theory-based correlates of PA or dietary behavior in EnCa survivors. This cross sectional study was among the first to examine the relationship between established SDT variables and PA and dietary behavior in EnCa survivors. These observational data will inform the design and delivery of a subsequent lifestyle intervention trial targeting EnCa survivors.

**Hypothesis 3:** Our third hypothesis was that both SCT and SDT variables would be associated with level of physical activity and dietary practices. Specifically, higher levels of Self-efficacy (SCT) and higher competence and intrinsic motivation (SDT) will be associated with greater levels of PA and better dietary practices.

Participants completed assessments of their current level of physical activity (PA), information about dietary practices, functional limitations and co-morbidities. Psychosocial constructs regarding domains of both health related quality of life (HRQL) and quality of life (QOL) (perceived stress, depression, sleep quality, and mindfulness) were also examined. One study aim was to explain relationships among disease profiles and the associated psychosocial variables within the framework of Self-Determination Theory (SDT) or Social Cognitive Theory (SCT). It should be noted that for the current survey study we did not specifically assess lower limb lymphedema as part of functional limitations due, in part, to the following reasons: 1) As per the current clinic guidelines there are no standard assessments outside of a general clinical evaluation and interview with the subject. 2) This would be timeous and difficult to replicate using a questionnaire and 3) as we do not feel this is directly relevant to the outcomes of this proposed phase of
the study. Should we continue to examine patients within a lifestyle intervention phase of the study such information may be necessary.

**Recruitment strategy, informed consent, and risk/benefit evaluation**

**Participants**

The target was to survey between 150 to 200 EnCa patients and given the exploratory nature of certain aspects of this survey, keep the eligibility quite broad. All patients were screened for eligibility initially through the gynecologic oncology outpatient clinic and at that time directed to take a survey should they so wish. This survey was administered through the REDcap online survey software and the data managed by the administrators of that software in accordance with IRB protocols regarding anonymity and privacy as determined in the HIPAA guidelines. The OSU CCTS Research Informatics Services Core will be used as a central location for data processing and management. Vanderbilt University, with collaboration from a consortium of institutional partners (including OSU) and the NIH National Center for Research Resources, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the CCTS Research Informatics Services Core.

As part of the data dictionary development process, individual fields can be denoted as “identifiers”. When exporting a de-identified dataset, these variables are
omitted. Additionally, the data export tool also allows for the shifting of dates for a limited data set export. REDCap provides a secure, web-based application that is flexible enough to be used for a variety of types of research, provides an intuitive interface for users to enter data and has real time validation rules (with automated data type and range checks) at the time of entry. It offers easy data manipulation with audit trails and ad hoc reporting functionality for reporting, monitoring and querying patient records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). REDCap is 21 CRF Part 11 capable. Currently, REDCap installations support electronic signatures by positively identifying the user through a unique username and password combination. The provisioning of accounts and user access to specific database(s) is integrated with the OSU Medical Center LDAP authentication service, and the provisioning of access and specific user rights are managed by CCTS staff.

**Eligibility**

We targeted these women because they are most at risk for disease recurrence, future comorbidity (CVD and type II diabetes) as well as experiencing compromised physical function due to sedentary lifestyles and poor dietary practices. The following were the inclusion and exclusion criteria for participation:

*Inclusion criteria*

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- Female
- English speaking
- Previous diagnosis of grade 1 or 2, stage I or II endometrioid endometrial cancers (“Type I cancers”)

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— Anytime from treatment
— Treating oncologist consent
— Ambulatory

Exclusion Criteria

— No prior type I endometrial cancer diagnosis;
— Prior diagnosis of other cancer
— Non-ambulatory;
— Concurrent diagnosis of organic brain syndrome, dementia, mental retardation, or significant sensory deficit;
— Major mental illness (e.g., schizophrenia, major depressive disorder);
— Unwilling to give consent

Informed consent

Upon arriving to the Mill Run Clinic or the Stefanie Spielman Comprehensive Breast Center (SPCBC) for their scheduled physician visit, patients were approached by a study assessor—research nurse or research assistant—to determine interest and eligibility in the study. The assessor then described the study purpose, procedures, risks and benefits, provided patients with an opportunity to discuss their questions and concerns. Interested subjects were then given the option to take the survey in a number of ways depending on whether they wanted to complete an electronic or a paper version of the survey. If the participant was willing to take an electronic version of the survey, this was offered in two ways: a) to start the survey whilst waiting for their scheduled appointment on a tablet device or b) offered the opportunity to take the survey at a later stage via a
provided online link (email) to the REDcap survey. For the online electronic versions of
the survey, HIPAA and OSU privacy practices information was provided at the time the
subject activated the link to the online survey. If the participant chose a paper version of
the survey they were provided with and asked to sign the informed consent in the clinic
before being provided with the paper version. As a further recruitment strategy to
complete the targeted accrual, the oncologists at the research clinics also identified recent
patients who were eligible for study participation from patient records. These patients
were mailed an introductory letter and asked whether they were interested in the study.
Patients interested in participating could follow a link in the mailed letter to accept the
consent online and take the survey. We did not mail out paper versions for reposting due
to cost. Informed consent was documented by acceptance of either the online forms or the
printed consent (same) approved by the OSU Institutional Review Board. Patients were
informed that participation was voluntary and would in no way affect their medical
treatment or their relationship with the OSUCCC or the University. The study team
obtained informed consent before the survey was started.

**Minority Representation**

Given the division of gynecologic oncology’s established success in recruiting
EnCa patients and survivors in prior clinical studies, we anticipated being able to
successfully recruit a representative proportion of minority women who were treated
through the James/OSUCCC in study I. Currently the Non-Caucasian population of
females patients is roughly 10% overall at OSU for endometrial cancers (8% African
American, 1% Asian, 1% Hispanic).
Risks to the Study Participant

There were minimal risks associated with participating in this study. Participants completed a one-time survey during which a self-report of lifestyle behaviors was obtained. Thus, in light of the medical screening prior to study inclusion, the risk associated with conducting this survey was minimal. One possible psychological risk was that some individuals may have experienced some guilt or embarrassment in self-reporting dietary practices or sedentary behavior. Safety of the participants following the survey was monitored during recurring clinic visits, appropriate medical screening from referring oncologists, medical prescreening conducted by the research staff, or the primary care physician. Collectively, the participants assumed no more than minimal risk in completing the assessment protocol.

Confidentiality

The administrators of the REDcap online survey software maintain patient confidentiality of records. Individuals were not be identified by name or by any other personal identifying information in reports, or publications resulting from this study. Thus, risk of disclosure of confidential medical information will be essentially nonexistent. Additionally, all data was number coded and stored in a locked research office that could only be accessed by the research staff. These procedures have been successfully used to protect confidentiality in Dr. Focht’s prior completed research.

Benefits of participation

Although there was essentially no direct benefit to the subject regarding participation in the this survey, participation could help provide scientific data for
investigators to assess the relationship of habitual physical activity levels and dietary practices to physical function and quality of life of women who are survivors of EnCa. The benefits to the scientific community and the public are potentially large. We did not provide any monetary or other incentives to participants in this study. Due to the nature of the motivational construct’s being surveyed in the context of the SDT we believe these incentives to be extrinsically motivating and that they would therefore affect our data.

Measures

The survey was administered via the REDcap online survey technology. This allowed the generation of “links”, which were emailed to patients, shared via social media or delivered in person with the use of currently available technologies such as tablets in the clinical setting. The entire battery included measures that demonstrate excellent validity and reliability in prior research.

Measures included in the current study will aim to elucidate information regarding the following:

Demographics: Information regarding age, race, height, weight, level of education and income will add to the already growing body of information relating to this specific understudied female carcinoma. Importantly, we aimed to gather information about underserved communities that are representative of the ethnic diversity of the Columbus Metropolitan area. We also asked questions about quality of life, depression, mindfulness, perceived social stress and functional limitations. As we intended to examine behavior within the framework of current psychological theory (SDT or SCT) we also asked questions regarding motivation and self-efficacy.
Physical Activity (PA): PA participation was one of the primary lifestyle behaviors of interest in the present investigation. PA was assessed using the Modified Paffenbarger Questionnaire (PAQ) (Paffenbarger, Blair, & Lee, 1993) to sample the typical levels of physical activity engaged in by EnCa survivors. The PAQ allows for the assessment of the amount of time typically spent by an individual in various types of physical activity including stair climbing, walking and structured exercise. Comparison of the level of accumulated weekly PA can be made with the current HHS guidelines of 150 minutes of moderate to vigorous PA per week. This measure also allows the calculation of a rough caloric expenditure for a typical week. Prior research has demonstrated the PAQ has well established validity and reliability.

Diet: In addition to PA, the other main behavior of interest was current dietary patterns. Information regarding the typical dietary practices of an EnCa population would serve to inform the best approach to changing this lifestyle behavior and will augment the important goal of weight loss in an EnCa population. Current evidence supports the use of both PA and dietary intervention for the most effective and healthy weight loss.

Understanding where this particular patient population falls compared with other chronic disease populations is of critical importance for clinical practice. To measure the food intakes of EnCa survivors we used the Food Habits Questionnaire (FHQ) (Silverstein, 1997), which was originally developed as a screening tool for dietary quality related to the prevention of cancer and cardiovascular disease, with a focus on the assessment of dietary fats and whole grains. It typically includes 49 questions related to frequency of food intake over 6 categories. In the RENO diet heart study the test restest reliability of this measure was (Pearson $r=0.92$) and a Cronbach’s alpha level of 0.85. It
is recognized that there are more in depth analysis of food intakes available, however for the purposes of this study we chose this measure for its brevity as well as ability to capture meaningful data in conjunction with other measures as part of a larger survey.

**Quality of Life:** We assessed this construct from both a global perspective as well as within a more disease specific context (HRQL). Globally we used the Satisfaction with life Scale (SWLS), a 10 item, likert type questionnaire with reported validity and reliability (Diener, Emmons, Larsen, & Griffin, 1985) and for the disease specific aspects of QOL related to EnCa we used the Functional Assessment for Cancer Therapy-Endometrial (FACT-En), which is a well known measure within the cancer literature that has acceptable validity and reliability (Cella et al., 1993) and been adapted for this population.

**Mindfulness:** Mindfulness is a complex construct that has been operationalized in different ways but which is essentially and for our purposes a skill that allows an individual to pay attention to the present moment in a non-judgmental or reactive way. Originally Buddhist mindfulness meditation was a specific technique proposed to enhance the skill of mindfulness. Being more mindful is seen as a way to reduce the stress and anxiety encountered by appraising a given life situation as threatening, uncontrollable or unpredictable. In more recent explorations a number of different questionnaires have aimed to measure underlying aspects of mindfulness. We will use the Five Factor Mindfulness Questionnaire (FFMQ) that has been created by using factor analysis to combine the most relevant aspects of separate mindfulness constructs targeted by different survey tools and has demonstrated acceptable psychometric properties. Alpha coefficients for all facets ranged from 0.67 – 0.92 (Baer et al., 2006; R.A. Baer et
The five underlying constructs targeted are: **Observing, Acting with awareness, Non-reacting, Non-judging, and Describing**—all of which show strong expected relationships with psychological variables.

**Perceived Stress Scale (PSS):** This is a measure of the perceived level of stress an individual feels they are currently experiencing in their lives. The items in the questionnaire are designed to tap into specifically, how overloaded, unpredictable and uncontrollable people may find their lives. This is a 10-item survey asking participants how often they felt a certain way in the past month. There is good validity and reliability of this measure with respondents scoring higher on the scale having more reported health status problems including health-seeking behavior and higher susceptibility to life-event elicited depressive symptoms (Cohen, Cohen, & Syme, 1985).

**Self-efficacy & Barriers Efficacy:** Self-efficacy beliefs are the primary motivational construct within Bandura’s larger Social Cognitive Theory (SCT) (Bandura, 1986). In this manner SE is thought to be involved in a reciprocally deterministic relationship, with both physical barriers and environmental factors influencing the choices and therefore the behaviors an individual engages in. Having a high self-efficacy for a specific task increases the likelihood an individual will attempt that behavior (e.g. Physical Activity). In turn engaging in PA will serve to increase SE for that task. In a similar fashion Barriers efficacy relates to an individuals perception of their capacity to overcome perceived barriers to engaging in an activity (e.g. physical activity) A single global measure of self-efficacy—the multidimensional exercise self-efficacy scale (MESES)—will address underlying aspects of self-efficacy and has been developed and
validated through a factor analysis method in reported three separate studies (Rodgers, Wilson, Hall, Fraser, & Murray, 2008).

Motivation: Within the Self Determination Theory (SDT)—previously described—there are 3 main constructs related to health-care behavior (Deci & Ryan, 1985; Ryan et al., 2008). The first is the Treatment Self-Regulation Questionnaire (TSRQ); the second is the Perceived Competence Scale (PCS); and the third is the Health Care Climate Questionnaire (HCCQ). For this study we decided not to ask the health care climate section as we did not want patients in the clinic to feel that they would be at risk of any reprise should they unfavorably report on their health care providers. Each questionnaire has four versions, relating to four different health relevant behaviors: namely, smoking cessation, diet improvement, exercising regularly, and drinking responsibly. For the current study we will only use the diet and exercising regularly measures. The questions are asked with a likert type scale ranging from 1 (Not at all true) to 7 (very true). These questionnaires will aim to assess autonomy, competence, and relatedness as they affect persons within the EnCa survivorship continuum.

Sleep quality and quantity: An understudied aspect of health is the quality and quantity of sleep a person is able to regularly get. Lower levels of sleep are related to cardiovascular problems, fatigue, depression and may importantly influence the quality of life of a patient. We will use the Pittsburg Sleep Quality Index (PSQI) to sample typical sleep patterns over the previous month, which is determined to be a time frame within which transient issues with this aspect of normal functioning may vary. The measure has been shown to be valid and reliable in prior research (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).
**Depression:** It is common for persons diagnosed with critical or life threatening diseases to experience depressive symptoms. Left unnoticed or untreated this can become a chronic depressed state. Depression further exacerbates perception of fatigue, decreases immune function and reduces QOL. Consequently, self-reported depressive symptoms were assessed using the Center for Epidemiological Studies–Depression (CES-D), a measure with strong validity and reliability (Radloff, 1977). The CES-D is a 20 item self-report questionnaire often used to screen and manage depression in the general population as well as having been used in cancer patients (Courneya et al., 2005).

**Procedure**

After the subject had initially been screened and had met the inclusion criteria, she was emailed a link or provided with a hard copy of a link to the online survey or asked to complete the survey using a tablet device within the clinic. Upon activating the survey, participants were required to complete the informed consent document prior to initiating the survey. Once the patient accessed the website they were additionally informed of the purposes and the benefits of the research study and of the expected time commitment. They were informed that the survey was voluntary, and that they may stop at any time should they wish. They were then asked for their consent in order to proceed. During the survey, the subject could save their progress and complete at a later time if they so wished. Private and confidential space was available in the division of gynecologic oncology for completion of the survey while at their clinic visit.

**Statistical Analyses**

The OSU CCTS Research Informatics Services Core was used as a central location for data processing and management. Vanderbilt University, with collaboration
from a consortium of institutional partners (including OSU) and the NIH National Center for Research Resources, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the CCTS Research Informatics Services Core. As part of the data dictionary development process, individual fields can be denoted as “identifiers”. When exporting a de-identified dataset, these variables are omitted. Additionally, the data export tool also allows for the shifted of dates for a limited data set export. REDCap provides a secure, web-based application that is flexible enough to be used for a variety of types of research, provides an intuitive interface for users to enter data and has real time validation rules (with automated data type and range checks) at the time of entry. It offers easy data manipulation with audit trails and ad hoc reporting functionality for reporting, monitoring and querying patient records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). REDCap is 21 CRF Part 11 capable. Currently, REDCap installations support electronic signatures by positively identifying the user through a unique username and password combination. The provisioning of accounts and user access to specific database(s) is integrated with the OSU Medical Center LDAP authentication service, and the provisioning of access and specific user rights are managed by CCTS staff. In addition to the standard OSU REDcap data management procedures; the PIs (Dr. Focht and Alexander Lucas) were responsible for all aspects of data management, quality
control, and statistical analysis. Dr. Focht has worked with data management on several previous large PA studies.

In analyzing the data it was taken into account that all subjects will have been treated in accordance with the same protocol and will additionally control for the effects of time since treatment has occurred. Preliminary bivariate correlation analyses were conducted to determine the significance of relationships between PA and dietary behavior and QOL.

**Objective 1.** To test hypotheses for the primary objective; Multiple Linear Regression was be used to explore the relationships between lifestyle PA/dietary behavior and QOL. In Model 1 (direct effects model) the regression model will examine the direct effect of PA and dietary behavior on QOL. In Model 2 (indirect effects model), we tested the direct effects of PA and dietary behavior on select SCT and SDT variables. We also tested the indirect effects of the SCT and SDT variables on QOL using a meditational analysis (Baron & Kenny, 1986). These models allowed us to determine whether the cross sectional relationship between PA and dietary behavior was direct or indirect operating through the select SDT and SCT variables. In addition we will include differences in treatment modality and time from diagnosis as a control in the analysis. We in addition wanted to examine the reciprocal determinism theorized in SCT by looking at the effect of SCT variables on lifestyle behaviors.

**Objective 2.** To test hypotheses for the secondary objective, Regression will again be used to explore the relationships between SDT and SCT variables and self-reported participation in lifestyle PA/dietary behavior.
**MIM + Diet Feasibility and Efficacy Intervention (Study II)**

**Study Design and Overview**

Although the study was initially intended to be a 3-arm intervention study comparing MIM+D \((n=20)\) to aerobic exercise + dietary counseling \((n=20)\) or usual care \((n=20)\) in a sample of 60 surgically staged (I&II) and treated Type I EnCa patients, due to the aforementioned recruitment challenges, study II was refocused upon the objective of evaluating the feasibility and preliminary efficacy of the MIM+D intervention. While not ideal it was thought to be more likely to inform further studies than if a very small sample were randomized to two groups that may lack characteristics of the intended intervention. Participants completed measures of study variables on three sampling occasions: 1) a baseline assessment 2) follow-up assessment after 8 weeks active intervention and 3) follow-up assessment at 14 weeks. The study variables included measures of physical activity (self-report and accelerometry), functional performance, self-reported functional limitations, body composition (Percent body fat and BMI), and quality of life. The active intervention was examined for preliminary efficacy and feasibility in a sample of 17 women.

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*Figure 5 Study Flow*
**Objective 1:** The primary objective of study II was to determine the feasibility and efficacy of delivering a lifestyle intervention (MIM + Diet) for endometrial cancer survivors.

**Hypothesis 1:** Our hypothesis is that lifestyle interventions will be safe and tolerable for EnCa patients.

**Objective 2:** The secondary aim of this study was to determine whether gentle yoga and mindfulness (MIM) coupled with dietary counseling could improve physical function and quality of life.

**Hypothesis 2:** Our second hypothesis was that there would be an improvement in physical function and quality of life for EnCa survivors. An ancillary hypothesis was that those participants exhibiting the best adherence to the intervention would demonstrate the most favorable improvements in the outcomes of interest.

**Recruitment Strategy, Informed Consent, and Risk/Benefit Evaluation**

**Participants**

In collaboration with Ohio State University GYN oncology clinic this study used Dr. David Cohn as the focal point for recruitment of women for this study. Other GYN oncology specialists were also referring physicians that aided in recruiting women into the sample. Alexander Lucas and study staff conducted a telephone-screening interview to confirm participants satisfy the eligibility criteria for the study and scheduled the baseline assessment visits. All possible subjects must have been surgically staged and treated for type 1, early stage (I, II) endometrial cancer. The number of required
participants is based on prior studies of behavior change and the required power to detect meaningful differences between groups post intervention.

*Eligibility*

The gynecologic oncology clinic has previously completed accrual to other behavioral research clinical trials and has the necessary infrastructure and resources to support such an effort. We are targeting these women because they are most at risk for disease recurrence, future comorbidity (CVD and type II diabetes) as well as experiencing compromised physical function due to sedentary lifestyles and poor dietary practices. The following were the inclusion and exclusion criteria for participation:

*Inclusion Criteria*

— Female

— English speaking

— Previous diagnosis of grade 1 or 2, stage I or II, endometrioid endometrial cancers (“Type I cancers”) — confirmed during surgical intervention for treatment.

— Overweight or Obese (>25kg/m²)

— Anytime from treatment

— Treating oncologist consent (OSUGYN)

— Ambulatory or able to engage in walking for at least 45 minutes per intervention visit.

— Sedentary lifestyle, as engaging in less than 100 minutes structured aerobic walking, cycling or swimming per week.
Exclusion Criteria

— No prior type I endometrial cancer diagnosis;
— Prior diagnosis of other cancer
— Currently (previous 6 months) engaged in structured exercise either aerobic or yoga based.
— Severe Heart or Systemic Disease: evidence of documented myocardial infarction, chronic unstable angina, symptomatic congestive heart failure, uncontrolled hypertension.
— Severe Musculoskeletal Disease: Severe muscle or joint disorders due to disease or trauma, amputations, or any condition that significantly impair physical capabilities, as defined by the physician.
— Non-ambulatory;
— Concurrent diagnosis of organic brain syndrome, dementia, mental retardation, or significant sensory deficit;
— Major mental illness (e.g., schizophrenia, major depressive disorder);
— Unwilling to give consent.

Informed Consent

Subjects were prescreened and recruited in the SPCBC Clinic by clinic staff and Alexander Lucas, Eligible volunteers were subsequently contacted by Alexander Lucas to conduct a telephone screening interview to confirm participants satisfied the eligibility criteria for the study and confirm scheduling for the baseline assessment visit. Upon arrival for the baseline screening visit—on the ground floor of the PAES Building on the Ohio State University Main Campus—study staff (Lucas) reviewed the consent
document, purpose of the study, the procedures, risks and benefits, confidentiality, and options for withdrawal from the study with each participant. No assessments took place before the signing of consent. Patients were informed that participation was voluntary and would in no way affect their medical treatment or their relationship with the OSUCCC or the University. Participants then completed the consent form, which was approved by The OSU Institutional Review Board (IRB). Upon completing the informed consent process, the HIPAA and OSU privacy practices information was provided. Informed consent was documented by acceptance and signing of the printed consent approved by the OSU Institutional Review Board. The risks of the study protocol were expected to be low but were carefully monitored.

**Minority Representation**

Given the division of gynecologic oncology’s established success in recruiting EnCa patients and survivors in prior clinical studies, we anticipated being able to successfully recruit a representative proportion of minority women who were treated through the James/OSUCCC in the proposed study. Currently the Non-Caucasian population of females patients is roughly 10% overall at OSU for endometrial cancers (8% African American, 1% Asian, 1% Hispanic).

**Summary of the OSUCCC Data and Safety Monitoring Plan**

The Ohio State University Comprehensive Cancer Center [OSUCCC] places the highest priority on ensuring the safety of patients participating in clinical trials. Every therapeutic interventional trial conducted at the OSUCCC must include a plan for safety and data monitoring. Specific plans may vary based on the degree of risk involved in participation and the size and complexity of the clinical trial. The development of
protocol monitoring plans and reporting requirements are dependent upon the study sponsor, nature of the investigational agent, and phase of trial. Trials include studies of cytotoxic and cytostatic agents in treating cancer in an active disease or adjuvant setting, agents targeting biologic endpoints, and interventional studies in cancer control and cancer prevention. Clinical trials sponsored by the NCI Cooperative Group Program [CALGB, GOG, NSABP, CCG, ACoS, RTOG, and SWOG] will be monitored by long-standing and established systems for cooperative group data submission, reporting, review, and monitoring.

All local, investigator-initiated therapeutic clinical trials, such as this proposal, are required to have specific data and safety monitoring plans based on the size and complexity of each trial and the potential risk to patients. Local, investigator-initiated Phase I trials are required to be continuously monitored by the principal investigator of the study with quarterly safety and monitoring reports submitted to the CCC Data and Safety Monitoring Committee [DSMC]. Local, investigator-initiated Phase II protocols will require monthly monitoring by the principal investigator of the study with biannual reports submitted to the DSMC. Phase I/II studies sponsored by NCI/CTEP will be monitored by the principal investigator with required reporting to NCI/CTEP using the Clinical Trials Monitoring Service [CTMS], the Clinical Data Update System [CDUS], and/or the Adverse Event Expedited Reporting System [AdEERS]. Due to the difficulty in accessing this data for data and safety monitoring locally, investigators of NCI-supported studies outside the cooperative group mechanism must report to the DSMC as required for local investigator-initiated phase I/II trials. Local, investigator-initiated randomized Phase III clinical trials will be monitored by protocol-specific data and safety
monitoring boards [DSMB]. Formal DSMBs will consist of clinical investigators, biostatisticians, clinical trial experts, and lay patient advocates independent of investigators involved in the design and conduct of the trial. Following protocol review and monitoring, all DSMB recommendations and reports will be forwarded to the IRB, DSMB, the CCC Associate Director for Clinical Research, and the principal investigator.

All data and safety monitoring reports for local, investigator-initiated studies included the number of patients entered, number of patients treated, dose level of agent[s] involved, summary of all adverse events reported to date using CTCAE 3.0 grading, a specific list of adverse events requiring expedited reporting to include ALL serious adverse events [SAEs], and, on an annual basis or as it arises, significant literature reporting developments that may affect the safety of participants or the ethics of the study. Data safety and monitoring activities for each study will continue until all patients have completed their treatment and all patients are beyond the time point at which study-related adverse events would likely be encountered. Multi-center, limited-institution randomized phase III trials will be held to the same standards as local, investigator-initiated phase III trials and be required to submit formal data and safety monitoring plans including the establishment of an appropriate DSMB prior to activation.

All serious adverse events experienced by patients at the OSUCCC will be immediately reported to the OSUCCC Clinical Trials Office, the DSMC, the Cancer IRB, and the study sponsor. Protocol administration and individual patient clinical data will be subject to random audits by the OSUCCC Office of Protocol Compliance to insure data accuracy and compliance with protocol-directed patient management. In the event that data and safety monitoring by the DSMC results the Associate Director for Clinical
Research suspending or terminating a trial, the principal investigator, the OSUCCC Director, the Cancer IRB, the CSRC, and the study sponsor [to include NIH, Department of the Army, pharmaceutical industry sponsors, and other external sponsors] will be notified within 24 hours of such action.

The OSUCCC DSMC will additionally submit an annual report to the OSUCCC Director and OSUCCC Associate Director for Clinical Research on activities of the past year and make recommendations to improve data and safety monitoring activities. All data and safety monitoring plans, institutional as well as individual protocol-specific, must be reviewed and approved by the OSU Cancer IRB prior to protocol initiation.

**Risks to the Study Participant**

The risks associated with this protocol were expected to be minimal. Participants completed 3 experimental assessment visits during which measurement of all study variables was obtained. The assessment of body composition via IDXA involves no exertion or risk whatsoever. The functional performance tests involve walking, stair-climbing, and functional performance tasks that are of no more than the minimal risk associated with performing typical activities of daily living. Moderate intensity aerobic exercise has inherent risk of minor muscular strains and sprains as well as mild discomfort initially. This would be no more than usually experienced should a person start a walking program. Gentle yoga carries similar risks to walking however the novelty of the modality means licensed yoga practitioners designed the level of yoga to be specific to the needs and capabilities of the cancer patients. The supervised sessions were designed to teach safe, effective techniques, which would foster a safe transition to home
practice. Thus, in light of the medical screening prior to study inclusion, the risk associated with conducting these tests and intervention was minimal. Additionally, Dr. Focht and the research assistant (Alexander Lucas) who were directly involved in conducting and supervising the completion of the functional and strength tests are both certified exercise leaders who have conducted thousands of prior exercise tests through past research and clinical experience. There are minimal risks associated with completing the self-report measures for this study. One possible psychological risk is that some individuals may experience some guilt or embarrassment in self-reporting functional limitations or sedentary behavior. Safety of the participants during the functional performance testing was ensured through several strategies; appropriate medical screening from referring oncologists, medical prescreening conducted by the research staff, primary care physician, and strict adherence to established testing protocols demonstrated to be safe in prior research. Collectively, the participants were assuming no more than minimal risk in completing the assessment protocol and the minimal risk inherent to completing the assessments was mitigated via stringent pre-test medical screening and during testing supervision.

**Safety**

Dr. Cohn was to be notified immediately of any adverse events and these would then be reported to the OSU-IRB as required. We would follow the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0. The CTCAE document is over 70 pages long and is not included with this dissertation, but can be found at the following web address:


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**Confidentiality**

Patient confidentiality of records was maintained. Individuals were not identified by name or by any other personal identifying information in laboratory records, reports, or publications resulting from this study. Thus, risk of disclosure of confidential medical information is essentially nonexistent. Additionally, all data is number coded and stored in a locked research office that can only be accessed by the research staff. These procedures have been successfully used to protect confidentiality in both Dr. Focht and Dr. Cohn’s prior completed research.

**Benefits of Participation**

Participation in this study could help provide scientific data for investigators to assess the efficacy of gentle yoga+ diet for improving lifestyle in EnCa patients. Lifestyle changes can lead to higher levels of physical function and improved quality of life in aged women with EnCa. Furthermore providing patients with the tools to reduce stress and risk for future disease recurrence and comorbidity is a significant benefit. It is well established that patients participating in physical activity, diet, and stress reduction studies derive significant emotional and psychological benefits. These involve feelings of self-empowerment and pride in contributing to scientific knowledge. Given the limited extant lifestyle intervention research in EnCa survivors, the benefits to the scientific community and the public are potentially meaningful. In order to provide scientifically supported lifestyle recommendations to the public, it is critical that we obtain a clearer understanding of the relationship of different types of lifestyle interventions to changes in physical function and quality of life in this specific cancer survivorship population. Additionally, understanding whether different patients are more
suited to alternative forms of PA that will encourage adherence to lifestyle change in the long term is both novel and significant.

**Research Design**

The final design of study II involved a single arm intervention study examining change in select quality of life and physical function outcomes in a group of surgically treated, early stage (I &II) type I endometrial cancer patients (EnCa). Gentle Yoga (Mindfulness in Motion)+ Diet was followed for a period of 8 weeks—during which subjects will attend 1 x weekly session of 45-60 minutes. Additionally participants will be directed to supplement their onsite mindfulness practice with home-based gentle yoga and meditation to allow a transition to complete home-based activity during weeks 8-14 and beyond. Participants completed measures of study variables on 3 sampling occasions: 1) a baseline assessment which was obtained from participants who have been surgically staged and treated; 2) follow-up assessment after 8 weeks of being in the intervention and finally 3) follow-up assessment after 14 weeks (6 weeks post intervention). Adherence will be tracked through attendance to study session and with the use of exercise and dietary self-report logs.

**Measures**

Diet was monitored with both weekly food logs and additionally sampled during the intervention period using the Food habits Questionnaire. Physical function was measured with a battery of tests designed to test the functional capacity of the subject relative to their level of expected activity and daily living requirements. They included a 400m-walk test (Newman et al., 2006; Simonsick, Montgomery, Newman, Bauer, &
Harris, 2001), The Short Physical Performance Battery (SPPB) (Guralnik et al., 1994) a stair climb task and a Lift and Carry task. Quality of life (QOL) was assessed from both a global sense as well as within a more disease specific context. We used the satisfaction with life scale (SWLS) (Diener et al., 1985) the Rand SF-36 for physical and mental functioning subdomains, as well as the functional assessment of cancer therapy-Endometrial (FACT-En). Additional constructs to be measured included mindfulness questionnaires; the Five Factor Mindfulness Questionnaire (FFMQ) and the Mindfulness Attention Awareness Scale, a sleep quality questionnaire—the Pittsburg Sleep Quality Index (PSQI)—and the CES-D for depression.

**Physical Function Battery**

Functional Performance was assessed using 3 valid and reliable timed performance-related mobility tasks: 400 meter walk, stair-climb, and lift and carry task (Peters, Lotzerich, Niemeier, Schule, & Uhlenbruck, 1994; Peters, Lotzerich, Niemeir, Schule, & Uhlenbruck, 1995; Reboussin et al., 2000; Rejeski et al., 1995). Assessments of *Mobility-Related Self-Efficacy* to complete each functional task was also completed with the tests.

For the 400 m walk, participants completed 10 clockwise laps around a 40m indoor course as quickly as possible. For the stair-climb task, participants were timed while they ascended a set of 10 stairs turning around at the top of the platform, and then descending the stairs. In the lift and carry task, participants picked up a container—a 10lb weight—with both hands, turned and walked around a cone placed 5 meters away. They then returned to the shelf to place the container down. Performance on each test was measured in the total time (in minute and/or seconds) to complete the task. Mobility-
related self-efficacy was also assessed by asking participants to rate their confidence in successfully completing incrementally more challenging amounts of the 400 Meter Walk and Stair Climb tasks. For walking self-efficacy, participants were asked to rate their confidence on a 0 (no confidence at all) to 10 (completely confident) scale in completing 2, 4, 6, 8, and 10 laps around the cones without stopping. For stair climb self-efficacy participants were asked to rate their confidence in successfully completing 2, 4, 6, 8, and 10 trips on the stairs without stopping. Mobility-related self-efficacy scores were calculated for each task by summing the total, dividing by the total number of ratings, and multiplying by 10 to yield a score ranging from 0 to 100.

**Physical Activity (PA)**

PA level was measured with both subjective self-report and objective assessments at Baseline, 8 week follow-up and finally at 14 week follow-up. This approach has successfully been used to quantify objective and subjective activity in intervention trials with older adults (Ayabe et al., 2010). Self-reported PA was measured using the CHAMPS physical activity questionnaire (Stewart et al., 2001). The CHAMPS is a valid reliable measure of PA and EX that has been used extensively in previous exercise research among older adults. The LIFECORDER Plus (Suzuken-Kenz, Inc. Nagoya, Japan) accelerometer contains an acceleration/deceleration signal that is digitized by an analog-to-digital converter and numerically integrated over a pre-programmed epoch interval. The LIFECORDER Plus is a valid, reliable objective activity monitor that provides assessments of total minutes of activity, total minutes of light, moderate, and vigorous physical activity, total energy expenditure, and total steps taken.
**Quality of Life (QOL)**

Assessments of both global and disease-specific indices of HRQL were obtained using several valid and reliable scales. Globally, QOL was measured using the Satisfaction with Life Scale (SWLS) (Diener et al., 1985) and HRQL was measured with the SF-36 (Ware & Sherbourne, 1992) and the Functional Assessment of Cancer Therapy-Endometrial. The SWLS is a 5-item measure of global life satisfaction and the SF-36 is 36-item generic measure of HRQL that consists of norm-based physical health and mental health composite scales and eight subscales. Disease and function specific QOL measures will include the Functional Assessment of Cancer Treatment-Endometrial (FACT-En) survey (Cella et al., 1993). The 12-items of the FACT-En scale designed to assess concerns specific to EnCa patients will be assessed. Symptoms of pain and fatigue will also be assessed.

**Body Composition**

Body composition was assessed using the IDXA dual X-ray absorptiometry scanning device. Body composition (fat mass and lean body mass) will be assessed with dual-energy X-ray absorptiometry (Lunar iDXA, GE Lunar, Madison, WI, USA). This scan gives you about the same amount of radiation, as you would get from living in a high altitude city such as Denver for 2 days, or taking 1-airplane flight from New York to Los Angeles. This assessment method offers extremely high precision as well as being able to quantify regional body composition and bone mineral density.

**Behavioral and Feasibility Measures:**

Physical activity was assessed using the CHAMPS (Stewart, 2003). Objectively determined physical activity will also be recorded using the LIFECORDER Plus.
Accelerometer (Suzuken-Kenz, Inc. Nagoya, Japan). Adherence to the MIM intervention was assessed using attendance logs. Participants were also encouraged to record all home-based mindfulness practice independently. Exercise-Related Self-Efficacy was assessed using valid and reliable Exercise Self-Efficacy, Barrier Self-Efficacy, Multi-dimensional scales (McAuley, 1993; Melzack, 1987; Rodgers, Wilson, Hall, Fraser, & Murray, 2008) Dietary tracking was encouraged using either apps or paper based logs. All behavioral and self-efficacy assessments have established validity and reliability and have been successfully integrated in Dr. Focht’s prior research. Feasibility Measures. Descriptive statistics for assessments of recruitment rates, intervention adherence, adverse events, and retention rates were calculated prospectively throughout the trial. Feasibility assessments of participants’ satisfaction with the exercise and dietary intervention will also be completed at the end of the 8-week intervention.

**Mindfulness in Motion & Dietary Counseling Intervention**

**Background and Rationale**

Reducing psychological and social stress through building of resilience and encouraging healthy dietary practices are increasingly advocated in the medical management of chronic disease progression. Unfortunately interventions targeting EnCa survivors at risk for recurrence, and mortality due to CVD and type II diabetes, are significantly lacking. Another aspect not well understood in this population of cancer survivors is long-term adherence to lifestyle change. Consequently, identifying innovative approaches for promoting healthy lifestyles including healthy dietary practices and increased physical activity is integral for the successful behavioral management of
cancer survivorship. Furthermore, whilst the efficacy of traditional physical activity modalities is well established, the examination of alternative—possibly more tolerable—exercises such as yoga in this population of survivors is lacking. It is also important to take into account that a primary characteristic of EnCa survivors is high levels of obesity and overweight. Given that exercise alone is not enough to promote weight loss, the implementation of a gentle yoga (MIM) and dietary interventions as an introduction to lifestyle change may a more achievable goal. In essence this approach could be a primer for more intensive exercise or physical activity being introduced to patients.

**Gentle Yoga and Mindfulness**

This aspect of the intervention was be based on the Mindfulness in Motion protocol (Klatt et al., 2009), designed by Maryanna Klatt PhD., and is an abbreviated 8 week program based on Mindfulness-Based Stress Reduction that emphasizes mindful yoga as a way to invite you into a healthy relationship with your body. Mindfulness in Motion is a mindfulness based intervention that is an 8 week program for adults interested in learning a practical strategy for stress reduction, intended to be delivered on the worksite or home. The movements and breathing exercises are simple and can be practiced daily. Gentle piano music accompanies this practice as an invitation, a cue, to relax your body, mind, and spirit. The yoga and gentle music are meant to facilitate your ability to become aware of the life you are living. The MIM intervention was delivered using facilities at the same location. In a similar fashion yoga was be delivered at a tolerable level for these patients. The active intervention was 8 weeks after which the MIM will be transitioned to a predominantly home-based prescription. We provided safely demonstrated guidelines for home exercise (yoga) as has been done in prior
studies. After 14 weeks we completed a second follow up to determine the adherence to either condition and compared with control to determine the efficacy of such an approach.

**Dietary Counseling**

This aspect of the lifestyle interventions included 8, 30-min nutritional counseling sessions with a registered dietitian. In consultation with Dr. E. Grainger RD, who has previous experience delivering the same intervention to prostate cancer patients within a research intervention context, Ashley Harris, RD was recruited to consult for the study. The 8 counseling sessions were conducted once/week immediately following a center-based MIM session during weeks 1-8. The specific dietary objectives were consistent with the Therapeutic Lifestyle Changes recommended in the Adult Treatment Panel III Report of the National Cholesterol Education Program (Expert Panel on Detection, 2001) and the American Institute of Cancer Research (World Cancer Research Fund, 2007). The nutrition intervention encourages reductions in portion size and caloric and fat consumption together with a gradual transition from an animal-based diet to a more plant-rich diet while still incorporating animal foods including milk and meat with an emphasis on monitoring food proportion and portion size. Specific goals of the dietary component include: (a) reduction in energy intake by 500-1000 kcal per day (for women with a BMI of \( \geq 27 \text{kg/m}^2 \) only, women with a healthy BMI will be instructed to maintain caloric intake); (b) reduction in total fats to 25-30%, saturated fats to 7%, and protein to 15% of total calories; (c) increase in fruit and vegetable consumption to 5 servings per day; (d) intake of 3 or more servings per day of whole grains per day and a gradual increase to at least 25 grams of dietary fiber per day. The nutrition counseling used a
motivational interviewing approach that has been demonstrated to be an effective approach to promote behavior change in cancer patients (Campbell et al., 2009; Carels et al., 2007). The nutrition counseling also builds upon cognitive-behavioral self-management strategies as well as aspects of mindfulness utilized in the MIM intervention. These included self-monitoring, building self-efficacy, goal setting, and anticipating and overcoming barriers to dietary behavior change. Participants complete dietary logs to help with self-monitoring. All of the behavioral counseling conducted during intervention is designed to facilitate the development of behavioral self-regulatory skills needed to successfully adopt and maintain change dietary behavior. An outline of the topics addressed in the exercise and dietary counseling portion of the intervention is provided in the appendices.

**Analysis Plan**

Significance tests for the efficacy of the lifestyle intervention on the longitudinally gathered data at 8 and 14 weeks will be individually standardized by baseline values and will be evaluated using a weighted repeated measures analysis of variance statistical model adjusting for the effect of age and time from surgical intervention (Study Objective #1). The primary aim is to estimate effect sizes for a future application. To evaluate the effect sizes we used Cohen’s $d$, assessed with the following formula:

$$
Cohen's \, d = M_1 - M_2 / s_{\text{pooled}}
$$

Where $s_{\text{pooled}} = \sqrt{\left(\frac{s_1^2 + s_2^2}{2}\right)}$

The values and meanings for the effect size estimates are; a) a small effect size ($d=0.2$), b) a moderate effect size ($d=0.5$) and c) a large effect size ($d=0.8$).
Although the initial sample size of 60 women (20 per group) would not provide optimal statistical power to detect treatment effects, it seemed a feasible sample to recruit given the time and resources provided by the funding mechanism. However during the actual recruitment process for study I & II, it was realized that given the time frame we would need to focus on a single intervention arm. It was hoped the final sample size of 17 women in the MIM group would allow for adequate assessment of the feasibility of the intensive lifestyle intervention and obtain the effect size estimates necessary for the design of a large randomized controlled lifestyle intervention trial. Analyses were conducted using the intention to treat principle with last value carried forward approach used to account for data missing due to participant attrition. Descriptive statistics for the feasibility measures were calculated prospectively throughout the trial.

**Recruitment**

**Recruitment strategies**

Recruitment for the stage I and II studies was primarily conducted through the clinics of Dr. David Cohn of The James OB/GYN cancer care center located at 1145 Olentangy river road, Columbus Ohio. Patients who had been surgically staged and treated for Type I endometrioid adenocarcinomas were identified via a number of mechanisms for eligibility in both the survey study (study I) and the lifestyle intervention study (study II). Initially patients were approached during in-clinic visits as to their interest in taking a survey aimed at improving the understanding of factors associated with lifestyle and health outcomes. Many of these patients were then later approached again about interest in participating in an actual intervention study that offered a gentle
yoga and mindfulness based intervention. The precise recruitment approaches for each study will be described below.

Strategy 1: Patients who were determined to be eligible for the study based on their diagnosis were identified the day before clinic. The first approach to making contact with eligible patients was through the clinic nurse who was completing check out for patients. At the Mill run clinic initially and then at the Stefanie Spielman Comprehensive Breast Center (SSCBC); patients would check in, have their appointment with the treating oncologist and then proceed to the nurse for follow-up. At this time the nurse would ask the patient if they were interested in participating in a survey regarding quality of life for endometrial cancer patients and how it may be related to aspects of their lifestyle. If the patient was interested they were directed to Alexander Lucas who would provide more detail of the study. The patient would then choose a method of survey completion; a paper version with prepaid envelope, or providing an email address to have a link sent to them. This strategy of approaching subjects following the clinic visit was proving to be unsuccessful, particularly at the SBCBC. The researchers suspected that the difference in nursing staff may have been affecting the likelihood of the patients agreeing to participate. As such an attempt was made to encourage the promotion of the study. This still did not have the desired effects.

Strategy 2: The first adjustment to the above approach was to have the secretary who was checking the patients in for their clinic visit ask if they may be interested in speaking with a researcher about quality of life for endometrial cancer patients and how it may be related to aspects of their lifestyle. If the were interested, Alexander Lucas then described the study and offered the same options for taking the study as before. This
adjustment was made to try and speak with a patient before rather than after their appointment—when they may be tired and wish to get home—in the hopes it may increase recruitment. This approach did increase interest in the study to some degree and will be clarified in the results section, however the rate of recruitment was still very slow and we had now reached the stage of wanting to recruit to the lifestyle intervention study. This lead to Strategy 3.

Strategy 3: Dr. Cohn was consulted during a meeting of the advisory committee and the proposed study II. It was decided that contact would be made with clinicians at two local medical centers; Mount Carmel and Riverside Hospital in order to increase the number of patients being seen. Alexander Lucas met with and explained the goals of the study, the benefits and the possible outcomes of conducting a study in this population. After a few months of this approach and no further progress towards recruitment efforts we implemented strategy 4.

Strategy 4: Based on evidence from interventions of physical activity and lifestyle literature we decided to identify past patients who had been treated through the OSUGYN clinic and mail them an invitation to participate in both study I and study II. Using data monitoring records the first time frame used was all patients with a diagnosis of 182.0 (ICD 10) seen at OSUGYN between October 2011-September 2012. We further applied a filter to the patient’s names to target only those who were in the Columbus telephone code. This was done to exclude patients who would be too far to travel to intervention. This mail out markedly increased the rate of response and interest for both study I & study II, however still not to a target level. Using the same strategy we conducted a second mail out for the time frame October 2012-September 2013. This
again helped increase numbers for both studies but still short of targets. At the same time
as strategy 4 was being implemented Alexander Lucas the clinical trials coordinator for
OSUGYN division in a bid to have CCTS staff approach eligible patients in clinic visits,
this did not affect accrual at all.
Chapter 4: Results

In addressing the projects results we will: a) begin by summarizing the results of the recruitment process, b) we will then address the results of the cross sectional survey study (study I) and c) conclude with the findings of the MIM+Diet intervention study (study II).

Recruitment

With regard to the recruitment findings we will combine the results of both study I and study II as the efforts to recruit samples to both studies overlapped. For the cross sectional survey we had a final response rate of 71 participants of which 58 had complete data for the entire survey. This response was achieved over a period of roughly 14 months. While short of the targeted 150-200 responses we were able to examine relationships between key variables of interest. The recruitment process for MIM+Diet intervention yielded 43 patients who showed an interest in the intervention with a final 17 participants having baseline assessments. We did lose 4 of these participants to follow up.

We received IRB clearance from the Cancer review board of the Ohio State University for study 1 (Appendix A), and began the recruitment process in October 2010. The initial response to the in clinic recruitment efforts seemed promising. At the Mill Run clinic—an offsite OSU OBGYN location—we saw the first 4 potential subjects after their routine clinic visit. Of the 4 patients approached 2 agreed to participate (50%). Very
early became apparent that the method of approaching women to take the survey in the clinic on the tablet device would not be feasible. The length of the survey was such that insufficient time would be available to complete the survey and also in part because some older patients seemed uncomfortable with the technology for the most part. An older population of women may not have been used to the touch screen technology. We therefore asked whether the subjects would prefer a paper version to mail back or provide us with an email so we could send them a link. When we started the same process at the primary clinic of one of the oncologists involved in the study we had more potential patients per clinic day but were achieving a lower rate of response. Over the first two months of recruitment we saw a marked difference in the accrual rate between clinic sites. At the offsite location we had fewer clinic visits—11 in total—but of those 11 patients 7 agreed to participate and a final 5 completed surveys, a recruitment rate of 63% and a successful completion rate of 71%. In contrast the other clinic location had more potential subjects—40 in two months, however only 15 agreed to participate of which 3 completed the surveys. Of the patients who agreed to participate at both sites, we had 7 (31.8%) request paper copies and 15 (68.2%) provide us with an email address. A further advantage of being provided an email address was that subjects could be reminded again should they not complete the survey initially. The REDCap system allowed us to track this response rate and the degree to which the survey was complete. This resulted in a recruitment rate of 37% and a final successful completion rate of 20%. Combined, our recruitment rate was 22 from 51 possibles (43%) and the completion rate was 8 from 22 or 36%. At this rate from 2 months of clinic visits it would take a projected 36 months to reach our target accrual of 150 subjects or 50 months to achieve 200. This was obviously
not feasible as the timeframe had originally been 6 months and furthermore, study I was to inform aspects of the lifestyle interventions to be delivered in the MIM+Diet intervention study.

Following discussion with the research team it was decided that the recruitment process should be adjusted. This lead to the implementation of strategy 2 described in the methods section. Following the change in approach there was a marked increase in the number of patients who indicated a willingness to participate in the survey study (study I). During the rest of 2012 (December) the total number of patients who had agreed to participate had risen to 32, of which 21 completed the survey (65%).

Table 2
Recruitment Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Total Possible</th>
<th>Actual Responses</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional Survey Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In clinic</td>
<td>110</td>
<td>36✽</td>
<td>32.7%</td>
</tr>
<tr>
<td>Mailout</td>
<td>401</td>
<td>35</td>
<td>8.7%</td>
</tr>
<tr>
<td>Total</td>
<td>511</td>
<td>71</td>
<td>13.8%</td>
</tr>
<tr>
<td>MIM+Diet Intervention Study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In clinic</td>
<td>37</td>
<td>3</td>
<td>11.0%</td>
</tr>
<tr>
<td>Mailout</td>
<td>401</td>
<td>40</td>
<td>10.7%</td>
</tr>
<tr>
<td>Total</td>
<td>438</td>
<td>43✝</td>
<td>9.8%</td>
</tr>
</tbody>
</table>

Note ✽=52% online, 48% paper, ✝=17 eligible (39.5%)
There was then a period of less clinic time as a scheduling conflict meant the primary investigator could only attend one clinic day a week. Over the next 9 months of 2013 an additional 40 patients agreed to participate, with only 15 (37.5%) finally completing the survey. Over the total time of in-clinic recruitment efforts—1 day per week over roughly 1 year—there was a total of 110 possible patients approached about the survey. It should be noted this was primarily the patients of one specialist. Of the 110 possible subjects, 72 (65.5%) agreed to participate in the survey. Unfortunately only 36 (50%) of these patients completed the survey. From these patients who agreed to participate 54% preferred to take the survey via online link. Further of the completed surveys 52% were via online link and 48% were mailed back paper versions. Overall this was a further indication of the need to adjust the recruitment strategy again.

The new strategy to increase patients involved asking doctors from two outside clinics if they would be willing to provide information to their patients regarding the intervention (study II). By this time we had received IRB clearance for the second study—May 29th 2013—and in order to achieve the targeted accrual we would need to approach a high number of patients. Unfortunately this did not increase accrual at all save one patient who was referred and recruited into the intervention.

The final strategy was implemented with a goal of achieving target accrual for the survey and MIM+Diet studies. In order to achieve this goal we submitted an amendment to the Institutional Review Board to allow us to identify patients with the diagnostic code of 182.00 (endometrial adenocarcinoma) between Aug 2011-July 2012. This yielded a possible 1048 patients who had been treated through the OSUMC OBGYN. To further filter by patients who lived in an area accessible to the proposed intervention site, we
identified those who had a Columbus area telephone dialing code. This yielded 284 patients who were subsequently mailed a letter regarding both the survey study and the MIM+Diet lifestyle intervention. See Appendix C&D. From the first mailout we had a response from 23 (8%) women who were interested in the gentle yoga intervention. Of the 23 women who showed an interest we conducted baseline testing on 11 (47%) women who met initial eligibility criteria. Due to the recruiting challenges and the primary objective of determining the feasibility and efficacy of the Mindfulness in Motion coupled with dietary counseling MIM+Diet approach, the lifestyle intervention was offered to all 11 subjects. At the end of the first groups’ intervention period we again identified patients seen through the OSU OBGYN clinics—this time between September 2012-September 2013. This period yielded 939 patients of which 271 had the 614-dialing code. Additionally, as there were a number of patients who were on continuing treatment we identified new patients since the previous mailout and those who were receiving a second mailout. There were 130 new patients and 141 whom had already received a mailout once from the previous round. There were a total of 43 women—from both mailouts—who responded to the invitation to the intervention study. After exclusion for being too active, underweight or overweight, stage III or greater cancer and wrong diagnosis (type II endometrial cancer), 17 women were scheduled for a baseline visit.

From the initial 17 subjects, 3 (17%) women did not start intervention due to scheduling conflicts. Of those that started 2 women attended the first session only and a final 12 completed 6 out of the 8 sessions for the active intervention. Unfortunately 2 of these 12 did not complete follow up assessments. The final adherence to the intervention,
if started, was determined by counting the number of actual attended sessions divided by the total number of possible sessions and was 77%. If the two women who only attended the first session are excluded then the attendance is 90%.

Following the mailout, there was also an increase in response to the survey. The final total of 71 (47.3%) responses was still short of the targeted accrual of 150-200. While the success of the survey response was low as a proportion of mailouts—35 or (8%)—this was achieved in a relatively short time when compared with the 36 over a nearly 12 months of in-clinic visits.
Figure 6 CONSORT diagram
During the administration of the survey there were 2 separate cases of women responding to the study staff that once they had started the survey they had begun to feel uncomfortable as the line of questions had led them to feel responsible for their having become ill.

The CONSORT diagram above (Figure 6) indicates the flow of participants into the survey study initially, followed by the lifestyle intervention. We also document the retention and adherence to the Mindfulness in Motion with dietary counseling (MIM+Diet) intervention over the course of the two groups that had completed the program.

For Study I (survey) we started the analyses by exporting the data set from the online software—REDCap—to SPSS version 21. The initial process was to examine the data set for completeness. The most obvious aspect of missing information in the data set was due to subjects beginning the survey and not completing it. This meant for 71 subjects we had demographics data but had only a final of 59 (83.1%) subjects with complete surveys.

For missing data values within each sub-scale we took the approach of computing a mean value based on other items for that subject on the same scale. If the scale had a mix of positively scored and negatively scored items we took the average of the items scored the same way as that variable. We then scored the scales for all data where there was at least a 70% completion rate. For example, if a sub scale had 5 out of 7 responses we calculated missing scores. The next step we took was to code and calculate scores for questionnaires within the survey that had sub–scales. To do this we used the “compute variable” command within SPSS according to the scoring protocol for each measure.
Once we had completed this process we explored the data for outliers, normalcy of distribution and homogeneity of variance for key variables of interest.

**Cross-Sectional Survey Study (Study I)**

The following section will address the results of study I, a cross-sectional survey examining correlates of physical activity and dietary behavior among type I endometrial cancer survivors. In this study data from 71 subjects who started the survey with 58 complete responses was examined. Table 3 is an overview of some of the basic demographic information from this sample. In this section, we begin with a summary of basic descriptive statistics of the measures of interest and subsequently report the findings of the correlational and regression analyses addressing the primary hypotheses of interest.

We also examined BMI by category to better illustrate the distribution within the sample (Figure 8). From this figure it can be seen that there are a wide distribution of subjects by BMI category, further while there are women who fall in the normal and overweight categories the majority are obese. It should also be noted that BMI is not ideal for body composition but is easily computed from self-reported data.

Endometrial cancer subjects have been previously reported to engage in low levels of physical activity and to have poor dietary practices (von Gruenigen et al., 2011). The current study assessed both the estimated caloric expenditure through a combination of exercise and daily activity modalities (stair climbing) as well as time spent in walking. As many as 30-40% of women who are EnCa survivors are morbidly obese it was determined that walking would be an important form of low impact activity feasible for this population.
Table 3

**Demographics**

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td>61.7 (8.0)</td>
<td>43–84</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td>34 (10.5)</td>
<td>21.3–67.5</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>56 (82%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>5 (7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>16 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>36 (56%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate School or Higher</td>
<td>12 (19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Employment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently working</td>
<td>24 (39%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>28 (45%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Household Income</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75, 000 or more (highest)</td>
<td>28 (41%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Physical Activity

Below is a summary of the physical activity characteristics as determined from the survey using the modified Paffenbarger physical activity questionnaire (PAQ) (table 4). Of the 67 subjects that reported on physical activity roughly 13% acquired no reported daily energy expenditure from activity. 66% and 65% of subjects respectively, reported getting some walking related activity (exercise or commuting) and or engaging in some stair climbing each day. Despite this, the range and standard deviation of reported activity of this type was extremely large. For walking 82% of subjects would not have accumulated 150 minutes per week and the mean number of minutes walked per week was only 72 or just over an hour a week. Only 34% of subjects reported getting any
moderate to vigorous activity through a number of other activities that included stationary bicycling, Yoga/Tai Chi or Pilates, dancing/aerobics and weight training.

Table 4

Physical Activity Characteristics

<table>
<thead>
<tr>
<th>Mode of Activity</th>
<th>Subjects Reporting</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking (minutes/week)</td>
<td>44 (66)</td>
<td>72.4 (83.8)</td>
<td>0–315</td>
</tr>
<tr>
<td>Stairs (flights/day)</td>
<td>43 (65)</td>
<td>6.5 (12.7)</td>
<td>0–70</td>
</tr>
<tr>
<td>Cycling</td>
<td>8 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Training</td>
<td>8 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yoga/Tai Chi/Pilates</td>
<td>4 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dance/aerobics</td>
<td>6 (9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Caloric Expenditure (Kcal/week)</td>
<td>58 (86.6)</td>
<td>932 (1105)</td>
<td>0–4410</td>
</tr>
</tbody>
</table>

Diet

For the dietary habits reported by the research subjects there was complete data on 58 subjects, which was 83% of the sample. The scores for each food group and what they mean are shown below (Table 5) to make comparison with the survey samples scores (Table 6) more clear. For each of the categories the scores are representative of a slightly different quality of eating habits. Of the 58 subjects who reported on their dietary habits over the month prior to the survey 32 (55%) had poor choices in the grains category, which was an indication that not enough fiber and or not enough complex
carbohydrates were being consumed. In fact of the 32 that were below 11, a further 14 (25%) had scores of below 8, which is an indication of high risk for cancer.

For scores in the fruits and vegetables category only 2 subjects (3.5%) had a score in the poor choices range, 11 subjects (19%) in the fair choices range, while a majority of subjects scored in the fairly good range 26 (44%) and a further 19 subjects (33%) scored in the excellent range for fruits and vegetables.

Dairy scores showed that only 5 subjects had poor choices that required a change (9%). The majority of subjects 37 (64%) had fair choices that could use some improvements while 15 (26%) were making good choices and only 1 subject was considered to be making excellent choices when it came to their dairy selections.

Meat scores for the sample are a measure of protein intake and include items such as beans and fish. Scores in this category indicated that no subjects were in the poor category and at the opposite end no subjects were in the excellent category. This would seem typical for the American diet. However the majority of subjects scored in the fair category 36 (62%), which may mean it could improve for most, especially choosing lean proteins. A further 22 subjects (38%) scored in the good category for meat or protein choices.

In the fats and oils section a subject’s score indicates the general way a person may cook their meals or the type of meals they typically choose if eating out. 10 subjects (17%) scored in the poor category where a change would be highly recommended. Given the subject sample this is not surprising. 28 (48%) subjects reported scores in the range for good choices and the rest of the sample—20 subjects (35%) were making excellent choices.
The final category was “other” and referred to choices that included fast food, sugary foods and items such as alcoholic beverages. In the current sample 19 subjects (32%) were making poor choices and should take measures to improve. 23 (40%) subjects were making fairly good choices while 16 (28%) were making excellent choices.

Table 5

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Poor</th>
<th>Fair</th>
<th>Fairly Good</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains</td>
<td>8–11</td>
<td>12–15</td>
<td>&gt;16</td>
<td></td>
</tr>
<tr>
<td>Fruits &amp; Vegetables</td>
<td>&lt;11</td>
<td>11–16</td>
<td>17–22</td>
<td>&gt;23</td>
</tr>
<tr>
<td>Dairy</td>
<td>&lt;22</td>
<td>23–31</td>
<td>32–42</td>
<td>&gt;43</td>
</tr>
<tr>
<td>Meat</td>
<td>&lt;16</td>
<td>17–23</td>
<td>24–31</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Fats &amp; Oils</td>
<td>&lt;24</td>
<td>25–29</td>
<td>&gt;30</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>&lt;21</td>
<td>21–27</td>
<td>&gt;28</td>
<td></td>
</tr>
</tbody>
</table>

The results for the diet and physical activity patterns of a sample of type I endometrial cancer survivors does show that while some individuals are reporting levels and habits that are considered excellent, the vast majority could improve their lifestyle habits. The next step in the examination of the data was to determine the self reported quality of life of the sample and then finally to test the proposed hypotheses.
Table 6

Food Habits Questionnaire Scores

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains</td>
<td>10.5 (3.5)</td>
<td>2–17</td>
</tr>
<tr>
<td>Fruits &amp; Vegetables</td>
<td>19.7 (4.8)</td>
<td>7–28</td>
</tr>
<tr>
<td>Dairy</td>
<td>29.1 (5.7)</td>
<td>13–47</td>
</tr>
<tr>
<td>Meat</td>
<td>22.4 (3.3)</td>
<td>17–30</td>
</tr>
<tr>
<td>Fats &amp; Oils</td>
<td>27.7 (4.0)</td>
<td>20–37</td>
</tr>
<tr>
<td>Other</td>
<td>24.2 (4.1)</td>
<td>16–33</td>
</tr>
<tr>
<td>Total FHQ Score</td>
<td>133.9 (14.4)</td>
<td>102–172</td>
</tr>
</tbody>
</table>

Quality of Life and Health Related Quality of Life

Quality of life was examined using global and a more disease specific approaches, by a variety of measures. The scores for the various measures are reported in Table 7 below.

The disease specific measure of Health related Quality of Life (HRQL) is derived from the Functional Assessment of Cancer Therapy–General (FACT-G), with the added Endometrial specific component to produce the Functional Assessment of Cancer Therapy–Endometrial. The Fact-G is a well known measure within the cancer literature for assessing HRQL in a variety of samples of cancer patients and survivors. It can further be scored with subcomponents that include measures of functional well-being, physical well-being, social/family well-being and emotional well-being. The current sample of survivors had mean FACT-G scores of 85.9, which is a high mean score as
compared with previous studies with both a mixed cancer population and a population of the general public. In addition the scores for all the subcomponent scales had a mean at a level higher than or equal to norms. This is an indication that overall the sample had a high mean HRQL as reported by the FACT-G measure. It should be noted however that there were fairly large ranges on all scores with 33% of the sample scoring 80 or below. The minimum score reported was 21, which is extremely low.

Table 7

Quality of Life Measures

<table>
<thead>
<tr>
<th>Quality of Life Measure</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACT–G</td>
<td>85.9 (17.4)</td>
<td>21–107</td>
</tr>
<tr>
<td>Functional Well-being</td>
<td>21.7 (5.4)</td>
<td>2–28</td>
</tr>
<tr>
<td>Physical Well-being</td>
<td>23.2 (4.8)</td>
<td>9–28</td>
</tr>
<tr>
<td>Emotional Well-being</td>
<td>19.8 (4.4)</td>
<td>7–24</td>
</tr>
<tr>
<td>Social Well-being</td>
<td>21.2 (6.1)</td>
<td>0–28</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>54.0 (7.7)</td>
<td>33–64</td>
</tr>
<tr>
<td>FACT–EN</td>
<td>139.8 (21.8)</td>
<td>54–171</td>
</tr>
<tr>
<td>Perceived Social Stress</td>
<td>19.3 (3.8)</td>
<td>7–29</td>
</tr>
<tr>
<td>CES-D</td>
<td>16.9 (4.7)</td>
<td>7–29</td>
</tr>
<tr>
<td>Pittsburgh Sleep Quality Index</td>
<td>6.0 (3.5)</td>
<td>1–18</td>
</tr>
<tr>
<td>Satisfaction with Life Score</td>
<td>25.3 (7.0)</td>
<td>5–35</td>
</tr>
</tbody>
</table>
The perceived social stress scale (PSS) is a widely used measure of perceived stress and has been validated regularly with higher scores associated with failed efforts to stop smoking, failed efforts to control blood sugar among diabetic patients and higher incidence of colds. The mean score for the current population was higher than norms generated for females (13.8), white race (12.8) and age group >55 (11.9) indicating this sample did perceive their stress to be fairly high on average. Again there was a large range in scores with a low of 7 and a high of 29.

The Center for Epidemiological Studies Depression Scale (CES-D) was used to screen for depression and showed the current sample had mean scores for depression that on average were slightly above 16—an arbitrary cut point that is often used to determine a level that indicates depressive symptoms and while the measure is not for diagnostic purposes it may indicate high risk for depression.

The Pittsburgh Sleep Quality Index (PSQI) is a self-report measure of sleep quality. 7 distinct component scores are calculated and then used to produce an overall composite score. Higher scores indicate poorer quality of sleep. Specifically a score over 5 is associated with a poor sleep quality. In the current sample the mean score was a 6.0. As with many other measures the range in scores is large with a low (good sleep quality) of 1 and a high of 18.

The global measure of quality of life was assessed with the Satisfaction with Life Scale (SWLS). Findings yielded a mean score of 25, which according to the norms provided by Diener, would be considered high. This is again an indication that there was an overall high level of quality of life reported within this sample. However, it should
again be noted that within the sample there were individuals who had a really poor score on this measure with a low score of 5 reported.

**Hypothesis 1 & 2:** Our hypothesis was that higher levels of PA and better dietary practices would be associated with higher self reported QOL. Secondary hypotheses were that psychosocial variables would mediate this relationship.

To test these hypotheses we began by examining the bivariate correlations between all variables of interest. We set the level for significance at $p<0.05$ (two-tailed). In the bivariate analysis we included as a variable the BMI by category and whether subjects reported moderate or vigorous PA—which was coded as a dichotomous variable. (0=No, 1=Yes).

The bivariate correlations that showed significant relationships are reported in the correlation matrices below. The first matrix reported (Table 8) shows the bivariate correlations between physical activity and dietary measures and self reported quality of life as measured with the FACT-G, FACT-En and the SWLS.

From this matrix we can see that body composition—measured in terms of BMI category—was negatively associated with physical activity ($r=-.402, p<0.01$ and $r=-.263, p<0.05$) for PAQ kcal and MVPA respectively. PAQKcal is reflective of total self reported kcal of weekly energy expenditure and MVPA is a dichotomous variable—reporting or not reporting moderate or vigorous activity. Notably body composition was not associated with either HRQL or QOL measures in this sample.
Table 8

*Bivariate Correlations Between Lifestyle & Psychosocial Variables*

<table>
<thead>
<tr>
<th></th>
<th>BMI category</th>
<th>PAQ Kcal</th>
<th>MVPA</th>
<th>FHQ</th>
<th>FACT-G</th>
<th>FWB</th>
<th>PWB</th>
<th>SWLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI category</td>
<td>1</td>
<td>- .402**</td>
<td>- .263*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAQ Kcal</td>
<td>1</td>
<td>1</td>
<td>.372**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVPA</td>
<td>1</td>
<td>.290*</td>
<td>.346**</td>
<td>.290*</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHQ</td>
<td>1</td>
<td>- .268*</td>
<td>- .298*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACT-G</td>
<td>1</td>
<td>1</td>
<td></td>
<td>.587**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FWB</td>
<td>1</td>
<td>1</td>
<td></td>
<td>.663**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWB</td>
<td>1</td>
<td>1</td>
<td></td>
<td>481**</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWLS</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: **= p < 0.01, *= p < 0.05

Furthermore, self reported (SR) dietary behavior and self reported moderate to vigorous activity were associated with aspects of both domain specific HRQL (FACT-G, PWB and FWB) and also global QOL (SWLS). Interestingly, the food habits score was negatively associated with self reported HRQL as measured by the FACT-G ($r = -0.268$, $p = <0.05$) and more specifically the Functional Well-Being (FWB)($r = -0.298$, $p = <0.05$) sub-scale of the FACT-G. In terms of PA, SR moderate to vigorous weekly activity was associated with higher functional well-being (FWB)($r = 0.290$, $p = <0.05$), physical well-being (PWB)($r = 0.346$, $p = <0.01$) and global satisfaction with life (SWLS) ($r = 0.290$, $p = <0.05$). More proximal aspects of HRQL—FACT-G, FACT-En, FWB and PWB—were all positively associated with a more distal, global quality of life ($r = 0.587$, $p = <0.01$)($r = 0.577$, $p = <0.01$)($r = 0.663$, $p = <0.01$)($r = 0.481$, $p = <0.01$) respectively.
These results provide partial support to our 1st hypothesis with greater physical activity being associated with more favorable quality of life. However, in contrast to our hypothesis dietary habits were negatively associated with select aspects of quality of life.

In examining the 2nd hypothesis we first examined the associations between the social cognitive theory (SCT) and self-determination theory (SDT) variables and the lifestyle factors and quality of life factors before using a multiple regression model to test for mediation. The Table 9 below shows a correlation matrix used to explore the bivariate associations between SCT, SDT and lifestyle factors.

Table 9

Bivariate Correlations Between Lifestyle & Motivation

<table>
<thead>
<tr>
<th></th>
<th>BMIcategory</th>
<th>PAQ Kcal</th>
<th>MVPA</th>
<th>FHQ</th>
<th>MESES</th>
<th>AMS</th>
<th>AMOT</th>
<th>PCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMIcategory</td>
<td>1</td>
<td>-.402**</td>
<td>-.263*</td>
<td>-.288*</td>
<td>-.491**</td>
<td>.457**</td>
<td>-.379**</td>
<td></td>
</tr>
<tr>
<td>PAQ Kcal</td>
<td>1</td>
<td></td>
<td>.580**</td>
<td>.376**</td>
<td>464**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVPA</td>
<td>1</td>
<td></td>
<td>.560**</td>
<td>.267*</td>
<td>.398**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FHQ</td>
<td>1</td>
<td></td>
<td></td>
<td>-.268*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MESES</td>
<td>1</td>
<td>.429**</td>
<td>-.311*</td>
<td>.708**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMS</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMOT</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: MESES= self-efficacy (SCT), AMS=Autonomous Motivation, AMOT=Amotivation, PCS=Perceived Competence (all SDT)

Note: **=p<0.01, *=p<0.05
From the above matrix it can be seen that body composition is associated with aspects of exercise self-efficacy (SCT) and autonomous motivation, amotivation and perceived confidence (SDT) for exercise. Higher self-efficacy for exercise (MESES) is associated with lower BMI category ($r = -0.288$, $p = <0.05$). Similarly, higher autonomous motivation (AMS) ($r = -0.491$, $p = <0.01$), and higher perceived competence (PCS) ($r = -0.379$, $p = <0.01$) for exercise were associated with lower category of BMI. Higher levels of amotivation (AMOT) were associated with higher BMI category ($r = 0.457$, $p = <0.01$).

Of the SCT and SDT variables, only MESES and PCS scales were associated with aspects of HRQL (FACT-G, PWB and FWB). In addition while PCS had slightly stronger relationships than MESES, ($r = 0.359$, $p = <0.01$) and ($r = 0.297$, $p = <0.05$) respectively, both had similar strength relationships with FWB and PWB. MESES with PWB and FWB ($r = 0.414$, $p = <0.01$), ($r = 0.451$, $p = <0.01$) and PCS ($r = 0.389$, $p = <0.01$), ($r = 0.297$, $p = <0.05$). There was also a strong correlation between MESES and PCS ($r = 0.708$, $p = <0.01$). Overall these results suggest the select variables of social cognitive theory (self-efficacy) and self-determination theory were associated with exercise in the expected direction. Because these variables all correlated in the expected way, we decided to test multi dimensional self-efficacy (MESES), a single construct variable as a mediator of the effect of lifestyle on health related quality of life for hypothesis 3.

For the first model (A) we conducted a multiple linear regression (MLR) of HRQL (Functional Well-Being) onto lifestyle factors, including self reported weekly moderate/vigorous exercise and food habits score (FHQ) while controlling for BMI category. This model explained 25% of the variance in functional well-being ($R^2 = 25.4$, $p = <0.01$) ($F = 8.515$). The next MLR (B) regressed global quality of life (SWLS) onto
more proximal aspects of HRQL (FWB) and lifestyle factors controlling for BMI. This model explained 50% of the variance in global quality of life ($R^2=51.7$, $p=<0.01)(F=9.815$).

To look at the unique variance in global quality of life explained by lifestyle factors we regressed SWLS on BMI category, reporting moderate/vigorous exercise and food habit score (C). This model showed that lifestyle factors accounted for roughly 16% of the variance in global quality of life or life satisfaction ($R^2=16.3, p=<0.05)(F=3.116$).

![Figure 8 Analysis Model for Cross-sectional Survey Study](image)

Using the Baron and Kenny 4-step approach to test for a mediation effect we completed a number of simple regressions (Baron & Kenny, 1986). The first model was
similar to that in (A) where we regressed functional well being (FWB) on self reported moderate/vigorous exercise. This model was significant ($R^2 = 11.9$, $p = <0.01$). The 2nd step we regressed multi dimensional self-efficacy (MESES) on self reported moderate/vigorous exercise (D). This model was also significant ($R^2 = 31.8$, $p = <0.01$). In the 3rd step we regressed FWB on MESES (F) which was also significant ($R^2 = 11.6$, $p = <0.01$). The final step involves regressing FWB on both MESES and moderate/vigorous exercise. When controlling for MESES the coefficient for MVPA becomes non significant, Standardized Beta $= .225$, ($t = 1.495$ $p = <0.141$). However the reverse was also true and when controlling for MVPA, MESES was also non significant, Standardized Beta $= .214$, ($t = 1.420$ $p = <0.161$). This suggests that when controlling for MESES the effect of moderate and vigorous exercise is no longer significant and therefore its effects are mediated through self-efficacy. This finding means we cannot definitively say MESES mediates the effects of MVPA on FWB and therefore we reject hypothesis 2 in this case. However, in an exploratory step we conducted the same mediation analysis steps as above but used PCS instead of MESES. In this case we did find a mediation model was accepted. So if using perceived competence for exercise we would accept the second hypothesis.

**Hypothesis 3:** Our third hypothesis was that both SCT and SDT variables would be positively associated with both level of physical activity and better dietary practices. Specifically higher levels of self-efficacy (SCT) and higher competence and intrinsic motivation (SDT) would predict variability in the level of PA and dietary practices. This hypothesis was supported. First we tested a simple regression model where reporting moderate and vigorous exercise was regressed onto multi dimensional exercise self-
efficacy. This model was significant and supported the hypothesis that self-efficacy would also influence the level of MVPA in a reciprocal manner, which is in line with the theoretical model of SCT, ($F_{\text{change}}=26.138$) ($R^2=31.8$, $p=<0.01$). When regressing self-reported MVPA onto PCS we also found it significantly predicts self-reported MVPA, ($F_{\text{change}}=10.375$) ($R^2=.159$, $p=<0.01$), however it does not explain the same degree of variance. If we added, autonomous motivation (Intrinsic motivation) to the model we do not significantly increase the variance explained.
MIM + Diet Intervention (Study II)

The primary objective of study II was to examine the feasibility and preliminary efficacy of combining a mindfulness-based intervention with dietary counseling in the treatment of EnCa survivors. Consistent with the approach of reporting the results of study I, we begin with a summary of the basic descriptive statistics of the study sample and measures of interest and then subsequently report on the findings of the effects of the MIM+Diet intervention. Assessments of all outcomes of interest were obtained at baseline, 8-weeks and 14 weeks follow up after completion of the MIM+Diet intervention. The effects of the MIM+Diet intervention on changes in all outcomes of interest were analyzed using repeated measures ANOVA. Analyses were conducted using the intention to treat principle with the last value carried forward approach used to account for missing data. Where assumptions of sphericity were violated as determined by Mauchley’s test, we used the Greenhouse-Geisser adjustment to interpret main effects. Given this is a feasibility and preliminary efficacy study involving a small sample size effect sizes (Cohen’s $d$) were calculated by taking the mean difference and dividing by the pooled standard deviation to better estimate the meaningfulness of change for each observed outcome following the intervention. Finally we also conducted an exploratory analysis for intervention completers following the same steps as above where appropriate.

At completion of the MIM+Diet intervention, to assess the feasibility of our approach, participants were asked to evaluate the mindfulness and dietary counseling aspects of the study (Appendix F). Figure 7 below shows the responses out of a possible 5 for a number of categories including i) the professionalism of instructors, ii) Instructor knowledge, iii) Content usefulness for managing stress, iv) Needs as an EnCa survivor
met, v) Recommend MIM+Diet to others and vi) Time frame for MIM+D suitable. This indicates a high level of satisfaction with the intervention by those that completed.

Figure 7 Intervention Completion Survey

The demographics of the participants of Study II are reported below in Table 10. There was not much difference in the age of the study sample ($M = 61.1 \ SD$ 7) compared with the sample from the survey ($M = 61.7 \ SD$ 8).
### Table 10

**Demographics MIM+Diet Study**

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td>61.1 (7.0)</td>
<td>45–70</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td></td>
<td>33.8 (6.5)</td>
<td>23.0–49.5</td>
</tr>
<tr>
<td><strong>% Body Fat (IDXA)</strong></td>
<td></td>
<td>46.8 (6.6)</td>
<td>30.3–50.3</td>
</tr>
<tr>
<td>T2D Diabetes Mellitus</td>
<td>5 (29.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (64.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>4 (23.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>2 (11.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>15 (88%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>2 (12%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>3 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>10 (60%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate School or Higher</td>
<td>4 (23.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Employment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently working</td>
<td>6 (35%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>9 (53%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Household Income</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75,000 or more (highest)</td>
<td>9 (53%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The average BMI was in the class I obese category, and despite aiming to recruit a sample with a minimum BMI of 25 we did have two subjects who would be considered normal weight status. However, as can be seen from the body fat % measured with the
IDXA, none of the sample had a body fat % below 30 and a $M 46.8 \ SD \ 6.6$ for the sample.

**Physical Activity**

PA was assessed both with self-report (SR) and objective measures. SR physical activity was assessed with the modified PAQ. The accelerometer allowed for a step count for each day of a 7-day period. In addition, we had estimates of exercise intensity and minutes spent in that level of intensity each day. Light activity was 1-3 MET’s, moderate activity was 3-6 MET’s and vigorous activity was >6 MET’s. There was complete accelerometer data on 14 of the 17 subjects tested at BL. Below is a summary of the physical activity characteristics as determined from the LIFECORDER*plus* and the PAQ questionnaire.

Of the 17 subjects that self-reported on physical activity roughly 13% acquired no daily energy expenditure from activity. 66% and 65% of subjects reported getting some walking related activity (exercise or commuting) and or engaging in some stair climbing each day respectively. Despite this, the range and standard deviation of reported activity of this type was extremely large. From the LIFECORDER accelerometer, 82% of subjects would not have accumulated 150 minutes per week and the mean number of minutes of moderate to vigorous physical activity (MVPA) per week was only 72 or just over an hour a week.
Table 11

Physical Activity Characteristics

<table>
<thead>
<tr>
<th>Mode of Activity</th>
<th>Baseline Mean (SD)</th>
<th>Follow Up 1 Mean (SD)</th>
<th>Follow Up 2 Mean (SD)</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>LIFECORDER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steps/day</td>
<td>5334 (2686)</td>
<td>5272 (3820)</td>
<td>5714 (4069)</td>
<td>.14</td>
</tr>
<tr>
<td>LPA mins/wk</td>
<td>330 (129)</td>
<td>324 (150)</td>
<td>349 (169)</td>
<td>.13</td>
</tr>
<tr>
<td>MVPA mins/wk</td>
<td>65.7 (81.1)</td>
<td>82.6 (162.4)</td>
<td>88.0 (161.0)</td>
<td>.17</td>
</tr>
<tr>
<td>PAQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking (minutes/week)</td>
<td>57.5 (68.7)</td>
<td>72.8 (101.1)</td>
<td>123.4 (214.5)</td>
<td>.41*</td>
</tr>
<tr>
<td>Stairs (flights/day)</td>
<td>4.0 (5.4)</td>
<td>4.3 (5.3)</td>
<td>3.8 (3.5)</td>
<td></td>
</tr>
</tbody>
</table>

Note: MVPA = (3-6 METs), LPA = (1-3 METs)

Only 34% of subjects reported getting any moderate to vigorous activity through a number of other activities that included stationary bicycling, yoga/tai chi or Pilates, dancing/aerobics and weight training. The walking minutes were $M = 56$ per week from self-report (PAQ), a very low level of activity, however the range does indicate that some participants were engaging in a fair level of walking for activity purposes. Finally, stair climbing was reported at a mean level of 4 flights per day, however again the large range indicates that some participants walked up no flights of stairs while one participant in particular walked up roughly 20 flights per day.

Over the course of the intervention steps per day had increased on average by 380 steps and while this was not significant $F (2, 18) = 1.58, p = 0.233$, the effect size of
approached a small effect. Given the large SD we can see that some women in
the sample increased walking minutes a good deal. In terms of light physical activity (1-
3MET’s) we again did not see a significant increase $F (1.004, 9.036)=2.0, p =0.164$. The
effect size was also not large at ($d=0.13$). Again while not significant $F (1.002,
9.02)=2.603, p =0.141$, the increase in weekly MVPA approached a small effect ($d=0.13$).
The data for the persons who completed the intervention showed enhanced changes. For
steps per day the effect size was ($d=0.53$) a moderate effect, LPA ($d=0.28$) and MVPA
($d=0.45$). However, is should be noted this effect is due to a few individuals who increased
their exercise markedly over the course of the intervention. In terms of PAQ self report
for walking the pattern was the same with an effect size change to ($d=0.53$).

Physical Function

Another aspect of assessment in the current study was physical function (PF)—a
measure of the capacity of participants to complete tasks of daily living and an indication
of the capacity for independent living (table 12). The first battery of tests were for the
short physical performance battery (SPPB)—a balance test, a 4m usual pace gait speed
test, and a repeated stand from seated position in a chair. These items are individually
scored out of 4 and together form a total out of a possible 12 points. The majority of the
participants were high functioning with the overall SPPB score of $M 10.4 SD (1.0)$. More
specifically gait speed was measured at of $M 1.1 SD (.22) m/s$, which is indicative of
good function. Of the 3 tasks all women scored maximum points for balance but where
the most challenge was experienced was in the timed chair stands. The average time for 5
continuous stand from seated positions was $M 14.6 SD (5.0)$ seconds. Furthermore some
of the participants took more than 20 seconds for this task.
Other measures of physical function were the 400m-walk test—a measure that includes a component of cardiovascular function and which has been strongly correlated with morbidity and mortality outcomes—the stair climb test and the lift and carry test. The 400MWT time was $M \pm 342.5 SD 64.8$ seconds. All participants completed the task without exception. For the stair climb test again all participants completed the test without any trouble with a mean time to completion being 10.73 seconds. The lift and carry test, similar to carrying a load of laundry around the house or carrying a box with household items took $M \pm 11.49 SD 2.4$ seconds to complete. For all tests of PF there was a larger range in scores with some participants scoring on the low end and therefore indicative of some deficits in functioning.

The results of repeated measures ANOVA showed that there was a significant main effect of time on SPPB $F (1.38, 22.01)=6.55, p =0.011$. Effect size estimates revealed a moderate effect size ($d =.60$). For the chair stand aspect of the SPPB, results showed a significant main effect of time on chair stand performance $F (2, 32)=6.38, p =<0.01$. Effect size estimates indicated a moderate effect ($d=0.42$). The final repeated measure ANOVA indicated no significant effect main effect of time on stair climb time $F (2, 32)=0.02, p =0.98$, however there was a small effect size ($d=0.17$).

There were no other significant effects of the intervention on aspects of PF including the 400MWT or the lift and carry test. Due the fact that we did not specifically focus on aspects of physical fitness and or muscle strengthening exercises these results were to be expected. It is however an interesting finding that some aspects of physical functioning, an indication of the capacity to be independent, did improve over the course of the intervention, though it is possible this is partly a testing effect.
Table 12  

*Physical Function*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline Mean (SD)</th>
<th>Follow Up 1 Mean (SD)</th>
<th>Follow Up 2 Mean (SD)</th>
<th>Effect Size Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPPB</td>
<td>10.4 (1.0)</td>
<td>10.8 (1.1)</td>
<td>11.0 (1.0) ★</td>
<td>.60*</td>
</tr>
<tr>
<td><em>Gait Speed (m/s)</em></td>
<td>1.11 (.22)</td>
<td>1.14 (.20)</td>
<td>1.14 (.20) ★</td>
<td>.14</td>
</tr>
<tr>
<td><em>Chair Stand (secs)</em></td>
<td>14.6 (5.0)</td>
<td>13.0 (3.4)</td>
<td>12.6 (4.6) ★</td>
<td>.42*</td>
</tr>
<tr>
<td>400M Walk Time (secs)</td>
<td>342.5 (64.8)</td>
<td>342.9 (64.8)</td>
<td>338.5 (69.0)</td>
<td>.06</td>
</tr>
<tr>
<td>Stair Climb Time</td>
<td>10.7 (3.4)</td>
<td>10.7 (3.1)</td>
<td>10.7 (3.2)</td>
<td>0</td>
</tr>
<tr>
<td>Lift and Carry</td>
<td>11.5 (2.4)</td>
<td>11.3 (2.0)</td>
<td>11.1 (2.2)</td>
<td>.17*</td>
</tr>
</tbody>
</table>

Note: ★ Significant at the level <0.05, * = small to moderate effect size (0.2-0.7)

An ancillary analyses for those who completed the intervention revealed that ES estimates for SPPB went from (d=.60) to (d=.80), Gait speed went from (d=.14) to (d=.32), Chair stand time from (d=.42) to (d=.40), 400m walk time from (d=.06) to (d=.34), stair climb time from (d=0) to (d=.12), and lift and carry time from (d=.17) to (d=.23). While these are not large changes most aspects of PF would be considered to have improved by a small margin, though not statistically significantly. One exception is that a repeated measure ANOVA indicated a significant main effect of time on chair stand performance $F(1, 9)=16.958, p=0.003$.

*Diet*

For the dietary habits reported by the research subjects there was complete data on 16 subjects at BL, which was 94% of the sample. The scoring system for each food
group is reported in Table 8 previously. For each of the categories the scores are representative of a slightly different quality of eating habits.

Of the 16 subjects who reported on their dietary habits over the month prior to the start of the study 2 (12%) had poor choices in the grains category which was an indication that not enough fiber and or not enough complex carbohydrates were being consumed. 7 subjects in this sample had scores in the excellent range (44%), with the rest making fairly good choices.

For scores in the fruits and vegetables category, only 3 subjects (18.8%) had a score below the excellent choices range, with all 3 being in the fairly good category. This is somewhat similar to the responses to the survey in study I, where the majority of self-reported food choices indicate good choices are being made here.

Dairy scores showed that 4 subjects indicated poor choices that required a change (25%). The majority of subjects, 9 (56%) had fair choices that could use some improvements while 2 participants (12%) were making good choices while no participants were considered to be making excellent choices when it came to their dairy selections.

Meat scores for the sample is a measure of protein intake broadly and includes items such as beans and fish. Scores in this category indicated that no participants were in the poor category however at the opposite end of the range only 1 participant was making choices in the excellent category. This would seem typical for the American diet. The majority of subjects scored in the fairly good category 10 (62%), which may mean most participants are getting adequate protein, however the source of protein is not determined from this assessment for example choosing lean proteins.
In the fats and oils section scores indicate the general way a person may cook their meals or the type of meals they typically choose if eating out. 14 participants (87.5%) scored in the poor category where a change would be highly recommended. Given the subject sample this is not surprising. 2 (12.5%) of the participants reported scores in the range for good choices while no participant was making excellent choices.

The final category was “other” and referred to choices that included fast food, sugary foods and items such as alcoholic beverages. In the current sample 12 participants (75%) were making poor choices and should take measures to improve. 4 (25%) participants were making fairly good choices while again no participants were making excellent choices. Table 13 below shows the mean scores by category and the range of scores for each category.

As can be seen from Table 13, for four of the categories (Meat, Fats & Oils, Other, Total FHQ scores) self-reported scores were worse following the intervention. A repeated measures ANOVA’s revealed there were no significant main effects of time on self-reported food habits. However, when looking at data from subjects who completed (N=10) the intervention, effect size estimates (Cohen’s d) show that from Baseline to 8-weeks (follow up 1) the intervention did have some positive effects on the following categories of dietary habits; Grains (d=.06), Fruits & Vegetables (d=.37), Dairy (d=.17) and Total FH Score (d=.07), however for Grains (d= -.17), and the total FH Score (d= -.21) by follow up 2 the effect was negative meaning scores had worsened for these categories.
For other categories there were apparently no effects or negative effects from baseline to follow up 1 and follow up 2 for Meat ($d=0$) (No change) and ($d=−.13$), Other ($d=−.17$) and ($d=−.27$), Fats & Oils ($d=−.25$) and ($d=−.59$) respectively.

Table 13

**Food Habits Scores for MIM+Diet Study**

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Baseline Mean (SD)</th>
<th>Follow Up 1 Mean (SD)</th>
<th>Follow Up 2 Mean (SD)</th>
<th>Effect Size Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains</td>
<td>15.9 (3.1)</td>
<td>16.0 (3.5)</td>
<td>15.5 (3.4)</td>
<td>.03</td>
</tr>
<tr>
<td>Fruits &amp; Vegetables</td>
<td>27.3 (4.2)</td>
<td>28.1 (4.0)</td>
<td>27.6 (4.4)</td>
<td>.20*</td>
</tr>
<tr>
<td>Dairy</td>
<td>26.0 (5.2)</td>
<td>27.0 (6.5)</td>
<td>26.4 (6.5)</td>
<td>.17*</td>
</tr>
<tr>
<td>Meat</td>
<td>25.2 (3.5)</td>
<td>25.2 (3.6)</td>
<td>24.9 (3.7)</td>
<td>-.08</td>
</tr>
<tr>
<td>Fats &amp; Oils</td>
<td>21.8 (2.7)</td>
<td>21.0 (3.5)</td>
<td>20.4 (3.6)</td>
<td>-.44*</td>
</tr>
<tr>
<td>Other</td>
<td>17.0 (4.6)</td>
<td>16.9 (3.5)</td>
<td>16.5 (4.0)</td>
<td>-.12</td>
</tr>
<tr>
<td>Total FHQ Score</td>
<td>136.4 (19.3)</td>
<td>134.3 (15.3)</td>
<td>131.6 (17.2)</td>
<td>-.26*</td>
</tr>
</tbody>
</table>

Note: Cohen’s $d$ calculated for the largest differences, * = small to moderate effect size (0.2-0.7) intent to treat analysis

The results for the diet and physical activity patterns of a sample of type I endometrial cancer survivors does show that while some individuals are reporting levels and habits that are considered excellent, the vast majority could improve their lifestyle habits. The next step in the examination of the data was to determine the self reported quality of life of the sample.
Quality of Life and Health Related Quality of Life

Quality of life (QOL) was examined from both a global (Satisfaction with Life Scale) and a more disease specific, health related quality of life (HRQL) approach, by utilizing a variety of measures (FACT-G, FACT-En, RAND SF-36 and PSQI). The scores for these measures are reported in Table 14 below.

Table 14

Quality of Life Characteristics

<table>
<thead>
<tr>
<th>Quality of Life Measure</th>
<th>Baseline Mean (SD)</th>
<th>Follow Up 1 Mean (SD)</th>
<th>Follow Up 2 Mean (SD)</th>
<th>Effect Size Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>FACT–G</td>
<td>91.8 (12.6)</td>
<td>90.2 (12.5)</td>
<td>90.9 (10.4)</td>
<td>.06</td>
</tr>
<tr>
<td>Functional Well-being</td>
<td>23.0 (4.6)</td>
<td>22.9 (4.6)</td>
<td>23.0 (3.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Physical Well-being</td>
<td>25.7 (2.0)</td>
<td>25.4 (1.8)</td>
<td>25.7 (1.7)</td>
<td>.17*</td>
</tr>
<tr>
<td>Emotional Well-being</td>
<td>20.2 (4.2)</td>
<td>19.2 (4.7)</td>
<td>20.1 (3.9)</td>
<td>.21*</td>
</tr>
<tr>
<td>Social Well-being</td>
<td>22.9 (4.8)</td>
<td>22.8 (5.0)</td>
<td>22.2 (5.2)</td>
<td>-.14</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>54.1 (10.6)</td>
<td>53.5 (10.8)</td>
<td>53.8 (11.0)</td>
<td>.02</td>
</tr>
<tr>
<td>FACT–EN</td>
<td>142.7 (22.8)</td>
<td>143.7 (20.7)</td>
<td>144.7 (20.0)</td>
<td>.09</td>
</tr>
<tr>
<td>SF-36 MHS</td>
<td>75.9 (17.2)</td>
<td>80.1 (12.6)</td>
<td>80.6 (9.6)</td>
<td>.34*</td>
</tr>
<tr>
<td>SF-36 PHS</td>
<td>81.7 (10.0)</td>
<td>83.3 (9.9)</td>
<td>83.0 (9.5)</td>
<td>.13</td>
</tr>
<tr>
<td>PSQI</td>
<td>11.8 (3.2)</td>
<td>10.7 (2.8)</td>
<td>10.5 (2.5)</td>
<td>.45*</td>
</tr>
<tr>
<td>SWLS</td>
<td>25.6 (8.1)</td>
<td>27.5 (6.4)</td>
<td>27.1 (7.2)</td>
<td>.20*</td>
</tr>
</tbody>
</table>

Note: Cohen’s d calculated for the largest differences * = small to moderate effect size (0.2-0.7) intent to treat analysis
The current sample of survivors had a FACT-G scores of $M = 91.7$ $SD = 12.6$, which is a high mean score as compared with previous studies including both a mixed cancer population and a population of the general public. In addition the scores for all the subcomponent scales had a mean at a level higher than or equal to norms. This is an indication that overall the sample had a high mean HRQL as reported by the FACT-G measure. It should be noted however that there were fairly large ranges on all scores with a proportion of the sample reporting less than favorable scores. The minimum score reported was 21, which is extremely low.

Repeated measure ANOVA’s to determine the effects of the MIM+D intervention on FACT-G and subscales, were all non significant and are thus not reported.

For FACT-G and all but one subscale (SWB) of FACT-G, it seemed that there was a slight decline in score from Baseline to follow up 1 at 8 weeks, however this was not statistically significant. From the 8-week point to the final follow up at 14 weeks all the scores had returned to a baseline level, again this was not statistically significant, however Cohen’s $d$ effect sizes are reported in Table 14 to reflect the change from 8 weeks to 14 weeks. Only physical well-being and emotional well-being (PWB and EWB) had effect sizes approaching what would be considered a small effect ($d=.20$).

The mental health and physical health summary (MHS and PHS) scores from the RAND SF-36 were not statistically different across the time course of the intervention, however both showed slight improvement according to effect size estimates. MHS changed more as a result of the intervention ($d=.34$), a moderate effect, while that for PHS ($d=.13$) was a negligible effect.
The Pittsburgh sleep quality index (PSQI) is a self-report measure of sleep quality as measured over 7 categories, which are used to produce a composite score. Higher scores indicate poorer quality of sleep. Specifically a score over 5 is associated with a poor sleep quality. In the current sample the score at baseline was $M = 11.8\ SD = 3.2$ indicating that all participants in the study had a compromised sleep quality. The range in scores was also relatively large with a low (good sleep quality) of 7 and a high of 20.

A repeated measure ANOVA found no significant main effect of time on sleep quality $F (1.38, 22.07) = 3.04, p = 0.084$. However on conducting an effect size analysis we found there to be a moderate effect ($d = 0.45$). It is worth noting that despite the effect of the intervention on sleep quality the overall mean score following intervention ($M = 10.5\ SD = 2.5$) still indicated compromised sleep quality for all subjects.

The measure of global quality of life (SWLS) indicated a score of $M = 25.6\ SD = 8.1$, which according to the norms provided by Diener would be considered high. This is again an indication that there was an overall high level of global quality of life reported within this sample. However, it should again be noted that within the sample there were 4 individuals who had a relatively poor scores on this measure ($Range = 11-14$).

A repeated measure ANOVA indicated there was no significant main effect of time $F (1.25, 20.06) = 3.04, p = 0.089$ on SWLS. Despite the lack of significance there was a small effect size ($d = 0.20$).

The ancillary analyses for those who completed follow up 1 & 2 visits revealed the following. ES estimates for FACT–G Cohen’s $d$ increased from ($d = 0.06$) to ($d = 0.25$), for FWB from ($d = 0.02$) to ($d = 0.17$) PWB from ($d = 0.17$) to ($d = 0.53$), for EWB from ($d = 0.21$) to ($d = 0.49$), for SWB from ($d = -0.14$) to ($d = 0.12$) for ENC from ($d = 0.02$) to ($d = 0.25$) and finally
FACT–En from ($d=.09$) to ($d=.38$). These are all positive changes that result in small to moderate ES estimates.

ES estimates for the MHS and the PHS changed from ($d=.34$) to ($d=.32$) and from ($d=.13$) to ($d=.05$) respectively. Both of these composite scales decreased however the ES for MHS was still moderate in size. For the PSQI, ES estimates changed from ($d=.45$) to ($d=.40$) which is a reduction but still a moderate ES and finally for SWLS we found a change from ($d=.20$) to ($d=.52$), which was a moderate effect size increase.

The final outcomes of interest related to the intervention were scores on two separate mindfulness measures. The scores for the mindfulness attention awareness scale (MAAS), and the five-factor mindfulness questionnaire (FFMQ) are reported in Table 15 below. The MAAS is a one-dimensional measure while the FFMQ is composed of 5 separate but related underlying constructs.

There were no significant main effects of time on any of the five factors analyzed as part of the FFMQ. There were some small effect sizes as calculated using Cohen’s $d$. However, only the Observe ($d=.17$) and Non-react ($d=.22$) constructs had values that represented any meaningful effect. Exploratory analyses for completers showed no significant main effects for any of the FFMQ subscales as a result of the intervention.
Table 15

*Mindfulness Measures*

<table>
<thead>
<tr>
<th>Mindfulness Measure</th>
<th>Baseline Mean (SD)</th>
<th>Follow Up 1 Mean (SD)</th>
<th>Follow Up 2 Mean (SD)</th>
<th>Effect Size Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FFMQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Observe</em></td>
<td>30.2 (5.1)</td>
<td>31.1 (5.3)</td>
<td>30.7 (5.7)</td>
<td>.17*</td>
</tr>
<tr>
<td><em>Non-judge</em></td>
<td>30.8 (6.3)</td>
<td>30.2 (6.6)</td>
<td>30.6 (5.7)</td>
<td>-.03</td>
</tr>
<tr>
<td><em>Non-react</em></td>
<td>23.9 (4.8)</td>
<td>23.2 (5.5)</td>
<td>24.4 (5.6)</td>
<td>.22*</td>
</tr>
<tr>
<td><em>Describe</em></td>
<td>30.1 (5.5)</td>
<td>29.9 (5.9)</td>
<td>30.1 (4.8)</td>
<td>.04</td>
</tr>
<tr>
<td><em>Act with Awareness</em></td>
<td>28.9 (3.9)</td>
<td>28.8 (3.4)</td>
<td>29.2 (3.7)</td>
<td>.11</td>
</tr>
<tr>
<td><strong>MAAS</strong></td>
<td>66.6 (12.0)</td>
<td>68.1 (8.8)</td>
<td>70.4 (9.9)</td>
<td>.35*</td>
</tr>
</tbody>
</table>

*Note: Cohen’s d calculated for the largest differences*  
*    * = small to moderate effect size (0.2-0.7) intent to treat analysis

A repeated measure ANOVA found no significant main effect of time on mindfulness as measured with the MAAS $F(1.43, 22.95) = 2.01, p = 0.165$. The calculation of Cohen’s $d$ indicated a small to moderate effect size of the intervention on aspects of mindfulness as measured by the MAAS ($d = .35$).

However, a second repeated measure ANOVA for those persons who completed follow up, revealed a significant main effect of time on mindfulness as measured with the MAAS $F(2, 18) = 3.924, p = 0.039$. Further ES estimates for this data resulted in a moderate effect ($d = .62$). Figure 8 below shows the resultant graph of the change in MAAS with time.
Figure 8 Mindfulness Over Time Assessed with the MAAS for Intervention Completers
Chapter 5: Discussion

The current dissertation included two separate but related studies and had the following aims: 1) To describe and evaluate the procedures and challenges of the recruitment of a population of endometrial cancer (EnCa) survivors to lifestyle related research, 2) Explore the relationships between the theory-based correlates of physical activity and dietary habits (lifestyle) and quality of life outcomes (study I). 3) To test the feasibility and preliminary efficacy of delivering a single-arm mindfulness based intervention coupled with dietary counseling to a population of EnCa survivors (study II).

Cross sectional survey (study I)

Our findings partially supported hypothesis 1 with physical activity but not dietary habits being associated with aspects of quality of life. In addition, participants who reported higher caloric expenditure as a result of physical activity (PA) and who reported engaging in moderate to vigorous physical activity (MVPA) were in a lower BMI category. Regarding hypothesis 2, we did not conclusively find multi-dimensional exercise self-efficacy, a theory based psychosocial construct, to mediate the relationship between PA and select quality of life outcomes. However perceived competence for exercise did mediate this relationship. Hypothesis 3 was that higher levels of self-efficacy (SCT) and higher perceived competence and intrinsic motivation (SDT) would be associated with greater levels of PA and better dietary practices. Again, the findings only provide
partial support for the 3rd hypothesis, as higher levels of self-efficacy and perceived competence, but not intrinsic motivation, were associated with PA.

*MIM+Diet Feasibility and Efficacy Study (Study II)*

From a feasibility standpoint we did experience challenges to the recruitment process. However, using a number of adjusted approaches over the course of many months did eventually lead to accruing a sample of EnCa survivors who were interested and participated in the MIM+Diet intervention. Future studies will certainly benefit from the information obtained in this process. With regard to feasibility, the intervention was considered safe and tolerable. Study completion surveys revealed high levels of satisfaction with the intervention and that participants would recommend it other EnCa survivors (Figure 9). The time frame for the active intervention (8-weeks) and the time commitment (1 hour per week) were deemed to be appropriate and sufficient to yield improvement in the targeted outcomes. Despite some participant attrition, there were no participant complaints or adverse events during the intervention. With respect to the efficacy of the intervention, the observed effect sizes suggest that participants who attended regularly and adhered to the program experienced meaningful improvements in sleep quality, physical function and quality of life outcomes. Additionally, some participants lost weight, improved dietary patterns and began to exercise at levels more consistent with national guidelines. With a high proportion of participants having comorbidity, these are findings that reflect positive lifestyle changes.

**Significance**

There were an estimated 56,230 new cases and 8,590 deaths as a result of endometrial cancer in 2014 (Siegel et al., 2014). However, survivorship odds are
particularly high with an estimated 95% of patients surviving 5 years or more if diagnosed with localized disease (Siegel et al., 2013). One of the most significant challenges for EnCa survivors is in preventing recurrence, maintaining their health status and reducing risk for the onset of comorbidity—of which endometrial cancer survivors are at a disproportionately high risk. One of the primary means by which EnCa patients can maintain and even improve health in survivorship is by improving their lifestyle behaviors (Courneya et al., 2005). This approach includes eating a healthy diet low in fat (Dalvi, Canchola, & Horn-Ross, 2007), engaging in regular physical activity and managing psychological stress. To date there have been limited examinations of the most effective way to change lifestyle in this high-risk population (McCarroll et al., 2013). It is however recognized that well designed, theory-based interventions are an important step in the process of refining recommendations to this end. The first step is to engage a population of endometrial cancer patients in this research process.

**Recruitment**

A significant challenge to conducting research with a population of endometrial cancer survivors was in recruiting a representative sample. Endometrial cancer survivors are subject to a number of challenges across the cancer experience. These include comorbidity associated with obesity, such as TTDM, CVD and a decline in physical function, which may lead to a loss of independence (von Gruenigen et al., 2006; von Gruenigen et al., 2011; Ward et al., 2012). Lifestyle related interventions for a population of survivors that are inactive, obese and who have poor dietary habits may be a daunting challenge and therefore a hard sell. Previous research has shown that the diagnosis of EnCa does not seem to lead to this population making lifestyle changes (Basen-Engquist
et al., 2009). However, for many patients the diagnosis of cancer has been suggested as a “teachable moment”, whereby attempts at lifestyle change may be more successful due to the nature of the individual’s motivation (Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005).

The initial strategy of recruiting the current patients of OSUMC gynecological oncologists during their regular clinic visits was seen as an appropriate approach. Based on early consultations and a review of the number of patients seen on an annual basis we were optimistic that target accrual would be successfully achieved. Unfortunately, a number of factors may have hindered this approach. 1) *Using technology to conduct real-time surveys*: Many of the patients were older women who had limited experience with technology. This was understood fairly early in the recruitment process and paper versions of the survey were provided as an alternative approach. Fortunately many women did use email and consented to having an online link to the survey emailed to them. The benefit of this approach was that follow-up reminders could be sent from the REDcap software and we were able to determine who had responded. Roughly half of the final responses from in clinic approaches were paper and half were online. 2) *In clinic vs. Mailout*: There were 110 possible patients seen in clinic over a 12 month period and based on our target accrual this method was inefficient. Only one recruiter was approaching patients on a clinic day, therefore the amount of time spent per patient who actually responded to the survey made this approach unfeasible. A further factor that influenced the receptiveness of patients to the survey process was how the researcher had access to patients. Understandably nurses in the clinic are busy with regular aspects of their job, however depending on the buy in of the nursing staff to the research process,
the study was either described to patients in a good light or not really given much attention. Future approaches that determine how to most effectively involve and engage clinic staff in the recruitment process are warranted (Pisu, Manne, Basen-Engquist, & Alfano, 2014). Despite lower than anticipated response rate (Table 2) to the mailout invitations for both the survey and the intervention, the reduced time relative to a larger pool of patients means this approach is recommended in future approaches.

Overall, to recruit the original number of patients targeted in the intervention (40), we would have needed to see roughly 280 patients in clinic or mail out an invitation to 950 local Columbus based patients. In a single year–period there were roughly 260-280 eligible Columbus based patients who were treated through the OSUCCC. Therefore to increase the numbers of patients seen it would also be recommended to develop relationships with clinics outside of the OSU system. While this was attempted, it was difficult to establish a relationship given the current resources of the study. Thus, subsequent optimally powered lifestyle intervention studies may require a multi-center research approach from both a feasibility and efficacy perspective.

Notwithstanding the challenges of recruitment, it should be noted that barriers are common for many researchers who are aiming to deliver interventions to cancer survivors. At a recent national conference, a panel discussion highlighted the following recruitment approaches and results (Pisu et al., 2014). In the Steps to Health program, 646 endometrial cancer survivors from MD Anderson were invited to participate in a study of lifestyle behavior change that included physical activity. In the initial period from March to August only 1 patient had been recruited. Of the final 646 eligible patients 185 (28%) showed an interest in the study and 100 (15.4%) had baseline visits conducted.
These numbers are slightly higher than those for the current study however this was a large randomized controlled trial with an R01 funding mechanism. Furthermore the intervention offered in this study was to be delivered from distance as opposed to requiring a weekly time commitment. This approach incorporating momentary ecological assessment (EMA) is novel and would negate a common barrier to participation—travel to the intervention location. One interesting observation from the study investigators was that the most important factors influencing whether patients showed interest in the study was having a face to face contact to describe aspects of the intervention and also having physicians telling their patients they thought the study was important. Consequently, these may be particularly critical aspects in successfully recruiting EnCa patients and/or survivors into future lifestyle intervention studies.

For the next study, accrual targets for an intervention were expected to take 15 months but ended up taking 39 months at 13 different recruitment sites. Another study reporting on recruiting couples—one partner having had a diagnosis of cancer—to participate in an intervention related to intimacy following prostate cancer. 2250 couples were approached to accrue 300 participating couples (14%) over 7 years. Other examples of cancer populations being recruited into interventions reported approaching 828 subjects to randomize 126 subjects, a response rate of 15.2%. In summary, the panel’s researchers suggested that including samples with more than one cancer type could help to increase the pool of survivors being approached. However, the challenge to this strategy was that funding agencies tended to favor homogenous populations of survivors to better isolate mechanisms of benefit. Another suggestion was to use national registries to approach patients at multiple sites. These methodologies involve large resource pools
in terms of both funding and personnel.

The response rate to the MIM+D intervention was somewhat lower (9.8%) than that observed in the prior studies discussed above. However, the survey (13.8%) was consistent with that observed in these previous studies. Given the limited resources of this investigation and the time frame available this was acceptable. Future approaches do need to take into account the specific challenges of each unique environment and the implementation of lessons learnt from other studies can help to overcome recruitment barriers. If the resources allow, using consultants with marketing experience could aid in recruitment to research studies as they are essentially a “product” that may help a cancer survivor. Those who completed the current intervention reported that they would have liked to have been offered this kind of program when they were first diagnosed with endometrial cancer. In contrast the majority of patients in the current intervention were recruited via patient records meaning many of them were in the final phases of their 5-year follow up care. Referring back to the “teachable moment” hypothesis—patients newly diagnosed may be more likely to think about making lifestyle choices than those who have been surgically treated “cured”, and who after 5 years are not as concerned about the risk factors and their disease. Furthermore, there were cases of patients who on being approached about participation during clinic visits responded that “they were cured of cancer and why would they need an intervention”. This may shed light on the mindset of many survivors who due to the successful nature of treatment for early stage (I&II), type I endometrial cancer do not feel lifestyle change is necessary. In contrast, a recent study of Danish breast cancer survivors, found that of 1281 eligible subjects, those that showed an interest in a psychosocial intervention involving MBSR were younger and
further from initial diagnosis than survivors who declined participation. There was not found to be any other significant difference based on comorbidity, work place stress etc. (Wurtzen et al., 2013).

In summary, regarding the recruitment process, cancer patients and endometrial cancer survivors in particular are in need of lifestyle change. Being able to more effectively communicate the importance of this change to these patients may improve recruitment. Having the buy-in of physicians and their staff will aid in emphasizing this importance. It is, however, recognized that the treatment regimen requires significant resources and prioritization is paramount. Therefore, for many newly diagnosed patients, direct cancer therapy that involves surgery is the first line of defense. Stress reduction and lifestyle changes may however support this approach.

Development of recruitment approaches that can capture the largest pool of eligible patients via mailout, online and multiple patient databases will aid in this endeavor. In addition to the large-scale efforts involving databases, by concurrently approaching newly diagnosed patients during clinic visits we could also improve interest. While this investigation showed that many older patients may be challenged by research approaches involving technology, as time moves forward and technology becomes more available and understood, incorporating these approaches will yield increasingly favorable results.

**Demographics**

In the following section will address and compare the demographics from both study I and study II concurrently as we targeted the same group for both. From the survey results we saw that the mean age for participants was 61.7 years of age with a range of
roughly 40 years (Table 3). The mean calculated BMI was 34kg/m², which would be considered obese class I. 60% of the total sample had a BMI over 30kg/m², 73% of participants were overweight or obese and 25% of the sample were considered to be class III or morbidly obese with a BMI >40kg/m². When looking at BMI by category we saw a fairly large range of scores. While there were a fair number of normal BMI participants, a large proportion were obese and obese class III. This is in line with the typical patient demographics that are reported in the literature.

Courneya et al., (2005) reported that 72% their sample of 386 female endometrial cancer survivors were overweight or obese. Similar to the present study the mean age of the sample was 64±10, and the majority of participants were college educated and currently retired. This seems to be an indication that this population of survivors is fairly homogenous. Interestingly they reported that roughly 50% of their population was under the age of 65 while 75% of our population was 65 or younger. Given that the Courneya and colleagues study was conducted 10 years ago, this may represent a shift towards women being diagnosed with EnCa at a younger age. Furthermore with the current trends in obesity this would be possible. As is common in research trials, the majority of this population was also white and 40% were considered to be in the highest income bracket. 45% of the sample was retired but there were still a large proportion of women currently working full time (39%).

With regards to the demographics of the MIM+Diet participants, BMI was very similar to those in the survey 33.8 vs. 34kg/m². One extra level of measurement was from the IDXA scanning device. This device is now considered the gold standard for body composition testing and allows measurement at high degree of precision. The current
sample had extremely high levels of body fat \( M \ 46.8\% \ SD \ 6.6 \). Furthermore, what is interesting to note is that despite two participants in the intervention being normal weight by BMI criteria, neither had a baseline body fat \% below 30. In fact the participant with the lowest BMI at \((23 \text{ kg/m}^2)\) had a body fat percentage closer to 40\%. This is an important finding. If patients who are at risk for disease progression are screened by BMI criteria only we may miss the high level of adiposity, which could have future implications for disease risk. This may be especially important in a population of endometrial cancer survivors where there is a strong link between adiposity and disease. This further highlights the need for healthy lifestyle activities, even for women that may not seem overweight. As is the case with most research trials, participants interested in the MIM+Diet program were also well educated and from higher levels of socioeconomic status. This is certainly not representative of the larger population of survivors and finding ways of advertising and making available services that can offer benefit to all patients and survivors is critical.

Another observation is that many of the demographic characteristics of these women are no different from that of the general population. There are a large number of overweight and obese women at risk for chronic disease so why should there be a special approach for these women? It is plausible to suggest that despite aspects of this being true, one difference is the psychological effect of a cancer diagnosis. This has previously been framed in the context of a “teachable moment” and may offer a very unique opportunity to make lifestyle changes. It is however important to do this at a time when the significance of a diagnosis is most impactful.
Cross-sectional Associations among Physical Activity, Diet and QOL

As expected the majority of EnCa survivors—who are typically overweight or obese—did not engage in physical activity levels associated with health promotion and disease prevention. Only 18% of women achieved a self-reported level of activity consistent with the current national physical activity guidelines. Given that self-reported physical activity is frequently overestimated it is possible that even a smaller proportion of the sample was actually accruing recommended amounts of physical activity (Baranowski, 1988). More specifically, it was observed that only 35% of women reported doing any type of moderate or vigorous activity (MVPA), which could essentially be called exercise. Whether the intensity of the exercise was actually moderate or not is difficult to determine. However, what does support the fact that this activity was at a level required to achieve health benefits is the association between reporting moderate exercise and both physical well being (PWB) and functional well being (FWB)—as assessed with sub scales of the functional assessment of cancer therapy (FACT). Also, self-reported moderate levels of exercise was associated with global quality of life (SWLS). Although reporting any amount of MVPA (yes/no) was associated with BMI category, physical activity energy expenditure (PAEE) that included walking and stair climbing was more strongly related to BMI category than MVPA alone. This could be interpreted to suggest that exercise (MVPA) is associated with HRQL, global QOL and body composition, but taking into account daily activity such as walking and stair climbing strengthens the relationship between activity and these outcomes. Assessing overall physical activity related caloric expenditure through the tracking of multiple modes of daily activity is one way to do this and has been previously used as a method to
quantify physical activity energy expenditure (PAEE) (Jakicic, Wing, & Winters-Hart, 2002; Jeffery, Wing, Sherwood, & Tate, 2003).

For a population of obese individuals, who are unlikely to be exercising at the level of the current guidelines, we may need to tailor our approach to fostering lifestyle change. While beginning to exercise is a valuable endeavor, it should not be an all or nothing approach. Simply increasing daily activity through stair climbing and or walking can impact health outcomes. Once this is achieved a further adjustment to include higher intensities of exercise may be more feasible. Given that the relationships are cross-sectional in nature it is also possible that BMI category is associated with greater self-reported MVPA because lower BMI persons are more capable of engaging in exercise. There is some evidence to suggest obese individuals are at greater risk of injury when starting to exercise, especially in high impact activities and at relatively high intensities. Vincent (Vincent & Vincent, 2013), examined the differences in biomechanics of gait and ground reaction forces in obese compared with non-obese subjects at two different walking speeds. They found alterations in gait and muscle recruitment in obese subjects that could make them susceptible to injury when beginning to walk or walking at higher intensities. This finding implies that the initiation of even low levels of activity and further exercising at moderate to vigorous levels is not without risk. Given that physical activity should be a lifestyle change it is our opinion that initiation should be either under the direct guidance of exercise professionals or at a low level initially. Once a basic level of fitness is engendered a more progressive program may be advised.

Regarding the assessment of food habits, while there was a relationship between higher (better) general food habits scores and physical activity related caloric
expenditure, there did not seem to be a relationship between food category scores and any health outcomes, either in terms of body composition or quality of life. However, one interesting negative relationship was found between total food habits score, possibly driven by the dairy category, and FACT score. This may have been driven by the relationship with the functional well being (FWB) sub scale, however it is unclear as to why higher (better) scores in the dairy category or total food habits scores would be associated with lower HRQL or lower functional well being. The specific items of the FACT that made up the FWB sub scale included questions such as “I am able to work” and “I have accepted my illness” but also questions that are more global in nature such as “I am able to enjoy life”. One possibility is that persons who feel they should limit or restrict certain aspects of their diet to “eat well or healthily” may experience a reduction in a sense of enjoyment of life.

Given that the food habits questionnaire (FHQ) was designed with the food pyramid in mind and that many of the current guidelines are taught based on the new MyPlate (Agriculture & Services, 2010) guidelines, this measure may not have been the most suitable. Nonetheless, it does capture broad food related choices and is useful as a screening tool. In the original RENO diet-heart study (Silverstein, 1997) the FHQ was designed to be used in conjunction with food records and more detailed assessments of caloric intake. Given the current surveys length, anything more would have been cumbersome. The authors did report that the food categories had less internal reliability (chronbachs alpha=<0.7), except for fruits and vegetables, than did the total food score. This may be one reason significant associations between these food categories and outcomes of interest were not consistently observed in the present study.
In terms of the usefulness of the FHQ to identify areas of concern relating to an individual’s diet, we did see that the majority of participants reported less favorable dietary habits. Mean scores for Grains were in the poorest category, Dairy and Meat scores were considered fair—the second lowest level—while Fats and Oils and Other were fairly good. It is apparent that Fruits and Vegetable scores were better than all the other for choices which may be an indication that the information about eating 5 or more fruits and vegetables a day for cancer survivors is well marketed and understood. It may however also be the case that cancer survivors know they are meant to be eating lots of fruits and vegetable and so their self report is reflective of bias towards this. In a study conducted by Brug et al., (1994), assessments were made of persons attitudes and beliefs towards eating a low fat diet in conjunction with actual dietary fat intake measurements. Results revealed a relatively low correlation between the two. Thus, despite people having positive attitudes towards low fat diets, they did not report consistently eating low fat foods. Additionally, in the original validation of the FHQ, responses were compared with actual intake as assessed with a 1-day recall. Significant correlations were found between food category scores for Dairy, Meat, Fats and Oils, Other and total caloric intake, carbohydrate intake and fat intake. Total FH scores were also associated with the same aspects of caloric intake. The authors did suggest that as the questionnaire was designed on the food pyramid and respondents were rewarded for low fat choices that this bias may have been behind some of the relationships seen.

**Health Related Quality of Life**

Given the low levels of physical activity, prevalence of obesity and older age of the sample, it was expected that there would be deficits in self reported aspects of both health
related quality of life and a more global well being. However, the overall mean FACT-G and FACT-En scores for the sample did not indicate low levels of HRQL. In a previous study by Fader et al (Fader, Frasure, Gil, Berger, & von Gruenigen, 2011), quality of life as measured by the FACT-G and sub scales in a sample of 152 overweight and obese endometrial cancer survivors found similar levels of functional well being, physical well being and overall FACT scores observed in the present sample. In their analysis they broke down HRQL scores by BMI and found that the mean scores for women considered normal/overweight was 88.1, which is slightly higher than our total sample mean of 85.9 and also higher than the general population norm of 80.1 from a Brucker et al’s (Brucker, Yost, Cashy, Webster, & Cella, 2005) normative data study. However, in the normative data study comparing Cella’s original validation sample of cancer patients and the U.S population sample there were a wide range of ages including people 18-45. Fader’s study used a one-way ANOVA to compare BMI category by FACT-G and sub scales and found that there were only significant differences in the PWB sub scale by BMI category. They did break down their BMI categories differently to the current study using normal weight/overweight (<30), obese (30–39.9) and morbidly obese (>40). For comparisons sake we readjusted our data to fit their categories, which gave us a more even distribution among categories and found that our normal/overweight group had a similar mean FACT-G score of 88.4, however our obese category was lower with a score of 79.8 vs. their 83.6. Noticeably our morbidly obese group—smaller in sample than the other two groups—had a score slightly higher than our normal group at 88.8. This is difficult to explain as this would be considered a high level of health related quality of life and nearly 6 points higher than the same BMI category in the Fader study. Overall the current
sample reported a good level of health related quality of life, however there is a large range in scores and 31% of the sample had total FACT scores below the U.S. population norm.

In terms of the sub scales our sample had FWB and PWB scores of 21.7 and 23.2 respectively, and these sub scales were almost identical to scores in the Fader study with their obese population having scores of 21.8 and 23.9. These scores were again higher than the norms for general cancer patients and the US population.

Overall, with many respondents to the survey indicating high health related quality of life and quality of life, there would theoretically not be much room for improvement (ceiling effect) should these same persons be interested in an intervention. In contrast it may also be that individuals who are lower in terms of HRQL to begin with are the ones that are interested in some form of intervention. This has previously been suggested regarding a sample of women who participated in a yoga intervention (Kraemer & Marquez, 2009).

Social Cognitive Theory and Self Determination Theory

Given that one of the primary goals of the cross sectional survey was to explore whether a framework for lifestyle change could be based on sound psychosocial theory, we wanted to explore how either SCT or SDT theory variables would be associated with both lifestyle and HRQL and QOL. Results revealed that multidimensional self-efficacy for exercise behavior (SCT), intrinsic motivation and perceived competence were similarly related with physical activity and MVPA (exercise) as well as with aspects of HRQL and global QOL. These findings suggest that when designing interventions to change lifestyle behaviors, we should take theory driven approaches into account as they
can enhance the efficacy of the treatment effect. For example previous studies have found self-efficacy to mediate the effects of physical activity on health status and global quality of life (McAuley et al., 2006). In this study McAuley and colleagues examined physical activity behavior, exercise self-efficacy, health status, and global quality of life in a sample of older women (M age 68). Using a structural equation modeling approach they examined 3 different models to test the direct and indirect effects of PA on health status, and global quality of life. The model that fit the data the best supported a social cognitive theory based understanding. PA had direct effects on self-efficacy (r=.66) and in turn self-efficacy was associated with better mental health status (r=.39) and physical health status (r=.68), which were both then associated with global quality of life (r=.58) and (r=.53) respectively.

Interestingly, our measure of multidimensional exercise self-efficacy (MESES), which significantly predicted HRQL both independently and as part of a regression model controlling for MVPA, did not mediate the relationship between MVPA and HRQL. However PCS, which is very similar to self-efficacy, did mediate this relationship. Thus it appears that each of these measures is tapping slightly different aspects of self-belief in ability. It may be that MESES, which can also be scored as 3 subscales, is a slightly different construct to PCS. Multidimensional exercise self-efficacy takes into account, task efficacy, scheduling efficacy and coping efficacy. Nevertheless, there is support for the idea that aspects of motivational style and self-regulation are important psychosocial constructs in the context of behavior change.

Therefore, one of the targets for improving both mental and physical health status as well as more global quality of life will be self-efficacy or perceived competence for
lifestyle habits. Improving diet, exercise or physical activity is important but improving the participants self-efficacy or belief in their ability can further enhance the likelihood they will engage in that health behavior as well as adhere to it after initiation (Brassington, Atienza, Perczek, DiLorenzo, & King, 2002). There are recent examples of the social cognitive theory based, group mediated cognitive behavioral (GMCB) approach to designing interventions. This technique aims to target aspects of behavioral regulation that include, social support (group), goal setting (outcome expectancy), self monitoring and barrier/problem solving to help maintain physical activity behavior as well as lead to improvements in self-efficacy. Rejeski et al., (2003) randomized 147 older adults into two exercise intervention arms. Those in the GMCB group had favorable improvements when compared with the traditional exercise group on all measures. Further the authors reported that improved barriers efficacy—the ability to successfully overcome barriers to exercise—was associated with successful adoption and maintenance of PA.

In a separate study, Dishman and colleagues (2010) examined the dose response of goal setting and moderators of goal setting, including aspects of self-efficacy, in a multiracial sample of worksite employees aiming to increase MVPA. Results showed a dose response relationship between increased levels of MVPA, goal setting, satisfaction and self-efficacy. Therefore the finding that self-efficacy is an important mediator of lifestyle behaviors in older adults supports its use when designing interventions for endometrial cancer survivors. Basen-Engquist and colleagues (2013) in the Steps to Health study, delivered a primarily home based exercise program to 100 recently post treatment endometrial cancer survivors. The study used ecological momentary
assessment (EMA) to assess whether morning self-efficacy and outcome expectations could predict afternoon exercise behavior. The results of the study did show that both morning self-efficacy and outcome expectations significantly predicted afternoon exercise, however in their model when they controlled for self-efficacy in their analysis the relationship for outcome expectations was attenuated.

With regards to SDT theory variables, there were strong associations with PA, health related quality of life and global quality of life. In addition, the SDT variables Autonomous Motivation and Perceived Competence were strongly associated with self-efficacy. The only difference being that perceived competence for exercise was associated with global satisfaction with life while exercise self-efficacy was not. This may point to the fact that the perceived competence scale is accounting for variance in QOL that multidimensional exercise self-efficacy is not.

While not conducted in the same age group, a recent study examined the relationship between exercise goals, self-determination theory variables, QOL and weight management in 580 adolescents. Using structural equation modeling to examine the meditational role of both intrinsic and extrinsic motivations to lose weight it was found that for those children who felt pressurized to lose weight there was a more extrinsic approach to exercise goals. Furthermore this was related to poorer exercise behavior and QOL compared with adolescents who were intrinsically motivated. This may indicate that when persons feel it is important for them to engage in a health behavior (exercise or diet) but don’t really value that behavior, that they are less likely to benefit from it. For example if they feel they should exercise or eat a better diet because it will please their doctor or family rather than valuing the benefits for their own sake, they are unlikely to
stick with it in the long term. Motivations to exercise that are primarily related to improving appearance are often classified as being extrinsic and have been related to less weekly hours of activity than motivations that are primarily competence and enjoyment related (intrinsic) in nature (Richard, CHRISTINA, DEBORAH, Rubio, & KENNON, 1997). However, more recently there have been indications that when starting exercise programs or health behavior change that having a identified regulatory style rather than completely intrinsic is more useful. More intrinsic styles are associated with long-term exercise adherence (Teixeira, Carraca, Markland, Silva, & Ryan, 2012).

Due to the close relationship between SCT and SDT variables in the model we tested we did not examine SDT in quite the same depth. Furthermore by the time we began examining the data from the survey study we had had to begin the MIM+Diet intervention. SDT as a theoretical approach was new to the authors and given our background and previous experience with SCT, we chose to use SCT as the underlying structure upon which to design the intervention. Based on the results of the survey however, future interventions will include and utilize SDT especially those that involve a mindfulness-based approach.

**Mindfulness in Motion and Dietary Counseling Intervention**

It was hypothesized that the MIM+Diet intervention would be a safe and tolerable lifestyle intervention for EnCa survivors. Findings supported this hypothesis as no adverse events were observed and participants reported a high degree of satisfaction with multiple aspects of the intervention. In the following section we will address the: i) *Feasibility* briefly and then the ii) *Efficacy* as it relates to each of the following outcomes;
a) Physical Activity, b) Diet c) Physical Function d) Quality of Life and e) Mindfulness.

The second hypothesis was specific to improvements in both physical function and quality of life aspects of efficacy.

Feasibility

As mentioned previously there were a number of challenges to the recruiting process, which resulted in a sample accrual that did not have optimal statistical power to detect significant effects for all outcomes of interest. Nonetheless, the feasibility and preliminary efficacy of the MIM+Diet intervention was examined after offering the intervention to a sample of 13 women. (2 did not start and 2 attended the first session only). Feedback from the participants who completed was very positive and based on that information we deem it feasible to offer this type of program in the future. From a recruiting standpoint, the multiple iterations led to a method that we believe is more refined and would yield larger numbers of patients for future trials. One significant aspect of feedback that was given by participants is that they would have liked to have been offered the program earlier in their treatment. This may counter the approach of mailout recruiting as catching women newly diagnosed would be very similar to the in-clinic approach. It is therefore the recommendation that future trials that need to be adequately powered and should be multi-center in nature. This approach is not without its own challenges (Treweek et al., 2013). In addition, by including type II endometrial survivors and similar cancer types such as ovarian and cervical, there can be benefit to multiple survivors while still taking into account the scientific methodology necessary to determine efficacy. A limit of this approach is that many funding agencies would prefer homogenous populations.
Efficacy

With regard to the preliminary efficacy of the intervention, for women who were able to commit to and attend the majority of sessions (at least 6 from 8) there were a number of benefits seen.

Physical activity: From a behavioral standpoint we did see that physical activity improved in a portion of the sample. While we did not specifically target PA behavior, in the course of the mindfulness and dietary counseling, lifestyle habits are often talked about. For example, select intervention content addressed issues such as: “things that can aid in the management of stress and health include engaging in physical activity, eating a healthy diet and taking time to relax and de-stress”. Additionally, mindfulness training aims to give people the tools to make better decisions regarding their health and is part of why this type of intervention is seen to go well with lifestyle change (Keng, Smoski, & Robins, 2011). In order to be more in touch with your own health and make choices to that end you have to be able to pay attention to the everyday processes of thought and action.

Another reason that PA may have increased in some of the sample is that when paying attention to one health behavior it may be beneficial to deal with others. There have been mixed findings in this regard with some researchers finding multiple health change interventions too taxing, however most of this literature is regarding the cessation of a negative habit such as smoking and increasing a positive one such as physical activity. There are multiple examples of combined physical activity and dietary interventions having success especially for long term maintenance of weight loss (Wing, 1999). In one study conducted in Wales (Butler et al., 2013), researchers examined
whether training 53 primary health care providers to deliver health behavior change counseling had any effect on health outcomes in 1827 patients. Health behaviors targeted were smoking, exercise, healthy diet and alcohol use. They found no significant effect on the main outcome—the proportion of patients who self reported improved health behaviors at 3 months and no change at 12 months on biometric and biochemical screenings. However, they did find the intervention participants compared with controls had made more attempts to change (39% vs. 32%) odds ratio 1.40 (1.15 to 1.70), reported a sustained behavior change at 3 months (35% vs. 28%), odds ratio 1.36 (1.11 to 1.65) and slightly improved eating habits at 3 and 12 months and had better activity at 12 months. This study was specifically designed to compare whether extra counseling training impacted behavior change compared with standard care. While some behaviors only showed slight improvement there is support for the idea that certain behaviors may cluster, such as diet and exercise. In the current study we did not attempt to change smoking or alcohol intake and while not directly examining PA it may easily fit into future interventions. One idea may be to increase the intervention requirements to 2 days per week with a second day focusing on physical activity. This may then be seen as a more comprehensive lifestyle intervention.

One of the strengths of the present study was the inclusion of an objective assessment of PA (i.e., Lifecorder accelerometer). This approach removes the potential bias that accompanies reliance on self-reported PA alone. However, the fact that we did not specifically attempt to increase the PA behavior of the sample may mean they also self-reported relatively accurately. In an exploratory sense we did see that self-reported
walking minutes were correlated with objective minutes of MVPA ($r=0.548, p=<0.05$), but not LPA or steps per day.

**Diet:** Regarding one of the primary targets during the intervention, dietary habits, analysis revealed that no statistically significant changes in these outcomes were observed at the 8 and 14-week post-intervention follow up assessments. While not statistically significant, the small effect size changes observed following the intervention are indicative of some positive dietary behavior adjustments. As previously mentioned the FHQ was designed as part of the RENO Diet–heart study (Silverstein, 1997) as a screening tool to be used in conjunction with both 7-day recall and FFQ’s. Together they form part of a comprehensive assessment of nutrient and caloric intake. Due to the feasibility and efficacy nature of the present study and the fact that the FHQ was used to screen dietary quality in the study I we chose not to assess diet in a more in depth way. The current approach to dietary counseling focuses on moving to a more plant based diet, reducing fat, increasing whole grains and choosing lean protein options as a smaller proportion of each meal. This approach has successfully been used to reduce overall caloric intake and emphasize a healthy change to dietary intake patterns in previous studies (Inoue-Choi, Robien, & Lazovich, 2013). This is also based on the framework provided by the American Institute for Cancer Research (AICR). Coupling the dietary intake with the mindfulness intervention was an attempt to improve the uptake of the dietary counseling information.

There were notable weaknesses to using the FHQ as a stand-alone measure of dietary quality. First, it is likely that because the participants knew they were entering a study involving dietary counseling they were biased in their reporting of their current...
intake habits. For example, aspects of dietary habits like Fats & Oils scores went down over the course of the intervention. This is hard to explain, because while there was not a focus on eating a low fat diet specifically we would have expected choices in this area to improve. However, as mentioned previously Brug and colleagues (1994) found that self reported attitudes and intentions towards eating a low fat diet were not associated with actual low fat intakes. At baseline participants in the MIM+Diet study may have reported better fat choices than they were actually making knowing that it is an important tenant of healthy diets for cancer survivors. Additionally the FHQ was designed to be sensitive to fat intake as this was a specific target of the RENO diet-heart study and may be particularly effective in assessing this particular macronutrient.

A further example of possible bias may be in the fact that observed fruit and vegetable intake was overall excellent. Either these participants really were making excellent choices in this regard or the importance of fruit and vegetable intake is well marketed to cancer patients and survivors. Again knowing they were in a study focused on healthy eating may have led participants to favorably report their fruits and vegetables as excellent.

When comparing the scores from the MIM+Diet participants with overweight women from year 8 in the RENO diet-heart study, our sample scored higher in grains (15.9 vs. 12.4), fruits and vegetables (27.3 vs. 21.4), the same in meat (25.2 vs. 25.0) and lower in Other (17.0 vs. 26.2) and Fats & Oils (21.8 vs. 57.9). Total FHQ scores in our sample were also lower than the original study sample (136.4 vs. 141.9). This does indicate our sample had room to improve, but also that the current intervention may not
have been adequate to this end according to the specific needs of endometrial cancer survivors.

One aspect of diet not comprehensively addressed in the present study was dietary self-monitoring. While participants were encouraged to track their own intake regularly—as this is known to be associated with successful weight loss and management efforts—this tracking was not required as part of the MIM+diet intervention procedures. The reason we did not record this information is that we did not want to overburden the participants who were already being asked to track mindfulness and practice every day. As the study sample was already small we did not want to risk losing participants who felt they had too much to do.

Given the short time frame of the intervention we would not have expected to see significant changes in body composition due to dietary change. Dietary pattern change as part of a healthy lifestyle can lead to weight loss, however this may be a slow process if done in a healthful way. For women who are obese, weight loss may be even more difficult to achieve. Despite this we did have 4 women who reduced their % body fat, two of which lost up to 5% body fat over the 14-week period. Of those who did not lose % body fat, 5 women only gained between 0.2 and 0.4%. Due to the sensitivity of the IDXA measure we could also determine that some of the women who did not lose %BF actually lost weight, however it was lean muscle mass. This is often the case when weight loss is through diet alone and not in conjunction with exercise. Therefore we may have had significant improvement in dietary patterns in certain women but not had the measures sensitive enough to detect this change in diet. Many of the food scores are attributed arbitrary cut points as a marker of food quality, a change of 1 or 2 points would not
necessarily change a person's score from a fairly good to an excellent standing or from poor to fairly good. It is therefore difficult to interpret what meaningful change in a food category is. Finally as the period of recall is over the last month small changes that a participant had made for the better may not be noticeable to them in terms of their general approach to eating.

Future studies will need to incorporate more precise measures of dietary intake such as food frequency questionnaires and 7 day recalls as well as tracking the self-monitoring of diet.

**Physical function:** Physical functioning is a reflection of an individual’s capacity to live in an independent way. There are many components of health and fitness that may impact the ability of an individual to function optimally. A loss of the ability to function in a manner that allows an individual to successfully complete tasks of daily living can lead to impacts on both health-related quality of life and global well being. In the disablement process model (Verbrugge & Jette, 1994), it is proposed that acute or chronic impacts to physical or mental health can lead to declines in functioning of specific bodily systems. Personal or environmental risk factors lead to decline from pathology to impairments, then functional limitations, and finally disability. Disability is described as difficulty in any domain of life (sleep quality, daily activities such as transport or shopping, work or leisure) due to a health or physical problem.

Due to the high level of obesity and low physical fitness of the current population of survivors it was seen to be important to quantify the functional capacity of EnCa survivors and whether this may place these women at higher than normal risk for disablement. In a systematic literature review of longitudinal studies Stuck and
colleagues (1999) examined the risk factors for functional status decline and disability among older community dwelling adults. Some of the strongest evidence for risk of decline was for comorbidity, increases in BMI, lower extremity functional limitation and low physical activity.

In the present study, the short physical performance battery (SPPB), stair climb test and lift and carry test were used to assess physical function. For mobility and endurance we used the 400m-walk test. The SPPB combines tests for gait speed over 4m, balance in 3 tasks and lower extremity strength with a sit to stand 5 times. In the original study to test the battery, over 5000 older adults completed measures. Results indicated that performance on the SPPB was predictive of short-term mortality and nursing home admission. The stair climb and lift and carry tests have been used with other populations at high risk for disablement and loss of independence such as those suffering from osteoarthritis of the knee (KOA)(Focht et al., 2012). The 400m-walk measure was originally tested in over 3000 older adults to determine its prognostic value as a predictor of mortality and incident mobility disability (Newman et al., 2006). For those who were unable to complete the 400m walk, the risk was higher for mortality (212.6 vs. 79.1 events/1000 person-years; adjusted HR, 1.86; 95% CI, 1.58-2.18; \( p<.001 \)) and mobility disability (85.2 vs. 28.8 events/1000 person-years; adjusted HR, 1.95; 95% CI, 1.56-2.44; \( p<.001 \)). For persons able to complete the walk, each additional minute of performance time was associated with an adjusted HR of 1.29 (95% CI, 1.12- 1.48) for mortality, 1.20 (95% CI, 1.01-1.42) for incident cardiovascular disease, 1.52 (95% CI, 1.41-1.63) for mobility limitation, and 1.52 (95% CI, 1.37-1.70) for disability.
In the MIM+Diet group we did have fairly high functioning persons for the most part. Total SPPB scores ranged from 9-12 with the baseline mean of 10.4. In the validation study it was shown that there was a clear difference in risk for those scoring 10 compared to those scoring 11 and 12 respectively. This is an important aspect of this measure.

While the hypothesis was supported, that is, significant improvement in SPPB was observed, this was primarily due to the statistically significant improvement in chair stand time. This is perhaps the measure most indicative of leg strength. During the mindfulness intervention we do engage in some gentle yoga based movement activity, however this would not have been enough to significantly improve leg strength. The primary activity that we would expect to be related to increases in physical function would be moderate to vigorous exercise and as this was not a target of the intervention the strength of this effect was surprising (Cohen’s $d=.60$). It may be a case of improved testing ability that is reflected in the improved chair stand time, however given that standing from seated is an activity that would be engaged in regularly during the course of a day we do not think this is the case.

The intervention yielded only a small effect size change in 400m walk time ($d=.06$). However, results of the completer analysis excluding those participants the observed effect size increased considerably ($d=.34$). Again as physical activity was not a primary target of the intervention we would expect this measure to be stable, and possibly get worse if a participant was very inactive. It may be that for those that were very inactive to begin with, even starting a small amount of PA may have led to improvements in mobility and fitness. In a secondary analysis of data from the LIFE study, it was found
that minimally clinically meaningful change for physical function measures included, 0.03–0.05m/s for gait speed over 4m, 0.3–0.8 points on the total SPPB and 20-30 seconds on the 400m walk test. By these standards subjects completing the MIM+Diet intervention approached meaningful change for gait speed (0.03m/s), SPPB (0.6 points) but not 400m walk time.

A final possibility relating to the improvement in physical functioning outcomes is that by follow up visits the participants had gotten to know each other and the researcher which led to greater efforts on measures of function. It is possible that participants wanted to show they were better and tried harder. Ideally, a person unknown to the participants should have carried out the follow-up assessments—in order to control for this possibility.

Health Related Quality of Life and Quality of Life: Measures of disease specific health related quality of life that included the FACT-G, FACT-En, summary scales of the RAND SF-36 and the PSQI all showed slight improvements as a result of the MIM+Diet intervention. While the scores for all aspects of the FACT-G/En indicated a high level of HRQL there were some subjects within the group who had lower scores. Interestingly when we calculated effect sizes (Table 14) we only had positive change between 8–14 week follow ups. In essence it seemed that FACT scores went down and then back up again albeit very slightly. When we examined the data for completers we then saw a more clear pattern of improvement with FACT-G, FWB, PWB and EWB and FACT-En all increasing by small to moderate effect sizes (Cohens $d$.25–.53). In the initial validation and development of the FACT measure, Cella and colleagues (1993) found that the FWB, PWB and EW B subscales were the most sensitive to change. A recent randomized
controlled trial to examine the effects of a weight loss intervention for endometrial cancer participants found that FACT-G scores did not differ significantly between intervention and control groups over the course of 3 and 12 months. This was despite significant changes in BMI for intervention participants. They did detect a within-subjects change for the intervention from 79.8 to 87.1. Given that our participants had a baseline mean score higher than this we may have struggled to increase HRQL by a more meaningful margin. Notwithstanding, this measure may be useful to screen for patients who are at high risk for functional and physical decline over time.

While we would expect increases in physical fitness and physical function measures to lead to increases in HRQL this may not actually happen at lower levels of activity such as seen in the current MIM+Diet sample. Another interpretation may be that as the mindfulness intervention would be more likely to affect mental and social aspects of HRQL it may not directly affect PWB and FWB, the most sensitive scales to change within the FACT. Furthermore, as our subjects did not lose significant body weight or %BF we would again not expect to see large increases in health related quality of life.

In support of this position, we did find that the mental health summary (MHS) scales of the RAND SF-36 improved \( (d=.34) \), while the physical health summary scales were relatively unchanged \( (d=.05) \) for completers. A study by Blissmer et al., (2006) examined health related quality of life (MHS and PHS) in response to a 24-month weight loss intervention. While there were improvements in both MHS and PHS immediately post intervention (6 months) when weight loss was highest, as the study progressed to 24 months these changes had diminished. Specifically, PHS scores had returned to baseline while the MHS had been somewhat sustained. In the MIM+Diet, we did not have
significant weight loss but a change in mindfulness may have impacted MHS indirectly through improved stress coping strategies. However in contrast, a study of 84 breast cancer survivors, randomized into a mindfulness based stress reduction (MBSR) intervention or usual care control group, found improvements in PHS but not MHS for those in the intervention compared with controls (Lengacher et al., 2009). The breast cancer survivors were all within 18 months of treatment and MBSR in this case may have included a larger physical component of yoga than in the MIM+Diet intervention. This could have led to greater physical improvements reflected in the PHS. MIM does include some gentle yoga but there is more of a focus on stress management and mindfulness than yoga per se.

Another important aspect of HRQL for EnCa survivors is sleep quality. The Pittsburgh Sleep Quality Instrument (PSQI) indicated that in contrast to other HRQL measures, sleep quality for participants in the MIM+Diet was considered poor. Furthermore, despite a significant improvement over the course of the intervention the scores at follow up remained indicative of poor sleep. One week of the MIM intervention specifically aims to target sleep quality and many participants reported feeling better as a result. Sleep quality has independently been associated with aspects of anxiety and stress and a recent study by Okubo et al., (Okubo et al., 2014) demonstrating the strong relationship between subjects with a high PSQI score and metabolic syndrome. The odds ratio of having metabolic syndrome among participants with PSQI score of 6 or more points was 2.37 (95% confidence interval: 1.23-4.58) for males and 2.71 (1.45-5.07) for females in contrast to those with 5 or less points. The fact that we saw improved scores as
a result of the MIM+Diet intervention is positive, however the high scores at follow up are still of concern.

Global quality of life as measured with the SWLS was also found to be on average fairly high in the MIM+Diet participants. This is an interesting finding and may be reflective of the fact that the population does not have deficits in more proximal aspects of HRQL and therefore this does not impact a more global sense of well-being. Given that the majority of survivors were significantly post treatment and had high survivorship odds it is understandable that we would not see low SWLS. It should be noted however that there were still certain participants who had scores below the cut point of 25 (23.5%). Furthermore these individuals all scored below 20 on this measure. As can be seen from the survey data, SWLS scores are strongly correlated with aspects of HRQL and it is therefore reasonable to expect that changes in HRQL might yield more favorable outcomes in global well-being. In the validation of the SWLS Diener did report the scale to be very stable and unlikely to change based on short-term mood fluctuations as opposed to more significant long term life events (Diener et al., 1985).

Overall the favorable changes in aspects of both disease specific and global quality of life observed following the intervention provides evidence supporting the preliminary efficacy of this approach for EnCa survivors. Perception of well-being and functional status can be important motivators and correlates of healthy lifestyle behaviors. HRQL and QOL are increasingly being evaluated as clinical outcomes due to the medical system’s more patient focused approach. Fader and colleagues (2011) highlighted the importance of measuring these aspects of health in obese endometrial cancer survivors specifically, because despite the high success rate of treatment, women
continue to suffer from deficits in aspects of physical well being, functional well being and overall PHS measures of health status (Fader et al., 2011). By screening and measuring these variables, treatments that support primary care approaches may be more efficacious.

**Mindfulness:** One of the primary focuses of the MIM intervention was on the development of a more mindful approach to daily life. This program invites participants to pay attention to the present moment in a non-judgmental or reactive way. Originally Buddhist mindfulness meditation was a specific technique proposed to enhance the skill of mindfulness. Being more mindful is seen as a way to reduce the stress and anxiety encountered by appraising a given life situation as threatening, uncontrollable or unpredictable. The focus of each week’s practice is slightly different and deals with topics such as mindful sleep and mindful eating among others. For example, it is thought that many people engage in poor eating habits in response to stress. By cuing participants to notice when they are feeling “stressed out” we may facilitate a more conscious approach to modulating that stress response—namely eating when not actually hungry. With regards to sleep disturbance, if individuals can consciously appraise negative and stressful thoughts in conjunction with a relaxation process they may be able to sleep better. Changes in these subtle mental processes as a result of mindfulness-based interventions have been shown to improve multiple outcomes. In a review of the evidence for the efficacy of mindfulness-based programs in cancer care settings, 13 studies, including 3 randomized controlled trials and 5 pre-post test designs gave support to improvements in anxiety, depression, immune function and stress. While the authors did highlight methodological weaknesses in the studies they did suggest a possible place for
mindfulness based approaches in acute as well as palliative care (Shennan et al., 2011). In another review of the role of mindfulness meditation for cancer patients Ott and colleagues (Ott, Norris, & Bauer-Wu, 2006) concluded that there was conclusive support for consistent improvements in psychological functioning, reduction of stress symptoms, enhanced coping and well being, however they too suggested a more rigorous methodology for evaluating the practice. This included more randomized controlled trials with an exploration of a dose response effect and minimally expected benefits. In addition to the typical self-report aspects of mindfulness measurement, finding ways to measure physiological and neurological processes that can change as a result of mindfulness training is important. The significant improvements and meaningful effect sizes accompanying changes in mindfulness outcomes observed following the MIM-Diet intervention provides additional support for the preliminary efficacy of this approach for EnCa survivors.

**Weaknesses and future directions**

Although results of the present studies expand current knowledge of the correlates of lifestyle behaviors (study I) and the feasibility and efficacy of the MIM-Diet intervention in the treatment of EnCa survivors (study II), there are also several limitations that should be acknowledged. The current series of studies (study I and study II) suffered from a lack of adequate statistical power. This was directly related to a smaller than targeted sample size. For the cross sectional survey we would have liked to have used a structural equation modeling (SEM) approach to more definitively examine the relationships between theory based correlates of physical activity and dietary behavior. This would have allowed us to test the comparative fit of two distinct
psychosocial theories of behavior as they may apply to a unique population of EnCa survivors. This evaluation of theory was then to directly inform the design of a lifestyle intervention (study II) with the aim of maximizing benefits in health outcomes. The recruitment process whilst refined and improved over time was inefficient to begin with. Too few patients were seen in a given period of time to accrue an optimal sample size for either study. Future attempts to examine these relationships may benefit from using national or similar size databases to approach as large a sample as possible. In a similar fashion by recruiting patients with similar diagnoses and possibly implementing interventions at multiple sites a larger more representative sample can be studied.

In terms of the actual intervention, we lost 4 subjects from baseline testing in an already small sample. Future efforts should aim to maximize retention of the sample following consent. Regarding the recruitment process, having conducted this feasibility and efficacy study a better understanding of the needs of EnCa survivors may allow future studies to be more targeted in nature.

Finally by incorporating physical activity into the MIM+Diet approach we may also improve the appeal of the intervention to a larger sample of survivors as well as increase the effectiveness of the intervention on body composition, physical function and quality of life outcomes. Moreover, in addition to self-reported aspects of well being and health status, assessments of biomarkers related to inflammation and physiological stress will help to validate the mindfulness based approach to lifestyle modification.

**Conclusion**

We believe that theory based approaches to examining behavior change are of paramount importance. By better understanding the correlates of distinct behavior
patterns we can more accurately assess and target them in interventions that may in turn lead to favorable outcomes. With a significant burden being placed on the personal finances and the resources of the health care system for the foreseeable future, finding ways for individuals to better manage their own health care is a notable objective. Prevention of disease progression through the impacts of stress and lifestyle habits is an achievable goal for many persons. Specifically a diagnosis of cancer may present a teachable moment, in which the opportunities to change behavior are more salient. While endometrial cancer patients and survivors have favorable outcomes following treatment, they are still subject to higher than normal risk of comorbidity including obesity, CVD and TTDM.

Mindfulness-based approaches to lifestyle change warrant further exploration within this unique population of cancer survivors. Psychologically and physiologically the stress response can result in increased levels of inflammation, reduced immune function and negatively impact quality of life outcomes. Building resilience may help to protect individuals from the impacts of stress and also place them in a position to make better lifestyle choices, specifically regarding diet and physical activity. In addition, by incorporating mindfulness training into their curriculum, previously validated approaches to lifestyle change could be further enhanced.

If we can provide everyday people with the tools to enhance their long term health, quality of life and well being we should certainly make every effort to that end.
References


American College of Cardiology, 50(15), 1435-1441. doi: 10.1016/j.jacc.2007.06.037


adults through fitness training. *Journal of Molecular Neuroscience*, 20(3), 213-221.


Appendix A: IRB approval (Study I)

Dear Dr. Focht,

The Cancer IRB APPROVED BY EXPEDITED REVIEW the above referenced research. The Board was able to provide expedited approval under 45 CFR 46.110(b)(1) because the research meets the applicability criteria and one or more categories of research eligible for expedited review, as indicated below.

Date of IRB Approval: July 20, 2012
Date of IRB Approval Expiration: July 20, 2013
Expedited Review Category: 7

If applicable, informed consent (and HIPAA research authorization) must be obtained from subjects or their legally authorized representatives and documented prior to research involvement. The IRB-approved consent form and process must be used. Changes in the research (e.g., recruitment procedures, advertisements, enrollment numbers, etc.) or informed consent process must be approved by the IRB before they are implemented (except where necessary to eliminate apparent immediate hazards to subjects).

This approval is valid for one year from the date of IRB review when approval is granted or modifications are required. The approval will no longer be in effect on the date listed above as the IRB expiration date. A Continuing Review application must be approved within this interval to avoid expiration of IRB approval and cessation of all research activities. A final report must be provided to the IRB and all records relating to the research (including signed consent forms) must be retained and available for audit for at least 3 years after the research has ended.

It is the responsibility of all investigators and research staff to promptly report to the IRB any serious, unexpected and related adverse events and potential unanticipated problems involving risks to subjects or others.

This approval is issued under The Ohio State University’s OHRP Federalwide Assurance #00006378.

All forms and procedures can be found on the ORRP website – www.orrp.osu.edu. Please feel free to contact the IRB staff contact listed above with any questions or concerns.

Thomas W. Rauch, OD, PhD, Vice-Chair
Cancer Institutional Review Board
Appendix B: IRB approval (Study II)

May 29, 2013

Protocol Number: 2013C0043
Protocol Title: LIFESTYLE INTERVENTIONS TO IMPROVE PHYSICAL FUNCTION AND QUALITY OF LIFE IN ENDOMETRIAL CANCER SURVIVORS: THE ROLE OF BOTH AEROBIC AND YOGA BASED EXERCISE PROGRAMS, Brian Focht, David Cohn, Maryanna Khat, Alexander Lucas, School of Physical Activity and Education Services
Type of Review: Initial Review
IRB Staff Contact: Ryan Lienemann
614-292-6243
Lienemann.1@osu.edu

Dear Dr. Focht,

The Cancer IRB APPROVED the above referenced research.

Date of IRB Approval: May 28, 2013
Date of IRB Approval Expiration: May 28, 2014

If applicable, informed consent (and HIPAA research authorization) must be obtained from subjects or their legally authorized representatives and documented prior to research involvement. The IRB-approved consent form and process must be used. Changes in the research (e.g., recruitment procedures, advertisements, enrollment numbers, etc.) or informed consent process must be approved by the IRB before they are implemented (except where necessary to eliminate apparent immediate hazards to subjects).

This approval is valid for one year from the date of IRB review when approval is granted or modifications are required. The approval will no longer be in effect on the date listed above as the IRB expiration date. A Continuing Review application must be approved within this interval to avoid expiration of IRB approval and cessation of all research activities. A final report must be provided to the IRB and all records relating to the research (including signed consent forms) must be retained and available for audit for at least 3 years after the research has ended.

It is the responsibility of all investigators and research staff to promptly report to the IRB any serious, unexpected and related adverse events and potential unanticipated problems involving risks to subjects or others.

This approval is issued under The Ohio State University’s OHRP Federalwide Assurance #00006378.

All forms and procedures can be found on the OHRP website - www.orp.osu.edu. Please feel free to contact the IRB staff contact listed above with any questions or concerns.

William Carson, M.D., Chair
Cancer Institutional Review Board
Appendix C: Survey Invitation letter

Dear Ms,

The Ohio State University Division of Gynecologic Oncology is contacting you to ask if you may be interested in participating in an anonymous research survey. As a patient currently or previously being seen for your endometrial cancer, the information you offer may assist us in providing improved care to you and other similar patients in the future.

This study would require you to answer some questions relating to your typical physical activity, dietary habits, and aspects of your quality of life. Should you be interested in taking the survey, you would follow the link provided at the bottom of this page. This will take you to the online survey, which should require 20-30 minutes to complete. If you are unable to finish the survey in one sitting you may save your progress and return at a later more convenient time.

Should you have any further questions relating to the study please feel free to contact the research staff at the number or email address below,

Thank you in advance for your help with this study,

Please type the following into your web browser  http://j.mp/OxqUe9

Alexander R. Lucas, MS  
Co-Investigator  
Health and Exercise Science, The Ohio State University  
Email: lucas.452@osu.edu  
Phone: 614-292-0458  
Address: PAES Building A12, 305 W. 17th Ave., Columbus, OH 43210-1224

David E. Cohn, MD  
Director, Division of Gynecologic Oncology  
Gertrude Parker Heer Chair in Cancer Research  
The Ohio State University  

Brian C. Focht, PhD, FACSM  
Principal Investigator  
Health and Exercise Science, The Ohio State University  
Email: fbocht@ehe.osu.edu  
Phone: 614-292-0757  
Address: PAES Building A45, 305 W. 17th Ave., Columbus, OH 43210-1224
Appendix D: MIM+Diet Invitation Letter

Dear Ms. ,

The Ohio State University Division of Gynecologic Oncology is contacting you to ask if you may be interested in participating in a research study aimed at improving quality of life in endometrial cancer survivors. As a patient currently or previously seen for your endometrial cancer, we feel you may benefit from participation in this study as well as being in a unique position to assist us in providing improved care to you and other similar patients in the future.

This study would require you to attend a 1-hour session per week for 8 weeks of a stress reduction and mindfulness program known as Mindfulness in Motion (MIM). This will be coupled with 20-30 minutes of dietary counseling. This program has successfully been used to teach stress reduction techniques to medical nurses as well as to workers in the corporate setting through The Ohio State University.

Should you be interested in participating in the study, or if you would like to know more about the study please contact;

Alex Lucas at 336-406-9269 or by email at Alexander.Lucas@osumc.edu

Thank you in advance for your help with this study,

Alexander R. Lucas, MS
Co-Investigator
Health and Exercise Science, The Ohio State University
Email: lucas.452@osu.edu
Phone: 614-292-0458
Address: PAES Building A12, 305 W. 17th Ave., Columbus, OH 43210-1224

David E. Cohn, MD
Director, Division of Gynecologic Oncology
Gertrude Parker Heer Chair in Cancer Research
The Ohio State University

Brian C. Focht, PhD, FACSM
Principal Investigator
Health and Exercise Science, The Ohio State University
Email: bfocht@ohio.edu
Phone: 614-292-0757
Appendix E: Telephone Screening Questionnaire

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you previously had a diagnosis of grade 1 or 2, stage I or II endometrioid endometrial cancers (“Type I cancers”) as confirmed during surgical intervention for treatment.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Are you currently able to engage in walking for at least 15 minutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Are you currently involved in any structured physical activity such as walking, biking swimming or running for more than 60 minutes per week?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Are you currently or have you been in the last 6 months engaged in any yoga based exercise or yoga classes for more than 60 minutes per week.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Have you had a previous diagnosis of other cancer?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Do you have severe Heart or Systemic Disease: evidence of documented myocardial infarction, chronic unstable angina, symptomatic congestive heart failure, uncontrolled hypertension.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Do you have a Severe Musculoskeletal Disease: Severe muscle or joint disorders due to disease or trauma, amputations, or any condition that significantly impair physical capabilities, as defined by the physician.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Date: ____________________________________  Tel. _____________________________________
Name: ____________________________________  Email: _______________________________
Height_________________ Weight_____________  BMI________________

Eligible  Yes  No
Appendix F: Intervention Completion Survey

Please answer the following questions based on the below scale

1 – Strongly Disagree
2 – Disagree
3 – Neutral
4 – Agree
5 – Strongly Agree

1. Mindfuless & Gentle Yoga Intervention was delivered in a professional manner

2. Person delivering Mindfuless & Gentle Yoga Intervention was knowledgeable and helpful as an instructor

3. Person delivering Mindfuless & Gentle Yoga Intervention provided useful tools for managing stress

4. Mindfuless & Gentle Yoga Intervention addressed your needs as an endometrial cancer survivor

5. You would recommend Mindfuless & Gentle Yoga Intervention to other patients or persons with your diagnosis

6. Dietary Counseling was delivered in a professional manner

7. Person delivering Dietary Counseling Intervention was knowledgeable and helpful as an instructor

8. Dietary Counseling Intervention addressed your needs as an endometrial cancer survivor

9. You would recommend the Dietary Counseling Intervention to other patients or persons with your diagnosis

10. The time frame for the Intervention is suitable
11. The time of day for the intervention was suitable ___________

Please take some time to offer any further thoughts and or feedback as per the intervention as a whole.

12. What did you like about the intervention?

13. What did you dislike about the intervention?

14. Other thoughts?