ONE SIZE DOES NOT FIT ALL: PREDICTING SUBGROUPS OF BREAST CANCER SURVIVORS WHO REPORT DIFFERENT PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR FROM PRE-DIAGNOSIS TO TEN YEARS POST-DIAGNOSIS

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A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Health Behavior.

Chapel Hill 2015

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ABSTRACT

Angela M. Stover: One size does not fit all: Predicting subgroups of breast cancer survivors who report different physical activity and sedentary behavior from pre-diagnosis to 10 years postdiagnosis (Under the direction of Christine Rini and Bryce B. Reeve)

Purpose: Despite increasing evidence that Physical Activity (PA) and Sedentary Behavior (SB) contribute to breast cancer prognosis, little is known about changes during survivorship and whether psychosocial variables predict change. In Study 1, I determined subgroups reporting different PA and SB trajectories from pre-diagnosis through ten years postdiagnosis. In Study 2, I predicted subgroup membership based on stress and coping theory constructs.

Sample: The NCI-funded Health, Eating, Activity, and Lifestyle (HEAL) study is a cohort of breast cancer survivors (stages 0-IIIA) diagnosed during 1995-1999. A subset of 938 survivors was analyzed who were ages 35-64 years at diagnosis. They were recruited from cancer registries in New Mexico, California, and Washington (36% African American, 12% Hispanic).

Methods: At six months post-diagnosis, breast cancer survivors reported their prediagnosis PA (hours/week of moderate-vigorous PA) and SB (hours/week sitting watching TV) and current PA and SB. Follow-up interviews occurred at two, five, and ten years post-diagnosis. Subgroup membership was determined with growth mixture modeling. Mediation was examined with structural equation modeling, where demographic and clinical characteristics were predictors, stress and coping variables were mediators, and subgroups were outcome variables.

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Results: In Study 1, two subgroups were identified: 1) 91% reported low PA that increased from six months through five years post-diagnosis and TV watching consistent with the U.S. average of 18-19 hours/week across all time points ("Low but Increasing PA and Average TV Subgroup"); and 2) 9% reported high PA declining over time and TV watching consistent with the U.S. average but increasing over time ("High but Declining PA and Average but Increasing TV Subgroup"). In Study 2, African American breast cancer survivors with higher fatigue, greater comorbid conditions, and lower education were more likely to report poor perceived health, and in turn were more likely to be in the "Low but Increasing PA and Average TV Subgroup."

Conclusion: Despite national PA guidelines, over 90% of breast cancer survivors followed a trajectory of low PA and watching TV for 18-19 hours/week from pre-diagnosis through ten years post-diagnosis, potentially putting them at risk for poor outcomes. Study 2 results can guide development of theory-informed interventions.

I dedicate this dissertation to my family in Pennsylvania who have always supported me and been a source of strength. I also dedicate my dissertation to Michael O' Malley, PhD, who was taken from us too soon. I wouldn't be where I am today without Michael's mentorship. I hope I can be as good a mentor someday as he was to me.

ACKNOWLEDGEMENTS

I would like to acknowledge the Lineberger Comprehensive Cancer Center's Cancer Control and Education Program (CCEP) pre-doctoral fellowship (5R25-CA057726) and Sheps Center for Health Services Research's National Research Service Award (5T32-HS000032-24). The Parent HEAL study was funded by NCI contracts N01-CN-75036-20, N01-CN-05228, and N01-PC-67010.

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LIST OF ABBREVIATIONS

GMM	Growth mixture modeling
HEAL	Health, Eating, Activity, and Lifestyle study
HRQOL	Health-related quality of life
LCM	Latent curve modeling
NCI	National Cancer Institute
PA	Physical activity
SB	Sedentary behavior
SCT	Social Cognitive Theory
SEER	Surveillance, Epidemiology, and End Results cancer registries
SEM	Structural equation modeling
TPB	Theory of Planned Behavior
TTM	Transtheoretical Model

CHAPTER 1. INTRODUCTION

My dissertation is composed of six chapters. In Chapter 1, I review: 1) background information on my outcome variables of physical activity and sedentary behavior during breast cancer survivorship and the ways in which these constructs are differentiated; 2) two studies examining PA trajectories in breast cancer survivors; 3) constructs in Lazarus and Folkman's (1987) Transactional Model of Stress and Coping and strengths and weaknesses of the model for examining physical activity and sedentary behavior as coping strategies; 4) my conceptual models for physical activity and sedentary behavior; and 5) the longitudinal dataset that I used to test my aims. I conclude the chapter with my Specific Aims. In Chapter 2, I review the empirical literature on PA and SB levels at different points during survivorship, describe empirical studies informing my conceptual models, and describe how I operationalized Transactional Model constructs. I conclude the chapter by describing the significance of my proposed work. In Chapter Three, I review my methodology, equations, and power calculations. Chapters Four and Five are my papers stemming from my dissertation research and Chapter Six is my concluding chapter discussing implications for cancer care and future interventions with breast cancer survivors.

1.1. Overview

1.1.1 Differentiating Physical Activity, Exercise, and Sedentary Behavior

The terms, "physical activity" and "exercise" are often used interchangeably but have distinct meanings. The American College of Sports Medicine conceptualizes physical activity (PA) as movement involving the skeletal muscles that raises energy expenditure above a resting

metabolic rate (2013). In contrast, exercise is defined as, "systematic, planned, or structured PA involving a specific frequency, intensity, duration, or mode performed regularly for the purpose of enhancing physical fitness" (American College of Sports Medicine, 2013, pg. 4). Thus, PA is broader in scope in that it captures unstructured and structured lifestyle activities. Moderate-vigorous PA is the dominant aspect of human movement studied in PA research and its significance to health outcomes is well supported by over 60 years of scientific inquiry (Katzmarzyk, 2010). Examples of moderate-vigorous PA include brisk walking, running, aerobics, and other activities that raise heart- and breathing-rates above a resting level and cause sweating to occur.

Sedentary Behavior (SB) is prolonged periods of sitting or reclining during waking hours with no skeletal muscle movement, such as sitting watching television or working at a desk for several hours in a row (Lynch, 2010). SB has a weak correlation with PA, which means that SB is not simply the opposite of PA (George et al., 2013a; Tremblay, Colley, Saunders, Healy, & Owen, 2010; Santos et al., 2012). PA and SB can vary independently and likely have different predictors and differential effects on health (Katzmarzyk, 2010).

Owen and colleagues (Owen, Leslie, Salmon, & Fotheringham, 2000) published a diagram differentiating PA and SB in different contexts (e.g., home, occupation), behavioral settings (e.g., indoor and outdoor activities), functions (e.g., home maintenance, commuting), and behavioral choices (e.g., watching television, cleaning) (see Figure 1.1). In this model, multilevel environmental factors such as socioeconomic status and poverty predict context, behavioral settings, functions, and health behavior choices (Owen et al., 2000). For instance, adults with limited resources may have less access to behavioral settings that cost money (e.g., a gym), may

work longer hours at one or more jobs, and may have sole childcare responsibilities, which all limit leisure time for engaging in PA.

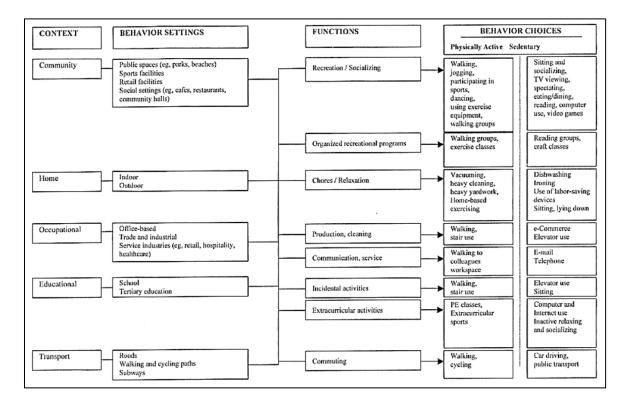


Figure 1.1. Owen's (2000) diagram.

1.1.2 Physical Activity, Sedentary Behavior, and Risk for Recurrence and Early Mortality

There is a growing body of evidence for the beneficial effects of PA for breast cancer survivors including better quality of life and reduced risk for recurrence and early mortality. Several systematic reviews have shown that PA improves physical function, mental health, fatigue, and quality of life in breast cancer patients (see Schmitz, 2011; Fong et al., 2012; McNeely et al., 2006).

Two systematic reviews and a meta-analysis have shown that PA is also associated with better overall survival and breast cancer-specific survival, with post-diagnosis PA being more beneficial than pre-diagnosis PA (Ballard-Barbash et al., 2012; Fontein et al., 2013; Ibrahim & Al-Homaidh, 2011). Ibrahim and Al-Homaidh (2011) conducted a meta-analysis of six studies with over 12,000 breast cancer survivors to determine the relationship between PA and mortality. Pre-diagnosis PA reduced risk of breast cancer-specific mortality by 18% and post-diagnosis PA reduced risk by 34%. Early mortality from other causes was reduced by 41%.

Ballard-Barbash and colleagues (2012) systematically reviewed studies that examined the relationship between PA and mortality (cancer-specific and all-cause) across several cancer types. Figure 1.2 shows the risk estimates for mortality based on 17 observational studies of PA in breast cancer survivors. The confidence intervals showed consistent evidence that PA was associated with reduced all-cause and breast cancer-specific mortality.

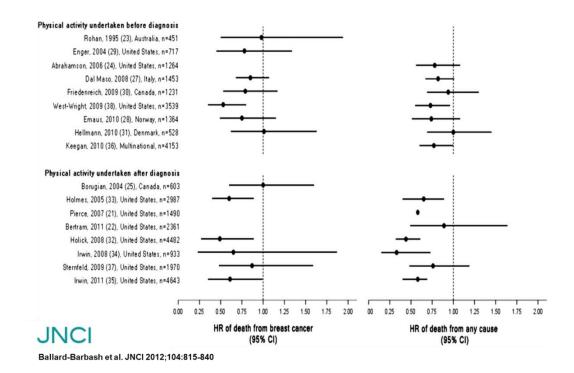


Figure 1.2. Observational studies of physical activity and mortality outcomes in breast cancer survivors.

Additionally, two cohort studies of initially healthy women examined PA and breast cancer recurrence and survival (Nurses' Health Study and the Women's Healthy Eating and Living trial). In both studies, women diagnosed with breast cancer who engaged in recreational PA for approximately two to three hours per week (i.e., meeting the national PA guideline) had a 30-34% lower risk of breast cancer recurrence and all-cause mortality than breast cancer survivors who did not meet the PA guideline (Holmes et al., 2005; Pierce et al., 2007). This decreased risk of recurrence and early mortality associated with PA was observed in both pre-menopausal and post-menopausal women and was independent of body mass index (i.e., the measure of relative weight based on an individual's mass and height).

Finally, one study (Sternfeld et al., 2009) found a negative association between PA and recurrence over a seven-year period when models were adjusted for age but the association was not significant when adjusted for other covariates such as race and education. Age-adjusted results from 1,970 women in the Life after Cancer Epidemiology study showed that higher PA was associated with reduced risk of recurrence and breast cancer-specific mortality. However, results were attenuated when adjusted for other demographic and clinical characteristics.

SB, such as hours spent sitting per day, is deleterious in its own right and uniquely contributes to negative health outcomes, above and beyond PA. Three systematic reviews (in general population samples) have shown that SB was correlated with all-cause mortality, cardiovascular disease mortality, and type II diabetes incidence, after controlling for PA (Biswas et al., 2015; Proper, Singh, vanMechelen, & Chinapaw, 2011; Wilmot et al., 2012). Proper and colleagues (2011) reviewed 19 studies and found significant correlations among SB, type II diabetes incidence, all-cause mortality, and cardiovascular disease mortality. Wilmot et al. (2012) reviewed 18 studies (16 prospective) with over 794,000 participants. The greatest

sedentary time, compared with the lowest, was associated with a 112% increase in relative risk for diabetes incidence, a 147% increase in risk for cardiovascular events, a 90% increase in risk for cardiovascular mortality, and a 49% increase in risk for all-cause mortality.

In addition to all-cause mortality, cardiovascular mortality, and type II diabetes incidence, Biswas et al. (2015) also found significant correlations with cardiovascular disease incidence and cancer incidence and mortality. They reviewed 41 prospective articles and performed metaanalyses on outcomes for cardiovascular disease and diabetes (14 studies), cancer (14 studies), and all-cause mortality (13 studies). Significant hazard ratio (HR) associations were found with all-cause mortality (HR: 1.240 [95% CI, 1.090 to 1.410]), cardiovascular disease mortality (HR: 1.179 [CI, 1.106 to 1.257]), cardiovascular disease incidence (HR: 1.143 [CI, 1.002 to 1.729]), cancer mortality (HR: 1.173 [CI, 1.108 to 1.242]), cancer incidence (HR: 1.130 [CI, 1.053 to 1.213]), and type II diabetes incidence (HR: 1.910 [CI, 1.642 to 2.222]). Hazard ratios associated with SB and outcomes were generally more pronounced at lower levels of PA than at higher levels.

In breast cancer survivors, no studies have examined SB and risk for recurrence. Early mortality risk and SB was examined in a Health, Eating, Activity, and Lifestyle (HEAL) study. George et al. (2013a) examined the association between television watching time and all-cause mortality after breast cancer. This HEAL study subset included 687 women diagnosed with local or regional breast cancer. At two years post-diagnosis, women completed self-report assessments on time spent sitting watching television/videos in a typical day in the previous year. Deaths were followed for seven years. Breast cancer survivors in the top tertile of television watching time had twice the risk of early mortality than survivors in the lowest tertile. However, PA may be able to attenuate this association. When the authors adjusted for moderate-vigorous PA, the

correlation between SB and early mortality was no longer significant. To date, no studies have examined SB and risk for recurrence.

The George et al. (2013a) HEAL study suggests that examining patterns of both PA and SB is important. A combination of long-term SB and low PA may be particularly detrimental to health. For instance, evidence from a meta-analysis in the general population suggests that a pattern of long-term SB paired with low levels of PA is associated with doubling the risk for diabetes and cardiac conditions (Edwardson et al., 2012). The health effects of a pattern of long-term SB paired with low levels of PA are unknown for breast cancer survivors but likely are harmful to health. Because evidence suggests that patterns of high SB paired with low PA are likely to place breast cancer survivors at risk for poor outcomes, as they do in other populations, my studies will determine if there is a subgroup of breast cancer survivors following a pattern of low PA and high SB, the percentage in this subgroup, and whether this subgroup is predicted by variables from Lazarus and Folkman's (1987) Transactional Model of Stress and Coping.

1.1.3 Biological Mechanisms Linking Physical Activity and Reduced Risk for Recurrence and Early Mortality

Although I will not be examining biological mechanisms linking PA and SB to cancer prognosis, it is useful to review biological pathways published in the literature to establish that increasing PA and decreasing SB in breast cancer survivors will likely reduce recurrence and early mortality.

In 2008, McTiernan published a diagram showing biological pathways in which PA may be impacting cancer prognosis. These pathways include lower levels of PA leading to decreased sex hormones, insulin resistance, inflammation, and obesity, and in turn to cancer recurrence and survival risk (see Figure 1.3). The outcome variable in Figure 1.3 is "cancer risk" but the article reviews identical mechanisms for cancer prognosis. It may be the case that several pathways

need to be impacted before effects of PA on cancer prognosis can be observed. The pathways may also vary by demographic, clinical, and treatment-related characteristics.

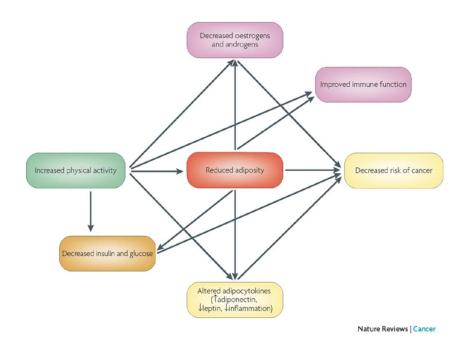


Figure 1.3. McTiernan's (2008) diagram showing hypothesized mechanisms linking physical activity to cancer risk and prognosis.

One systematic review also published a diagram showing hypothesized pathways in which SB may be influencing cancer progression and prognosis (Lynch, 2010). The hypothesized pathways for SB are identical to McTiernan's (2008) PA pathway diagram (sex hormones, metabolic dysfunction, and inflammation), with the addition of SB leading to decreased vitamin D levels, and in turn to cancer prognosis (see Figure 1.4).

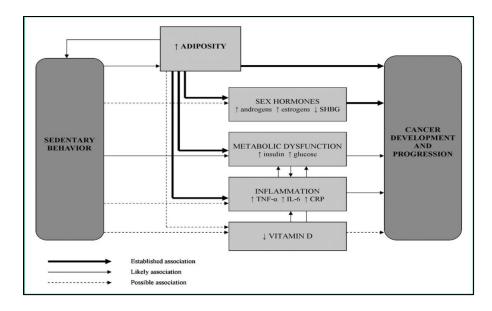


Figure 1.4. Lynch's (2010) diagram showing hypothesized mechanisms linking sedentary behavior to cancer prognosis.

1.1.4 Longitudinal Physical Activity and Sedentary Behavior during Survivorship

Despite PA and SB being likely determinants of outcomes after treatment for breast cancer, little is known about changes in PA and SB that may occur from pre-diagnosis through survivorship. Typically, self-reported PA levels are collected early in the post-treatment period and used to predict outcomes, such as survival and recurrence, several years later (Courneya, Mackey, & McKenzie, 2002; Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005; Ibrahim & Al-Homaidh, 2011; Kellen, Vansant, Christiaens, Neven, & Van Limbergen, 2009; Schmitz, 2011; Speck et al., 2010). However, this approach assumes that PA levels remain constant over time and fails to consider SB as an independent predictor of outcomes. It may be that PA and SB levels, independently or simultaneously, have mixed patterns over the course of survivorship, but empirical evidence is inadequate to date. In a review of cancer studies conducted during 1980-2003, the majority examined health behaviors during the diagnosis and treatment phases (Finney Rutten, Arora, Bakos, Aziz, & Rowland, 2005), indicating a critical need for research on health behaviors during long-term survivorship.

To my knowledge, no study has modeled longitudinal patterns (trajectories) of SB in breast cancer survivors and only two studies have modeled trajectories of PA. In the first of these two PA studies, Emery and colleagues (Emery, Yang, Frierson, Peterson, & Suh, 2009) modeled the mean PA trajectory over five years for 277 women treated for breast cancer. They found a curvilinear pattern from the time period between post-surgery and five years post-surgery: PA initially increased after surgery through 18 months, reaching recommended levels, and then gradually declined. At the 5-year post-surgery assessment, mean PA was lower than it was at baseline (Figure 1.5). However, this average trajectory may be masking individual variation and subgroups following different patterns. To date, no studies have modeled trajectories of longitudinal PA from the time of diagnosis to ten years post-diagnosis and no studies have modeled longitudinal SB trajectories.

In Figure 1.6, PA trajectories were stratified by perceived social support levels (groups were created with a median split). Social support was measured as general perceived social support that was not specific to PA (Perceived Social Support from Family and Friends). Breast cancer survivors with low perceived social support (dotted line in Figure 1.6) had higher PA after surgery but a steeper decline and significantly lower PA at five years post-surgery than breast cancer survivors with higher perceived social support (solid line in Figure 1.6). This finding provides intriguing evidence that breast cancer survivors who differ on characteristics relevant to coping resources may demonstrate different trajectories of PA.

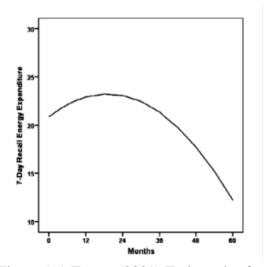


Figure 1.5. Emery (2009) Trajectories from post-surgery to 5 years post-surgery.

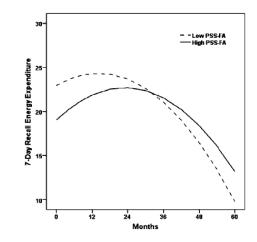


Figure 1.6. Emery (2009) trajectories stratified by perceived social support level.

The second study examined PA trajectories in 199 Canadian breast cancer survivors over a 15-month period (Brunet, Amireault, Chaiton, & Sabiston, 2014). Women were assessed at three, six, nine, twelve, and fifteen months post-treatment. The investigators identified five subgroups. The largest subgroup (49.2%) consistently met PA guidelines over the 15 months after treatment. The next largest subgroup (25.1%) was consistently active at levels that did not meet guidelines. The third subgroup (10.6%) reported being inactive at 3-9 months posttreatment but increased PA at 12 months post-treatment that was sustained at 15 months posttreatment. A fourth subgroup (9.5%) did not meet guidelines at three months post-treatment, met guidelines at six months post-treatment, dropped to not meeting guidelines again at nine months post-diagnosis, and reported no PA at 12-15 months post-treatment. The fifth subgroup (5.5%) consistently reported no PA (see Figure 1.7).

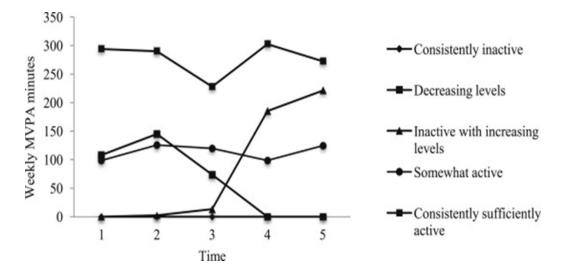


Figure 1.7. Brunet (2014) physical activity trajectories in 199 Canadian breast cancer survivors.

Three methodological concerns arise for the Brunet et al. (2014) study. First, the small sample size limits confidence in determining a reliable number of subgroups. Second, the authors did not adjust for sample size with the Bayesian Information Criterion (BIC) when enumerating the number of PA classes, which is biased toward too many classes (Enders, 2010b). Thus, five classes may be overstating the number of PA subgroups. Third, the sample was largely Caucasian (85%) and highly educated (50% with a college degree). These demographics may explain the surprising finding that the largest subgroup met PA guidelines at all time points. A more diverse sample of breast cancer survivors in the U.S. is unlikely to show the majority of the sample consistently meeting guidelines because lower PA levels are associated with minority heritage and less education, even after controlling for clinical and treatment characteristics (e.g., Hair et al., 2014; Hawkins et al., 2010; Patterson et al., 2003; Irwin et al., 2003; Pinto, Trunzo, Reiss, & Shiu, 2002).

Brunet et al. (2014) examined their subgroups in relation to demographic and clinical characteristics and symptoms such as depression and anxiety. Age, disease stage, time since

treatment, number of treatment types received, and physical symptoms did not predict PA trajectory group membership. Breast cancer survivors who reported higher depression and fatigue were less likely to be consistently sufficiently active compared to other groups. However, survivors who reported higher levels of cancer worry were more likely to be consistently sufficiently active. Brunet's small sample size limits confidence in determining reliable correlates of trajectories. However, this study suggests that there may be considerable value in examining whether subgroups of breast cancer survivors are following different trajectories and whether psychosocial variables are better predictors of subgroups than demographic and clinical characteristics. It may be the case that psychosocial variables are acting as mediators between demographic and clinical characteristics and subgroups of breast cancer survivors following different PA trajectories.

Neither the Brunet et al. (2014) nor the Emery et al., (2009) studies attempted to capture PA levels prior to cancer diagnosis; thus limiting our understanding of how trajectories of PA after treatment are associated with pre-diagnosed PA levels. Also, neither study examined SB trajectories, which ignores how the majority of leisure time is spent. No studies to date have estimated PA and SB in the same model for breast cancer survivors. Modeling PA and SB together would yield a fuller picture of how breast cancer survivors are spending their leisure time and which PA-SB trajectories may jeopardize long-term health.

In sum, little is known about how PA and SB change over the course of survivorship and whether there are groups of breast cancer survivors that follow different PA and SB trajectories based on demographic, clinical, and treatment-related characteristics. Prior research has assumed that PA levels remain constant over time and failed to consider SB as an independent predictor of outcomes. To address these gaps, my dissertation is focused on modeling breast cancer

survivors' PA and SB changes, from pre-diagnosis to 10 years post-diagnosis, and examining potential cognitive and emotional predictors informed by Lazarus & Folkman's (1987) Transactional Model of Stress and Coping.

1.2. Transactional Model of Stress and Coping

In addition to the fact that PA and SB have never been studied together from pre-diagnosis through ten years post-diagnosis in cancer survivors, using a research design that enables examination and comparison of their trajectories simultaneously, research on PA and SB has rarely used a theoretical approach. Of the limited studies, the most commonly applied theories with cancer survivors (and in the general population) are Social Cognitive Theory (SCT), the Theory of Planned Behavior (TPB), and the Transtheoretical Model (TTM) (Pinto & Floyd, 2008). I will describe these theoretical approaches in Section 1.2.2 and compare their strengths and weaknesses to the Transactional Model of Stress and Coping, described in the next section.

1.2.1 Transactional Model Constructs

After understanding how PA and SB patterns change over the course of survivorship, the next logical step is to determine important demographic, clinical, and treatment-related characteristics, as well as psychosocial variables, that may be associated with them. Demographic, clinical, and treatment-related characteristics are important for identifying subgroups of women in need of intervention. Psychosocial variables from the Transactional Model of Stress and Coping that prove to be mediators may be mutable intervention targets in the future.

Theories, such as the Transactional Model of Stress and Coping, are useful in several ways for identifying intervention targets for future research. Theory is helpful for selecting psychosocial variables to study because the framework shows a mediational process of how psychosocial variables affect the outcome of interest. Theory also aids in interpreting results in

light of the functions that psychosocial constructs may be playing in important health-related processes. Psychosocial variables are an important component of the Transactional Model of Stress and Coping, in that they describe how cognitive and affective perceptions predict the coping process.

The central tenets of the Transactional Model are four-fold: 1) Perception of a stressor is considered to be "transactional" because it is formed by an individual's cognitive and emotional appraisal of the stressor and the environmental context in which it occurs; 2) Individuals vary in their perception of stressors and availability of coping resources; 3) Coping strategies are a process determined by how threatening the situation is perceived to be and what coping options are perceived to be available; and 4) Coping is conceptualized as dynamic in that it varies by situational context, even within individuals (Lazarus & Folkman, 1987; Lazarus, 1999; Hill Rice, 2000). The Transactional Model makes no a priori assumptions about what constitutes "good" or "bad" coping strategies (e.g., Folkman & Lazarus, 1985). Coping is simply an individual's efforts to manage a stressor when demands exceed coping resources.

Figure 1.8 shows the 1987 version of the Transactional Model that represents Lazarus and Folkman's later thinking. In the diagram, a stressor is assumed to be occurring in order for appraisal processes to be initiated (but does not appear in the diagram itself). A stressor is a danger or demand originating from the internal or external environment that upsets homeostasis and requires action to restore balance (Glanz & Schwartz, 2008; Lazarus & Laupier, 1978). Lazarus and Folkman (1987) make a distinction between an objective, versus a perceived, threat (e.g., perceived risk for breast cancer recurrence may or may not align with objective risk). Their model assumes that perceptions of a stressor are better predictors of coping strategies than more objective assessments.

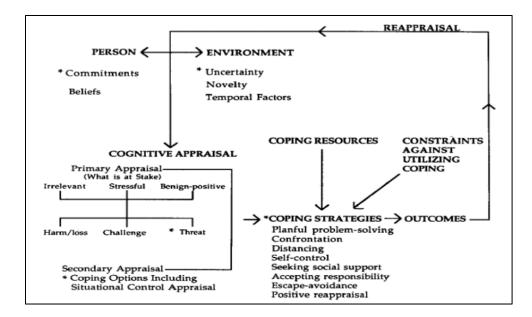


Figure 1.8. Transactional model of stress and coping.

Lazarus and Folkman describe two types of cognitive and emotional appraisals that impact coping behavior: primary and secondary appraisal. They argue that, before emotion occurs, individuals make a primary appraisal, which is an automatic, often unconscious, assessment of what is happening and what it may mean for them personally or for loved ones. In primary appraisal, a situation or stressor is judged on whether it is germane to well-being, i.e., whether the stressor is irrelevant, stressful, or benign-positive (lower left corner of Figure 1.8). If the situation is judged to be benign or positive, it has the potential for a positive outcome (labeled "benefit" in the Transactional Model literature but not shown in Figure 1.8). A situation perceived to be stressful is broken down further into three parts: harm/loss, future threat, and challenge (Lazarus & Folkman, 1987). "Harm or loss" is conceptualized as negative consequences attributed to the stressor that have occurred to date; "threat" is anticipated harm for the future; and "challenge" is the potential for mastery or gain. A secondary appraisal also occurs. This appraisal relates to the perception of whether any action(s) can be taken to reduce or eliminate the stressor, and if so, which coping strategies might be effective (Lazarus & Folkman, 1987; Lazarus, 1999). Coping strategies are the cognitive, affective, and behavioral efforts to manage a situation perceived to be a stressor (Lazarus & Folkman, 1987).

Primary and secondary appraisals are explicitly described as influencing each other but not having a temporal dimension. In other words, the appraisal that something (or nothing) can be done about a stressor may be made before the individual has determined what is personally at stake. The Transactional Model predicts that when stakes are perceived to be high, mobilization of coping resources will occur. When the stake is substantial and coping resources are judged to be inadequate, a negative emotional response is predicted to occur. The greater the imbalance between stakes and coping resources, the greater the negative emotional response is predicted to be.

The Transactional Model of Stress and Coping suggests that breast cancer survivors who perceive recurrence to be an important future threat, and who appraise their coping resources as adequate to manage future recurrence risk, will change their behavior as a coping strategy. For instance, breast cancer survivors may increase their PA or change their diet to increase overall health and reduce future health threats. Breast cancer survivors may choose to change PA (instead of, or in conjunction with, other health behaviors) because of media reports on PA and cancer, a clinician's recommendation to increase PA, or other sources of information.

Because few researchers have explicitly framed PA and SB as coping strategies, virtually no research exists about when they are used to deal with a stressor and when they are due to other circumstances or personal characteristics. I examined longitudinal PA and SB trajectories

as proxies for coping strategies after a breast cancer diagnosis. These ideas will be covered more fully in Section 1.2.4. In the next section, I discuss the strengths and weaknesses of the Transactional Model in relation to my dissertation.

1.2.2 Strengths and Weaknesses of the Transactional Model

A review conducted in 2007 found only 30 published articles using a theoretical framework to understand a range of health behavior changes among cancer survivors (Park & Gaffey, 2007). The most commonly applied theories were Social Cognitive Theory (SCT), the Theory of Planned Behavior (TPB), and the Transtheoretical Model (TTM) (Pinto & Floyd, 2008). SCT postulates that a health behavior is performed if an individual perceives control over the outcome, few external barriers, and confidence in ability (i.e., self-efficacy) (Bandura, 1986). TPB theorizes that an individual's intention to perform a behavior is a function of attitudes held toward the behavior, subjective norm (perception of how others want the person to act), and perceived behavioral control (Ajzen, 1991). TTM describes five temporal stages of readiness to change a behavior (Prochaska & DiClemente, 1983).

Criticisms of SCT, TPB, and TTM include three potentially flawed assumptions: 1) Behavior is always under conscious control; 2) Emotions and affective reactions are not important predictors of health behavior; and 3) Social, organizational, and cultural influences have minimal impact on health behavior (Armitage & Conner, 2000; Burke, Joseph, Pasick, & Barker, 2009; Brug, et al., 2005; Giles-Corti & Donovan, 2002). The Transactional Model addresses some of these criticisms: 1) Emotions and affective reactions are assumed to be influential predictors of health behavior, which allows for unconscious and non-rational explanations of behavior; 2) Inclusion of individual-level constructs such as primary appraisal, which reflects individual differences in the perception of a stressor; and 3) Inclusion of individual-level constructs assessing social, organizational, and cultural coping resources such as

perceived social support and religious coping resources (secondary appraisal), which may impact health behavior. These features of the Transactional Model allow for a richer examination of the functions that health behaviors, such as PA and SB, may serve in the context of women's responses to stressors associated with having been treated for breast cancer.

Despite its advantages, the Transactional Model also has several weaknesses. For instance, the Transactional Model fails to include potential effects of age, race, and gender differences on key model variables including perceptions of a stressor, perceived coping resources, and coping strategies. In Figure 1.8, the personal determinants of appraisals are focused on more intrapersonal cognitive constructs (e.g., commitments and beliefs) than on demographic characteristics. I included demographic, clinical, and treatment-related characteristics in my conceptual models in order to take a public health approach to understanding women's longitudinal PA and SB patterns after breast cancer.

The Transactional Model also lacks a variable such as self-efficacy for performing specific coping strategies. Self-efficacy has proven to be an important predictor of health behavior change in the general population (Armitage & Conner, 2000). However, it is arguable whether self-efficacy is implicitly included in the Transactional model. For instance, individuals are not likely to perceive something to be a coping resource unless they are able to access and use it.

Another important criticism of the Transactional Model is that it does not describe a specific reference period for coping efforts, which raises questions about whether the model describes only immediate responses or whether coping strategies can be maintained over time (De Ridder, 1997). Lazarus and Folkman (1987) deal with coping strategies over time by including a concept called "reappraisal." Reappraisal is essentially a feedback loop in the model

(see Figure 1.8) where individuals make re-assessments of primary and secondary appraisals based on changes to the stressor or in the environment, which implies a long-term time element.

I used the Transactional Model of Stress and Coping to investigate predictors of PA and SB trajectories after breast cancer because it includes constructs for emotional reactions and social and cultural coping resources, which typically are excluded from classic health behavior theories. I also included demographic, clinical, and treatment-related characteristics in my conceptual models to take a public health approach to better understanding the determinants of breast cancer survivors' PA and SB patterns. In the next section, I describe a study that applied primary and secondary appraisals to better understand the coping strategies used by breast cancer survivors. This study by Hilton (1989) illustrates that primary and secondary appraisal constructs are relevant to my target population (breast cancer survivors) and the ways in which they cope with a cancer diagnosis.

1.2.3 Applying Appraisals and Coping to Breast Cancer

Hilton (1989) used the Transactional Model to examine the relationships between anxiety about recurrence, perceived control, and coping strategies in a sample of 277 women recently diagnosed with breast cancer. Two patterns emerged that reflect Transactional Model predictions: 1) breast cancer survivors who had high anxiety about recurrence (proxy for primary appraisal) and low perceived control over the situation (proxy for secondary appraisal); and 2) breast cancer survivors who reported high anxiety about recurrence and high perceived control over the situation.

Breast cancer survivors who had high anxiety about recurrence and low perceived control were more likely to use escape-avoidance coping strategies and less likely to use positive reappraisal or to take control of the situation than breast cancer survivors who reported high anxiety about recurrence and high perceived control (Hilton, 1989). Breast cancer survivors who

reported high anxiety and high perceived control were more likely to use coping strategies such as planful problem solving, seeking social support, positive reappraisal, and self-control techniques than survivors who reported high anxiety and low control (Hilton, 1989). These two patterns of primary and secondary appraisals explained about a third of the variance in coping strategies used by survivors (1989).

Hilton (1989) did not report on whether women with low primary appraisal changed their coping strategies. However, the Transactional Model processes suggest that breast cancer survivors with low primary appraisal would not change their coping strategies because the situation is not seen as a stressor requiring action.

I hypothesized that similar patterns would emerge in my sample for primary and secondary appraisal clusters, which in turn would affect women's levels of PA as a coping response. Table 1.1 presents a simplified way of thinking about the patterns of PA predicted as a coping strategy in response to primary and secondary appraisals. (Note that this table does not take into account demographic, clinical, and treatment-related characteristics.)

If threat/primary appraisal is perceived to be high and coping resources/secondary appraisal are low, a pattern lower in PA over time is predicted (top row, right cell) because the woman would be expected to perceive breast cancer to be a high threat for future health but that she is unable to change the stressor with cognitive, behavioral, or affective efforts. In contrast, if threat and coping appraisal are both high, a pattern higher in PA over time is expected (bottom row, left cell) because the woman perceives a high future health threat and that she has the coping resources to successfully alter that threat. In the next section, I describe the ways in which PA and SB can function as coping strategies after a cancer diagnosis.

		Threat Appraisal					
		Low Medium High					
	Low	No Change in PA	↓ PA	↓ PA			
Coping Appraisal	Medium	No Change in PA	↑ PA	↑ PA			
	High	No Change in PA	↑ PA	↑ PA			

Table 1.1. Expected Patterns of Physical Activity in Response to Appraisals

1.2.4 Physical Activity and Sedentary Behavior as Coping Strategies

A breast cancer diagnosis represents a "teachable moment" where women may be more receptive to hearing information about making lifestyle changes to become healthier. It also represents a time where women may begin using coping strategies in response to the stressor of cancer and feelings of vulnerability about their current and future health. One type of coping strategy after diagnosis is to change health behavior, which may be health-promoting (e.g., increasing PA) or health-inhibiting (e.g., decreasing PA). In a population-based sample of survivors of different cancer types, almost 30% reported increasing their PA following diagnosis, about half remained the same, and 15% decreased PA following diagnosis (Hawkins et al., 2010). Thus, almost half of cancer survivors may be changing health behaviors in response to their cancer diagnosis.

In the coping literature, coping strategies are generally categorized as problem- or emotionfocused (Carver, Scheier, & Weintraub, 1989). Problem-focused coping strategies directly impact the threat or stressor. For instance, PA can be a problem-focused coping strategy because it directly impacts the threat of breast cancer recurrence by reducing risk [Ingledew, & McDonagh, 1998]). Emotion-focused coping strategies are used to manage the emotions and emotional reactions stemming from the stressor. A more emotion-focused aspect of PA may be managing feelings of anxiety and depression stemming from a cancer diagnosis.

However, this dichotomy of problem- vs. emotion-focused coping is potentially misleading. It is more likely that coping strategies serve both problem- and emotion-focused functions (Park & Iacocca, 2014) because they serve several purposes. For example, PA as a coping strategy may have both problem- and emotion-focused aspects by helping a woman to feel better physically and emotionally and increasing her feelings of control. SB may have problem- and emotion-focused aspects by directly impacting the stressor (e.g., helping a woman to feel better by resting during active treatment) and managing the emotional reactions to cancer (e.g., increasing time spent sitting watching TV to avoid thinking about cancer). The Transactional Model avoids labeling coping strategies in this way and assumes that coping strategies can be both problem- and emotion-focused.

In the context of the Transactional Model, I examined PA and SB as coping strategies in response to breast cancer. Conceptualizing PA and SB as long-term coping strategies is an innovative application of the Transactional Model. However, evidence from fields such as exercise science and health psychology support the notion that some individuals use PA explicitly for the purpose of coping with a stressor (e.g., Ingledew, Hardy, Cooper, & Jemal, 1996; Park & Iacocca, 2014). Research with breast cancer survivors is consistent with this function for PA. For instance, in a small qualitative study, breast cancer survivors spontaneously mentioned PA as an active coping strategy they employ to enhance feelings of personal control and to increase their physical and mental strength (Drageset, Lindstrom, & Underlid, 2009).

In 2007 and 2014, Park and colleagues surveyed the literature linking stress, coping, and health behaviors and noted that very little research has explicitly examined health behaviors as

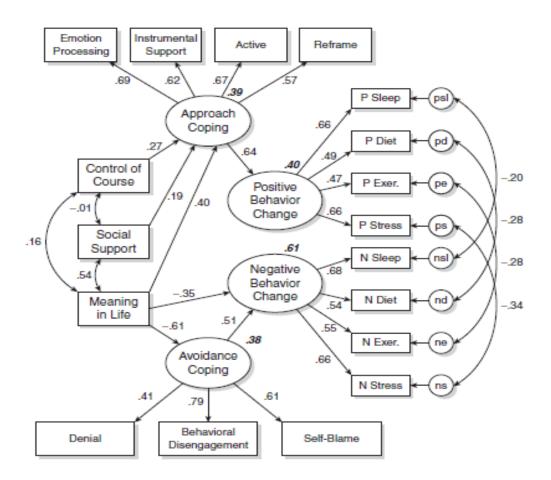
coping responses in general or medical populations (Park & Gaffey, 2007; Park & Iacocca, 2014). Because few researchers have explicitly framed health behaviors as coping strategies, little research exists about when health behaviors are used to manage a stressor. Park and Iacocca (2014) recommend using a Transactional Model approach to advance the understanding of health behaviors and to inform future intervention development.

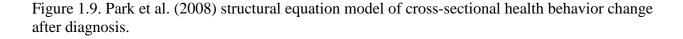
Park and colleagues (Park, Edmonson, Fenster, & Blank, 2008) successfully applied the Transactional Model to examine health behavior changes as coping strategies in response to cancer (see Figure 1.9). They examined cross-sectional positive and negative health behavior changes following diagnosis in 250 cancer survivors (almost 50% breast cancer, mean age: 45, 89% Caucasian). Health behaviors included PA, diet, sleep, and stress management.

Figure 1.9 is Park et al.'s (2008) structural equation model results showing that positive health behavior changes following diagnosis were related to social support, sense of control over disease course, meaning in life, and approach coping (composite index of emotion processing, instrumental support, active coping, and reframing the situation). Negative health behavior changes after a cancer diagnosis were related to a lack of meaning in life and avoidance coping (composite index of denial, behavioral disengagement, and self-blame) (Park et al., 2008). Positive and negative health behavior changes were predicted by different types of coping strategies, and thus appear to be distinct (but correlated) phenomena.

In sum, I examined PA and SB as coping strategies in response to cancer in the context of the Transactional Model. Very little research has explicitly examined health behaviors as coping responses. Park and colleagues (2008) applied the Transactional Model to examine crosssectional health behavior changes as coping strategies in response to cancer. Their results suggest that the Transactional Model is useful for understanding PA change in cancer survivors and that

PA change can be predicted from appraisals. In the next section, I describe my conceptual models for PA and SB that incorporate Transactional Model constructs as mediators.





1.3 Conceptual Models

In this section, I present the conceptual models for PA and SB separately, starting with PA. I also present a conceptual model for PA and SB estimated in the same model. Supporting empirical literature is reviewed in Chapter 2.

1.3.1 Conceptual Model for Physical Activity

My PA conceptual model was informed by Lazarus and Folkman's (1987) Transactional Model of Stress and Coping and a literature review of empirical research. The model represents the research question of whether primary and secondary appraisals (Transactional Model of Stress and Coping) mediate the relationships between demographic, clinical, and treatmentrelated characteristics and PA trajectories from pre-diagnosis through ten years post-diagnosis (see Figure 1.10).

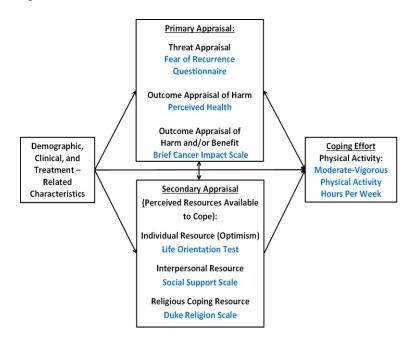


Figure 1.10. Conceptual model: Physical activity.

Specific demographic, clinical and treatment-related variables were selected for my conceptual model because they are important for breast cancer prognosis and are correlated with PA (see Chapter 2). Figure 1.10 shows that demographic, clinical, and treatment-related characteristics were expected to have both direct and indirect effects on PA.

Demographic characteristics included age at diagnosis, race/ethnicity, education, being partnered/married, and working outside the home. Clinical characteristics were operationalized

as disease stage, comorbid conditions, fatigue, and BMI. Treatment-related characteristics were operationalized as four variables: surgery (breast-conserving surgery or mastectomy); chemotherapy; radiation therapy; and taking tamoxifen. Tamoxifen is an oral medication that prevents estrogen from binding with breast cancer cells (Devita, Lawrence, & Rosenberg, 2010; Rubin, 2001). During the years of this cohort study (1995-2009), tamoxifen was typically prescribed for five years following diagnosis to prevent recurrence for women with hormonereceptor-positive tumors (Rubin, 2001). Tamoxifen can cause menopausal-like symptoms such as hot flashes, mood swings, or nausea.

Mediators (primary and secondary appraisals) were selected from an existing dataset (see Section 1.4) with the goal of identifying variables from that dataset that best represent Transactional Model constructs. I operationalized primary appraisal with three constructs: anxiety about recurrence (a proxy for anticipatory appraisal of threat); perceived health (a proxy for harm appraisal); and perceived impact of breast cancer (direct assessment of harm and benefit appraisals).

Anxiety about recurrence was chosen based on Folkman and Lazarus' (1985) idea that emotions reflect an individual's appraisal of the encounter. Anxiety about recurrence implies anticipatory concern or worry about a future health threat, and therefore is a good proxy for appraisal of threat.

Perceived health was chosen based on Lazarus and Folkman's outcome appraisal of a stressor as harmful because it reflects perceived consequences to physical health experienced to date. Having had breast cancer is a major event in many women's lives; thus it is very likely that breast cancer survivors would report adverse effects and symptoms related to treatment when asked about perceived health in general (in addition to other health symptoms).

Perceived impact of breast cancer was chosen based on Lazarus and Folkman's constructs of outcome appraisals of harm and benefit because breast cancer survivors report both negative and positive impacts of cancer on their lives (Alfano et al., 2006; Ganz et al., 2002). In other words, a negative perception of cancer impact represents harm appraisal and a positive perception represents potential benefit (e.g., post-traumatic growth such as re-evaluating what is important in life).

Secondary appraisal has been operationalized as perceived coping resources by several researchers, which I also did. Secondary appraisal was operationalized with three constructs: personal coping resources (generalized positive expectations for the future, or optimism); interpersonal resources (the presence of people to confide in, or perceived social support); and religious coping resources (measured by the proxy of religiosity/spirituality).

Optimism was selected as a personal coping resource based on work by Carver, Scheier, and Segerstrom (2010) showing that individuals with higher optimism (i.e., positive expectancies regarding future outcomes) use more problem-focused (engagement coping), which predicts better resilience against a health stressor. Perceived social support was chosen as an interpersonal coping resource based on Lazarus and Folkman's work on coping resources (1997).

Religiosity/spirituality was chosen as a proxy for religious coping resources because it provides a schema for making sense of adversity, increases feelings of control over a stressor (e.g., a belief that "God has a plan"), and may provide emotional, tangible, and informational support resources for individuals who are part of faith communities.

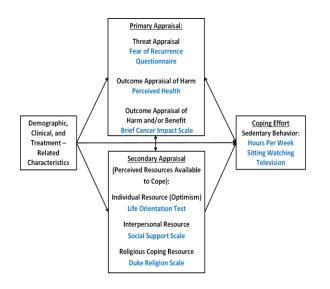
In my PA conceptual model (Figure 1.9), a bi-directional arrow was included between primary and secondary appraisal because Lazarus and Folkman (1987) described them as cooccurring and interacting. In addition, the individual constructs of anxiety about recurrence,

perceived health, perceived impact of breast cancer, optimism, religiosity/spirituality, and social support are correlated among breast cancer survivors (Alfano et al., 2006; Waters, Liu, Schootman, & Jeffe, 2013; Stolley, Sharp, Wells, Simon, & Schiffer, 2006). Finally, I operationalized longitudinal PA (as a coping strategy) as the number of hours of moderate-vigorous PA per week measured as trajectories from pre-diagnosis through ten years post-diagnosis.

1.3.2 Conceptual Model for Sedentary Behavior

My conceptual model for SB includes the same pathways as PA because they were correlated with SB in prior research or are predicted based on Transactional Model processes (see Chapter 2). SB was first included in a conceptual modeled by itself (see Figure 1.11) and then PA was added to the model as a separate outcome variable (see Figure 1.12). Conceptualizing SB individually and then simultaneously with PA was important because they are separate (but correlated) constructs that may have different predictors. Including PA and SB in the same conceptual model reflects the idea that different combinations of trajectory patterns are possible (e.g., low PA and high SB, or high PA and high SB).

All predictors and mediators of SB were operationalized in the same manner as PA. SB (as a coping strategy) was operationalized as hours per week sitting watching television because it is the most common way of measuring SB in the literature (Clark et al., 2009).



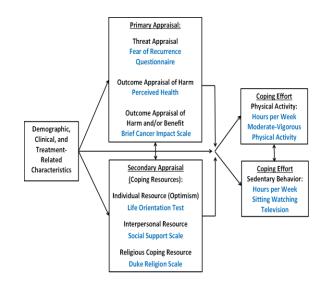


Figure 1.11. Conceptual model: Sedentary behavior.

Figure 1.12. Conceptual model: Physical activity and sedentary behavior modeled simultaneously.

1.4 Study Aims

The <u>objectives</u> of my dissertation were to determine the longitudinal trajectories of PA and SB and whether theoretically-based psychosocial constructs were important predictors. The <u>rationale</u> for these objectives was that the results would provide a better understanding of the mechanisms underlying PA and SB patterns during survivorship and inform the type of interventions women with breast cancer need to increase their PA to recommended levels and decrease time spent in SB.

My dissertation was informed by previously published empirical research and a *theoretical framework*, Lazarus and Folkman's (1987) Transactional Model of Stress and Coping. The Transactional Model predicts that two types of cognitive and affective appraisals will influence how an individual behaves in response to a stressor, primary and secondary appraisal. Primary appraisal is an assessment of a situation's potential for threat or benefit. It was operationalized with three constructs: anxiety about recurrence (proxy for anticipatory threat

appraisal), perceived health (proxy for harm appraisal), and perceived impact of breast cancer (direct assessment of harm and benefit appraisal). Secondary appraisal is an assessment of available coping resources. It was also operationalized with three constructs: optimism (personal coping resource), social support (interpersonal resource), and religiosity/spirituality (proxy for religious coping resources).

My <u>central hypotheses</u> were that 1) Groups of breast cancer survivors would follow different PA and SB patterns over time based on demographic, clinical, and treatment characteristics ("predictors"); and 2) Primary and secondary appraisals would be important mediators of associations between predictors and women's longitudinal PA and SB patterns during survivorship.

I examined these specific aims in a *prospective cohort study* called the "Health, Eating, Activity, and Lifestyle" (HEAL) study. HEAL is a cohort of 938 women diagnosed with breast cancer between 1995 and 1999. Women were recruited from cancer registries in New Mexico, California, and Washington. The sample is diverse with 61% non-Hispanic Caucasian, 36% non-Hispanic African American, and 12% Hispanic American. Their ages ranged from 35-64 years at the time of diagnosis. More detail is given about the HEAL study in Chapter 4.

Specific Aim 1: Estimate temporal patterns (trajectories) of PA and SB from 1 year prior to breast cancer diagnosis through 10 years post-diagnosis

<u>Aim 1a</u>: Determine the shape of the average PA and SB trajectories from pre-diagnosis through ten years following breast cancer diagnosis (estimated in separate models first and then in the same model) <u>Aim 1b</u>: Determine whether there is significant individual variability in the intercept and slope parameters for PA and SB trajectories from pre-diagnosis through ten years following breast cancer diagnosis (estimated in separate models first and then in the same model) <u>Aim 1c</u>: Determine whether there are subgroups of breast cancer survivors who follow different PA or SB trajectories from pre-diagnosis through ten years post-diagnosis (estimated separately

and then in the same model)

Specific Aim 2: Determine whether primary and secondary appraisal constructs from Lazarus and Folkman's (1987) Transactional Model of Stress and Coping predict PA and SB patterns for breast cancer survivors

<u>Aim 2a</u>: Determine which psychosocial constructs from the Transactional Model of Stress and Coping mediate relationships between demographic, clinical, and treatment-related characteristics and subgroup membership for breast cancer survivors following different PA trajectories from pre-diagnosis through ten years post-diagnosis

<u>Aim 2b:</u> Determine which psychosocial constructs from the Transactional Model of Stress and Coping mediate relationships between demographic, clinical, and treatment-related characteristics and subgroup membership for breast cancer survivors following different SB trajectories from pre-diagnosis through ten years post-diagnosis

<u>Aim 2c</u>: Determine whether different Transactional Model constructs mediate the relationships between demographic, clinical, and treatment-related characteristics and subgroups when PA and SB are estimated in the same model (rather than modeled separately)

In terms of *expected outcomes*, Aim 1 was expected to extend existing scientific knowledge of the longitudinal PA and SB patterns exhibited by breast cancer survivors from

pre-diagnosis through ten years post-diagnosis. Aim 1 was also expected to determine subgroups following different PA and SB patterns over time. Aim 2 determined if primary and secondary appraisals informed by the Transactional Model of Stress and Coping were important mediators between demographic, clinical, and treatment-related characteristics and PA and SB subgroup membership. Study 2 results may also guide development of theory-informed interventions for breast cancer survivors.

CHAPTER 2. LITERATURE REVIEW

In this chapter, I summarize the empirical and theoretical literature informing my hypotheses. I review: 1) PA and SB levels of breast cancer survivors at different time points during survivorship, 2) empirical studies and theoretical constructs informing the pathways in my conceptual models, and 3) an overview of how primary and secondary appraisal from the Transactional Model of Stress and Coping were operationalized. I conclude the chapter by describing the significance of my dissertation work.

2.1 Physical Activity and Sedentary Behavior Levels at Different Time Points during Survivorship

2.1.1 Physical Activity Levels

National guidelines for the recommended minimum amount of time per week to spend engaging in PA are identical for adults with and without cancer: 150 minutes per week of moderate PA or 75 minutes per week of vigorous PA (Rock et al., 2012; Haskell et al., 2007). Breast cancer survivors may be vulnerable to decreasing PA after diagnosis and throughout survivorship, and thus are at risk for not meeting recommended levels.

Table 2.1 shows six studies that examined longitudinal PA levels at different points during breast cancer survivorship. Only one examined trajectories (Emery et al. [2009]). These studies suggest that PA forms a non-linear pattern for breast cancer survivors but they are inconsistent in their characterization of the timing and direction of changes. Two studies showed a non-linear trend where PA increased during the first 12 months post-diagnosis and then declined around 18 months post-diagnosis (Harrison, Haves, & Newman, 2009; Emery et al., 2009). However,

Littman et al. (2010) observed a decrease in PA during the first 12 months post-diagnosis and an increase at 19-30 months post-diagnosis for women diagnosed with invasive breast cancer.

Inconsistencies in PA levels across these studies may be explained by differences in demographic, clinical, and treatment-related characteristics, or even inconsistent use of PA measures, but evidence to date is inadequate. Samples across these prior studies were homogenous for race (mostly Caucasian for the four studies conducted in the U.S.), age (around 50-55), education (high education level), and being partnered, and thus demographic differences cannot be compared. However, one study specifically examined PA levels by race (Hair et al., 2014). After adjustment for potential confounders, African American women were less likely to meet PA guidelines after diagnosis than Caucasian women (odds ratio, 1.38; 95% CI, 1.01-1.88) and reported less weekly post-diagnosis PA (12- vs. 14-MET hours) than Caucasian women.

Clinical and treatment-related characteristics may also account for a portion of the variance in PA across studies. The four cohort studies with a higher proportion of women with stage II and III disease reported decreases in PA after diagnosis (Littman et al., 2010; DeVoogdt et al., 2010; Andrykowski et al., 2007; Hair et al., 2014). In contrast, the two studies with larger proportions of women with early stage disease showed increases in PA after diagnosis (Harrison et al., 2009; Emery et al., 2009). The inconsistencies in the timing and direction of PA patterns underscore the importance of my dissertation research to model PA trajectories from prediagnosis through ten years post-diagnosis in a diverse cohort of breast cancer survivors, as well as the importance of understanding how those trajectories may vary according to demographic, clinical, and treatment-related characteristics.

First Author (Year)	Time Period	PA Level	Treatment Types	Main Findings
		Women Followed	Up To 12 Mont	hs Post-Diagnosis
Devoogdt (2010): 267 Flemish Breast Cancer Survivors	Before surgery and 1, 3, 6, and 12 months post- operative	Pre-Surgery: 269 MET- hours/week of TOTAL PA* <u>1 Month Post-</u> <u>Tx</u> : 241 MET- hours/week <u>3 Months</u> : 244 MET- hours/week <u>6 Months</u> : 248 MET- hours/week <u>12 Months</u> : 256 MET- hours/wek	Mastectomy: 45%, Lumpectomy: 55%, Chemo: 51%, Radiation: 87%, Hormonal: 80%	PA significantly decreased between week prior to surgery to first month after surgery and did not recover during first year. At each follow-up, total PA lower than before surgery. Mean age: 55 (21-90), Mean BMI: 25, race not reported (Flemish), education not reported. Greater age and smoking predicted decrease in moderate PA, not having a spouse predicted decrease in household activities. *TOTAL PA = light+moderate+vigorous
Andry- kowski (2007): 257 American Breast Cancer Survivors from 2 Treatment Centers	Between time of surgery and start of adjuvant therapy and 2 and 6 months post-tx	After Surgery: Radiation: 150 min/week Chemo: 150 <u>After Adjuvant</u> <u>Therapy</u> : Rad: 100 Chemo: 100 <u>2 Months</u> <u>Post-Tx</u> : Rad: 150 Chemo: 150 <u>6 Months</u> <u>Post-Tx</u> : Rad: 125 Chemo: 175	Radiation: 143 (56%) Chemo+ Radiation: 114 (44%)	Significant decreases, relative post- surgery baseline, in total weekly MET-minutes of leisure-time exercise during adjuvant therapy for both radiotherapy and chemotherapy + radiation groups. Levels did not differ from post-surgery by 2 and 6 months after adjuvant therapy. Groups not significantly different for demographics or PA. Mean age: 55 (29-82), 92% Caucasian, 74% Partnered, 28% high school education or less, mean BMI: 27

Table 2.1. Longitudinal Physical Acitivty Levels during Survivorship

First Author (Year)	Time Period	PA Level	Treatment Types	Main Findings
Hair (2014): 1,735 U.S. women with invasive breast cancer from Phase 3 Carolina Breast Cancer Study	Pre- (recalled) and post- dx	<u>3 Months Prior</u> <u>to Diagnosis</u> (<u>Recalled):</u> Sample: 473.9 minutes/week White: 491.0 Black: 420.1 <u>6 Months Post- Diagnosis:</u> Sample: 245 minutes/week White: 263.8 Black: 144.7	Chemo: 51%, chemo+ radiation: 14%, no chemo or radiation: 23%, radiation: 12%	35% met PA guidelines after diagnosis. 59% reported decrease in PA after diagnosis, with average reducing PA by 15 MET-hours (95% CI: 12 -19). After adjustment, black women less likely to meet PA post-dx (OR = 1.38; 95% CI, 1.01-1.88) and reported less weekly postdx PA (12 MET hours vs 14 MET hour). In adjusted stratified analyses, receipt of chemo or radiation significantly associated with postdx PA in black women. In fully adjusted models, racial differences in postdx PA and changes not significant. Erroneously classified low PA as SB. Ages 20-74.
	Women	Followed Throug	ph 13 or More N	Ionths Post-Diagnosis
Harrison (2009): 287 Australian Breast Cancer Survivors	6, 12, 18 months post-dx	<u>6 months post-</u> <u>dx</u> : 283 minutes of TOTAL PA/ week <u>12 months</u> <u>post-dx</u> : 307 min/week <u>18 months</u> <u>post-dx</u> : 227 min/week	73% local exision, 27% mastectomy, 28% radiation	Harrison (2009): 80% reported engaging in some PA between 6 and 18 months following diagnosis, mostly moderate-intensity activities, with only 20–30% reporting either vigorous intensity or strength-based exercise. 45% met national guidelines for sufficient PA. Treatment-related complications related to lower PA. Mean age: 55, no other demographics reported (Australia) *TOTAL PA = light+moderate+vigorous PA
Emery (2009): 277 U.S. women (1/2 random- ized to PA inter-vention trial but inter-vention not success- ful)	Post- surgery to 5 years post-tx	Baseline: 16.6 METs/week* <u>4 months</u> : 24.5 <u>8 months</u> : 26.6 <u>1 year</u> : 31.3 <u>18 months</u> : 25.4 <u>2 years</u> : 22.3 <u>30 months</u> : 23.2 <u>3 years</u> : 19.6 <u>42 months</u> : 21.0 <u>4 years</u> : 16.8 <u>54 months</u> : 13.8 <u>5 years</u> : 14.3	Surgery (57%), RT (54%), Chemo (84%), Tamoxifen (75%)	Curvilinear trajectory where PA initially increased from surgery through 18 months to recommended levels and then gradually decreased until 5-year assessment. Higher social support associated with slower decline from 18- 42 months. Mean age: 51 (20-84), 90% Caucasian, 67% married, average of 14 years of education. *MET = ratio of energy consumption during specific activity to reference metabolic rate, e.g., 18 MET- hours/week equivalent to moderate- paced walking for 50 minutes/day

First Author (Year)	Time Period	PA Level	Treatment Types	Main Findings
		Pre-Treatment	to 30 Months P	Post-Treatment
Littman (2010): 315 American Breast Cancer Survivors Residing in Washing- ton State	2-year period before diagnosis and at 3 intervals after dx (1-12, 13- 18, and 19-30 months post-dx)	2 years pre-dx: Total: 18.8 MET-h/wk Vigorous: 8 Moderate: 4.2 <u>0-12 months</u> <u>post-dx:</u> Total PA: 9.2 Vigorous: 2.9 Moderate: 1.6 <u>13-18 months</u> : Total: 15.3 Vigorous: 5.8 Moderate: 3.1 <u>19-30 months</u> : Total: 15.0 Vigorous: 5.8 Moderate: 2.6	Chemo and radiation (61%), Chemo (20%), Radiation (12%)	Longitudinal cohort study. Mean PA levels decreased by 50% in 12 months after dx relative to before dx. At 19-30 months post-dx, overall PA increased from low levels reported in first year after diagnosis, but remained ~3 MET- hours/wk lower than before dx. [18.8 MET-h/wk s equivalent to walking ~50 min per day.] Mean age: 52 (21-74), 85% Caucasian, 72% partnered, 50% college education or higher, 56% BMI of ≥ 25 Diagnosed with invasive breast cancer between 2002-2004 and identified by population-based registry

2.1.2 Studies Examining Both Physical Activity and Sedentary Behavior Levels at Different Points during Survivorship

SB, such as sitting watching television for several hours in a row, has only recently been examined in the context of breast cancer. No studies to date have examined SB changes after diagnosis without also examining PA. As such, three studies are reported that examined both PA and SB (Kim et al., 2013; Lynch et al., 2010; Rogers, Markwell, Courneya, & McAuley, 2011). It is important to note that these studies reported both PA and SB, but they did not model them together to determine if they were inter-related.

Table 2.2 summarizes two studies that looked at PA and SB cross-sectionally (Kim et al., 2013; Rogers et al., 2011) and one that used a longitudinal design (Irwin et al., 2003). Kim and colleagues (2013) examined cross-sectional PA and SB levels using a nationally representative sample (NHANES) of women with and without breast cancer. One-hundred and thirty-two breast cancer survivors, who had a mean age of 62 and were an average of four years post-diagnosis, completed self-reports on PA and SB. After adjusting for demographics, BMI, and smoking,

breast cancer survivors were more likely than women without cancer to report spending more than eight hours per day in SB (OR = 1.99, 95% CI: 1.25 to 3.19), suggesting that breast cancer survivors are inactive for longer periods of time than women without cancer (Kim et al., 2013). Interestingly, breast cancer survivors were also more likely than women without breast cancer to report spending up to 60 minutes per day engaged in moderate or vigorous PA (OR = 1.74, 95% CI: 1.07 to 2.83) (Kim et al., 2013). This result highlights the importance of examining subgroups of breast cancer survivors who report different combinations of PA and SB patterns.

In contrast, Rogers et al. (2011) observed very different proportions of a day spent in PA and SB as reported by rural breast cancer survivors. These women had a mean age of 63, were approximately 39 months post-diagnosis, and were living in rural counties in a Midwestern state in the U.S. Rural breast cancer survivors self-reported approximately four hours of sitting time per day, 44 minutes spent walking (proxy for light PA), and 139 minutes in moderate-vigorous PA per day. The authors speculated that this low level of SB may have been due to higher levels of walking for transportation purposes, domestic activities, gardening, and farming among rural breast cancer survivors. The inconsistencies in proportion of a day spent in PA and SB highlights the importance of considering the characteristics of the women, such as demographics, which may be playing a role in PA and SB patterns.

First Author (Year)	Time Period	Sedentary Time	Treatment Types	Main Findings
Kim (2013): NHANES 2007- 2010 women with (132) and without breast cancer	Cross- sectional: average of 4 years post- diagnosis (<3 years post-dx excluded)	>8 hours/day	Unknown in NHANES	After adjusting for demographics, BMI, smoking, breast cancer survivors more likely than women without cancer to report spending >8 hours/day in SB (OR = 1.99, 95% CI: 1.25 to 3.19) and to spend up to 60 minutes/day engaged in moderate or vigorous PA (OR = 1.74, 95% CI: 1.07 to 2.83). Mean age: 62, 86% Caucasian, mean BMI of 29, 58% >high school, partnered not reported
Rogers (2011): 483 breast cancer survivors living in the most rural counties of a Midwest, U.S. state	Cross- sectional: 39 months post-dx	Daily SB: 4.2 hours Walking, MET- mins/week: 968.5±2064 (= 44 min/day) Moderate- Vigorous MET- mins/week 2969±3048 (= 139 min.day)	Not reported	Rogers (2011): SB: no difference in age, race, or months since dx. Greater minutes sitting associated with less education. Women reporting ≥ 360 daily minutes of sitting also reported less education when compared with those reporting > 120 to < 360 min. Higher SB associated with higher # comorbidities. Mean Age: 63, 96% Caucasian, mean 13 years educ, partnered not reported

Table 2.2. Cross-Sectional Physical Activity and Sedentary Behavior Levels during Breast Cancer Survivorship

First Author (Year)	Time Period	Sedentary Time	Treatment Types	Main Findings
Irwin (2003): 812 from HEAL (New Mexico and W. Washing -ton sites) *Exclude d Californi a site where all African America n women were recruited	Longi- tudinal: Pre-dx to 6 months post-dx	SB: Surgery Pre-dx: 41.3 hrs/wk Post-dx: 44.1 Surgery+RT pre-dx: 39.7 post-dx: 41.0 Surgery+Chemo pre-dx: 43.4 post-dx: 49.4 Surgery, RT, Chemo pre-dx: 37.8 post-dx: 45.9 PA: Surgery pre-dx: 18.9 hrs/wk post-dx: 17.3 Surgery+RT pre-dx: 18.7 post-dx: 17.4 Surgery+Chemo pre-dx: 19.7 post-dx: 16.1 Surgery, RT, Chemo pre-dx: 18.9 post-dx: 15.3	No differences in PA or SB by stage. Surgery (n=266), Surgery and radiation (n=329), Surgery and chemotherapy (n=52) Surgery, radiation, and chemo (n=165)	 HEAL patients decreased total PA by 2 hours per week from pre-dx to post-dx (11% decrease). Greater decreases in moderate-vigorous PA observed for radiation and chemotherapy (50% decrease) compared with women who underwent surgery only (24% decrease) or who were treated with radiation only (23%). Greater decreases in PA among obese patients (41% decrease) compared with normal weight (24% decrease), implying a potential for greater weight gain among women who already are overweight. Mean age: 55, mean BMI: 27, 90% Caucasian, 98% high school graduates (breakdown not reported), partnered not reported

One additional study examined PA and SB longitudinally (Irwin et al., 2003). This prior HEAL study used data from two out of three sites (Washington state and New Mexico) and excluded the California site where all African American women in the HEAL study were recruited (because data were not available yet). Irwin and colleagues (2003) found differences in PA and SB levels by treatment type. HEAL breast cancer survivors who underwent surgery and received radiation therapy reported a 1-hour increase in SB and a 45-minute decrease in PA per week from pre- to post-diagnosis. Women who received chemotherapy, in addition to any other therapy type, fared the worst for PA and SB. They reported a six-hour increase in SB and a 1.5hour decrease in PA per week from pre- to post-diagnosis. Across treatment types, the level of increase in SB was not equivalent to the decrease in moderate-vigorous PA, reflecting the differences in the constructs.

In sum, three studies have examined both PA and SB for breast cancer survivors (two cross-sectional and one longitudinal). Inconsistencies in PA levels across studies may be explained by differences in demographic, clinical, and treatment-related characteristics. Samples across prior studies were homogenous for race, age, education, and being partnered/married, and thus demographic differences cannot be determined from prior studies. Therefore, I included race/ethnicity, education, age at diagnosis, and marital/partnered status in my conceptual models. A longitudinal study indicated that PA and SB levels vary by treatment type, and thus I included surgery, radiation, chemotherapy, and tamoxifen in my conceptual models. In the next section, I review the literature supporting the proposed pathways in my conceptual model for PA.

2.2 Empirical Research Informing My Conceptual Model for Physical Activity

For Aim 2a, I examined whether primary and secondary appraisals mediated the relationships between demographic, clinical, and treatment-related characteristics and PA patterns from pre-diagnosis to ten years post-diagnosis. Demographic, clinical, and treatment-related characteristics are important variables to include because perceptions of harm, threat, and coping resources may vary by them.

Table 2.3 summarizes prior research showing correlates of PA in breast cancer survivors (demographic, clinical, and treatment-related characteristics, and primary and secondary appraisals). The direction of the relationship is also specified. A dashed line indicates that the relationship has not been examined empirically. For instance, no studies have examined PA and tamoxifen use but it is important to determine whether it exerts an effect on PA, and thus needs to be taken into consideration for the structural equation model.

In my study, demographic characteristics were operationalized as age, race/ethnicity, education, and being partnered/married because there is strong evidence suggesting that Caucasian race, younger age, higher education, and being partnered/married are correlated with higher PA levels in breast cancer survivors, even after controlling for clinical characteristics (e.g., Hawkins et al., 2010; Irwin et al., 2003; Patterson et al., 2003; Pinto et al., 2002; Kampshoff et al., 2014).

Clinical and treatment-related variables have all been negatively correlated with PA after diagnosis (higher BMI, later disease stage, higher fatigue, greater number of comorbid conditions, and receipt of mastectomy or chemotherapy) (e.g., Charlier et al., 2013; Harrison et al., 2009; Hawkins et al., 2010; Irwin et al., 2003; Patterson et al., 2003; Pinto et al., 2002; Courneya et al., 2014; Kampshoff et al., 2014) (see Table 2.3).

PA has also been correlated with primary and secondary appraisals (mediators), although no studies have examined all constructs in the same model. Two of my constructs assessing primary appraisal were negatively related to PA (anxiety about recurrence and perceived impact of breast cancer) and one was positively related (perceived health). Breast cancer survivors who reported lower anxiety about recurrence, higher perceived health status, or higher perceived impact of breast cancer (primary appraisal indicators) or higher optimism, religiosity/spirituality, or social support (secondary appraisal indicators) increased their PA at a greater rate, and sustained lifestyle changes longer, than survivors lower in these characteristics (Costanzo, Lutgendorf, & Roeder, 2011; Hawkins et al., 2010; Park et al., 2008; Park & Gaffey, 2007; Pinto et al., 2002). See Table 2.3 for a summary that links citations to each correlate.

Correlate	Direction of Relationship with PA	First Author (Year)	
BMI	Negative	Hong (2007); Lynch (2010); Irwin (2003); Sabiston (2014); Charlier (2013); Harrison (2009); Hawkins (2010); Patterson (2003); Pinto (2002); Courneya (2014)	
Comorbid conditions	Negative	Irwin (2003); Sabiston (2014); Charlier (2013); Harrison (2009); Hawkins (2010); Patterson (2003); Pinto (2002)	
Fatigue	Negative	Irwin (2003); Sabiston (2014); Charlier (2013); Harrison (2009); Hawkins (2010); Patterson (2003); Pinto (2002)	
Stage of cancer	Negative	Sabiston (2014); Charlier (2013); Harrison (2009); Hawkins (2010); Patterson (2003); Pinto (2002); Courneya (2014); Courneya (2008); <i>Irwin (2003): no relationship;</i>	
Mastectomy	Negative	Harrison (2009); Irwin (2003); Andrykowski (2007); Devoogdt (2010); Hawkins (2010); Hong (2007); Patterson (2003); Pinto (2002)	
Radiation	Negative	Harrison (2009); Irwin (2003); Andrykowski (2007); Hawkins (2010); Hong (2007); Patterson (2003); Pinto (2002); Vallance (2010)	
Chemotherapy	Negative	Harrison (2009); Irwin (2003); Andrykowski (2007); Hawkins (2010); Hong (2007); Patterson (2003); Pinto (2002); Courneya (2014); Vallance (2010)	
Tamoxifen			
Partnered/ married	Positive	Hawkins (2010); Patterson (2003); Pinto (2002); Kampshoff (2014)	
Age	Negative	Hawkins (2010); Patterson (2003); Pinto (2002)	
Education	Positive	Hawkins (2010); Patterson (2003); Pinto (2002); Vallance (2010)	
Racial/ethnic Minority Status	Negative	Hong (2007); Irwin (2003); Hawkins (2010); Patterson (2003); Pinto (2002); Hair (2014); Courneya (2008)	
Anxiety about Recurrence	Negative	Park (2008); Park (2007); Pinto (2002); Hawkins (2010)	
Perceived Health	Positive	Emery (2009); Park (2008); Park (2007); Pinto (2002); Hawkins (2010)	
Perceived Impact of Breast Cancer	Negative	Alfano (2006); Costanzo (2011)	
Optimism	Positive	Park (2008); Park (2007); Pinto (2002); Carver (2010); Harper (2007); Hawkins (2010); Rogers (2007)	
Religiosity/ Spirituality	Positive	Hawkins (2010); Gall (2005); Karvinen (2014); Strawbridge (2001)	
Social Support	Positive	Emery (2009); Park (2008); Park (2007); Pinto (2002); Harper (2007); Hawkins (2010); Rogers (2011)	

Table 2.3. Summary of Correlates of Physical Activity in Breast Cancer Survivors

In my PA and SB conceptual models, appraisals are mediators, and thus are predicted by demographic, clinical, and treatment-related characteristics. Table 2.4 summarizes existing research showing demographic, clinical, and treatment-related correlates of relevant indicators of

primary and secondary appraisals and the direction of the relationship for breast cancer survivors (dashed line indicates that the relationship has not been examined empirically).

Demographic characteristics have been correlated with indicators of primary appraisals (anxiety about recurrence, perceived health, and perceived impact of breast cancer). The most consistent predictors of anxiety about recurrence have been younger age, lower education level, being partnered/married, and having Caucasian or Hispanic ancestry (Crist & Grunfeld, 2013; Deimling et al., 2006; Janz et al., 2011; Simard & Savard, 2009; Simard, Savard, & Ivers, 2010; Vickberg, 2003). Better perceived health has been associated with younger age, higher education, and being partnered (Ashing-Giwa, Tejero, Kim, Padilla, Hellemann, 2007; Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005). Demographic characteristics associated with a more negative impact of breast cancer include younger age and not being partnered (Alfano et al., 2007). Older women (ages 60 and older at diagnosis) have reported less impact from breast cancer than younger survivors for educational plans, work life, diet, family plans, social life, finances, exercise, romantic relationships, retirement plans, and ability to be a caregiver (Ganz et al., 2002).

In the general population, demographic characteristics have also been associated with the secondary appraisal constructs in my conceptual model (optimism, religiosity, and social support). Greater optimism has been correlated with older age and higher education (Ek, Remes, & Sovio, 2004; Palgi et al., 2011; Benyamini et al., 2005). Religiosity/spirituality has been correlated with older age (Beeghley et al., 1981). The correlation between education and religiosity/spirituality varies by race, such that higher religiosity/spirituality has been reported by Caucasian individuals with higher education and African American individuals with lower education (Beeghley et al., 1981; Koenig, 1998). Finally, higher perceived social support is

associated with being partnered, younger age, and higher education (Bloom et al., 2013; Drageset & Lindstrom, 2005).

Clinical characteristics have been examined in prior research with breast cancer survivors with respect to two of my primary appraisal constructs (anxiety about recurrence and perceived health). The evidence is mixed for relationships between anxiety about recurrence and clinical characteristics. Disease stage has been inconsistently related to anxiety about recurrence for breast cancer survivors with seven studies finding no relationship and three studies finding that higher disease stage was associated with greater anxiety about recurrence (Ganz et al., 1993; Van den Beuken-van Everdingen et al., 2008; Mellon et al., 2007; Northouse, 1981; Johnson Vickberg, 2001; Park, Cho, Blank, & Wortmann, 2013; Rakovitch et al., 2003). The most consistent clinical predictors of perceived health status have been comorbid health conditions and fatigue (Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005; Montazeri, 2008). Clinical characteristics have not been examined with respect to perceived impact of breast cancer and indicators of secondary appraisals (optimism, religiosity, or social support).

Treatment-related characteristics have been correlated with all three of my primary appraisal constructs (anxiety about recurrence, perceived health, and perceived impact of breast cancer) in breast cancer survivors. Receipt of chemotherapy or radiation therapy has been the most consistent treatment-related characteristics associated with higher anxiety about recurrence (Crist & Grunfeld, 2013; Deimling et al., 2006; Janz et al., 2011; Mehnert et al., 2009; Mellon et al., 2007), lower perceived health (Mols et al., 2005; Montazeri, 2008), and a negative perception of the impact of breast cancer (Alfano et al., 2006). Receiving a mastectomy was inconsistently related to anxiety about recurrence with eight studies finding no relationship and four studies

with mixed results. No studies have examined treatment-related characteristics in relation to secondary appraisal constructs (optimism, religiosity, and social support).

	Anxiety about Recurrence	Perceived Health	Perceived Impact of Breast Cancer	Optimism	Religiosity/ Spirituality	Social Support
BMI						
Comorbid conditions	Inconsistent: no relationship (Liu (2011), positive (Janz (2011)	Negative: Mols (2005);				
Fatigue	Positive: Clayton (2006); Crist (2013)	Montazeri (2008)				
Stage of cancer	Inconsistent: 7 studies no relationship (Ganz (1993); Van den Beuken (2008); Mellon (2007); Northouse (1981); Johnson Vickberg (2001); Park (2013); Rakovitch (2003) 3 positive: McGinty (2012); Janz (2011); Liu (2011)					
Mastect-omy	Inconsistent: 8/12 no relationship: Curran (1998); Janz (2011); Lasry (1992); Mehnert (2009); De Haes (2003); Johnson Vickberg (2001); Liu (2011)					
Radiation	Positive:	Negative:				
Chemo	Crist (2013); Deimling (2006); Janz (2011); Mehnert (2009); Mellon (2007)	Mols (2005); Montazeri (2008)	Positive: Alfano (2006)			
Tamoxifen						

Table 2.4. Summary of Correlates of Primary and Secondary Appraisals

	Anxiety about Recurrence	Perceived Health	Perceived Impact of Breast Cancer	Optimism	Religiosity/ Spirituality	Social Support
Partnered/ Married	Negative: Crist (2013); Deimling (2006); Janz (2011); Simard (2009): Simard	Ashing- Giwa (2007); Negative: Mols Crist (2013); Deimling (2005);	Negative: - Alfano		Inconsistent: Wolfinger (2008)	Positive: Bloom (2013); Drageset (2005)
Age			(2006)	Positive:	Positive: Beeghley (1981)	Negative : Bloom (2013); Drageset (2005)
Education	(2010); Vickberg (2003)	Positive: Ashing- Giwa (2007); Mols (2005); Schmitz (2013)		- Ek (2004); Palgi (2011); Benyamin i (2005)	Varies by Race: Caucasian: Positive and African American: Negative (Beeghley, 1981; Koenig (1998)	Positive: Bloom (2013); Drageset (2005)
Minority	-				Positive: Koenig (1998)	

In sum, the demographic, clinical, and treatment-related correlates of PA are well established for breast cancer survivors (with the exception of tamoxifen). The state of the evidence for correlates of primary and secondary appraisals is limited and more research is warranted to establish these associations. In the next section, I present a summary of the empirical literature supporting the pathways specified in my SB conceptual model.

2.3 Empirical Research Informing My Conceptual Model for Sedentary Behavior

In Aim 2b, I proposed to examine whether primary and secondary appraisals mediated the relationships between demographic, clinical, and treatment-related characteristics and SB trajectories. Very little is known about SB in both breast cancer survivors and the general population. As such, I present SB research for both breast cancer survivors and the general population in order to better understand how SB may be affected by demographic, clinical, and treatment-related characteristics.

Table 2.5 summarizes the predictors of SB that have been examined in the general population and in breast cancer survivors (dashed line indicates that the relationship has not been examined empirically). In breast cancer survivors, demographic correlates of higher SB included fewer years of education and minority race or ethnicity (Rogers et al., 2011). Inadequate evidence is available for breast cancer survivors on whether age is correlated with SB. In the general population, age was positively related to SB and education was negatively related (Rhodes et al., 2012; Owen et al., 2000).

In terms of clinical characteristics for breast cancer survivors, higher SB levels were associated with higher fatigue (Rogers et al., 2011) and higher BMI (Sabiston et al., 2014; Irwin et al., 2003; Lynch et al., 2010) in breast cancer survivors. In the general population, higher BMI was also associated with greater SB (Rhodes et al., 2012; Owen et al., 2000).

Treatment-related characteristics for breast cancer survivors correlated with higher SB levels include mastectomy, radiation, and chemotherapy (Irwin et al., 2003). Greater comorbid conditions have been associated with higher SB (Rogers, 2011). No research exists on the relationships between SB, tamoxifen, being partnered, primary appraisals (anxiety about recurrence, perceived health, and perceived impact of breast cancer), and secondary appraisals (optimism, religiosity/spirituality, social support). More work is needed to establish these relationships in breast cancer survivors.

Correlate	<u>Breast Cancer</u> <u>Survivors</u> : Direction of Relationship with SB	First Author (Year)	<u>General</u> <u>Population</u> : Direction of Relationship with SB	First Author (Year)
BMI	Positive	Sabiston (2014); Irwin (2003); Lynch (2010)	Positive	Rhodes (2012); Owen (2000)
Comorbid Conditions	Positive	Rogers (2011)		
Fatigue	Positive	Rogers (2011)		
Stage of disease	Insufficient Evidence	Irwin (2003): no relationship	N/A	N/A
Mastectomy	Positive	Irwin (2003)	N/A	N/A
Radiation	Positive	Irwin (2003)	N/A	N/A
Chemotherapy	Positive	Irwin (2003)	N/A	N/A
Tamoxifen			N/A	N/A
Partnered/Married				
Age	Insufficient Evidence	Rogers (2011): no relationship	Positive	Rhodes (2012)
Education	Negative	Rogers (2011)	Negative	Rhodes (2012); Owen (2000)
Minority status	Positive	Rogers (2011)		
Anxiety about Recurrence				
Perceived Health				
Perceived Impact of Breast Cancer			N/A	N/A
Optimism				
Religiosity/Spirituality				
Social Support				

Table 2.5. Summary of Correlates of Sedentary Behavior

In summary, little research has been conducted on demographic, clinical, and treatmentrelated correlates of SB. I conducted a literature review to inform my hypotheses about which demographic, clinical, and treatment-related characteristics have been shown to affect primary and secondary appraisal variables and SB. Higher SB is related to fewer years of education, minority race or ethnicity, greater age, higher BMI, higher fatigue, and receipt of a mastectomy, radiation, or chemotherapy, and thus these are included in my conceptual model and hypotheses. In the next section, I give an overview of the constructs I used as proxies for primary and secondary appraisals and describe how these constructs were operationalized.

2.4 Operationalizing Transactional Model Constructs

In Aims 2a-2c, I applied Lazarus and Folkman's (1987) Transactional Model of Stress and Coping to determine important cognitive and affective variables associated with longitudinal patterns of PA and SB during breast cancer survivorship. Below I describe how key Transactional Model variables were operationalized.

2.4.1 Operationalizing Primary Appraisal

Folkman and Lazarus (1985) operationalized primary appraisal as an individual's appraisal of the encounter as harmful, threatening, challenging, and/or benign or positive. There are two types of theorized primary appraisals: 1) *anticipatory appraisals* of threat (e.g., fear and worry) and challenge (e.g., eagerness and confidence) and 2) *outcome appraisals* of harm (e.g., anger/disgust) and benefit (e.g., relief/happiness). For instance, in one study Folkman and Lazarus (1985) measured the extent to which undergraduate students facing an upcoming exam experienced various emotions that theoretically reflected anticipatory and outcome appraisals. The items for threat were "worried, fearful, and anxious" and the challenge items were "confident, hopeful, and eager." The items used to assess harm were "angry, disappointed, and guilty" and the benefit items were "pleased, happy, and relieved." If a student reported feeling worried about the upcoming exam, Lazarus and Folkman felt that that emotion represented appraisal of the exam as a threatening situation.

Later researchers have operationalized primary appraisal by assessing how threatening and/or challenging a situation is perceived to be and the level of harm attributed to the stressor. Three studies show examples of prior variable operationalization. For instance, Chang (1998) operationalized primary appraisal with three items when examining the appraisal process during exams for undergraduate students: "How important was the event?"; "How threatening (could have negative consequences for you) did you find the event?"; and "How challenging (could

have positive consequences for you) did you find the event?" Parle and Maguire (1995) used the item, "I see my illness as a challenge," with cancer survivors. Finally, Hilton (1989) used the Fear of Recurrence Questionnaire (Northouse, 1981) to operationalize threat appraisal with breast cancer patients, reflecting a primary concern of women who have had breast cancer. I used the same questionnaire to operationalize threat appraisal. In a meta-analysis of coping and appraisals during cancer survivorship by Franks and Roesch (2006), harm appraisal in cancer patients was typically assessed as the physical and mental aspects of harm attributed to cancer.

I operationalized harm appraisal in two ways, selecting from variables available in the HEAL dataset guided by the foregoing research. First, I used an item assessing perceived health that was administered at several time points (six months post-diagnosis, and two and ten years post-diagnosis). Second, I used a questionnaire called the "Brief Cancer Impact Assessment" (Alfano et al., 2006; Ganz et al., 2002), which assesses the perceived impact, negative and positive, that cancer has had in four domains: caregiving/financial, exercise/diet, social/emotional, and religiosity/spirituality. In Sections 2.4.1.a - 2.4.1.c below, I give an overview of each of the primary and secondary appraisal proxies and describe how they were operationalized. Measures are described in detail in Chapters 4 and 5.

2.4.1.a Anxiety about Recurrence

Vickberg (2003) defined fear of recurrence as, "worry or concern about breast cancer coming back in the same breast or another area of the body, or a new breast cancer in either breast" (pp. 18). While most women with breast cancer may not experience a high degree of global distress, the single largest concern reported by women with breast cancer is the possible recurrence of cancer (Spencer et al., 1999). Anxiety about recurrence is not usually experienced continuously but may be induced by triggers that require effort to dismiss (Simard, Savard, & Ivers, 2010; Simard et al., 2013; Johnson Vickberg, 2001; Whitaker, Watson, & Brewin, 2009).

Factor analytic studies show that anxiety about recurrence encompasses uncertainty about the future and perceived loss of control (Johnson Vickberg, 2001; Simard & Savard, 2009; Simard, Savard, & Ivers, 2010; Simard et al., 2013; Spencer et al., 1999). Anxiety about recurrence implies anticipatory concern about a future cancer threat, and thus is a good proxy for threat appraisal.

However, uncertainty about the future and perceived loss of control are descriptions of anxiety instead of fear. Fear is an acute and automatic response caused by the belief that someone or something is dangerous. By definition, fear cannot be sustained and therefore is not the best description of women's experience. Thus, I use the term "anxiety about recurrence" instead of "fear of recurrence" in my dissertation.

I measured anxiety about recurrence with the Fear of Recurrence Questionnaire (Northouse, 1981), which has six items assessing anxiety-related features of future health threat. For instance, two items are, "I worry that my cancer will return" and "I am bothered by the uncertainty of my health status." Hilton (1989) also used this scale to operationalize the Transactional Model construct of "threat" with breast cancer survivors. I reverse-coded positively worded items so that higher scores indicated higher primary (threat) appraisal. The Fear of Recurrence Questionnaire was administered at approximately 39 months post-diagnosis, as part of a quality of life supplement.

2.4.1.b Perceived Health

In Lazarus and Folkman's Transactional Model, one aspect of primary appraisal is an assessment of harm or loss attributable to the stressor. "Harm or loss" is usually operationalized as the perceived negative consequences that have occurred because of the stressor (as opposed to "threat" which is anticipated harm in the future) (Franks & Roesch, 2006).

Perceived health is an assessment of one's current health status that takes into account past health status. Being treated for breast cancer is a major event in many women's lives; thus, it is very likely that breast cancer survivors would report adverse effects and symptoms related to treatment when asked about perceived health in general. Previous qualitative research indicates that when respondents were asked to define the item, "How was your health in general?," the majority referred to one or more aspects of physical health (Simon, de Boer, Joung, Bosma, & Mackenbach, 2005). For instance, respondents mentioned the effects of chronic health conditions on physical health, physical problems, medical treatment, and age-related complaints (Simon et al., 2005). Therefore, perceived health is a good proxy for the amount of perceived harm to physical health after a breast cancer survivor diagnosis.

In HEAL, perceived health was measured at several time points with the item, "How would you describe your general health status?" Response options are 1) *Excellent*; 2) *Very Good*; 3) *Good*; 4) *Fair*; 5) *Poor*. These response options were not reverse-coded because they are already in the direction of higher harm.

Even though it is only one item, this general health question is widely used, including in multiple epidemiological surveys (e.g., Behavioral Risk Factor Surveillance System; Hagan Hennessy, Moriarty, Zack, Scherr, & Brackbill, 1994) and has powerful predictive properties. It is strongly associated with a person's objective physical and mental health status (DeForge, Sobal, & Krick, 1989; Permanyer-Miralda et al., 1991; Stewart et al., 1989) and these relationships persist across age and cultural groups (Cockerham, Kunz, & Lueschen, 1988; Kawachi et al., 1999). Self-rated health is sensitive to changes in comorbid conditions and is a predictor of mortality (DeSalvo, Bloser, Reynolds, He, & Muntner, 2006). Poor perceived health has also been correlated with health risk behaviors, including heavy alcohol consumption,

smoking, and low PA (Colsher et al., 1990; Lamb, Brodie, Minten, & Roberts, 1991; Segovia, Bartlett, & Edwards, 1989), and it is associated with demographic and social factors such as socioeconomic status and lack of access to health care (Schroll et al., 1991).

2.4.1.c Perceived Impact of Breast Cancer

Perceived impact of breast cancer is focused on past and current levels of harm/loss and/or benefit attributable to breast cancer, and thus is a direct assessment of harm and benefit appraisals. HEAL used the Brief Cancer Impact Assessment (BCIA) (Alfano et al., 2006; Ganz et al., 2002), which assesses the perceived impact, negative and positive, that cancer has had in four domains: caregiving/financial, exercise/diet, social/emotional, and religiosity/spirituality. Scale scores differed by demographic and treatment characteristics, and the pattern of correlations with HRQOL scales generally supported the construct validity of the scales (Alfano et al., 2006). Positively worded items were reverse-coded so that higher scores indicate higher threat appraisal.

The BCIA is a relatively new scale and has not been tested with respect to the Transactional Model. However, a small study of 77 breast cancer survivors three months postdiagnosis suggests that women who believed their cancer had more severe consequences are more likely to report improvement in diet or PA (Costanzo, Lutgendorf, & Roeder, 2011). The authors speculated that changing health behaviors after a breast cancer diagnosis may help manage the uncertainty that many women feel related to the possibility of recurrence and the loss of their "safety net" after active treatment ends (Costanzo, Lutgendorf, & Roeder, 2011), and thus it is consistent with Transactional Model processes.

2.4.2 Operationalizing Secondary Appraisal

A secondary appraisal involves an assessment of action(s) that can be taken to reduce or eliminate the stressor and the perceived availability of coping resources (Lazarus & Folkman,

1987; Lazarus, 1999). Lazarus and Folkman measured secondary appraisal with four general items assessing evaluations of whether a situation could be changed, had to be accepted, required more information before acting, and whether self-restraint was required (e.g., Folkman, 1982).

Later researchers have operationalized secondary appraisal as perceived coping resources (Schwarzer & Leppin, 1991; Gall et al., 2005). Following their model, I operationalized secondary appraisal with three constructs: personal coping resources (generalized positive expectations for the future, or optimism), interpersonal resources (the perceived presence of people to confide in, or perceived social support), and religious coping resources (spiritual beliefs as a cognitive schema shaping perceptions of stress and creating meaning, or religiosity/spirituality as a proxy). Optimism, religiosity/spirituality, and perceived social support were not reverse-coded because they are already in the direction of higher secondary appraisal (higher coping resources).

2.4.2.a Personal Resource: Optimism

Optimism is the extent to which an individual holds generalized favorable expectations for the future (Carver, Scheier, & Segerstrom, 2010). Adults with higher optimism have been shown to be more persistent in pursuing goals, used more active coping strategies, and had better overall health, which allowed them to translate these tendencies into long-term coping resources (see Carver, Scheier, & Segerstrom, 2010 for a review).

It may be that optimists safeguard their health (preventive or proactive behavior) because they feel more control over outcomes, and thus engage in more health-enhancing behavior (Carver, Scheier, & Segerstrom, 2010). In several cross-sectional studies, breast cancer survivors who reported higher optimism also reported increasing their PA after diagnosis (Harper et al., 2007; Hawkins et al., 2010; Park, Edmondson, Fenster, & Blank, 2008; Park & Gaffey, 2007; Pinto, Trunzo, Reiss, & Shiu, 2002). Perhaps optimists are more likely to set health behavior

change goals and persevere in these goals because they believe these goals can be achieved, which is similar to Bandura's work on self-efficacy and positive outcomes expectancies (Bandura, 1986). In another cross-sectional study of breast cancer survivors, women who expected more positive outcomes (optimistic expectations) from PA itself (e.g., reducing fatigue and depressive symptoms) were more likely to report being physically active after diagnosis (Rogers, Courneya, Shah, Dunnington, & Hopkins-Price, 2007).

Optimism has also been found to be associated with specific coping strategies (Carver, Scheier, & Segerstrom, 2010; Scheier, Weintraub, & Carver, 1986). In the general population, a meta-analysis determined that optimism was correlated with higher levels of engagement coping (coping with a stressor by directly dealing with the stressor to reduce threat or the emotions stemming from it) and lower levels of disengagement or avoidance coping (escaping the stressor or emotions stemming from it) (Solberg Nes & Segerstrom, 2006).

There is evidence that this is also true for breast cancer survivors with higher optimism. Namely, Carver et al. (1993) observed that before and after surgery, breast cancer survivors who were more optimistic used more coping that involved accepting the reality of the situation, placing a positive light on the situation, and relieving tension with humor, which resulted in lower distress. Breast cancer survivors who were more pessimistic used more coping strategies focused on overt denial (pushing the reality of the situation away) and were more prone to giving up on goals (Carver et al., 1993). Thus, optimism can be viewed as an indicator of secondary appraisal because a woman has favorable expectations that she has the resources necessary to support active coping and feels more control over coping resources.

The most common way of operationalizing optimism is with Scheier and Carver's (1985) Life Orientation Test (LOT). The LOT is a series of statements about generalized future

expectations. For instance, one LOT statement is, "I'm always optimistic about my future." I also operationalized optimism with the LOT.

In sum, optimism is a generalized positive expectation about the future, which can be situation-specific (e.g., medical contexts) and clusters with other coping resources such as social, status, and economic resources. Optimism can be an indicator of secondary appraisal because an individual who feels that she has the resources necessary to support a coping strategy may also feel more control over the situation. This supports using optimism as a proxy for secondary appraisal.

2.4.2.b Interpersonal Resource: Perceived Social Support

Perceived Social support is a multidimensional construct encompassing emotional, tangible, and informational functions. Lazarus and Folkman conceptualized social support as a coping resource because it is a transactional process that changes with demands of a stressor (1987). This conceptualization is consistent with the view of perceived social support as an indicator of secondary appraisal, that is, women who perceive that they have support available to them if they need it are more likely to view a stressor as something they can cope with successfully.

Social support has been extensively studied in the context of stressors and chronic health conditions. In the 1980s, health psychology researchers were examining the ways in which social support impacts chronic health conditions. Cohen and Wills popularized the "buffering hypothesis" in their review of social support models (1985). This hypothesis states that the positive association between social support and health/well-being is attributable to a process through which support protects individuals from potentially adverse effects of stressful events. In other words, social support is predicted to "buffer" against stressors (Cohen & Wills, 1985), and thus serves as a coping resource (Schwarzer & Leppin, 1991). The buffering hypothesis appears

to be relevant for breast cancer survivors. Waters and colleagues (Waters, Liu, Schootman, & Jeffe, 2013) found that early-stage breast cancer survivors who reported higher perceived social support experienced better perceived health in the first six months after diagnosis and had a shorter recovery period than women with lower social support. Perceived social support also predicted 5-year trajectories of PA for breast cancer survivors (Emery et al., 2009).

In the HEAL study, an item assessing confidant network size was available as a proxy for perceived social support. This item assesses how many family or friends the woman confides in. The item assumes that a larger confidant network represents greater perceived social support. It was administered at 39 months post-diagnosis. At that time, breast cancer survivors were also asked to recall their number of confidants at the time of diagnosis. Given that breast cancer survivors were recalling past perceived support, recall bias may be an issue. Women may have remembered better or worse perceived social support at the time of diagnosis than was actually the case. See Cohen, Underwood, & Gottlieb (2000) for a discussion of social support measures and test-retest reliability.

2.4.2.c Religious Coping Resource: Religiosity/Spirituality

Religiosity/spirituality functions as a coping resource in three ways: 1) it provides a schema for that helps people achieve an understanding of adversity to facilitate cognitive processes and situational meaning making (i.e., a way of comprehending a stressor in relation to attitudes and beliefs about the world and a higher power); 2) it increases feelings of control over a stressor (e.g., a belief that "God is in control" or "God has a plan"); and 3) it may provide emotional, tangible, and informational support resources for individuals who are part of faith communities (see Harrison et al., 2001 for a review). Therefore, religiosity/spirituality is conceptualized in my dissertation as a proxy for perceived religious coping resources.

In a qualitative study with breast cancer survivors, religiosity and spirituality were reported to be critical aspects of HRQOL and experiences in the post-treatment period. Breast cancer survivors described religiousness and spirituality as playing three major roles: 1) providing global guidance; 2) guiding illness management efforts; and (3) facilitating recovery (Puchalski, 2012; Regan Sterba et al., 2014; Schreiber, & Brockopp, 2012). Women's religious and spiritual beliefs and behaviors were used to cope with breast cancer in terms of making sense of the illness and to manage the physical and emotional aspects of breast cancer (Puchalski, 2012; Regan Sterba et al., 2014; Schreiber, & Brockopp, 2012). The ability to create meaning when faced with a stressful event has been associated with successful coping, adaptation, and well-being in both cancer and non-cancer populations (Koenig, 1997; Park & Folkman, 1997; Schreiber, & Brockopp, 2012). In contrast, the inability to find meaning during a stressor has been correlated with psychological distress and uncertainty, which in turn can lead to inhibition of effective coping behaviors (Koenig, 1998; Pargament, 1997).

In the HEAL study, religiosity/spirituality was measured with the Duke Religion Index (Koenig, Parkerson, & Meador, 1997), which assesses religiosity/spirituality in terms of organizational, individual, and intrinsic religiosity. The items include: 1) "How often do you attend faith community or other religious meetings?" 2) "How often do you spend time in private religious activities, such as prayer, meditation or Bible study?" 3) "In my life, I experience the presence of God or the Divine"; 4) "My religious beliefs are what really lie behind my whole approach to life"; and 5) "I try hard to use my religion in all aspects of my life." In the general population, religious/spiritual beliefs have been correlated with an active attitude toward coping, higher perceived social support, and more hopeful attitudes in response to a stressor (Koenig,

1997), which supports my decision to include religiosity/spirituality as one of three proxies for secondary appraisals.

In sum, religiosity/spirituality is a good proxy for religious coping resources because it provides a schema for making sense of adversity, increases feelings of control over a stressor (e.g., a belief that "God has a plan"), and, for individuals who are part of faith communities, enhances the potential real or perceived availability of support resources.

2.4.3 Operationalizing Coping Processes

In the context of the Transactional Model, I examined longitudinal PA and SB trajectories as proxies for coping strategies in response to breast cancer. In this section, I discuss ways in which coping processes have been previously operationalized and provide a justification operationalizizing PA and SB patterns as coping strategies.

Lazarus and Folkman assessed coping processes with their Ways of Coping Questionnaire (1987), but it has been criticized for several psychometric weaknesses and the generic nature of the coping responses. This 60-item questionnaire assesses four categories of general coping: direct action, inhibition of action, information search, and psychological coping. Respondents are asked to identify a recently experienced stressful situation and identify if each type of general response was used to cope with the stressor. Although widely used, the Ways of Coping Questionnaire has been criticized for having low internal consistency, poor test-retest reliability, and different factor analysis patterns depending on the sample (Parker & Endler, 1992; Stone et al., 1992; Vitaliano, Russo, Carr, Maiuro and Becker, 1985). Folkman and Lazarus (1987) themselves recommended conducting factor analyses on every sample. Thus, many researchers have dropped or changed items on the Ways of Coping Questionnaire, which makes results incomparable. Given the problems encountered with the Ways of Coping Questionnaire, other

researchers have instead assessed specific coping strategies, such as problem- or emotionfocused strategies, in response to specific stressors.

In the context of the Transactional Model, I examined PA and SB as long-term coping strategies in response to the stressor of breast cancer. Conventionally, the Transactional Model has not been applied to health behaviors. However, Shaw (1999) published a helpful framework that explains health behaviors during chronic health conditions through a combination of transactional coping processes from Lazarus and Folkman (1987), illness representations from Leventhal's parallel process model (Leventhal & Nerenz, 1985), and behavioral intentions from the Theory of Planned Behavior (Ajzen, 1991). Figure 2.1 shows that Shaw's framework begins with appraisals and first leads to a decision as to whether symptoms represent a health threat. This threat appraisal then leads to an appraisal of the perceived severity of the health threat, behavioral intentions, and then finally to health behaviors as the coping strategy. In this framework, appraisals are dependent on an individual's personal perception of what an illness is, and thus are predicted by demographic and personality characteristics, values and goals, illness representations, previous experience, and locus of control. A secondary appraisal of perceived coping resources is also undertaken. In the final pathway, health behaviors predict outcomes such as adapting to chronic illness, well-being, or distress (Shaw, 1999).

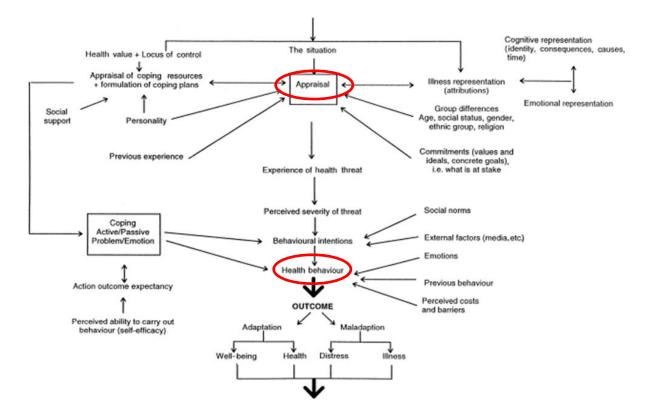


Figure 2.1. Shaw's (1999) framework of coping, illness representations, health behaviors, and outcomes.

I operationalized PA as hours per week of moderate-vigorous PA from pre-diagnosis through ten years post-diagnosis. I operationalized SB as hours per week sitting watching television (the most common way of measuring SB in the literature [Clark et al., 2009]) from pre-diagnosis through ten years post-diagnosis. Given dataset limitations, I was not able to directly assess if women were perceiving their PA or SB to be coping strategies in response to breast cancer. Instead, I will estimate PA and SB as latent variables and infer whether they are being used as a coping strategy by the associations with primary and secondary appraisals. In the next section, I describe the significance of my dissertation work.

2.5 Significance of Dissertation Aims

This is the first study among breast cancer survivors to examine psychological mechanisms underlying PA and SB patterns from pre-diagnosis through ten years post-diagnosis. A priori mediation models were informed by Lazarus and Folkman's (1987) Transactional Model of Stress and Coping. I used the Transactional Model of Stress and Coping to investigate predictors of PA and SB patterns after breast cancer because it includes constructs for emotional reactions and social and cultural coping resources, which typically are excluded from classic health behavior theories.

Conceptualizing PA and SB as long-term coping strategies is an innovative application of the Transactional Model of Stress and Coping and my dissertation results will determine if the Transactional Model is useful for explaining PA and SB patterns in cancer survivors. Additional strengths of my studies included: 1) a diverse sample from three U.S. sites; 2) data that spanned an eleven-year period and included pre-diagnosis data; and 3) treatment-related data that was collected through the Surveillance, Epidemiology, and End Results cancer registries; and 4) a statistically rigorous design that corrected for shortcomings in the HEAL dataset.

A better understanding of the cognitive and affective mechanisms underlying PA and SB patterns during breast cancer survivorship may inform better methods to intervene with women to increase PA and decrease SB.

CHAPTER 3. STUDY DESIGN AND METHODS

In this chapter, I review: 1) missing data procedures; 2) latent curve modeling (for Aim 1); 3) growth mixture modeling (for Aim 2); 4) a factor analysis to determine if mediators could be used as composite variables for primary and secondary appraisals; and 5) power calculations for structural equation modeling. Hypotheses will be described in chapters four and five.

3.1 Missing Data Procedures

Before analyses were performed, an examination of the extent and pattern of missing data was conducted for all measures. In order to assess the pattern of missingness, I created dummy variables (missing value =1, non-missing value=zero) and examined correlations with all variables in the model (including time-varying variables at different time points). A significant correlation indicated that missing data was related to variables in the dataset, and therefore, formed a pattern (Enders, 2010a; Fox-Waslyshyn & El-Masri, 2005).

Missing data for each variable was classified into one of three categories: missingcompletely-at-random, missing-at-random, or systematic (Fox-Waslyshyn & El-Masri, 2005). These categories determined how the missing data was treated. Missing data was categorized as *missing-completely-at-random (MCAR)* if the dummy variable was unrelated to all other variables in the dataset (e.g., individual physical function items missing intermittently but the non-response was unrelated to any other variable); *missing-at-random (MAR)* if the dummy variable was related to other variables in the dataset but not the outcome variable (e.g., physical function items missing for older respondents but unrelated to PA or SB); or *systematic* if the dummy variable was related to the outcome variable but not demographic characteristics (e.g., physical function items missing for individuals reporting low levels of PA but were not related to demographics) (Enders, 2011; Fox-Waslyshyn & El-Masri, 2005).

Missing data found to be MAR was estimated through a full-information maximum likelihood model-fitting program. MPLUS uses full-information maximum likelihood techniques as the default setting for structural equation modeling (SEM) (Muthen & Muthen 1998-2012). Full-information maximum likelihood uses all data points to construct first- and second-order estimates for the missing data (Allison, 2003; Fox-Waslyshyn & El-Masri, 2005). Violations of the multivariate normality assumption generally do not compromise SEM estimates in MPLUS because the default uses standard error estimates and test statistics that are robust to departures from normality (Allison, 2003). Full-information maximum likelihood is appropriate for imputation when up to 20% of data are MAR, regardless of the pattern of missingness (Roth, 1994).

Missing data found to be MCAR or systematic was estimated from multiple imputation techniques. Multiple imputation predicts the values of missing data in an equation based on iterated linear regression analyses where each variable with missing data is regressed on other variables in the dataset (Allison, 2003). Multiple imputation is appropriate when up to 20% of data are MCAR or up to 10% systematically missing (Roth, 1994). Variables exceeding 20% missing data were reviewed with my chairs and the HEAL group for possible deletion from the model.

3.2 Latent Curve Modeling

In Aim 1a, I used latent curve modeling to determine if PA and SB patterns over time can best be described as linear or curvilinear (i.e., quadratic) trajectories. Latent curve modeling is a modern longitudinal analysis technique in the SEM framework to estimate patterns of change.

Newer analytic methods were necessary because the HEAL dataset has a complex data structure that is not appropriate for traditional methods such an ANOVA. For instance, PA and SB variables in the HEAL dataset violate ANOVA's four main assumptions: 1) no missing data; 2) equally spaced time points; 3) normal distribution; and 4) homogeneity of variance and covariance over time. Additionally, growth modeling may be a better tool than traditional methods for examining individual-level change described in theoretical models of health behavior. For example, Lazarus and Folkman's Transactional Model of Stress and Coping provides an explanatory model of individual-level change in percevied threat, resources, and coping behavior. ANOVA would not be an appropriate test of this individual-level change because it test differences in groups means over time and cannot parse out individual-level change.

Therefore, latent curve modeling (LCM) was chosen as the analytic method. LCM relaxes the assumption that all individuals are drawn from a single population, resulting in separate intercepts, slopes, and variance parameters for each participant (Roth, 1994). LCM is flexible and robust to the following challenges encountered in the HEAL dataset: partially missing data, unequally spaced time points, non-normally distributed repeated measures, heterogeneity of variance and covariance over time, complex trajectories, and time-varying covariates (see Roth, 1994; Cohen & Cohen, 1983).

LCM has two parts: a measurement model and a structural model. The measurement model for LCM is a multivariate regression model that describes the relationship between one or more measured indicators and one or more latent variables (Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007). The structural model for LCM describes three types of relationships in one set of

multivariate regression equations (relationships among latent variables alone, outcome variables alone, and latent and outcome variables together) (Goodman, 1974).

In LCM, repeated measures for a given individual are expressed as an additive function of the underlying trajectory weighted by time. Most breast cancer survivors in HEAL had data available for five time points (pre-diagnosis, six months post-diagnosis, and two, five, and ten years post-diagnosis), and thus five time points appear in the equation. For each time point, the general equation for an observed trajectory was in the form:

Observed trajectory for individual = intercept + slope(weighted by time) + error Therefore, an individual breast cancer survivor's linear model equation with five time points is:

$$y_{ti} = \dot{\eta}_{1i} + \dot{\eta}_{2i}\lambda_1 + \dot{\eta}_{2i}\lambda_2 + \dot{\eta}_{2i}\lambda_3 + \dot{\eta}_{2i}\lambda_4 + \dot{\eta}_{2i}\lambda_5 + \varepsilon_{ti}$$
(1)

where t=time, i=individual, $\dot{\eta}_{1i}$ = intercept for individual i, λ =time point, $\dot{\eta}_{2i}$ = slope for individual i, and ϵ =error.

The equation is expanded to include a third eta ($\dot{\eta}$) at each time point for a quadratic (i.e., curvilinear) model:

$$y_{ti} = \dot{\eta}_{1i} + \dot{\eta}_{2i}\lambda_{1} + \dot{\eta}_{2i}\lambda_{2} + \dot{\eta}_{2i}\lambda_{3} + \dot{\eta}_{2i}\lambda_{4} + \dot{\eta}_{2i}\lambda_{5} + \dot{\eta}_{3i}\lambda^{2}_{1} + \dot{\eta}_{3i}\lambda^{2}_{2} + \dot{\eta}_{3i}\lambda^{2}_{3} + \dot{\eta}_{3i}\lambda^{2}_{4} + \dot{\eta}_{3i}\lambda^{2}_{5} + \epsilon_{ti}$$
⁽²⁾

where t=time, i=individual, $\dot{\eta}_{1i}$ = intercept for individual i, λ =time point, λ^2 =quadratic time point, $\dot{\eta}_{2i}$ = slope for individual i, $\dot{\eta}_{3i}$ =quadratic term for individual i, and ϵ =error.

Next, the mean linear trajectory with a covariate was calculated. The measurement equation is:

$$\mathbf{y}_{i} = \Lambda \dot{\boldsymbol{\eta}}_{i} + \boldsymbol{\varepsilon}_{i} \tag{3}$$

where i=individual, Λ = factor loading, η = factor score, and ε = item residual.

The corresponding <u>structural equation</u> for the <u>mean linear trajectory with covariates</u> for the intercept and slope, respectively, is:

$$\begin{split} \dot{\eta}_{1i} &= \alpha + y_{11} x_{1i} + \zeta_i \\ \dot{\eta}_{2i} &= \alpha + y_{21} x_{1i} + \zeta_i \end{split} \tag{4}$$

where $\dot{\eta}$ = factor score, i=individual, α = factor mean, y and x = covariates, and ζ = factor disturbance.

Thus, these 2 mean linear trajectory with covariates equations reduced to:

$$y_{ti} = \Lambda_1(\alpha_1 + \alpha_2 \lambda_t + y_{11} x_{1i} + y_{21} \lambda_t x_{1i}) + (\zeta_{1i} + \zeta_{2i} \lambda_t + \varepsilon_{ti})$$
(5)

where i=individual, Λ = factor loading, α = factor mean, λ =time point, y and x = covariate, ζ = factor disturbance, and ε = item residual.

The <u>mean linear trajectory</u> is represented by the following structural equation model:

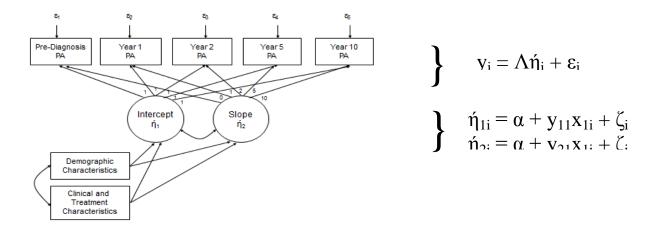


Figure 3.1. Mean linear trajectory structural equation model for physical activity (PA).

For a mean <u>quadratic</u> trajectory, the measurement equation is identical to the linear equation with 1 exception: the covariance matrix was expanded to include a third eta representing the quadratic function. Therefore, the <u>quadratic</u> trajectory equation is:

$$y_{ti} = \Lambda_1(\alpha_1 + \alpha_2\lambda_t + \alpha_3\lambda_t + y_{11}x_{1i} + y_{21}\lambda_tx_{1i} + y_{31}\lambda_tx_{1i}) + (\zeta_{1i} + \zeta_{2i}\lambda_t + \zeta_{3i}\lambda_t + \varepsilon_{ti})$$
(6)

where i=individual, Λ = factor loading, α = factor mean, λ =time point, y and x = covariate, ζ = factor disturbance, and ε = item residual. The structural equation model for the mean <u>quadratic</u> trajectory is:

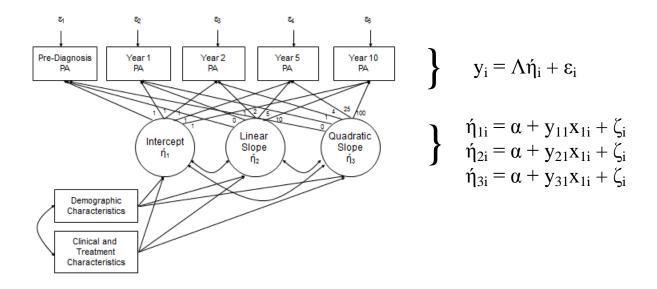


Figure 3.2. Mean quadratic trajectory model for physical activity (PA).

Finally, PA and SB were modeled simultaneously using a growth modeling procedure called, "pararell process."

The equation for a <u>parallel process linear</u> model with a covariate is:

$$\underline{y_i} = \Lambda_1(\alpha_1 + \alpha_2\lambda_t + \alpha_3\lambda_t + \alpha_4\lambda_t + y_{11}x_{1i} + y_{21}\lambda_tx_{1i}) z_i + (\zeta_{1i} + \zeta_{2i}\lambda_t + \zeta_{3i}\lambda_t + \zeta_{4i}\lambda_t + \varepsilon_{ti})$$
(7)

where i=individual, Λ = factor loading, α = factor mean, λ =time point, y and x = covariates, ζ = factor disturbance, and ε = item residual.

The equation for <u>a parallel process quadratic</u> model with a covariate is:

$$\underline{y_i} = \Lambda_1 (\alpha_1 + \alpha_2 \lambda_t + \alpha_3 \lambda_t + \alpha_4 \lambda_t + \alpha_5 \lambda_t + \alpha_6 \lambda_t + y_{11} x_{1i} + y_{21} \lambda_t x_{1i} + y_{31} \lambda_t x_{1i}$$

$$+ y_{12} x_{2i} + y_{22} \lambda_t x_{2i} + y_{32} \lambda_t x_{2i})$$

$$+ (\zeta_{1i} + \zeta_{2i} \lambda_t + \zeta_{3i} \lambda_t + \zeta_{4i} \lambda_t + \zeta_{5i} \lambda_t + \zeta_{6i} \lambda_t + \varepsilon_{ti})$$

$$(8)$$

where i=individual, Λ = factor loading, α = factor mean, λ =time point, y and x = covariate, ζ = factor disturbance, and ε = item residual.

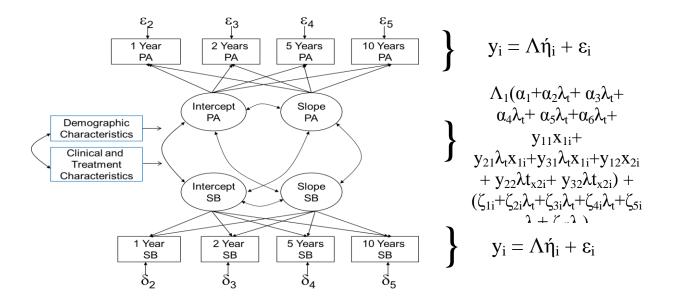


Figure 3.3. Parallel process model diagram for physical activity (PA) and sedentary behavior (SB).

Mean variances for each parameter (intercepts, slopes, and quadratic coefficients) were examined to determine if they were significantly different from zero. Variance was calculated by subtracting each woman's PA and SB estimates from the group mean and squaring the difference (Bollen & Curran, 2006). These differences were then averaged. High intercept variance indicates significant individual variation in PA and SB levels reported for pre-diagnosis. High slope variance indicates large differences across women in propensity to change over time. Taken together, significant variance in intercept and slope coefficients implies the likely existence of subgroups of women following different trajectories. However, the methodology of latent curve modeling cannot determine the number of subgroups. Thus, a second methodology was needed.

3.3 Growth Mixture Modeling

In the previous section, I discussed using growth modeling to determine mean PA and SB trajectories. However, mean trajectories neglect individual variation in starting points and change over time. Therefore, I also used growth mixture modeling to determine if there were subgroups of women following different PA and SB trajectories. Demographic, clinical, and treatment-related characteristics of the subgroups were determined with multinomial regression.

Growth Mixture Modeling (GMM) is a statistical method for classifying a set of observations into two or more mutually exclusive groups where subgroup membership is not known but inferred from the data (Collins & Lanza, 2010; Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov & Muthen, 2007). GMM is a person-centered approach to data analysis where latent variables and their relationship to other variables are modeled (Goodman, 1974). In Aim 1b, I used GMM to classify each HEAL breast cancer survivor into her most likely latent class of PA, SB, and simultaneously modeled PA-SB trajectory. These latent classes

were then used as the outcome variable for growth mixture modeling. Thus, my outcome variables were categorical and appropriate for GMM.

The measurement equation for the growth mixture model is:

$$(\mathbf{y}_i \mid \mathbf{C}_i = \mathbf{c}) = \Lambda^{(c)} \dot{\boldsymbol{\eta}}_i + \boldsymbol{\varepsilon}_i$$
(9)

where i=individual, c = latent class (e.g., $C_i = 1$ for subgroup 1 and $C_i = 2$ for subgroup 2, etc.), $\Lambda =$ factor loading, $\eta =$ factor score, and $\varepsilon =$ item residual.

The corresponding structural equation for the growth mixture model is:

$$(\dot{\eta}_i \mid C_i = c) = \alpha^{(c)} + \zeta_i \tag{10}$$

where i=individual, c = latent class, $\dot{\eta}$ = factor score, α = factor mean, and ζ = factor disturbance.

Thus, these 2 growth mixture model equations reduced to:

$$(\mathbf{y}_i \mid \mathbf{C}_i = \mathbf{c}) = \Lambda^{\mathbf{I}} \boldsymbol{\alpha}^{\mathbf{I}} + \Lambda^{\mathbf{I}} \boldsymbol{\zeta}_i + \boldsymbol{\varepsilon}_i$$
(11)

$$C_i \sim Multinomial (\Pi^{(1)}, \Pi^{(2)}, \Pi^{(K-1)})$$
 where PROB $(C_i = c) = \Pi^{1/2}$

where i=individual, c = latent class, Λ = factor loading, α = factor mean, ζ = factor disturbance, ϵ = item residual, K = number of mutually exclusive unobserved groups, Π^{I} = probability that a randomly selected person would belong to group c (probabilities are mutually exclusive and sum to 1.0).

Growth mixture models are not graphically depicted with model diagrams. Instead, they are presented as subgroups on a graph.

These equations were implemented using MPLUS software (Muthen & Muthen, 1998-

2014). The PA and SB variables were not normally distributed (skewed), and thus maximum likelihood with robust standard errors was used as a correction (Duncan, Duncan, & Strycker, 2006).

Optimal parameter estimates were then determined with model fit statistics. Optimal parameter estimates are typically viewed as those that minimize the difference between the

observed and model-implied estimates. Model fit for GMM was examined in two ways: absolute fit and relative fit. Absolute model fit examines whether the model is an accurate reflection of variability in the data. A log likelihood statistic was reported. A model with a higher log likelihood were considered to fit the data (Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007).

Relative model fit compares two or more models with different numbers of latent classes (e.g., would three latent classes of PA fit just as well as four while maintaining the ability to explain variability?). To identify the number of classes, models with incremental increases in the number of classes were compared. In general, as the number of latent classes increases, model fit gets better until there are no statistical differences with the addition of another class (Collins & Lanza, 2010; Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007).

A parsimony index called the sample-size-adjusted Bayesian Information Criterion (ssBIC) fit criteria was compared across models as the number of latent subgroups increased (Collins & Lanza, 2010; Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007). Models with <u>lower</u> ssBIC indicate better parsimony. In general, given two models with equivalent fit to the data, the model with the fewest parameters was selected (assuming theoretical relevance) (Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007).

3.4 Structural Equation Modeling

SEM is a set of statistical procedures used to simultaneously estimate parameters and the adequacy of model fit to the data, which keeps the Type I error rate from inflating (Bollen, 1989; Byrne, 2011). The pattern of relationships is specificied *a priori* but typically, several versions of

a model are evaluated in order to identify the most plausible model and to estimate individual parameters (Curran & Bauer, 2012; Curran et al., 2013).

SEM has a number of additional advantages over multiple regression techniques. For example, SEM estimates the inter-relationships between variables rather than assuming they are independent; and latent error terms may be included in order to estimate the effects of omitted variables and measurement error (Bollen, 1989; Curran & Bauer, 2012; Curran et al.,

2013). Conventional multivariate techniques cannot assess, or correct for, measurement error,

but SEM provides estimates of error variance (Byrne, 2011).

The equations for the measurement and structural models with a <u>categorical outcome</u> are:

Linear predictor_i = $v + \lambda \dot{\eta}_i$

$$H_{i} = \alpha + B\dot{\eta}_{i} + \Gamma x_{i} + \zeta_{i} \quad (\text{where var}(\zeta_{i}) = \Psi)$$
(12)

v = intercept term $\lambda = \text{factor}$ $\dot{\eta} = \text{latent variable/common factor}$ $\alpha = \text{vector of regression intercepts}$ $B = p \ x \ p \ (\# \text{ endogenous } x \ \# \text{ endogenous}) \text{ matrix of regression slopes}$ $\Gamma = p \ x \ q \ (\# \text{ endogenous } x \ \# \text{ exogenous}) \text{ matrix of regression slopes}$ x = vector of observed exogenous variables $\zeta = \text{vector of distrurbances/residuals}$ $\Psi = \text{covariance matrix of disturbances}$ i = varies by individuals

Note that these are the equations used no matter how many variables are in the model.

The corresponding SEM diagram is:

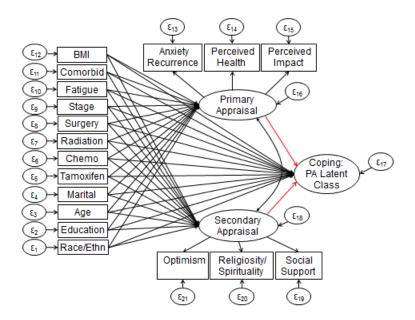


Figure 3.4. Structural equation model.

SEM can handle categorical outcome variables (PA and SB patterns) with minor changes to the model, hypothesis, and MPLUS code (Byrne, 2011; Curran & Bauer, 2012). The fundamental hypothesis for <u>categorical outcomes</u> is H₀: $\Sigma^* - \Sigma^*(\Theta) = 0$, $\mu^* - \mu^*(\Theta) = 0$ (Curran & Bauer, 2012). A plausible model is one where the null hypothesis is <u>not rejected</u>; that is, the specified model is correct in the population and lack of fit arises from sampling error.

An estimator option in MPLUS is maximum likelihood estimation, which is applicable for both continuous and categorical outcomes (Muthen & Muthen, 1998-2015; Byrne, 2011; Curran & Bauer, 2012). Maximum likelihood allows estimation of the fit of direct and indirect path coefficients, accommodates a large number of items and variables, permits mixed variable types, and provides asymptotically unbiased and maximally efficient estimates (Curran & Bauer, 2012). Full-information is particularly useful in that it retains cases with partially missing data and introduces adjustments that correct for non-normal distributions (Curran & Bauer, 2012). Maximum likelihood assumes: 1) sufficiently large sample size; 2) independence of residuals (no two residuals are any more/less similar than others); and 3) multivariate normality of residuals for continuous dependent variables (categorical require Poisson distribution). No assumptions are made about independent variables (e.g., predictors and mediators can be skewed, binary, ordinal, nominal, etc.).

SEM model fit was evaluated in three ways: 1) Theoretical fit; 2) Parsimony; and 3) Empirical criteria. Theoretical fit indicated whether revisions to the model were consistent with the Transactional Model of Stress and Coping (Lazarus & Folkman, 1987). Parsimony indicated that when two models fit equally well, the preferred model was the one with fewest parameters (Curran & Bauer, 2012).

Empirical criteria for model fit was evaluated by several criteria:

1) Chi-square and its p-value were examined to determine whether to reject the null hypothesis that the model fits the data well (i.e., in a well fitting model, the null hypothesis was <u>not rejected</u>).

2) Chi-square was examined to determine if it is more than two times the model degrees of freedom (indicating misfit).

3) CFI (Comparative Fit Index) (Hugh & Bentler, 1999) and TLI (Tucker-Lewis Index) (Tucker and Lewis, 1973) were examined against the criterion of ≥ 0.90 (maximum is 1.0).

4) RMSEA (root mean square error of approximation) 90% confidence interval was examined to see if it was below the criteria of 0.06, included 0 in the confidence interval, and had no values greater than 0.10 (Steiger, 1990).

5) Significance of individual parameters was examined (e.g., regression coefficients between constructs and the amount of variance explained).

6) Modification indices larger than the minimum value default of ten in MPLUS were evaluated for additional pathways to be added to improve model fit (e.g., correlating error terms or adding covariances).

3.5 Factor Analysis of Mediators (Primary and Secondary Appraisals)

Confirmatory factor analyses, within the SEM framework, were conducted to determine if mediators could be used as composite variables for primary and secondary appraisals. The potential composite index for primary appraisal included variables representing anxiety about recurrence (higher score indicates greater anxiety about recurrence), perceived health (higher score indicates better perceived health), and impact of breast cancer (higher impact score indicates more negative impact). The confirmatory factor analysis showed poor fit for treating primary appraisal as a composite index. The chi-square was highly significant ($\chi^2 = 2719.5$, df = 252, p < .00001), indicating that the null hypothesis of one factor is rejected), the RMSEA was higher than the <.06 criterion (90% confidence interval: 0.106 - 0.113), and CFI and TLI were well below the criterion of ≥ 0.90 (0.44 and 0.39, respectively). The Cronbach's alpha for internal reliability of the primary appraisal composite index did not reach the criterion: 0.80 (criterion: ≥ 0.90).

Correlations were small to moderate among anxiety about recurrence, perceived health, and impact of breast cancer. Anxiety about recurrence and perceived health were negatively correlated at r = -0.27 (p < .0001) (higher anxiety about recurrence correlated with worse perceived health). Anxiety about recurrence and impact of breast cancer were positively correlated at r = 0.37 (p < .0001) (higher anxiety about recurrence correlated with more negative impact). Perceived health and impact of breast cancer were negatively correlated at r = -0.16 (p < .0001) (better perceived health correlated with more positive impact). Given the poor fit for a 1-factor model and low Cronbach's alpha, primary appraisal will be measured as three separate

variables (anxiety about recurrence, perceived health, and impact of breast cancer) in structural equation models. Using separate variables for the mediators will also simplify interpretation. Covariances between the three variables will be tested in structural equation models given the small to moderate correlations.

The potential composite index for secondary appraisal included variables for optimism, social support (confidant network size), and religiosity/spirituality. The confirmatory factor analysis also showed poor fit for treating secondary appraisal as a composite index. The chi-square was highly significant ($\chi^2 = 6402.7$, df = 495, *p*<.00001), indicating that the null hypothesis of one factor was rejected), the RMSEA was higher than the <.06 criterion (90% confidence interval: 0.128 - 0.134), and CFI and TLI were well below the criterion of \geq 0.90 (0.30 and 0.25, respectively). The Cronbach's alpha for internal reliability of the secondary appraisal composite index did not reach the criterion: 0.78 (criterion: \geq 0.90).

Correlations were small among optimism, religiosity, and social support. Optimism and religiosity were positively correlated at r=0.18 (p<.0001) (higher optimism correlated with higher religiosity). Optimism and social support were positively correlated at r=0.15 (p<.0001) (higher optimism correlated with higher social support). Religiosity and social support were also positively correlated at r=0.12 (p<.0001) (higher religiosity correlated with higher social support). Given the poor fit for a one-factor model and low Cronbach's alpha, secondary appraisal will be measured as three separate variables (optimism, religiosity, and social support) in structural equation models. Using separate variables for the mediators will also simplify interpretation. Covariances between these three variables will be tested in structural equation models given the small correlations. In the next section, I provide power calculations for my

structural equation models when primary and secondary appraisals are treated as six separate mediators.

3.6 Power Calculations

Power is conceptualized as the probability of correctly rejecting the null hypothesis if the null hypothesis is false. No formal approach for calculating power for GM or GMM is available. Some researchers have used the guideline of 5-10 participants per latent class expected with GMM. With over 900 breast cancer survivors in HEAL, it is difficult to imagine a scenario where GMM power would be a problem.

For SEM power calculations, primary and secondary appraisals were treated as six separate mediator variables based on factor analytic results presented in the last section. Power is calculated in three ways for SEM. First, power is based on the number of parameters to be estimated. Generally, five to ten participants per parameter are recommended (MacCullum, Browne, & Sugawara, 1996; Curran & Bauer, 2012). Parameters are a function of the number of pathways in a model, means and variances for all variables, and covariances (the value of X_1 while holding X_2 constant).

For Aim 2a, 1 latent variable (PA) and 18 observed variables (12 predictors and six mediators) were modeled. This resulted in 87 parameters to be estimated (19 means, 19 variances, seven covariances, and 42 pathways) and a necessary sample size of 435-870 breast cancer survivors. At the ten-year assessment, 552 women ages 35-64 were available for analyses, which was sufficient for the PA model. For Aim 2b, the SB model had identical parameters to be estimated (87) as PA, and thus sufficient sample size at the ten-year assessment.

For Aim 2c, the model had 2 latent variables (PA and SB) and 18 observed variables, which resulted in 105 estimated parameters (20 means, 20 variances, seven covariances, and 58 pathways) and a necessary sample size of 525-1050 breast cancer survivors. At the ten-year

assessment, 552 women ages 35-64 are available for analyses, which was sufficient (but at the low end) for this model.

Second, model identification determines if there is enough observed information to provide unique estimates of every parameter in the model. Models can be over-identified, which means it has more pieces of observed information than parameters to be estimated; just-identified meaning it has the same number (i.e., regression model); and under-identified meaning it has fewer pieces of information than parameters to be estimated. The "t-rule" for model estimation requires that the number of observations (means, variances, co-variances), k, be greater than the number of free parameters, t (Curran & Bauer, 2012). Second, the "t-rule" for model estimation requires that the number of observations (means, variances, co-variances), k, be greater than the number of free parameters, t (Curran & Bauer, 2012). Second, the "t-rule" for model estimation

For Aim 2a, p represented the number of endogenous variables in the model (seven variables with predictors) and q represented the number of exogenous variables (12 variables without predictors):

$$k = \frac{[(p+q)(p+q+1)]}{2} + (p+q)$$

$$k = \frac{[(7+12)(7+12+1)]}{2} + (7+12) = 209$$
(13)

Thus, the criterion was met for the "t-rule" because 209 observed means, variances, and covariances was greater than 87 estimated parameters. This model was over-identified and appropriate for SEM.

For Aim 2b, the SB model was identical to the Aim 2a for PA in that it has 1 latent variable (SB) and 18 observed variables (12 predictors and six mediators). Thus, power for Aim 2b was identical to Aim 2a (sufficient).

In Aim 2c, the model had 20 variables (2 latent: PA and SB, 18 observed) so the number of observations was 230, which exceeded the 105 estimated parameters (and the "t-rule" was met).

$$k = \frac{\left[(8+12)(8+12+1)\right]}{2} + (8+12) = 230$$

Third, power is determined for fit indices such as the Root Mean Square Error of Approximation (RMSEA). Tests of model exact fit (χ^2) may be rejected with a large sample size (even though a large sample size is required for parameter estimation) so alternative fit indices such as RMSEA are essential tools for model fitting (Curran & Bauer, 2012). MacCallum, Browne, and Sugawara (1996) recommended calculating power for RMSEA using the degrees of freedom, significance level (α), sample size, a null value of RMSEA, and an alternative value of RMSEA. The null RMSEA value of 0.00 is usually used as it indicates a perfect fit and a common alternative RMSEA value is 0.05 (MacCullum, Browne, & Sugaware, 1996).

For Aim 2a, the degrees of freedom were 209 observations subtracted by 87 estimated parameters, which was 122. Using a significance level of 0.05, a null RMSEA value of 0.00, alternative RMSEA value of 0.05, and a sample size of at least 400, the model was powered at 100% (with a sample size of at least 300, power was greater than 0.993) (MacCallum, Brown, & Sugawara, 1996). Aim 2b also has degrees of freedom equal to 122, and thus the SB model is also powered at 100% (MacCullum, Brown, & Sugawara, 1996).

In Aim 2c, the degrees of freedom were k-t = 230 - 105 = 125. Using a significance level of 0.05, a null RMSEA value of 0.00, alternative RMSEA value of 0.05, and a sample size of at least 400, the model was powered at 100% (with a sample size of at least 300, power was greater than 0.993) (MacCallum, Brown, & Sugawara, 1996).

In sum, power for SEM analyses was adequate for all time points through ten years postdiagnosis when treating mediators as six separate variables. In the next section, I provide a chapter summary.

3.6 Chapter Summary

Chapter Three provided an overview of the statistical methodology that I used to conduct my specific aims. Before analyses were performed, an examination of the extent and pattern of missing data was conducted for all measures. Three statistical techniques were used to test my aims. In Aim 1, I used latent curve modeling and growth mixture modeling. In Aim 2, I used structural equation modeling.

Confirmatory factor analyses showed that treating primary and secondary appraisals as composite indices was a poor fit. Therefore, three variables each were used as proxies for primary appraisal (anxiety about recurrence, perceived health, impact of breast cancer) and secondary appraisal (optimism, religiosity, and social support) in structural equation models. Power was adequate for all time points through ten years post-diagnosis when mediators were treated as six separate variables. Covariances among mediators will be tested in SEM given their small correlations.

CHAPTER 4. ONE SIZE DOES NOT FIT ALL: SUBGROUPS OF BREAST CANCER SURVIVORS REPORT DIFFERENT PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR PATTERNS FROM PRE-DIAGNOSIS THROUGH TEN YEARS POST-DIAGNOSIS

In this chapter, I summarize my results from Aim 1. I review results related to: 1) determining whether the average PA and SB trajectories for breast cancer survivors follow linear or non-linear patterns from pre-diagnosis to ten years post-diagnosis; 2) determining whether there is significant individual variation in PA and SB intercepts and slopes (suggesting subgroups of women following different trajectories); and 3) determining the number of subgroups following different trajectories and the percentage of women in each subgroup. I conclude the chapter with a discussion section describing the significance of this aim and how my results compare to the broader literature. In chapter 5, I summarize the results of Aim 2 where I determined demographic, clinical, and psychosocial correlates of subgroup membership.

4.1 Introduction

Despite increasingly strong evidence that Physical Activity (PA) and Sedentary Behavior (SB) contribute to breast cancer outcomes, little is known about changes in PA and SB that may occur from pre-diagnosis through long-term survivorship. Typically, self-reported moderatevigorous PA is collected soon after a cancer diagnosis and used to predict outcomes such as survival and quality of life several years later (Courneya, Mackey, & McKenzie, 2002; Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005; Ibrahim & Al-Homaidh, 2011; Kellen, Vansant, Christiaens, Neven, & Van Limbergen, 2009; Schmitz, 2011; Speck et al., 2010). However, this approach assumes that PA remains constant over time, and it fails to consider SB as an independent predictor of outcomes. SB, defined as prolonged time spent sitting or reclining during waking hours (e.g., sitting at a desk, watching television) (Wilmot et al., 2012), is not just the converse of PA; evidence suggests it uniquely contributes to negative health outcomes for cancer survivors such as increased risk for recurrence, secondary cancers, and early mortality (Holmes, Chen, Feskanich, Kroenke, & Colditz, 2005; Rock et al., 2012). In general population samples, three systematic reviews have shown that SB is correlated with all-cause mortality, cardiovascular disease mortality, and type II diabetes incidence, after controlling for PA (Biswas et al., 2015; Proper, Singh, vanMechelen, & Chinapaw, 2011; Wilmot et al., 2012). These reviews are consistent with other research highlighting that PA and SB are weakly correlated and that they can vary independently to some degree in both cancer and non-cancer populations (George et al., 2013a; Tremblay, Colley, Saunders, Healy, & Owen, 2010; Santos et al., 2012).

There is compelling evidence from meta-analyses of randomized controlled trials that increasing moderate-vigorous PA improves physical and mental functioning, fatigue, and quality of life in breast cancer patients (Fong et al., 2012; McNeely et al., 2006). Systematic reviews demonstrate that moderate-vigorous PA is also associated with overall survival, with postdiagnosis PA being more beneficial than pre-diagnosis PA (Fontein et al., 2013; Holick et al., 2008; Holmes, Chen, Feskanich, Kroenke, & Colditz, 2005; Ibrahim, & Al-Homaidh, 2011; Pierce et al., 2007). Despite these health benefits, breast cancer survivors report an average of only 35-105 minutes per week of moderate intensity PA at diagnosis and during early survivorship (Lynch et al., 2010; Sabiston et al., 2014), far less than the recommended 150 minutes (Rock et al., 2012). In a review of cancer studies conducted during 1980-2003, the majority of studies examined moderate-vigorous PA during the diagnosis and treatment phases (Finney Rutton, Arora, Bakos, Aziz, & Rowland, 2005), and thus very little is known about PA patterns later in cancer survivorship (from approximately two to ten years post-diagnosis).

To my knowledge, no study has modeled SB trajectories in breast cancer survivors and only two have estimated PA trajectories. In the first of these two PA studies, Emery and colleagues (Emery, Yang, Frierson, Peterson, & Suh, 2009) modeled an average PA trajectory over five years for 277 American women treated for breast cancer. They found a non-linear pattern: moderate-vigorous PA initially increased after surgery (approximately six months postdiagnosis) through 18 months, reaching recommended levels, and then gradually declined through the five-year assessment. At five years, mean PA was lower than it was at baseline. No pre-diagnosis PA data was available, and thus it is unknown how breast cancer survivors' PA trajectories changed from pre- to post-diagnosis.

A second study found subgroups of breast cancer survivors following different PA trajectories during early survivorship for 199 Canadian women (Brunet, Amireault, Chaiton, & Sabiston, 2014). Brunet et al. (2014) identified five different moderate-vigorous PA subgroups over 15 months after treatment. The largest subgroup (49%) consistently met PA guidelines over 15 months post-treatment (note that Canada's national PA guideline is identical to the U.S.: at least 150 minutes/week of moderate PA [http://www.csep.ca/english/view.asp?x=949]). The next largest subgroup (25%) was consistently active at levels that did not meet guidelines. The third subgroup (11%) reported being inactive at 3-9 months post-treatment but increased PA at 12-15 months post-treatment. A fourth subgroup (10%) did not meet guidelines at three months post-treatment, met guidelines at six months post-treatment, dropped to not meeting guidelines again at nine months post-diagnosis, and reported no PA at 12-15 months post-treatment. The fifth subgroup (6%) reported no PA across all time points.

Three methodological concerns arise for the Brunet et al. (2014) study. First, the small sample size limits confidence in determining a reliable number of subgroups. However, this study suggests that there may be considerable value in examining whether subgroups of breast cancer survivors are following different PA trajectories. Second, the authors did not adjust for sample size in the Bayesian Information Criterion (BIC) for model fit, which has been shown to enumerate too many classes (Enders, 2010b). Therefore, five classes may be overestimating the number of PA subgroups. Third, the sample was largely Caucasian (85%) and highly educated (50% with a college degree) women from Canada. These demographic characteristics may explain the surprising finding that half of the sample (largest subgroup) met PA guidelines at all assessments. A more diverse sample of breast cancer survivors is unlikely to show the majority consistently meeting guidelines, because PA levels are associated with race/ethnicity and education, even after controlling for clinical and treatment characteristics (e.g., Hair et al., 2014; Hawkins et al., 2010; Patterson et al., 2003; Irwin et al., 2003; Pinto, Trunzo, Reiss, & Shiu, 2002).

Neither the Brunet et al. (2014) nor the Emery et al., (2009) studies attempted to capture PA levels prior to cancer diagnosis; thus limiting our understanding of whether PA trajectories after treatment are associated with pre-cancer PA levels. Also, Brunet et al. (2014) and Emery et al. (2009) did not examine SB trajectories. Studies are needed that estimate PA and SB together in the same model to obtain a more complete picture of the activity and sedentary patterns of breast cancer survivors and lay the groundwork for future intervention work. For instance, breast cancer survivors following different combinations of PA-SB trajectories may need different intervention strategies to achieve the goal of increasing PA to guideline levels and decreasing SB.

The importance of examining PA and SB together is bolstered by a recent meta-analysis in the general population, which showed that a pattern of long-term SB paired with low levels of PA doubles the risk for diabetes and cardiac conditions (Edwardson et al., 2012). Because evidence suggests that patterns of high SB paired with low PA may place breast cancer survivors at risk for poor outcomes, as they do in other populations, it is important to determine the proportion of breast cancer survivors who report this pattern from pre-diagnosis through longterm survivorship.

The purpose of this study was to estimate breast cancer survivors' average PA and SB patterns from pre-diagnosis through ten years post-diagnosis, and to determine if subgroups of breast cancer survivors report different PA and SB trajectories over time. PA was defined as minutes per week of moderate-vigorous PA. SB was measured with a proxy of minutes per week sitting watching TV.

4.2 Hypotheses

4.2.1 Aim 1a

<u>Aim 1a</u>: Determine the shape of the average PA and SB trajectories from pre-diagnosis through ten years following breast cancer diagnosis (estimated in separate models first and then in the same model)

<u>Hypothesis 1.a.1</u>: The mean PA trajectory for breast cancer survivors will decrease from prediagnosis to six months post-diagnosis, rebound at two years post-diagnosis to pre-diagnosis levels, and then steadily decline through five and ten years post-diagnosis.

<u>Hypothesis 1.a.2</u>: The mean SB trajectory for breast cancer survivors will increase from prediagnosis to six months post-diagnosis, decline at two years post-diagnosis back to pre-diagnosis levels, and then steadily increase through five and ten years post-diagnosis.

<u>Hypothesis 1.a.3</u>: When estimated in the same model, PA and SB trajectories will continue to demonstrate the same non-linear shapes as when they were estimated in separate models.

For PA, I hypothesized that the mean trajectory from pre-diagnosis to ten years postdiagnosis would be non-linear based on the duration of recovery time after active treatment and a literature review of PA reported in cohort studies. I expected PA to first decline from prediagnosis to six months post-diagnosis because breast cancer survivors are undergoing active treatment during this period, such as breast-conserving surgery and radiation, and thus are likely decreasing their PA because of treatment recovery and symptom burden. For instance, ionizing radiation may cause damage to normal and malignant cells and side effects such as fatigue generally occur from damage to normal tissue (Rubin, 2001). During active treatment, and through approximately 18 months post-diagnosis, over 80% of breast cancer survivors report fatigue, 70% report breast sensitivity, and over 50% report sleep disturbance (Janz et al., 2007; Montazeri, 2008; Mortimer et al., 2010; Nihal Guleser et al., 2012), all of which are known to affect PA after diagnosis (Alfano et al., 2007; Charlier et al., 2013; Fong et al., 2012; McNeely et al., 2006; Meeske et al., 2007).

Several cohort studies have also shown a decrease in PA from pre- to post-diagnosis for breast cancer survivors (Andrykowski et al., 2007; Devoogdt et al., 2010; Hair et al., 2014; Irwin et al., 2003; Littman et al., 2000). For example, Hair et al. (2014) found that 59% of breast cancer survivors in a cohort study reported decreasing their PA from pre- to post-diagnosis, but the magnitude of change varied by race. After adjustment for potential confounders, African American women were less likely to meet PA guidelines after diagnosis than Caucasian women.

I also hypothesized that SB would increase from pre-diagnosis to six months postdiagnosis because breast cancer survivors are spending more time in hospital and outpatient

medical settings to receive treatment, and thus are sitting for longer periods, and perhaps watching more TV to pass the time, than they did prior to cancer treatment. Additionally, the majority of breast cancer survivors who are working take a leave of absence during active treatment (Balak, Roelen, Koopmans, ten Berge, & Groothoff, 2008), and therefore have more time to watch TV. For breast cancer survivors with early-stage disease, the mean duration of absence from work is approximately 4-6 months, with absences up to 11 months for women receiving chemotherapy (Balak et al., 2008).

Irwin and colleagues (2003) used data from two HEAL sites (New Mexico and Washington) and found that PA decreased, and SB (TV watching) increased, from pre- to postdiagnosis for Caucasian and Hispanic survivors, and that the magnitude of these changes varied by treatment type. HEAL breast cancer survivors who underwent surgery and received radiation therapy reported a one-hour increase in TV watching and a 45-minute decrease in PA per week from pre- to post-diagnosis. Women who received chemotherapy, in addition to any other therapy type, fared the worst for PA and SB. They reported a six-hour increase in TV watching and a 1.5-hour decrease in PA per week from pre- to post-diagnosis.

I hypothesized that mean PA would rebound to the pre-diagnosis level at two years postdiagnosis for two reasons: 1) symptoms, such as fatigue and breast sensitivity, generally resolve after recovery from active treatment at approximately 18 months post-diagnosis; and 2) cohort studies have shown that PA increased after active treatment was completed (at approximately 18-24 months post-diagnosis). I also hypothesized that SB would decline to pre-diagnosis levels from six months to two years post-diagnosis because the majority of breast cancer survivors are able to resume their normal activities after recovery (e.g., Montazeri, 2008, Mols et al., 2007),

and thus have less time to watch TV. For instance, the majority of breast cancer survivors return to work after recovering from surgery and radiation (Balak et al., 2008).

In general, younger and middle-aged breast cancer survivors need approximately 12-18 months to recover from symptoms such as fatigue and return to their usual activities (Hsu, Ennis, Hood, Graham, & Goodwin, 2013; Mols, Vingerhoets, Coebergh, van de Poll-Franse, 2005; Montazeri, 2008). This timing of symptom recovery is consistent with longitudinal studies in breast cancer survivors showing PA increases after completion of active treatment (Emery et al., 2009; Harrison et al., 2009; Littman et al., 2000). For instance, Emery and colleagues (2009) observed a PA trajectory that initially increased from the time of surgery through 18 months, and then gradually declined through the five-year assessment where mean PA was lower than baseline levels.

Finally, I hypothesized that PA would steadily decline, and SB would steadily increase, from five to ten years post-diagnosis because PA decreases with age for both the general population (Fan, Kowaleski-Jones, & Wen, 2013; Kim et al., 2013; Sun, Norman, & While, 2013) and cancer survivors (Bellury et al., 2012; Hong et al., 2007; Kim et al., 2013; Lynch et al., 2010); TV watching also increases with age for the general population (Kim et al., 2003; Mares & Woodard, 2006) and cancer survivors (Kim et al., 2003; Lynch et al., 2010).

4.2.2 Aim 1b

<u>Aim 1b</u>: Determine whether there is significant individual variability in the intercept and slope parameters for PA and SB trajectories from pre-diagnosis through ten years following breast cancer diagnosis (estimated in separate models first and then in the same model) <u>Hypothesis 1.b.1</u>: Significant individual variability in the mean PA trajectory intercept (starting point) and slope (change over time) parameters will be observed for breast cancer survivors.

<u>Hypothesis 1.b.2</u>: Significant individual variability in the mean SB trajectory intercept (starting point) and slope (change over time) parameters will be observed for breast cancer survivors. <u>Hypothesis 1.b.3</u>: Significant individual variability in the mean PA and SB intercepts (starting point) and slopes (change over time) will continue to be observed for breast cancer survivors when PA and SB are estimated in the same model.

I hypothesized that significant variability in the PA intercept and slope would be present because Brunet et al. (2014) reported significant variability in starting points and rate of change for a Canadian sample of breast cancer survivors, with some scores three or more standard deviations from the mean.

Significant individual variability in the mean SB intercept and slope was hypothesized because Irwin and colleagues (2003) observed variability in SB changes from pre- to postdiagnosis. On average, HEAL breast cancer survivors decreased their PA by 11% from pre- to post-diagnosis. However, greater decreases in PA were observed for women who received surgery, radiation, and chemotherapy (50% decrease) compared with women who underwent surgery and radiation (24% decrease). The Irwin et al. (2003) results varied by treatment type, and thus imply that significant individual variability around the mean intercept and slope is likely for my study.

4.2.3 Aim 1c

<u>Aim 1c</u>: Determine whether there are subgroups of breast cancer survivors who follow different PA or SB trajectories from pre-diagnosis through ten years post-diagnosis (estimated in separate models first and then in the same model)

<u>Hypothesis 1.c.1</u>: Four PA subgroups will be observed: 1) the largest subgroup will report little or no PA at pre-diagnosis and over ten years post-diagnosis [Consistently low PA]; 2) the second subgroup will be sufficiently active prior to cancer but decrease their PA over time to levels

below recommendations [Sufficiently active but decreasing]; 3) the next largest proportion will be a subgroup who was inactive at pre-diagnosis but increased their PA over time [Low but increasing PA]; and 4) the smallest subgroup will exceed PA guidelines at all assessments [Consistently high PA].

<u>Hypothesis 1.c.2</u>: Four SB subgroups will be observed: 1) the largest subgroup will report TV watching consistent with the U.S. average of 18-19 hours/week at all assessments [TV consistent with U.S. Average and stable over time]; 2) the second largest subgroup will report TV watching consistent with the U.S. average of 18-19 hours/week and steadily increase over time [TV consistent with U.S. average and increasing]; 3) the third subgroup will report watching more TV than the U.S. average and increase over time [Above U.S TV average and increasing]; and 4) the smallest subgroup will report TV watching that is consistently lower than the U.S. average of 18-19 hours/week [Consistently below U.S. TV average].

<u>Hypothesis 1.c.3</u>: Four subgroups of breast cancer survivors will be observed when PA and SB are estimated in the same model: 1) the largest subgroup will consistently report low PA from pre-diagnosis through ten years post-diagnosis and stable TV watching consistent with the U.S. average of 18-19 hours/week [Consistently low PA and TV consistent with U.S. average and stable over time]; 2) the second subgroup will be sufficiently active prior to cancer but decrease their PA over time to levels below recommendations and report TV watching consistent with the U.S. average of 18-19 hours/week at pre-diagnosis and steadily increase over time [Sufficiently active but decreasing and TV consistent with U.S. average and increasing]; 3) the next largest proportion will be a subgroup who was inactive at pre-diagnosis but increased their PA over time and was higher than the U.S. TV average at pre-diagnosis and increased over time [Low but increasing PA and Above average TV and increasing]; and 4) the smallest subgroup will exceed

PA guidelines and report average TV watching below the U.S. average at all assessments [Consistently high PA and Consistently below U.S. TV average].

My hypotheses for subgroups were informed by empirical and theoretical evidence. Empirical evidence included an article mentioned previously (Brunet et al. [2014] subgroup results in Canadian breast cancer survivors) and a population-based study conducted by the American Cancer Society (Hawkins et al., 2010). Brunet et al. (2014) determined that there were five PA subgroups for Canadian breast cancer survivors, but the study has several methodological flaws that imply that five subgroups may be too many. In the American Cancer Society's cross-sectional analysis of 7,900 survivors with different cancer types, 29% reported increasing their PA following diagnosis, 56% remained the same, and 15% decreased PA (Hawkins et al., 2010), and thus there may be three subgroups who increase, decrease, and remain constant for PA.

Theoretical evidence informing my subgroup hypotheses included Lazarus and Folkman's Transactional Model of Stress and Coping (1987). The Transactional Model describes two types of cognitive and affective appraisals that influence how an individual behaves in response to a stressor, primary and secondary appraisal. Primary appraisal is an assessment of a situation's potential for harm already caused and/or future threat. Secondary appraisal relates to the perception of whether any action(s) can be taken to reduce or eliminate the stressor, and if so, which coping strategies might be effective (Lazarus & Folkman, 1987; Lazarus, 1999). Coping strategies are the cognitive, affective, and behavioral efforts to manage a situation perceived to be a stressor (Lazarus & Folkman, 1987).

In the context of PA during survivorship, the Transactional Model suggests that breast cancer survivors who perceive recurrence to be an important future threat, and who appraise their

coping resources as adequate to manage future recurrence risk, will change their behavior as a coping strategy. For instance, breast cancer survivors may increase their PA or change their diet to increase overall health and reduce future health threats. Thus, I hypothesized that a subgroup of breast cancer survivors would increase their PA after recovery from treatment because they perceive themselves to be at risk for cancer recurrence and have the necessary resources to make health changes. In the Brunet et al. (2014) study, a subgroup of 11% of Canadian breast cancer survivors did report increasing their PA after their cancer diagnosis. In the American Cancer Society study, 29% of survivors with diverse cancer types reported increasing their PA following diagnosis (Hawkins et al., 2010).

Similarly, Transactional Model processes also suggest a subgroup of breast cancer survivors who decrease their SB in response to feeling vulnerable about their future health and recurrence risk, and who appraise their coping resources as adequate to make health behavior changes. No supporting empirical studies are available to inform hypotheses about changes in SB made in response to a cancer diagnosis.

4.3 Methods

4.3.1 Participants

The Health, Eating, Activity, and Lifestyle (HEAL) study is a prospective cohort study of breast cancer survivors funded by the National Cancer Institute. HEAL prospectively followed a multi-site cohort of women newly diagnosed with stages 0-IIIa breast cancer from approximately six months to ten years post-diagnosis (McTiernan et al., 1998).

HEAL enrolled 1,183 women through three SEER (Surveillance, Epidemiology, and End Results) cancer registries: Fred Hutchinson Cancer Research Center (FHCRC) covering western Washington state (21%), University of New Mexico (UNM) covering the state of New Mexico (42%), and University of Southern California (USC) covering Los Angeles County (36%). Given these recruitment sites, the HEAL sample is diverse with 36% of women self-identifying as African American and 12% as Hispanic. By design, the majority of African American women were enrolled at USC and the majority of Hispanic women were enrolled at UNM (Meeske et al., 2007; McTiernan et al., 1998).

Women were included in the current sample if they completed their initial visit within one year of diagnosis and they were ages 35-64 years at the time of diagnosis (see Figure 4.1 for a consort diagram). Women needed to enroll by one-year post-diagnosis in order to have at least one year between the initial visit and 2-year follow-up. The age range was chosen to limit known effects of older age (see Sun, Norman, & While, 2013) and comorbid conditions (see Stewart et al., 1994) on PA and SB. In addition, the three SEER sites had differing age ranges due to ongoing clinical trials (USC: ages 35-64 years; FHCRC: ages 40-64 years; UNM: \geq 18 years), and thus I restricted ages to 35-64.

Of the 1,183 women enrolled in HEAL, 938 were between the ages of 35 and 64 years at the time of diagnosis and completed their initial assessment within one year of diagnosis. Of these 938 women, 769 (82%), 667 (71%), and 552 (59%) completed the two-, five-, and ten-year follow-up assessments, respectively (see Figure 4.1). This retention rate is consistent with other cohort studies of breast cancer survivors (e.g., Ganz, Desmond, Leedham, Rowland, Meyerowitz, & Belin, 2002). For the current study, IRB exemption was granted from the University of North Carolina at Chapel Hill.

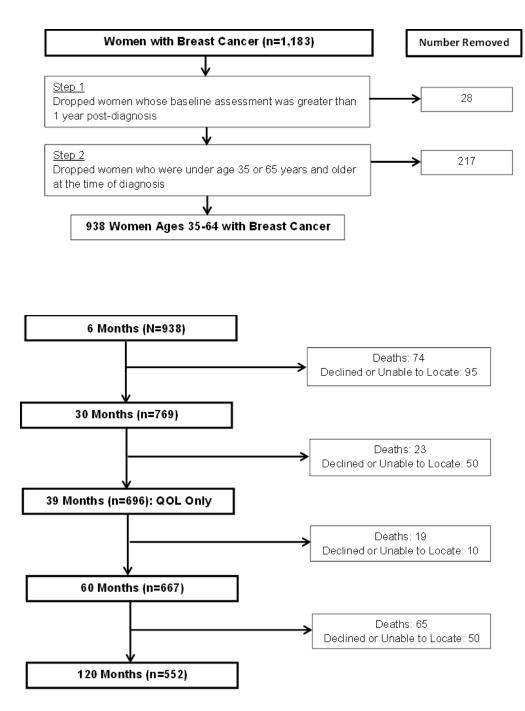


Figure 4.1. CONSORT diagrams for inclusion criteria and attrition.

4.3.2 Measures

<u>Moderate-vigorous Physical activity</u> was assessed by the Modifiable Activity Questionnaire (MAQ; Kriska, 1997), which was interviewer-administered at all time points (six months post-diagnosis for recall of pre-diagnosis PA and PA in the "last month", and at two, five, and ten years post-diagnosis). PA was defined as minutes/week in the last month spent doing 16 types of moderate-vigorous PA: fast walking, jogging, running, aerobics, Nordic track, tennis, golf, skiing, hiking, fast dancing, bowling, rowing, bicycling, calisthenics, swimming, and horseback riding. The MAQ has stable test-retest reliability and correlates positively with accelerometer data for younger and middle-aged women (Pettee, McClain, Schmid, Storti, & Ainsworth, 2010).

The assessment of PA and SB at enrollment (approximately six months post-diagnosis) was different among the three HEAL sites because USC was brought into the study later than UNM and FHCRC. At USC, pre-diagnosis PA data were collected as part of a case-control study where respondents recalled activity done regularly for at least one hour per week. The ages when the activity was performed, number of years, and average number of hours per week were recorded. Pre-diagnosis PA and PA in the last month were constructed from this lifetime history for USC. Data collection of SB was also affected. USC did not collect SB items at enrollment (including pre-diagnosis recall and six-month time point) and it could not be constructed from other data. Therefore, data were imputed using thirty variables for multiple imputation (see Section 4.4.3 for more details).

<u>Sedentary behavior</u> was assessed at the same time points as PA for the UNM and FHCRC sites (six months post-diagnosis for pre-diagnosis SB and SB in the "last month", and at two, five, and ten years post-diagnosis). USC completed the SB items at two, five, and ten years postdiagnosis. Women were asked the number of hours per day they spent sitting watching TV or videos on weekdays and weekends separately. Hours were converted into minutes and a variable

for overall TV time per week was calculated [(weekday TV minutes $\times 5/7$)+(weekend TV minutes $\times 2/7$)].

<u>Demographic variables</u> included self-reported race/ethnicity, education, marital status, and working status (working full- or part-time outside the home) at six months post-diagnosis. Race and ethnicity were combined into one variable: non-Hispanic Caucasian, non-hispanic African American, non-Hispanic other race, and Hispanic.

<u>*Clinical variables*</u> included body mass index, disease stage, and comorbid health conditions that limit activities. Body mass index (BMI) was calculated as kg/m² from self-reported height at age 18 and self-reported weight at six months post-diagnosis. Only two out of three HEAL sites (UNM and FHCRC) had weighed women, and thus we were not able to use weight obtained in the clinics. For all sites, the underweight category (BMI <18.4) was combined with the normal weight group (18.4-24.9) because there were too few women in the underweight category (e.g, n=28 at six months post-diagnosis) to estimate reliable parameters.

Disease stage was based on the American Joint Committee on Cancer (AJCC) stage of disease classification obtained from the Surveillance, Epidemiology and End Results (SEER) registry records. Women were included who were stages 0-IIIa. Recurrence is not tracked in SEER (http://appliedresearch.cancer.gov/seermedicare/aboutdata/program.html). Survivors' self-reported recurrence data may be unreliable because women were found to be reporting a "recurrence" in circumstances inconsistent with a recurrence, such as when a new primary breast cancer had occurred or when an irregular mammogram result was obtained. Thus, I was not able to control for recurrences or conduct sensitivity analyses.

Comorbid conditions were self-reported at two years post-diagnosis with two items: 1) asking if a doctor or other health professional had ever informed her that she had any of 17 health conditions: angina, myocardial infarction, congestive heart failure, high blood pressure, arthritis, osteoporosis, emphysema/chronic bronchitis, diabetes, gallbladder issues, endometriosis, cystic ovaries, liver disease, kidney disease, deep vein thrombosis, pulmonary embolism, stroke, and thyroid disease (Meeske et al., 2007); 2) if the survivor responded "yes" to a comorbid condition, a follow-up question was asked about whether the condition limited her activities. Comorbid conditions that limit activities were categorized as zero, one, or two or more and the categorical variable was used in analyses.

<u>Treatment variables</u> included surgery, radiation, and chemotherapy. Information on surgery and radiation therapy were obtained from SEER (George et al., 2013b) and coded as breastconserving surgery or mastectomy and radiation as yes/no. Chemotherapy data in SEER may be unreliable due to limited follow-up and a low correlation with chart reviews for women with breast cancer (Du et al., 2006). As such, physician and hospital records were used to create a yes/no variable for chemotherapy.

4.3.3 Missing Data Patterns and Multiple Imputation

PA and SB variables were examined for missing data to determine if the assumption of missing at random could be met. Each survivor's PA and SB variables were categorized as having no missing data, intermittently missing data (missing at one or more time points but completed the ten-year assessment), or attrition (at least two time points in a row missing and participant did not finish study). These missing data variables were then examined for correlations with demographic, clinical, and treatment-related variables to determine if multiple imputation was necessary.

A regression analysis was performed where categories of missing data were regressed on demographic, clinical, and treatment-related variables (entered simultaneously in the same step). As expected, missing data patterns were associated with African American race for PA (β =23.7,

p<.0001), SB (β =34.5, p<.0001), and PA-SB estimated in the same model (β =5.8, p<.0001). Given these correlations, the assumption of missing at random could not be met. Therefore, multiple imputation was conducted to correct for missing data. Multiple imputation is a state-of-the-art technique, compared to older methods such as mean replacement, that provides corrected standard errors by accounting for the uncertainty associated with missing data (Basagaña, Barrera-Gómez, Benet, Antó, & Garcia-Aymerich, 2013).

Sixteen variables were used for multiple imputation: demographic characteristics (SEER site, race/ethnicity[African American, Caucasian, Hispanic], education, marital status [time-varying], working status [time-varying]); clinical characteristics (body mass index [time-varying], age at diagnosis, comorbid conditions affecting activities, disease stage, menopausal status at enrollment); and treatment-related characteristics (radiation and chemotherapy treatment, surgery, self-reported tamoxifen use [time-varying]).

One-hundred imputed datasets were created and results were averaged across the datasets to determine final parameter estimates. The minimum recommendation is 20 imputed datasets in order to increase power and stabilize parameter estimates (Enders, 2010b), and thus favorable power and parameter stability were expected with 100 imputed datasets.

4.3.4 Statistical Models

4.3.4.a Latent Curve Modeling

Latent curve models were fit to estimate mean trajectories. Maximum likelihood with robust standard errors (MLR) was used as the estimator. Robust standard errors inflate or deflate the maximum likelihood standard errors according to the level of kurtosis in the data (Enders, 2010b), and thus correct for non-normality.

Linear, quadratic, and freed loading models were compared to determine the best fitting shape of the mean trajectory. Linear models imply steadily increasing or decreasing patterns

(equal change in outcome per unit of time regardless of where in time that occurs) whereas quadratic models allow for curvilinear (non-linear) patterns. A "freed loading model" is a nonlinear trajectory with unequal change per unit of time (i.e., factor loadings are not fixed and are therefore free to vary) and is the least restrictive of the models tested (Flora, 2008). In freed loading models, the mean and variance of the slope are interpreted as propensity to change nonlinearly over time.

Several empirical fit indices were used to compare latent curve models: chi-square, pvalue, and degrees of freedom. Chi-square can become biased with larger sample sizes (Enders, 2010b), and thus was not used as the sole criterion for assessing model fit. I also used the root mean square error of approximation (RMSEA, criterion: <0.08), Comparative Fit Index (CFI, criterion: >0.90), and Tucker-Lewis Index (TLI, criterion: >0.90). Additional empirical indicators included a parsimony index called the sample-size adjusted Bayesian Information Criteria (ssBIC) and the log-likelihood (in both cases, the lowest value indicates the model with better fit). ssBIC penalizes for model complexity (number of parameters estimated relative to sample size). In general, given two models with equivalent fit to the data, the most parsimonious model was selected (Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007).

PA and SB trajectories were estimated independently first and then together in the same model. Latent curve models were not adjusted for covariates because a later data step (growth mixture modeling) would determine subgroups based on a data-driven approach. In Chapter 5, I used the demographic, clinical, and treatment-related characteristics (along with psychosocial variables from the Transactional Model of Stress and Coping) to predict subgroup membership.

Next, the intercept, slope, and quadratic parameters were examined to determine if there was significant individual variability (significantly different from zero). Variance was calculated by subtracting each woman's PA and SB estimates from the group mean and squaring the difference (Bollen & Curran, 2006). These differences were then averaged to obtain the variance. In cases of statistically significant variance for the intercept and/or slope parameters, an additional analysis should be conducted to determine if subgroups are reporting different trajectories. This additional analysis is called "growth mixture modeling," which is described in the next section.

4.3.4.b Growth Mixture Modeling

The second methodology used was growth mixture modeling (GMM), which is a datadriven approach that categorizes each breast cancer survivor into her most likely PA or SB subgroup. GMM relaxes the assumption that all individuals are drawn from a single population, and thus separate intercepts, slopes, and variance parameters are calculated for each subgroup. GMM is flexible and robust to the following challenges encountered: partially missing data, unequally spaced time points, non-normally distributed repeated measures, complex trajectories, and time-varying covariates (Roth, 1994; Cohen & Cohen, 1983). Growth mixture models were also fit with multiple start values (300) in an effort to avoid a solution specific to one start value (i.e., a "local solution," see Curran et al., 2014).

The number of subgroups was determined by comparing fit indices across models with increasing numbers of subgroups (one through five subgroups). Relative model fit indices included the sample-size-adjusted Bayesian Information Criterion (ssBIC), entropy, and a minimum of five percent in each subgroup; ssBIC is a parsimony index where <u>lower</u> values indicate greater parsimony. Models with increasing numbers of subgroups were compared using

the change in ssBIC (calculated as two times the change in ssBIC [2 Δ BIC]). A cut-off value >10 indicated that the more complicated model had better fit (Kass & Wasserman, 1995).

Entropy is a measure of the precision of classification into subgroups (higher=more precision). It ranges from zero to one, where higher scores indicate better class separation. There is no standard cut-off value, but generally levels at or above 0.90 are considered acceptable (Jung & Wickrama, 2008).

A minimum percentage of 5% in each subgroup was used so that reliable parameter estimates could be determined for each subgroup (Enders, 2010b). Thus, the best fitting GMM had the highest entropy value, a 2 Δ BIC value greater than 10, and a minimum percentage of 5% in each subgroup (Curran & Bauer, 2013).

4.4 Results

4.4.1 Participant Characteristics

Breast cancer survivors had a mean age of 50.9 years (SD = 7.5, range: 35-64 years). The mean number of months between diagnosis and the initial interview was 5.9 months (SD = 2.3, range: 1-12 months). See Table 4.1 for demographic, clinical, and treatment-related characteristics. Women were recruited from cancer registries in New Mexico, California, and Washington (49% non-Hispanic Caucasian, 36% African American, and 12% Hispanic). At the initial assessment at six months post-diagnosis, 27% had completed high school or less education and 63% were married or cohabitating (23% separated/divorced, 5% widowed, and 9% had never married). Three-quarters of the women (76%) had been diagnosed with in situ or Stage I breast cancer. For treatment, 63% underwent breast-conserving surgery, 51% had radiation, and 36% had chemotherapy.

Approximately two-thirds (63%) of the sample reported having no comorbid conditions at two years post-diagnosis (13% reported one condition, 6% reported two or more conditions,

and 18% were missing). Stratifying by age group, 62% ages 35-44 years, 68% ages 45-54 years,

and 57% ages 55-64 years did not report comorbid conditions at two years diagnosis. Only 9%,

12%, and 18% of survivors ages 35-44, 45-54, and 55-64 years, respectively, reported one

comorbid condition.

	6 Months Post-
	Diagnosis
	(n=938)
SEER Site	200 (210/)
FHCRC: Fred Hutchinson Cancer Research	200 (21%)
USC: University of Southern California	340 (36%)
UNM: University of New Mexico	398 (42%)
Race/Ethnicity	
Non-Hispanic Caucasian	461 (49%)
Non-Hispanic African American	340 (36%)
Other (Non-Hispanic)	25 (3%)
Hispanic (any race)	112 (12%)
Missing	0
Education	
≤ High School	255 (27%)
Some College	355 (38%)
College	160 (17%)
Graduate Degree	168 (18%)
Missing	0
Marital Status	
Married/Cohabitating	592 (63%)
Separated/Divorced	217 (23%)
Widowed	48 (5%)
Never Married	81 (9%)
Missing	0
Working Status	
Working outside the home (full or part-time)	384 (41%)
Missing (*Not Collected at USC)	345 (37%)*
Body Mass Index	
≤ 24.9	530 (57%)
25-29 (Overweight)	248 (26%)
\geq 30 (Obese)	145 (15%)
Missing	15 (2%)

	6 Months Post- Diagnosis (n=938) n (%)
Comorbid Conditions that Limit Activities	
0	199 (21%)
1	240 (25%)
2 or more	333 (36%)
Missing	166 (18%)
Disease Stage	
0 (In Situ)	200 (21%)
I-IIa	518 (55%)
IIb-IIIa	137 (15%)
Missing	83 (9%)
Treatment Type	
Surgery	923 (98%)
Mastectomy	332 (35%)
Breast-Conserving Surgery	591 (63%)
No Surgery	15 (2%)
Missing	0
Radiation	476 (51%)
Missing	35 (4%)
Chemotherapy	335 (36%)
Missing	23 (2%)
Tamoxifen (anti-estrogen) at 6 Months Post-	195 (21%)
Missing	340 (36%)

Italicized: Different Treatment Types

4.4.2 Mean Physical Activity and Sedentary Behavior Trajectories

A quadratic model fit the data best for mean PA and SB trajectories when these outcomes were modeled independently (see Table 4.2), and thus were consistent with my hypotheses of non-linear trajectories.

	PA Linear	SB Linear
Intercept (SE)	111.7 (5.7)	1105.4 (17.0)
Slope (SE)	-1.4 (0.4)	6.2 (1.0)
ssBIC	60770.5	62242.5
Log Likelihood	-30366.9	-31103.4
Chi-Square	125.8	154.9
Degrees of freedom	10	10
RMSEA	0.11	0.13
CFI	0.82	0.91
TLI	0.82	0.91
	PA Quadratic	SB Quadaratic
Intercept	118.6 (10.9)	1077.6 (90.0)
Slope	-9.4 (2.1)	12.0 (15.2)
Quadratic Slope	-0.5 (0.1)	0.8 (0.6)
ssBIC	60466.9	61999.9
Log Likelihood	-30198.6	-30969.7
Chi-Square	3.4	12.9
Degrees of Freedom	1	3
RMSEA	0.05	0.06
CFI	0.99	0.99
TLI	0.96	0.98
	PA Freed Loading	SB Freed Loading
Intercept	91.8 (6.3)	1080.0 (20.1)
Slope	0.0 (0.4)	89.6 (16.4)
ssBIC	60715.6	62194.9
Log Likelihood	-30334.0	-31074.3
Chi-Square	209.4	104.7
Degrees of Freedom	7	7
RMSEA	0.17	0.13
CFI	0.71	0.94
TLI	0.54	0.92

Table 4.2. Parameter Estimates and Fit Criteria for Physical Activity and Sedentary Behavior Trajectories (Estimated Singly)

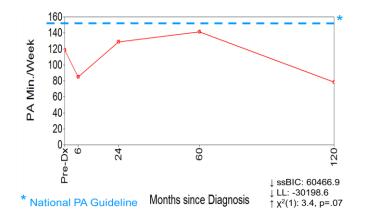
Criteria: RMSEA: <.08, CFI: ≥0.90, TLI: ≥0.90, ssBIC: lower value, chi-square: higher value Bold: best fitting model

The mean PA trajectory showed a decline of 34 minutes from pre-diagnosis (119 minutes/week) to six months post-diagnosis (85 minutes/week), and formed an inverse-U shape (increasing and then decreasing) from six months post-diagnosis through ten years post-diagnosis. The peak of the inverse-U occurred at five years post-diagnosis (141 minutes/week) with a considerable drop to 78 minutes/week at ten years post-diagnosis. For the mean PA trajectory, all assessment points were below the national guideline of at least 150 minutes/week of moderate PA. A decrease in PA between pre-diagnosis and six months post-diagnosis is

consistent with my hypothesis for the mean PA trajectory. However, I had hypothesized that the peak in the PA trajectory would occur at two years post-diagnosis. Instead, the peak occurred at five years post-diagnosis.

For SB, the mean trajectory showed an increase of one hour of TV watching per week from pre-diagnosis (18.0 hours/week) to six months post-diagnosis (19.1 hours/week). SB returned to pre-diagnosis levels by two years post-diagnosis (18.3 hours/week), and then steadily increased to a peak at ten years post-diagnosis (20.6 hours/week) (see Figure 4.3b). My SB mean trajectory results are consistent with my hypothesis of a non-linear trajectory that decreased between pre-diagnosis and six months post-diagnosis, returned to pre-diagnosis levels by two years post-diagnosis, and then steadily increased between five and ten years post-diagnosis.

When PA and SB were estimated simultaneously, a quadratic model continued to fit the data better than linear or freed loadings models (see Table 4.3). This result is consistent with my hypothesis that non-linear models would continue to be observed when PA and SB were estimated simultaneously.



4.2a. Physical Activity Model-Implied Mean Trajectory (Quadratic)

4.2b. Sedentary Behavior Model-Implied Mean Trajectory (Quadratic)

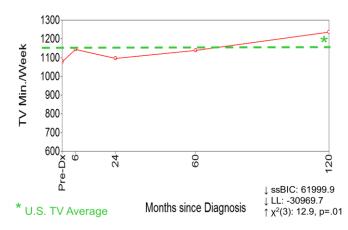


Figure 4.2. Best-fitting growth models for physical activity and sedentary behavior estimated singly.

	PA-SB Linear
PA Intercept	110.8 (5.7)
PA Slope	-1.4 (0.4)
SB Intercept	1113.2 (18.4)
SB Slope	6.0 (1.1)
ssBIC	138254.0
Log Likelihood	-69068.3
Chi-Square	1928.7
Degrees of Freedom	87
RMSEA	0.15
CFI	0.61
TLI	0.59
	PA-SB Quadratic
PA Intercept	94.8 (6.1)
PA Slope	8.7 (1.4)
PA Quadratic Slope	-0.5 (0.1)
SB Intercept	1122.2 (20.6)
SB Slope	-2.7 (3.6)
SB Quadratic Slope	0.4 (0.2)
ssBIC	129677.3
Log Likelihood	-64770.8
Chi-Square	218.6
Degrees of Freedom	28
RMSEA	0.09
CFI	0.94
TLI	0.90
	PA-SB Freed Loading Model
PA Intercept	130.1 (12.6)
PA Slope	-42.5 (15.5)
SB Intercept	1096.0 (27.2)
SB Slope	53.0 (36.6)
ssBIC	129815.1
Log Likelihood	-64852.5
Chi-Square	3640.9
Degrees of Freedom	35
RMSEA	0.20
CFI	0.77
TLI	Couldn't be calculated

Table 4.3. Physical Activity and Sedentary Behavior Modeled Simultaneously

Criteria: RMSEA: <.08, CFI: ≥0.90, TLI: ≥0.90, ssBIC: lower value, chi-square: higher value, Bold: best fitting model

When PA and SB were modeled simultaneously, the PA mean at pre-diagnosis was 120.9 minutes/week (SE=23.9) and watching 1145.6 minutes (SE=64.5) of TV per week (19.1 hours) in the year prior to diagnosis. Figure 4.3 shows that when PA and SB were estimated together,

the same quadratic shapes occurred as when they had been modeled singly, and thus my hypothesis was supported.

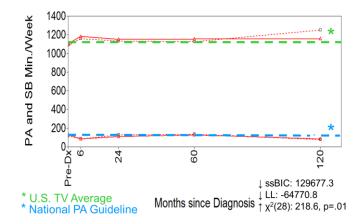


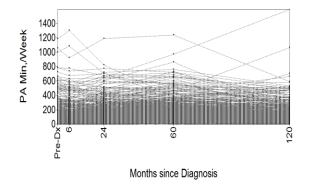
Figure 4.3. Physical activity and sedentary behavior estimated simultaneously.

4.4.3 Individual Variability in Trajectories

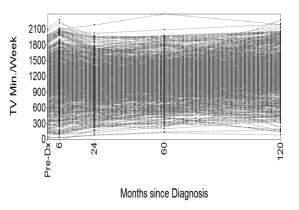
Significant individual variability was observed in all PA and SB parameters, and thus my hypotheses were supported. For PA, women demonstrated significant individual variation at prediagnosis (intercept variance= 23286.6) and change over time (linear slope variance=741.7, quadratic term variance=1.6) (all p<.0001). Figure 4.4a shows the individual variability in PA for all 938 women and Figure 4.4b shows 50 randomly selected PA trajectories to demonstrate high variance.

For SB, significant variability was also observed for pre-diagnosis TV watching (intercept variance=58501.8) and change over time (linear slope variance=4265.2, quadratic term variance=9.7) (all p<.0001). Figure 4.4c shows the individual variability in SB for all 938 women and Figure 4.3d shows 50 randomly selected SB trajectories to demonstrate high variance.

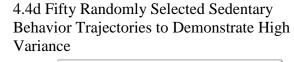
4.4a Individual Variability in Physical Activity Trajectories



4.4c Individual Variability in Sedentary Behavior Trajectories



4.4b Fifty Randomly Selected Physical Activity Trajectories to Demonstrate High Variance



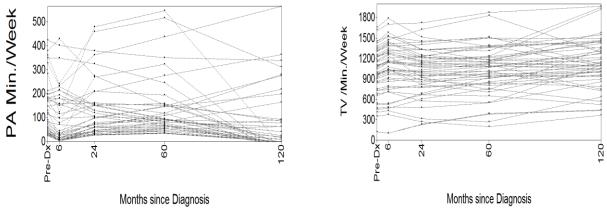


Figure 4.4. Individual variability in physical activity and sedentary behavior trajectories.

Given this substantial individual variation in starting values and slopes for PA and SB, I next examined whether there were subgroups of women following different trajectories. Subgroups were examined for PA estimated singly, SB estimated singly, and PA and SB estimated in the same model.

4.4.4 Subgroups of Women Following Different Trajectories (Latent Groups) 4.4.4.a Subgroups for Physical Activity

To determine the number of PA subgroups, models with increasing numbers of subgroups (one through five) were compared. A quadratic model fit best for the mean PA and SB trajectories, and thus quadratic models were also used in the growth mixture models.

When PA was modeled individually, ssBIC values for models with multiple classes were all lower than the one-class model, indicating that a subgroup model fit the data better than one class. ssBIC values decreased from one (60466.9) to two (59880.6) classes, increased to 60162.5 for three classes, and then decreased for four and five classes (59940.6 and 59828.3) (see Table 4.4). Change in ssBIC (two times the change in ssBIC [2 Δ BIC]) was used to compare models and a cut-off value of ten or more indicated that the more complicated model had better fit. For PA estimated individually, 2 Δ BIC exceeded ten when comparing one vs. two classes (1172.6), two vs. three classes (563.8), three vs. four classes (443.8), and four vs. five classes (224.6), which is consistent with better model fit as the number of classes increases.

Entropy values increased from two to three classes (0.97 to 0.98) and then decreased for four and five classes (both 0.96), indicating that there was higher precision for assigning women to classes within the two- and three-class models. The percentage of women assigned to each class was also examined. The models with a minimum percentage of 5% of women in each subgroup included the one- and two-class models. Taken together, the two-class model for PA met all criteria: significantly lower ssBIC than the one-class model, higher entropy than the oneclass model, and a minimum percentage of 5% of women in each class. I had hypothesized that four empirically distinct subgroups would be observed for PA trajectories, and thus my hypothesis is only partially supported.

Class #	Intercept (SE)	Slope (SE)	Quad- ratic (SE)	% in Sub- group	Minimum of 5% in Each Class?	ssBIC	Entropy
1 Class							
1	118.6 (10.9)	-9.4 (2.1)	-0.5 (0.1)	100	Yes	60466.9	N/A
2 Classes							
1	74.3 (34.4)	9.9 (48.6)	-0.5 (1.7)	92	– Yes	59880.6	0.97
2	659.7 (44.6)	-19.1 (41.0)	0.5 (13.5)	8	- 1es	39880.0	0.97
3 Classes							
1	331.0 (145.9)	64.7 (39.9)	-3.3 (1.7)	5			0.98
2	764.9 (220.2)	-84.2 (44.4)	4.5 (2.0)	1	No	60162.5	
3	77.1 (8.4)	6.7 (2.0)	-0.4 (0.1)	94	_		
4 Classes							
1	53.9 (4.8)	11.7 (1.4)	-0.6 (0.1)	88		59940.6	0.96
2	416.1 (27.0)	-21.5 (6.1)	0.5 (0.3)	10			
3	346.9 (143.9)	-25.4 (56.0)	3.7 (2.0)	0.3	– No		
4	1046.2 (120.4)	-63.3 (38.4)	1.9 (1.7)	1	_		
5 Classes							
1	54.6 (4.9)	8.9 (1.3)	-0.5 (0.1)	87			
2	133.6 (95.6)	104.1 (24.2)	-4.8 (1.1)	3	_		
3	1032.8 (99.9)	-57.7 (30.9)	1.6 (1.4)	1	No	59828.3	0.96
4	347.0 (144.0)	-25.4 (55.7)	3.7 (2.0)	0.3			
5	426.2 (29.4)	-26.7 (10.3)	0.7 (0.5)	9	_		

SE = standard error

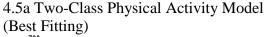
ssBIC = Sample-size adjusted Bayesian Information Criteria (lower is better) Entropy = precision of classification (higher is better)

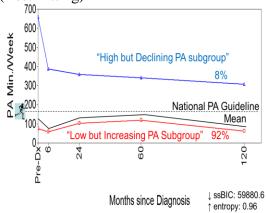
Figures 4.5a – 4.5d show the two-, three-, four-, and five-class model results for subgroups, respectively. Figure 4.5a shows the best fitting, two-class PA model. The largest subgroup (92%) reported consistently low PA across all time points and the smallest subgroup

(8%) reported high PA that steadily decreased over time. The shape of the PA trajectory for the large subgroup (92%) mirrored that of the mean trajectory for the whole group: a significant decline in PA from pre-diagnosis (74 minutes/week) to six months post-diagnosis (59 minutes/week), forming an inverse-U shape from six months post-diagnosis through ten years post-diagnosis. The peak of the inverse-U occurred at five years post-diagnosis (119 minutes/week) but did not reach the national guideline of at least 150 minutes/week of moderate PA.

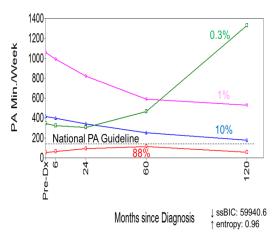
The smaller subgroup (8%) reported 660 minutes/week (11 hours/week) of PA prior to cancer diagnosis, with a sizeable drop to 388 minutes/week (6.5 hours) at six months post-diagnosis, and steadily declining to 307 minutes/week (5.1 hours) at ten years post-diagnosis.

As a sensitivity analysis, I examined whether more than one subgroup would be observed for low PA if the high PA subgroup was removed. Only one subgroup continued to be present for low PA when the high PA subgroup was removed (data not shown).





4.5c Four-Class Physical Activity Model



4.5b Three-Class Physical Activity Model

4.5d Five-Class Physical Activity Model

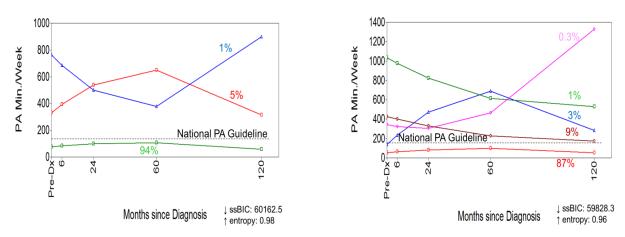


Figure 4.5. Physical activity subgroups (quadratic model).

4.4.4.b Subgroups for Sedentary Behavior

When SB was estimated independently, ssBIC values increased from one (61999.9) to two (62159.0) classes, decreased for three classes (62058.6), and then increased for four and five classes (62127.4 and 62108.5) (see Table 4.5). Two times the change in ssBIC (2Δ BIC) was also

used to compare increasingly complex models. For SB estimated independently, 2Δ BIC exceeded ten when comparing one vs. two classes (318.2), two vs. three classes (200.8), three vs. four classes (137.6), and four vs. five classes (37.8), indicating that models with two, three, four, or five classes had the best fit.

Entropy values steadily increased from two to five classes (0.66, 0.76, 0.85, and 0.87, respectively), indicating greater confidence in class enumeration as the number of classes increased. The percentage of women assigned to each class was also examined. The models with a minimum percentage of 5% of women in each subgroup included the one-, two-, three-, and five-class models. Considering the four criteria across models, the three-class SB model had the best fit: lower ssBIC than the two-class model, significant improvement in ssBIC over the two-class model, higher entropy than the two-class model, and a minimum percentage of 5% of women in each class.

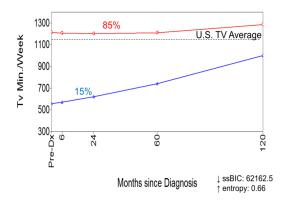
Class #	Intercept (SE)	Slope (SE)	Quad- ratic (SE)	% in Sub- group	Minimum of 5% in each Class?	ssBIC	Entropy
1 Class							
1	1077.6 (18.9)	5.1 (3.3)	0.2 (0.2)	100	Yes	61999.9	N/A
2 Classes							
1	664.9 (267.0)	22.2 (53.6)	-0.9 (3.3)	15	X 7	62159.0	0.66
2	1188.2 (65.9)	-3.3 (9.1)	0.4 (0.4)	85	– Yes		0.66
3 Classes							
1	320.9 (56.8)	49.2 (9.3)	1.5 (0.4)	18			
2	1151.3 (22.5)	0.6 (0.4)	0.8 (0.2)	66	Yes	62058.6	0.76
3	1591.3 (89.2)	85.8 (14.0)	-3.8 (0.6)	17			

Table 4.5. Sedentary Behavior Subgroup Estimates and Model Fit Indices

Class #	Intercept (SE)	Slope (SE)	Quad- ratic (SE)	% in Sub- group	Minimum of 5% in each Class?	ssBIC	Entropy
4 Classes							
1	1175.3 (24.3)	-0.1 (4.2)	-0.3 (0.2)	71			
2	730.0 (57.6)	-58.1 (9.4)	3.2 (0.4)	18	_	62127.4	
3	347.6 (284.1) (65.1)	134.2 (56.2) (18.6)	-3.7 (3.0)	1	No		0.85
4	1457.7 (79.2)	77.2 (13.5)	-3.3 (0.6)	10	_		
5 Classes							
1	1069.8 (26.3)	-9.8 (4.5)	0.8 (0.2)	45			
2	1309.2 (34.8)	23.7 (6.0)	-0.8 (0.3)	30		62108.5	
3	1225.0 (756.5)	-171.4 (122.8)	8.3 (5.5)	5	Yes		0.87
4	1538.9 (69.7)	84.5 (12.0)	-3.7 (0.6)	7			
5	650.2 (141.6)	-61.3 (13.5)	3.4 (0.7)	13			

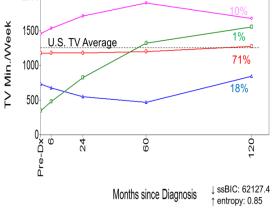
SE = standard error, ssBIC = Sample-size adjusted Bayesian Information Criteria (lower is better), Entropy = precision of classification (higher is better)

Figures 4.6a – 4.6d show the two-, three-, four-, and five-class model results for SB, respectively. Figure 4.6b shows the best fitting, three-class model. The largest subgroup (66%) reported consistently sitting watching TV for about 19 hours/week across all assessments. The low SB subgroup (18%) reported almost doubling their TV watching between pre-diagnosis (5.4 hours/week) and six months post-diagnosis (9.2 hours/week), and steadily increased to a peak of 14.2 hours/week at ten years post-diagnosis. The high SB subgroup (17%) reported a varying pattern with a large increase between pre-diagnosis (26.5 hours/week) and six months post-diagnosis (28.2 hours/week), dropping to 25.2 and 23.7 hours/week at two and five years post-diagnosis, respectively, and increasing to a peak of 28.4 hours/week at ten years post-diagnosis.



4.6a Two-Class Sedentary Behavior Model

4.6c Four-Class Sedentary Behavior Model



4.6d Five-Class Sedentary Behavior Model

4.6b Three-Class Sedentary Behavior Model (Best Fitting)

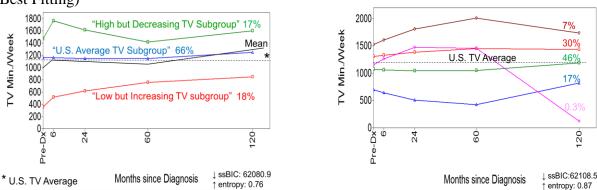


Figure 4.6. Sedentary behavior subgroups (quadratic models).

4.4.4.c Subgroups for Simultaneously Estimated Physical Activity and Sedentary Behavior

When PA and SB were estimated in the same model, there was a large decrease in ssBIC values from one (129815.1) to two (128752.0) classes, an increase for three classes (129281.4), and then a decrease for four and five classes (129115.7 and 129017.9) (Table 4.6). Two times the change in ssBIC (2 Δ BIC) was also used to compare models with increasing complexity. For PA and SB estimated simultaneously, 2 Δ BIC exceeded the cut-off of ten when comparing one vs.

two classes (2126.2), two vs. three classes (1058.8), three vs. four classes (331.4), and four vs. five classes (195.6), which indicates better fit with increasing numbers of subgroups.

Models with the highest entropy values (0.97) included the two-, three-, and four-class models, indicating greater confidence in class enumeration for these models. The models with a minimum percentage of 5% of women in each subgroup included the one- and two-class models. Considering these four model fit criteria, the two-class PA-SB model had the best fit for criteria: significantly lower ssBIC than the one-class model, significant improvement in ssBIC over the one-class model, the highest entropy value (tied with three- and four-class models), and a minimum percentage of 5% of women in each class (Figure 4.6c).

Class #	Intercept (SE)	Slope (SE)	% in Sub- group	Minimum of 5% in Each Class?	ssBIC	Entropy		
1 Class								
1: PA	130.1 (12.6)	-42.5 (15.5)	100	100	100	Yes	129815.1	N/A
1: SB	1095.8 (27.2)	53.0 (36.6)	100	105	129615.1	N/A		
2 Classes								
1: PA	81.8 (10.0)	5.5 (5.8)	91	- Yes 1	128752.0	0.97		
1: SB	1097.0 (20.7)	70.1 (14.5)	91					
2: PA	705.9 (154.7)	-347.5 (84.0)			128732.0	0.97		
2: SB	934.96 (70.1)	171.7 (58.4)	9					
3 Classes								
1: PA	673.8 (83.4)	-450.4 (85.6)	5					
1: SB	923.6 (99.6)	173.9 (73.4)		_				
2: PA	80.9 (7.5)	0.2 (4.8)	92	No	129281.4	0.97		
2: SB	1100.5 (21.1)	70.4 (15.4)		_				
3: PA	583.3 (141.9)	-43.5 (102.6)	3					

Table 4.6. Subgroup Estimates for Physical Activity and Sedentary Behavior Modeled Simultaneously

3: SB	932.7 (105.1)	135.8 (93.3)				
Class #	Intercept (SE)	Slope (SE)	% in Sub- group	Minimum of 5% in Each Class?	ssBIC	Entropy
4 Classes						
1: PA	1152.6 (110.0)	-326.1 (79.5)	1			
1: SB	836.9 (233.1)	123.0 (107.7)	1	_		
2: PA	60.8 (113.1)	6.6 (6.2)	88			
2: SB	1104.4 (91.3)	68.7 (16.5)	00	– No	129115.7	0.97
3: PA	-134.3 (81.5)	866.3 (124.7)		110	127113.7	0.97
3: SB	1627.8 (1374.3) (443.8)	229.3 (1085.8) (421.0)	0.1	-		
4: PA	485.3 (30.4)	-160.9 (41.1)	11			
4: SB	955.9 (51.0)	108.9 (42.2)				
5 Classes						
1: PA	708.1 (28.5)	-338.0 (35.9)	4			
1: SB	951.0 (80.9)	185.2 (66.4)		_		
2: PA	1462.0 (160.3)	-590.0 (124.7)	0.4			
2: SB	569.9 (204.7)	154.1 (104.3)	0.4	_		
3: PA	58.4 (13.2)	23.6 (9.3)	14			
3: SB	658.7 (206.5)	119.7 (121.5)	14	No	129017.9	0.80
4: PA	38.8 (4.1)	23.7 (4.2)	66			
4: SB	1212.6 (54.2)	60.3 (32.3)		_		
5: PA	335.3 (16.7)	-112.3 (13.7)	14			
5: SB	956.6 (44.8)	93.9 (32.4)	14			

SE = standard error, ssBIC = Sample-size adjusted Bayesian Information Criteria (lower is better), Entropy = precision of classification (higher is better)

Figures 4.7a - 4.7d show the model results for two-, three-, four-, and five-class models when PA and SB were estimated in the same model. Figure 4.7a shows the best-fitting, two-class model. In the largest subgroup, 91% of breast cancer survivors reported non-linear patterns of

PA and SB. At pre-diagnosis, they reported 1.4 hours/week of PA and 18.5 hours/week sitting watching TV. At six months post-diagnosis, PA dropped to 1.0 hour/week and TV increased to 19.5 hours/week. By two and five years post-diagnosis, respectively, PA (1.7 and 2.0 hours/week) had recovered to levels better than pre-diagnosis and SB (18.8 and 19.1 hours/week) increased slightly. However, at ten years post-diagnosis, PA had dropped back to 1.0 hour/week and SB had increased to a peak of 20.9 hours/week.

In the smaller subgroup, 9% reported non-linear patterns of high PA that exceeded national guidelines at all assessments and moderate SB that was lower than the U.S. average of 18-19 hours/week of TV watching (U.S. Bureau of Labor Statistics, 2014). At pre-diagnosis, this smaller subgroup reported a high of 10.1 hours/week for PA and a low of 15.2 hours/week for SB. At six months post-diagnosis, PA dropped by half to 5.4 hours/week and SB increased to 17.5 hours/week. At two years post-diagnosis, PA had increased to 5.9 hours/week and SB had decreased to 16.3 hours/week. At five years post-diagnosis, PA increased again to 6.9 hours/week and SB increased to 17.5 hours/week and SB increased to 17.5 hours/week. At ten years post-diagnosis, PA decreased to a low of 5.2 hours/week and SB increased to a peak of 18.6 hours/week.

A two-class model is not consistent with my hypothesis of four subgroups when PA and SB were modeled simultaneously. I had hypothesized four subgroups: Consistently low PA and TV consistent with U.S. average and stable over time, sufficiently active but decreasing and TV consistent with U.S. average and increasing, low but increasing PA and above average TV and increasing, and consistently high PA and consistently below U.S. TV average. However, the best fit to the data was a two-class model with one subgroup reporting low PA and TV consistent with the U.S. average and a second subgroup reporting high PA that decreased over time and TV watching below the U.S. average. Therefore, my hypothesis is not supported.

Figure 4.7a Two-Class PA-SB Model (Best

Fitting)

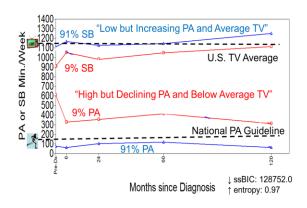


Figure 4.7b Three-Class PA-SB Model

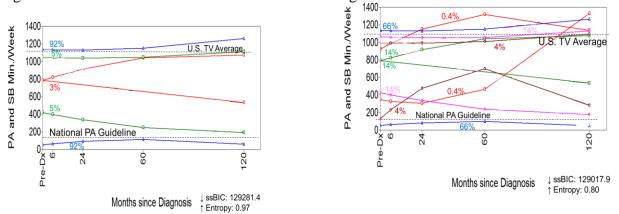


Figure 4.7. Subgroups when physical activity and sedentary behavior were estimated simultaneously.

4.5 Discussion

As a group, breast cancer survivors reported mean PA and SB patterns that were non-linear from pre-diagnosis through ten years post-diagnosis. However, a sizeable amount of variation occurred. Two PA subgroups following different trjectories fit the data better than a group average; and three subgroups for SB.

Figure 4.7c Four-Class PA-SB Model

National PA Guideline

Figure 4.7d Five-Class PA-SB Model

24

09

Months since Diagnosis

TV Average

Ó

↓ ssBIC: 129115.7

↑ Entropy: 0.97

1400

1200

1000

800

600

400

Pre-Dx

PA and SB Min./Week

4.5.1 Physical Activity

On average, breast cancer survivors were below the national guideline of at least 150 minutes per week of PA at all assessment points from pre-diagnosis through ten years postdiagnosis. The shape of the mean PA trajectory began with a decrease of 34 minutes per week between pre-diagnosis and six months post-diagnosis, rebounded to pre-diagnosis levels by two years post-diagnosis, increased to a peak of 142 minutes/week at five years post-diagnosis, and then decreased by over an hour to 78 minutes/week at ten years post-diagnosis.

This trajectory shape is consistent with Emery et al. (2009) where breast cancer survivors also reported an inverted-U shape, of increasing and then decreasing PA, from the time of surgery through five years post-treatment (Emery et al., 2009). In both studies, breast cancer survivors reported approximately 80-90 minutes/week of PA during early survivorship (after surgery in Emery [2009] and approximately six months post-diagnosis in the current study). Both studies also found similar PA levels at 18-24 months post-diagnosis (Emery: approximately 125 minutes/week at 18 months post-diagnosis vs. 129 minutes/week at 24 months post-diagnosis in the current study). After the two-year mark, the two studies started to diverge in patterns, however. The Emery (2009) survivors declined in PA from two to five years post-diagnosis, and the five-year PA was lower than at the time of treatment. However, in the current study, breast cancer survivors continued to increase their PA from two to five years post-diagnosis, to a peak of 142 minutes per week. At ten years post-diagnosis, a considerable drop in PA was reported.

There are demographic and clinical differences between between the two samples that may explain the diverging patterns after two years post-diagnosis. Demographically, the samples were similar with the exception of race/ethnicity (Emery: 10% non-white vs. 51% in the current sample) and age range (Emery: ages 28-84 with a mean of 50.9 vs. ages 35-64 with a mean of 51 in the current sample). Clinically, the Emery (2009) study enrolled survivors with higher disease stages (Emery: II-III vs. 0-IIIa in the current study) and a greater proportion receiving chemotherapy (Emery: over 80% vs. 36% in the current sample). The breast cancer survivors in the Emery (2009) study may have been experiencing a higher long-term symptom burden from more invasive therapy, or perhaps had more comorbid conditions, and therefore were unable to maintain PA levels as long as the survivors in the current study who had a lower disease stage and less invasive therapy.

Pre-diagnosis PA data was not collected in the Emery et al. (2009) study so no information is available about whether the breast cancer survivors decreased PA from pre- to post-diagnosis like the breast cancer survivors in the current study did. However, several cohort studies have also shown a decrease in PA from pre- to post-diagnosis for breast cancer survivors (Andrykowski et al., 2007; Devoogdt et al., 2010; Hair et al., 2014; Irwin et al., 2003; Littman et al., 2000). For example, Hair et al. (2014) found that 59% of breast cancer survivors reported decreasing their PA from pre- to post-diagnosis, but the magnitude of change varied by race. After adjustment for potential confounders, African American women were less likely to meet PA guidelines after diagnosis than Caucasian women.

Breast cancer survivors may be reducing their PA from pre- to post-diagnosis because they are undergoing active treatment, such as breast-conserving surgery and radiation, and experiencing symptoms such as fatigue and breast sensitivity. During active treatment, and through approximately 18 months post-diagnosis, over 80% of breast cancer survivors report fatigue, 70% report breast sensitivity, and over 50% report sleep disturbance (Janz et al., 2007; Montazeri, 2008; Mortimer et al., 2010; Nihal Guleser et al., 2012), all of which are known to affect PA after diagnosis (Alfano et al., 2007; Charlier et al., 2013; Fong et al., 2012; McNeely et al., 2006; Meeske et al., 2007; Smith et al., 2009).

In the current study, PA rebounded at two years post-diagnosis to nearly pre-diagnosis levels. This rebound is consistent with the timing of recovery from active treatment. In general, younger and middle-age breast cancer survivors need approximately 12-18 months to recover from treatment and return to their usual activities (Hsu, Ennis, Hood, Graham, & Goodwin, 2013; Mols, Vingerhoets, Coebergh, van de Poll-Franse, 2005; Montazeri, 2008). This timing of symptom recovery is consistent with longitudinal studies in breast cancer survivors showing PA increases after completion of active treatment (Emery et al., 2009; Harrison et al., 2009; Littman et al., 2000).

Finally, the current study observed a decline in PA from five to ten years post-diagnosis. This result may be due to PA decreasing with age. PA declines as individuals age have been observed for both the general population (Fan, Kowaleski-Jones, & Wen, 2013; Kim et al., 2013; Sun, Norman, & While, 2013) and cancer survivors (Bellury et al., 2012; Hong et al., 2007; Kim et al., 2013; Lynch et al., 2010). Fan et al. (2013) examined PA across 17 activity types for 3,952 women ages 25 years and older participating in the 2003-2006 National Health and Nutrition Examination Surveys (NHANES). Significant decline in leisure PA participation started at ages 35-44 years (e.g., running, dancing, treadmill, and team sports). Total PA also declined with age but significant declines did not occur until ages 55-64 years (e.g., participation in household PA and walking).

4.5.2 Sedentary Behavior

For SB, the mean trajectory began with an increase of over an hour of TV watching per week from pre-diagnosis to six months post-diagnosis, returned to nearly pre-diagnosis levels by two years post-diagnosis, increased by 44 minutes/week at five years post-diagnosis, and increased again by 97 minutes/week to a peak of 20.6 hours/week at ten years post-diagnosis. This mean SB trajectory was consistent with the U.S. national average of 18-19 hours per week of sitting watching TV (U.S. Bureau of Labor Statistics, 2014). The current study is the first to examine SB trajectories from pre-diagnosis to ten years post-diagnosis, and thus there are no prior studies available for comparison.

The increase in SB from pre- to post-diagnosis may be due to breast cancer survivors spending more time in hospital and outpatient settings to receive treatment. Breast cancer survivors may be sitting for longer periods, and perhaps watching more TV to pass the time, than they did prior to cancer treatment. Additionally, the majority of breast cancer survivors who are working take a leave of absence during active treatment (Balak, Roelen, Koopmans, ten Berge, & Groothoff, 2008), and therefore have more time to watch TV. For breast cancer survivors with early-stage disease, the mean duration of absence from work is approximately 4-6 months, with absences up to 11 months for women receiving chemotherapy (Balak et al., 2008).

Irwin and colleagues (2003) used data from two HEAL sites (New Mexico and Washington state) and found that PA decreased, and SB (TV watching) increased, from pre- to post-diagnosis for Caucasian and Hispanic survivors, and that the magnitude of these changes varied by treatment type. HEAL breast cancer survivors who underwent surgery and received radiation therapy reported a one-hour increase in TV watching and a 45-minute decrease in PA per week from pre- to post-diagnosis. Women who received chemotherapy, in addition to any other therapy type, fared the worst for PA and SB. They reported a six-hour increase in TV watching and a 1.5-hour decrease in PA per week from pre- to post-diagnosis.

In the current study, TV watching returned to pre-diagnosis levels by two years postdiagnosis, suggesting that breast cancer survivors had returned to usual activities, and thus were watching less TV. The majority of breast cancer survivors are able to resume their usual daily activities after recovery (e.g., Montazeri, 2008, Mols et al., 2007). For instance, the majority of

breast cancer survivors return to work after recovering from surgery and radiation (Balak et al., 2008), and thus may be decreasing their TV watching as normal activities are resumed.

TV watching began to increase again at five and ten years post-diagnosis. This result may be a function of lifestyle changes, or increasing comorbid health conditions, over the the lifespan. For instance, TV watching increases with age for the general population (Kim et al., 2003; Mares & Woodard, 2006) and in cancer survivors (Kim et al., 2003; Lynch et al., 2010). When PA and SB were estimated in the same model, breast cancer survivors reported an average pattern, from pre-diagnosis to ten years post-diagnosis, of spending 10-fold more time sitting watching TV than time spent engaging in PA.

4.5.3 Subgroups Reporting Different Physical Activity and Sedentary Behavior Trajectories

Given the sizeable amount of variation observed in mean PA and SB trajectories, subgroups of breast cancer survivors following different trajectories were a better fit to the data than average trajectories. Two PA subgroups were identified: 1) 92% reported a consistent pattern of low PA from pre-diagnosis through ten years post-diagnosis ("Low but Increasing PA Subgroup"); and 2) 8% exceeded PA guidelines at all assessments but reported a significant decline at 6 months post-diagnosis that persisted through ten years post-diagnosis ("High But Declining PA Subgroup").

My finding of two PA subgroups in a U.S. sample of breast cancer survivors is inconsistent with Brunet et al. (2014) who found five PA subgroups in Canadian survivors. Brunet et al. (2014) may have found more PA subgroups due to demographic differences between the samples and statistical issues. Demographically, the Canadian breast cancer survivors in the Brunet (2014) sample were largely Caucasian (85%) and highly educated (50% with a college degree), and thus the differences between these studies may be due to racial/ethnic, nationality, and educational differences. Statistically, Brunet et al. (2014) may have found a greater number of subgroups due to small sample size. Simulation studies have confirmed that too many classes may be enumerated when model fit criteria are not adjusted for sample size (Enders, 2010b).

Three SB subgroups were identified: 1) 66% had a flat trajectory of watching TV 19-20 hours/week, which is consistent with the U.S. average ("U.S. Average TV Subgroup"); 2) 18% reported watching fewer TV hours/week than the U.S. average at pre-diagnosis and steadily increased through ten years post-diagnosis ("Low but Increasing TV subgroup"); and 3) 17% reported greater TV hours/week than the U.S. average at all assessments, with increases at six months and ten years post-diagnosis ("High but Decreasing TV Subgroup"). When PA and SB trajectories were estimated in the same model, two subgroups were observed: 1) 91% reporting low PA and TV watching consistent with the U.S. average across all time points ("Low but Increasing PA and Average TV Subgroup"); and 2) 9% reporting high PA declining over time and TV watching consistent with the U.S. average increasing over time ("High but declining PA and Average TV Subgroup").

When PA and SB trajectories were estimated in the same model, two subgroups were observed: 1) 91% reporting low PA and TV watching consistent with the U.S. average across all time points ("Low but increasing PA and Average TV Subgroup"); and 2) 9% reporting high PA declining over time and TV watching consistent with the U.S. average increasing over time ("High but declining PA and Average TV Subgroup).

My subgroup results suggest that group means may be misleading in cancer survivors due to the presence of a small subgroup with high PA. For instance, if only the pre-diagnosis PA mean had been considered, breast cancer survivors as a group would have appeared to be

engaging in 44 more minutes/week of PA (118.6 minutes/week) than 92% of the sample reported (74.3 minutes/week). Future cancer control researchers should be cognizant that means for PA and SB in cancer survivors may be misleading, and thus should consider examining subgroups when significant variance is observed.

My results of differing subgroup patterns for PA and SB also has implications for future intervention development. Specifically, breast cancer survivors with different PA and SB patterns from pre-diagnosis to ten years post-diagnosis may need tailored intervention strategies to increase (or maintain) PA to guideline levels and/or to decrease SB. For example, the "High but Declining PA and Average TV Subgroup" may need an intervention focusing on maintaining PA and decreasing SB (e.g., getting up and walking during commercial breaks or in between shows). However, the "Low but Increasing PA and Average TV Subgroup" may need an intervention focusing on both overcoming barriers to increasing PA and decreasing SB (e.g., walking during commercial or show breaks).

The next logical step toward informing potential intervention strategies is to determine whether PA and SB subgroups are predicted by the same or different theoretical constructs from health behavior theories. Toward an intervention goal, future cohort studies with cancer survivors should consider adding questionnaires assessing theoretical constructs from health behavior theory.

Different theories may be needed to explain the health behaviors of subgroups of breast cancer survivors following different patterns. For instance, the largest subgroup in my study followed a pattern of low but increasing PA and TV watching consistent with the U.S. average. Theories targeting initiation of PA (or reduction of SB) may be best for changing health behaviors in this subgroup. A large body of work has tested PA initiation strategies in

randomized trials with breast cancer survivors (see Speck et al., 2010). Promising theoretical approaches include Social Cognitive Theory (Bandura, 1986), the Theory of Planned Behavior (Ajzen, 1991), and the Transtheoretical Model (Prochaska & DiClemente, 1983). However, no studies to date have tested an intervention targeting both increasing PA and decreasing SB.

A different theory may be necessary for the smaller subgroup who reported a pattern of high PA and TV watching lower than the U.S. average because these breast cancer survivors need to maintain PA, not initiate it. For instance, the Physical Activity Maintenance Theory (Nigg, Borrelli, Maddock, & Dishman, 2008) describes that PA maintenance is determined from individual psychosocial variables (e.g., goal-setting, motivation, barrier and relapse self-efficacy) and contextual constructs (e.g., PA environment and life stresses). More research is warranted to determine which health behavior theory constructs best predict subgroups when PA is estimated by itself, SB is estimated singly, and PA-SB are estimated in the same model.

Moving forward, observational and interventional research with cancer survivors would benefit from incorporating constructs from classic health behavior theories and the Transactional Model of Stress and Coping. Transactional Model constructs would enhance PA and SB research with cancer survivors because it assumes that emotions and affective reactions are influential predictors of health behavior (which allows for unconscious and non-rational explanations of behavior). It also includes individual-level constructs such as differences in the perception of a stressor and constructs assessing social, organizational, and cultural coping resources (e.g., perceived social support and religious coping resources), which may be able to be leveraged to change health behavior. These features of the Transactional Model allow for a richer examination of the functions that health behaviors, such as PA and SB, may serve in the context of women's responses to stressors associated with treatment and recovery from breast cancer.

4.5.4 Limitations

Several dataset limitations are noted. First, breast cancer survivors were asked to recall their pre-diagnosis PA and SB at the initial interview (at approximately six months post-diagnosis). Social desirability bias may have prompted women to recall more PA and less SB prior to their diagnosis. However, in a study with cancer patients, Hawkins et al., (2009) found no relationship between PA recalled at a later date and a measure of social desirability bias. This result suggests that breast cancer survivors in the current study may not have been exaggerating their pre-diagnosis PA and SB.

Second, SB items assessing time spent sitting watching TV have not been validated in cancer patients. Pedisic (2014) critically appraised 54 recent studies regarding their assessment of SB. Almost 60% of these measures had not been previously validated. Given that a SB scale with validation data did not exist until a few years ago, television watching time has been conventionally used as a proxy for leisure-time SB (Clark et al., 2009; Thorp, Owen, Neuhaus, & Dunstan, 2011). Self-reported television viewing time demonstrates moderate to large test–retest correlations across studies, indicating that questionnaires are likely prompting recall in a consistent way (Clark et al., 2009). Adults may have more accurate recall of television watching times than other types of sitting because specific shows or movies can be recalled, which may prompt better recall about leisure sitting time (Clark et al., 2009).

Third, the assessment of PA and SB at approximately six months post-diagnosis was different among the three HEAL sites because USC was brought into the study later than UNM and FHCRC. At USC, PA data for the pre-diagnosis and six months post-diagnosis time points were constructed from a lifetime history collected during a separate case-control study. At UNM and FHCRC, PA was collected with the Modifiable Activity Questionnaire. The same sixteen

exercise activities were used in the PA variable calculation, but different intervieweradministered questionnaires may have introduced differences in reporting.

Data collection of SB was also affected. USC did not collect SB items at enrollment (including pre-diagnosis recall and six-months post-diagnosis) and it could not be constructed from other data. Therefore, data were imputed using thirty variables for multiple imputation. Multiple imputation is a state-of-the-art missing data technique (Enders, 2010b), but future research studies are needed to confirm my results. All African American women were enrolled at the USC site, and thus more research is needed to examine how their SB changes from pre- to post-diagnosis, and whether there are differences from Caucasian and Hispanic breast cancer survivors.

4.5.5 Conclusion and Implications

This is the first study among cancer survivors to simultaneously examine PA and SB trajectories from pre-diagnosis through ten years post-diagnosis. Despite national PA guidelines, over 90% of breast cancer survivors reported a trajectory of low PA and watching TV for 18-19 hours/week from pre-diagnosis through ten years post-diagnosis, potentially putting them at risk for poor cancer outcomes. Future research should examine demographic and clinical characteristics associated with the patterns identified to target subgroups for intervention.

CHAPTER 5. STRESS AND COPING APPRAISALS DIFFERENTIALLY PREDICT LONG-TERM PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR PATTERNS IN BREAST CANCER SURVIVORS

In this chapter, I summarize my results from Aim 2. My objective was to determine which psychosocial constructs from the Transactional Model of Stress and Coping mediate the relationships between demographic and clinical characteristics and subgroups of breast cancer survivors who follow different PA and SB trajectories from pre-diagnosis to ten years postdiagnosis. The PA and SB subgroups identified in Aim 1 (Chapter Four) were used as the outcome variables for Aim 2 in the current chapter. In the next chapter (Chapter Six), I review the implications of my studies for clinical practice and future intervention development with breast cancer survivors.

5.1 Introduction

A breast cancer diagnosis may represent a "teachable moment" where women are more receptive to hearing information about making lifestyle changes to become healthier (Demark-Wahnefried, Aziz, Rowland, & Pinto, 2005). Diagnosis also represents a time where women may begin using coping strategies in response to the stressor of cancer and feelings of vulnerability about their current and future health. One type of coping strategy after diagnosis is to change health behavior, which may be health-promoting (e.g., increasing physical activity in an effort to reduce perceived health risks by becoming healthier) or health-inhibiting (e.g., decreasing physical activity in an effort to avoid physical symptoms, such as fatigue or breast sensitivity, that are unpleasant reminders of cancer). Evidence from fields such as exercise science and health psychology supports the notion that some individuals use physical activity (PA) explicitly for the purpose of coping with a stressor (e.g., Ingledew, Hardy, Cooper, & Jemal, 1996; Park & Iacocca, 2014). Moreover, research with breast cancer survivors offers evidence that is consistent with this function of PA. In a small qualitative study, breast cancer survivors spontaneously mentioned PA as an active coping strategy they employed to enhance feelings of personal control and to increase their physical and mental strength (Drageset, Lindstrom, & Underlid, 2009).

Park and colleagues (Park, Edmondson, Fenster, & Blank, 2008) successfully applied the Transactional Model of Stress and Coping (Lazarus & Folkman, 1987) to examine health behavior changes as coping strategies in response to cancer. They examined cross-sectional reports of positive and negative health behavior changes following diagnosis in 250 cancer survivors (almost 50% breast cancer, mean age: 45 years, 89% Caucasian). Health behaviors included PA, diet, sleep, and stress management. Positive health behavior change following diagnosis was related to social support, sense of control over disease course, meaning in life, and approach coping (a composite index including emotion processing, instrumental support, active coping, and reframing the situation).

Negative health behavior change after a cancer diagnosis was related to a lack of meaning in life and avoidance coping (composite index including denial, behavioral disengagement, and self-blame). Park et al. (2008) did not report on the percentage of cancer survivors who increased their PA after diagnosis. However, their results suggest that the Transactional Model of Stress and Coping is useful for understanding health behavior change in breast cancer survivors and that changes in PA can be predicted from Transactional Model constructs.

Park et al. (2008) also did not assess sedentary behavior (SB: proportion of waking hours spent sitting or reclining), and thus it is unknown if cancer survivors changed their SB as a coping strategy in response to diagnosis. It may be that some breast cancer survivors decrease their SB in an effort to become healthier overall and reduce perceived health risks. For others, SB may increase as part of avoidance coping. For instance, breast cancer survivors may increase the time they spend sitting watching TV because it provides behavioral disengagement from stressors related to cancer, such as active treatment and recovery or anxiety about cancer recurrence. Very little research has been conducted on long-term SB patterns in breast cancer survivors, and no studies to date have focused on explaining changes in SB with a theoretical approach.

In the current study, I used the Transactional Model of Stress and Coping (Lazarus & Folkman, 1987) to explain differences in PA and SB patterns over time for breast cancer survivors. In Chapter Four, I described my findings where two PA subgroups and three SB subgroups were identified for breast cancer survivors reporting different patterns from prediagnosis to ten years post-diagnosis. In the current study, these PA and SB subgroups served as outcome variables in mediation models. Specifically, I examined whether Transactional Model constructs mediated the relationships between demographic, clinical, and treatment-related characteristics and membership in PA and SB subgroups for breast cancer survivors. A brief overview of the Transactional Model of Stress and Coping is described next.

5.1.1 Overview of Transactional Model of Stress and Coping

In their discussion of the Transactional Model, Lazarus and Folkman (1987) describe two types of cognitive and emotional appraisals that are relevant for predicting behavior change: primary and secondary appraisal. They argued that before emotion occurs, individuals make a primary appraisal, which is an automatic assessment of what is happening and what it may mean

for them personally or for loved ones. A situation perceived to be stressful is appraised in terms of harm or loss and future threat (Lazarus & Folkman, 1987). "Harm and loss" are the negative consequences attributed to the stressor that have occurred to date; "threat" is anticipated harm for the future.

Secondary appraisal relates to the perception of whether any resources can be used to manage effects of the stressor, or whether action(s) can be taken to reduce or eliminate the stressor, and if so, which coping strategies might be effective (Lazarus & Folkman, 1987; Lazarus, 1999). The Transactional Model predicts that when stakes are perceived to be high, mobilization of coping resources will occur. Thus, coping strategies are cognitive, affective, and behavioral efforts to manage a stressful situation (Lazarus & Folkman, 1987). In the current study, my aim was to predict breast cancer survivors' membership in PA and SB subgroups based on Transactional Model constructs.

Extrapolating from the Transactional Model of Stress and Coping, a breast cancer survivor may make a primary appraisal about cancer (consciously or unconsciously) through threat appraisal (anxiety about recurrence) and harm appraisal (perceived health and perceived impact that breast cancer has already had on her life's goals, commitments, and loved ones). The greater the perceived "stakes" of the situation or stressor, the more intense her appraisal of threat and harm is predicted to be. Her secondary appraisal of available coping resources may include family and friends she can confide in (perceived social support), religiosity/spirituality as a coping resource in terms of a way of understanding adversity and potentially providing hope or tangible support, and her own personality characteristics such as the tendency to expect a positive outcome (optimism). These coping resources may be mobilized in order to reduce the

perceived threat to her current and future health. The implications of the Transactional Model for explaining my subgroup findings from Study 1 (Chapter Four) are described next.

5.1.2 Using the Transactional Model to Explain Subgroup Findings from Study 1 (Chapter 4)

Transactional Model processes may explain my results in Study 1 (described in Chapter 4) where two subgroups of breast cancer survivors reported different PA patterns from prediagnosis to ten years post-diagnosis. The smaller PA subgroup identified in Study 1 ("High but Declining PA subgroup") was comprised of 8% of breast cancer survivors who met PA recommendations at all assessments but experienced a drop in PA of approximately 200 minutes from pre-diagnosis to six months post-diagnosis and then never recovered their pre-diagnosis PA through ten years post-diagnosis.

In Chapter 4, I showed that the "Low but Increasing PA Subgroup" (92%) did not meet national PA guidelines from pre-diagnosis through ten years post-diagnosis. However, this subgroup did increase their PA at six months post-diagnosis and maintained the higher PA level through five years post-diagnosis, suggesting that they may have been experiencing different levels of perceived threat, harm, and coping resources than the "High but Declining PA Subgroup," and thus exhibited a different pattern of PA over time. For example, the "Low but Increasing PA Subgroup" may have had higher perceived threat and harm appraisals (higher anxiety about recurrence, worse perceived health, and more negative impact of cancer), and thus increased their PA after diagnosis to avoid perceived future health threats. The Transactional Model predicts that when a primary appraisal is activated, a secondary appraisal of coping resources also occurs. For instance, the "Low but Increasing PA Subgroup" may have considered their coping resources such as individual-level resources (optimism), interpersonal resources (social support), or religious coping resources (making sense of adversity, resources available through their faith communities, etc.) as resources they could use to increase their PA and reduce future health threat. If this is the case, then membership in the "Low but Increasing PA Subgroup" should be related to both primary and secondary appraisal variables.

The Transactional Model processes also make sense for why the "High but Declining PA Subgroup" decreased their PA at six months post-diagnosis and then maintained this lower PA level through ten years post-diagnosis. For instance, the "High but Declining PA Subgroup" may not have perceived a long-lasting threat to their current and future health, and therefore experienced low anxiety about recurrence and harm, and in turn did not make changes to their behavior. The Transactional Model predicts that if primary appraisal is not activated, then a secondary appraisal of coping resources will not occur. In other words, if the "High but Declining PA Subgroup" did not perceive threat and harm, then they would not have considered their coping options. If this is the case, then membership in the "high but Declining PA Subgroup" should not be related to primary and secondary appraisal variables. A major strength of my study is that I was able to examine whether these Transactional Model constructs mediated the relationships between demographic, clinical, and treatment-related characteristics and membership in PA and SB subgroups for breast cancer survivors.

Similar transactional processes may also explain the three patterns of SB that I found in Study 1 (described in Chapter 4). The first SB subgroup (18%) reported watching fewer TV hours/week than the U.S. average at pre-diagnosis and steadily increased through ten years postdiagnosis ("Low but Increasing TV subgroup"). Perhaps the "Low but Increasing TV subgroup" increased their TV watching over time because their perceived threat and harm were low (primary appraisal), and thus they did not need to consider coping resources to deal with a

stressor. Membership in the "Low but Increasing SB subgroup" should not be related to primary and secondary appraisal variables.

The second SB subgroup, "High but Decreasing TV Subgroup" (17%), reported greater TV hours per week than the U.S. average at all assessments, with increases at six months and ten years post-diagnosis but a steady decline between six months and five years post-diagnosis. The "High but Decreasing Subgroup" may have perceived higher threat and harm appraisals (higher anxiety about recurrence, worse perceived health, and more negative impact of cancer) and higher coping resources (higher optimism, religiosity, or social support) and in turn decreased their TV watching between six months and five years post-diagnosis . If this is the case, then membership in the "High but Decreasing Subgroup" should be related to primary and secondary appraisal variables.

Finally, the Transactional Model may also explain the flat trajectory of the "U.S. Average TV Subgroup" (66%) who reported consistently watching TV for 19-20 hours per week from pre-diagnosis to ten years post-diagnosis. Transactional Model processes predict that behavior will not change when perceived threat or harm is low. The "U.S. Average TV Subgroup" may not have perceived a threat to their current and future health, and thus did not experience anxiety about recurrence and perceived harm. They may have perceived that their health is fine and that cancer did not have a large impact on their life goals. In this case, no secondary appraisal of coping resources would be needed because cancer was not perceived to be a threatening or stressful situation. It is also possible that the perception of threat and harm from cancer was short-lived for this subgroup, and thus did not affect long-term health behavior such as TV watching.

In the next section, I describe my a priori models developed to test whether Transactional Model constructs mediated the relationships between the demographic, clinical, and treatmentrelated characteristics and membership in PA and SB subgroups identified in Study 1 (Chapter 4).

5.1.3 Hypothesized Mediation Model

In addition to Transactional Model constructs, my a priori model also included demographic (race/ethnicity, marital status, working status, education), clinical (disease stage, fatigue, comorbid conditions, body mass index), and treatment-related (mastectomy, radiation, chemotherapy, hormone therapy) characteristics because prior studies had found significant relationships with my proxy variables for primary and secondary appraisals for breast cancer survivors (for primary appraisal predictors, see Crist & Grunfeld, 2013; Hawkins et al., 2010; Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005; Alfano et al., 2006) (for secondary appraisal predictors, see Bloom et al., 2013; Drageset & Lindstrom, 2005). I also included demographic, clinical, and treatment-related characteristics in my a priori models to take a public health approach to better understanding the determinants of breast cancer survivors' PA and SB patterns.

There was also empirical evidence supporting associations between my proxy variables for primary and secondary appraisal and PA and SB. Breast cancer survivors who reported lower primary appraisal indicators (anxiety about recurrence, higher perceived health status, or higher perceived impact of breast cancer) or higher secondary appraisal indicators (perceived resources: optimism, religiosity/spirituality, or social support) increased their PA at a greater rate, and sustained lifestyle changes longer, than survivors lower in these characteristics when these variables examined separately across studies (Costanzo, Lutgendorf, & Roeder, 2011; Hawkins et al., 2010; Park et al., 2008; Park & Gaffey, 2007; Pinto et al., 2002). Therefore, my a priori

model hypothesized that primary and secondary appraisals would mediate the relationships between demographic, clinical, and treatment-related characteristics and PA and SB subgroup membership.

I also hypothesized direct relationships to PA for race/ethnicity, education, and body mass index because there is strong evidence suggesting that Caucasian race, higher education, and lower body mass index are correlated with higher PA levels in breast cancer survivors, even after controlling for other demographic and clinical characteristics (e.g., Hawkins et al., 2010; Irwin et al., 2003; Patterson et al., 2003; Pinto et al., 2002; Kampshoff et al., 2014). See Figure 5.1 for my hypothesized PA model.

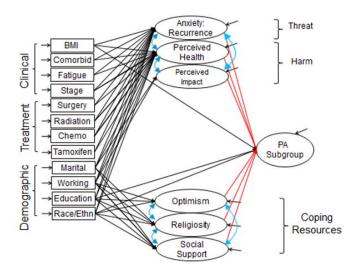


Figure 5.1. Hypothesized physical activity model.

In the next section, I further describe my hypotheses and rationale for each pathway in the a priori models.

5.2 Hypotheses

In this section, I first list the specific aim, describe the rationale for hypotheses, and finally list hypotheses for each aim. For mediation hypotheses, diagrams accompany hypotheses. **5.2.1 Aim 2a**

<u>Aim 2a</u>: Determine which psychosocial constructs from the Transactional Model of Stress and Coping mediate relationships between demographic, clinical, and treatment-related characteristics and subgroup membership for breast cancer survivors following different PA trajectories from pre-diagnosis through ten years post-diagnosis

The theoretical rationale for my a priori models was described in the introduction, and thus is not reviewed again. I also searched the empirical literature for correlational studies informing each pathway in Figure 5.2 because my mediation model has never been tested as a whole.

Starting with my PA subgroup outcome and working backward in Figure 5.2, PA has been correlated with primary and secondary appraisals in previous studies. Breast cancer survivors who reported lower anxiety about recurrence, higher perceived health status, or higher perceived impact of breast cancer (primary appraisal indicators) or higher optimism, religiosity/spirituality, or social support (secondary appraisal indicators) increased their PA at a greater rate, and sustained lifestyle changes longer, than survivors lower in these characteristics when examined separately across studies (Costanzo, Lutgendorf, & Roeder, 2011; Hawkins et al., 2010; Park et al., 2008; Park & Gaffey, 2007; Pinto et al., 2002).

Perceived social support, in particular, has been consistently associated with PA. In a study examining PA trajectories in Canadian breast cancer survivors, Brunet et al. (2014) found that anxiety about recurrence and perceived social support were better predictors of PA subgroups than demographic and clinical correlates. Perceived support from family was a

significant predictor of PA rate of change but not baseline PA (Brunet al., 2014). Breast cancer survivors with greater perceived family support reported increased PA during the first two years and gradually decreased during the subsequent three years. In contrast, survivors with lower perceived family support reported stable, higher PA during the first two years and a steady decrease thereafter. Perceived support from friends was not a significant predictor of PA at the time of treatment nor rate of change. Additionally, Park et al. (2008) found that perceived social support was related to making positive health behavior changes after a cancer diagnosis.

In Figure 5.2, primary and secondary appraisals are mediators, and thus are hypothesized to be predicted by demographic, clinical, and treatment-related characteristics. Prior studies showed that demographic, clinical, and treatment-related characteristics had important correlational relationships with my proxy variables for primary appraisal (anxiety about recurrence, perceived health, and perceived impact of cancer). The most consistent demographic predictors of anxiety about recurrence included younger age, lower educational level, being partnered, and Caucasian race and/or Hispanic ethnicity (Crist & Grunfeld, 2013; Deimling et al., 2006; Janz et al., 2011; Simard & Savard, 2009; Simard, Savard, & Ivers, 2010; Vickberg, 2003).

The evidence is mixed for relationships between anxiety about recurrence and clinical characteristics. Disease stage has been inconsistently related to anxiety about recurrence for breast cancer survivors with four studies finding no relationship and three studies finding that higher disease stage was associated with greater anxiety about recurrence (Ganz et al., 1993; Van den Beuken-van Everdingen et al., 2008; Mellon et al., 2007; Northouse, 1981; Johnson Vickberg, 2001; Park, Cho, Blank, & Wortmann, 2013; Rakovitch et al., 2003). The most consistent treatment-related characteristic associated with higher anxiety about recurrence was

chemotherapy (Crist & Grunfeld, 2013; Deimling et al., 2006; Janz et al., 2011; Mehnert et al., 2009; Mellon et al., 2007). Receiving a mastectomy has been inconsistently related to anxiety about recurrence with four studies finding no relationship and four studies with mixed results (Harrison et al., 2009; Irwin et al., 2003; Andrykowski et al., 2007; Devoogdt et al., 2010; Hawkins et al., 2010; Hong et al., 2007; Patterson et al., 2003; Pinto et al., 2002).

Better perceived health has been associated with younger age, higher education, being partnered, and working outside the home (Ashing-Giwa, Tejero, Kim, Padilla, Hellemann, 2007; Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005; Schmitz, 2011). The most consistent clinical predictors of perceived health status have been comorbid health conditions and fatigue (Mols, Vingerhoets, Coebergh, & van de Poll-Franse, 2005; Montazeri, 2008). Breast cancer survivors receiving more extensive treatment, such as chemotherapy, have reported worse perceived health than survivors who did not receive chemotherapy (Ganz et al., 2011).

A more positive perception of the impact of breast cancer has been associated with older age and being partnered (Alfano et al., 2006). Women ages 60 years and older at diagnosis reported less impact from breast cancer than younger survivors for educational plans, work life, diet, family plans, social life, finances, exercise, romantic relationships, retirement plans, and ability to be a caregiver (Ganz et al., 2002).

My hypothesized proxy variables for secondary appraisal (optimism, religiosity, and perceived social support) have also been correlated with demographic characteristics but have not been examined with respect to clinical or treatment-related characteristics affecting them. Greater optimism was correlated with older age and higher education (Ek et al., 2004; Palgi et al., 2011; Benyamini et al., 2005). Religiosity/spirituality was correlated with older age (Beeghley, 1981). In prior studies, the correlation between education and religiosity/spirituality

has varied by race, such that higher religiosity/spirituality was reported by Caucasian individuals with higher education and African American individuals with lower education (Beeghley et al., 1981; Koenig, 1998). Higher perceived social support was associated with being partnered, younger age, and higher education (Bloom et al., 2013; Drageset & Lindstrom, 2005).

Finally, I also hypothesized direct relationships to PA for race/ethnicity, education, and body mass index because there is strong evidence suggesting that Caucasian race, higher education, and lower body mass index are correlated with higher PA levels in breast cancer survivors, even after controlling for other demographic and clinical characteristics (e.g., Hawkins et al., 2010; Irwin et al., 2003; Patterson et al., 2003; Pinto et al., 2002; Kampshoff et al., 2014).

<u>Hypothesis 2.a.1</u>: Demographic, clinical, and treatment-related characteristics will be associated with primary appraisal variables of threat (anxiety about cancer recurrence) and harm (perceived health and impact of cancer), such that lower education, not being married/partnered, not working, African American or Hispanic ancestry, greater comorbid conditions, more fatigue, and chemotherapy will be associated with higher threat and harm appraisal (direct paths).

- Exploratory: higher body mass index (BMI), higher disease stage, mastectomy, tamoxifen (direct paths)

<u>Hypothesis 2.a.2</u>: Demographic variables will be associated with secondary appraisal variables of perceived coping resources (optimism, religiosity, and perceived social support), such that greater education and being married/partnered (direct paths), but not clinical and treatment-related characteristics, will be related to greater perceived coping resources.

- Exploratory: Caucasian ancestry (direct path), working status

<u>Hypothesis 2.a.3</u>: Primary and secondary appraisal will be associated with each other and with longitudinal PA trajectories (direct paths).

<u>Hypothesis 2.a.4</u>: Primary and secondary appraisals will partially mediate the relationships between demographic, clinical, and treatment characteristics and ten-year PA patterns for breast cancer survivors (see Figure 5.2).

- Demographic characteristics (education, married/partnered, race/ethnicity, working)
 will be associated with all mediators
- Clinical characteristics (BMI, comorbid conditions, fatigue, and disease stage) will be associated with primary appraisal variables (anxiety about recurrence, perceived health, and perceived impact of cancer) but not secondary appraisal variables (optimism, religiosity, and perceived social support)
- Treatment-related characteristics (surgery, radiation, chemotherapy, and tamoxifen)
 will be associated with primary appraisals (anxiety about recurrence, perceived
 health, and perceived impact) but not secondary appraisals (optimism, religiosity, and
 perceived social support)
- Note that I hypothesized that I would <u>not</u> find age at diagnosis to be a significant predictor of mediators because age at diagnosis was limited to 35-64 years in this sample. When a variable is restricted in range, the variation is also restricted, and thus the probability of finding a significant correlation is similarly reduced (Nie & Chu, 2011). In other words, I am hypothesizing that within this age range, there is no relationship between age and the mediators. I included age at diagnosis in the initial models to confirm the non-significance.

<u>Hypothesis 2.a.5</u>: Direct associations between predictors and PA subgroups are hypothesized for BMI, race/ethnicity, and education (see Figure 5.2).

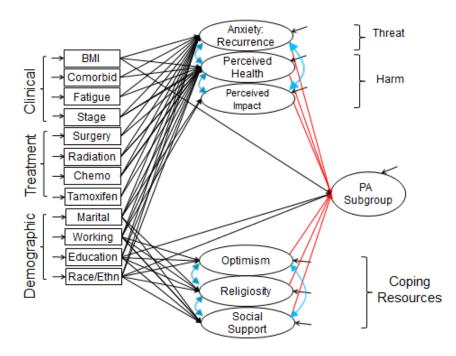


Figure 5.2. Hypothesized structural equation model for physical activity.

5.2.2 Aim 2b

<u>Aim 2b</u>: Determine which psychosocial constructs from the Transactional Model of Stress and Coping mediate relationships between demographic, clinical, and treatment-related characteristics and subgroup membership for breast cancer survivors following different SB trajectories from pre-diagnosis through ten years post-diagnosis

Correlations between predictors (demographic, clinical, and treatment-related characteristics) and mediators (primary and secondary appraisals) in the SB model were expected to be similar to PA reviewed in the previous section, and thus are not reviewed again. See

Section 5.2.2 for a description of how I used Transactional Model processes to hypothesize that SB subgroup membership would be predicted by primary and secondary appraisal variables.

I also hypothesized direct relationships between SB and race/ethnicity, education, and body mass index because several studies have observed significant correlations for breast cancer survivors (Rogers, 2011; Sabiston et al., 2014; Irwin et al., 2003; Lynch et al., 2010). No empirical research exists on the relationships between SB, tamoxifen, being partnered, primary appraisals (anxiety about recurrence, perceived health, and perceived impact of breast cancer), and secondary appraisals (optimism, religiosity, social support).

<u>Hypothesis 2.b.1</u>: Demographic, clinical, and treatment-related characteristics will be associated with primary appraisal variables of threat (anxiety about recurrence) and harm (perceived health and impact of cancer), such that lower education, not being married/partnered, not working, African American or Hispanic ancestry, greater comorbid conditions, more fatigue, and receipt of chemotherapy will be associated with higher threat and harm appraisal (direct paths).

- Exploratory: higher BMI, higher disease stage, receipt of mastectomy, receipt of tamoxifen (direct paths)

<u>Hypothesis 2.b.2</u>: Demographic characteristics will be associated with secondary appraisal variables of perceived coping resources (optimism, religiosity, and social support), such that higher education and being maried/partnered will be associated with greater perceived coping resources (direct paths), but not clinical and treatment-related characteristics.

- Exploratory: Caucasian ancestry (direct path)

<u>Hypothesis 2.b.3</u>: Primary and secondary appraisal will be associated with each other and with longitudinal SB subgroups (direct paths).

<u>Hypothesis 2.b.4</u>: Primary and secondary appraisals will partially mediate the relationships between demographic, clinical, and treatment characteristics and 10-year SB patterns for breast cancer survivors (see Figure 5.3).

- Demographic characteristics (education, being married/partnered, working, and race/ethnicity) will be associated with all mediators
- Clinical characteristics (BMI, comorbid conditions, fatigue, and disease stage) will be associated with primary appraisal variables (anxiety about recurrence, perceived health, and perceived impact of cancer) but not secondary appraisal variables (optimism, religiosity, and social support)
- Treatment-related characteristics (surgery, radiation, chemotherapy, and tamoxifen)
 will be associated with primary appraisals (anxiety about recurrence, perceived
 health, and perceived impact) but not secondary appraisals (optimism, religiosity, and socials support)
- Note that I hypothesized that I would <u>not</u> find age at diagnosis to be a significant predictor of mediators because age at diagnosis was limited to 35-64 years in this sample. When a variable is restricted in range, the variation is also restricted, and thus the probability of finding a significant correlation is similarly reduced (Nie & Chu, 2011). In other words, I hypothesized that there would be no relationship between age and the mediators. I included age at diagnosis in the initial models to confirm the non-significance.

<u>Hypothesis 2.b.5</u>: Direct associations between predictors and SB subgroups were predicted for BMI, fatigue, race/ethnicity, and education (see Figure 5.3).

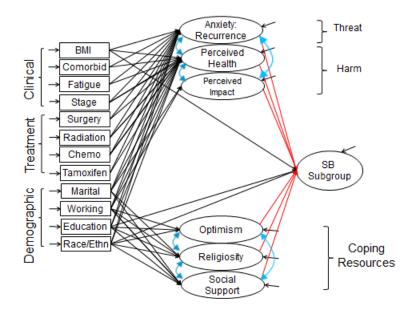


Figure 5.3. Hypothesized structural equation model for sedentary behavior subgroups.

5.2.3 Aim 2c

<u>Aim 2c</u>: Determine whether different Transactional Model constructs mediate the relationships between demographic, clinical, and treatment-related charactersistics and subgroups when PA and SB are estimated in the same model (rather than modeled separately)

Modeling SB individually and then simultaneously with PA is important because SB has a weak correlation with PA, which means that SB is not simply the opposite of PA (George et al., 2013a; Tremblay, Colley, Saunders, Healy, & Owen, 2010; Santos et al., 2012). PA and SB may have different predictors and influence health through different pathways (Katzmarzyk, 2010). Given that predictors are correlated, there is a finite amount of variance that can be used to explain PA and SB. Thus, the mediators may change when PA and SB are estimated in the same model. I hypothesized that all six mediators would still be significant for PA. However, I hypothesized that the SB mediators would include only perceived harm (perceived health and perceived impact) and a coping resource (social support).

<u>Hypothesis 2.c.1</u>: PA and SB subgroups will be associated with each other.

<u>Hypothesis 2.c.2</u>: When estimated in the same model, different Transactional Model mediators will predict SB than PA. Specifically, primary appraisals (anxiety about recurrence, perceived health, and perceived impact) and secondary appraisals (optimism, religiosity, and social support) will be significant mediators for PA. Fewer mediators are hypothesized for SB: two primary appraisals (perceived health and perceived impact) and one secondary appraisal (social support). See Figure 5.4.

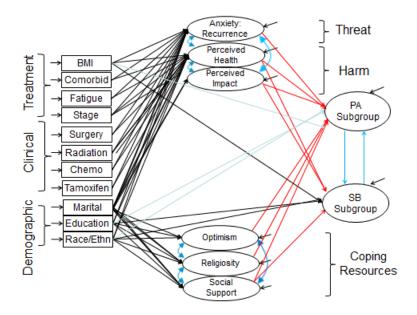


Figure 5.4. Hypothesized structural equation model when physical activity (PA) and sedentary behavior (SB) were estimated together.

5.3 Methods

5.3.1 Participants

The sample in the current study was identical to Chapter Four. Briefly, the NCI-funded Health, Eating, Activity, and Lifestyle (HEAL) study is a cohort of women diagnosed with breast cancer between 1995 and 1999 (stages 0-IIIA). A subset of 938 survivors was analyzed who were ages 35-64 years at the time of diagnosis. Women newly diagnosed with breast cancer were recruited from cancer registries in New Mexico (42%), California (36%), and Washington (21%). Approximately half (49%) reported being non-Hispanic Caucasian, 36% African American, and 12% Hispanic. A quarter (27%) of the sample had a high school education or less and 63% were married or living with a partner at six months post-diagnosis.

Three-quarters of the women (76%) were diagnosed at an early stage (0-IIA) and the average age at diagnosis was 50.9 years (SD=7.5). Almost two-thirds (63%) received breast-conserving surgery, 35% mastectomy, 51% radiation, and 36% chemotherapy. Of the 938 women, 769 (82%), 667 (71%), and 552 (59%) completed the two-, five-, and ten-year follow-ups, respectively. This retention rate is consistent with other cohort studies of breast cancer survivors (e.g., Ganz, Desmond, Leedham, Rowland, Meyerowitz, & Belin, 2002). For the current study, IRB exemption was granted from the University of North Carolina at Chapel Hill.

5.3.2 Measures

With the exception of appraisal variables, data collection and questionnaires were identical to those described in Chapter Four. See Table 5.1 below for a summary of data collection timing.

	Recalled Pre- Diagnosis	6 Months	24 Months	39 Months	60 Months	120 Months
РА	X	Х	Х		Х	Х
SB	X (2/3 Sites)	X (2/3 sites)	Х		Х	Х
Demographics		Х	X (updates)		X (updates)	X (updates)
Treatment	N/A	Х	X (updates)		X (updates)	X (updates)
Comorbid Conditions (Sum)		X (Medical Records)	X (Self- Report)			
Comorbid Conditions that Limit Activities			X (Self- Report)			
BMI (self-report)		Х			Х	Х
Fatigue (Piper Fatigue Scale-12)				Х		
Disease Stage	N/A	Х				
Perceived Health		Х		Х		Х
Social Support		X (Recalled)		Х		
Religiosity Optimism				Х		
Anxiety about Recurrence, Perceived Impact				Х		

Table 5.1. Summary of HEAL Data Collection Timing

Primary and Secondary Appraisal Variables

New variables added in this chapter include proxy variables for primary appraisal (anxiety about recurrence, perceived health, perceived impact of cancer) and secondary appraisal (optimism, religiosity, and social support). These mediators were chosen from the existing HEAL dataset that best represented Transactional Model constructs.

Anxiety about Recurrence

The Fear of Recurrence Questionnaire (FRQ, Northouse, 1981) was used to assess anxiety about recurence at 39 months post-diagnosis. The original questionnaire has 22 items. In order to limit respondant burden, HEAL administered six items: "I would like to feel more certain about my health," "I worry that my cancer will return," "I feel there is little need to worry about my future health status" (reverse-coded), "I am bothered by the uncertainty of my health status," "When I think about my future health status, I feel some uneasiness," and "I am preoccupied with thoughts of the cancer returning." Response options ranged from one (strongly disagree) to five (strongly agree), and thus higher scores represented higher fear of recurrence. Scores ranged from 6-30 and the mean in the HEAL sample was 19.3 (SD = 5.2, median = 20.0), indicating moderate anxiety about recurrence, on average, at 39 months post-diagnosis. Cronbach's alpha was favorable at 0.82. Research has demonstrated its construct and content validity across a range of treatment modalities for breast cancer (Mellon et al., 2007; Hilton, 1989; Stanton, Danoff-Burg, & Huggins, 2002; Thewes, Butow, Zacharie, Christensen, Simard, & Gotay, 2012; Simard et al., 2013).

Perceived Health Status

A commonly used general health item was used to assess perceived health at six and 39 months and ten years post-diagnosis: "How would you describe your general health status?" Response options ranged from one (excellent) to five (poor), and thus a higher score indicated worse perceived health. The mean score at six and 39 months and ten years post-diagnosis was 2.10 (SD = 0.94), 2.48 (SD = 1.02), and 2.45 (SD = 1.00), respectively, indicating generally positive perceived health.

Perceived Impact of Breast Cancer

The Brief Cancer Impact Assessment (BCIA; Alfano et al., 2006; Ganz et al., 2002) was used as a direct assessment of outcome harm and benefit appraisal at 39 months post-diagnosis. Breast cancer survivors reported how much of an impact their cancer experiences had had in fifteen areas. Response options included no impact (0), very positive impact (1), somewhat positive impact (2), somewhat negative impact (3), very negative impact (4).

Alfano et al., (2006) conducted an exploratory factor analysis in the HEAL sample for 783 breast cancer survivors who were ages 29 to 70 or more years at diagnosis (in the current study, the age range was 35-64 years). Alfano et al. (2006) found four subscales: caregiving/financial, exercise/diet, social/emotional, and religiosity/spirituality. Internal consistency coefficients in the current sample were similar to the Alfano et al. (2006) results for caregiving/finances (Alfano: 0.77 vs. current: 0.72) and social/emotional (Alfano: 0.75 vs. current: 0.73) subscales, but lower for exercise/diet (Alfano: 0.63 vs current: 0.49) and religiosity (Alfano: 0.81 vs. current: 0.64) subscales.

Given the low internal consistency values for the exercise/diet and religiosity subscales, an exploratory factor analysis was run with the current sample for up to four factors. One item had to be removed due to low variability (impact on religious activities where 49% reported no impact, 26% were missing due to attrition, 23% reported a positive impact, and only 2% reported a negative impact), and thus the EFA was run with 14 items. A four-factor solution also fit the current data but slightly different factors were found.

A four-factor solution fit the data better than a three-factor solution ($\chi^2 = 60.2$, df=11, p < .0001). Eigen values were above 1.0 for the first four factors and the fifth factor was below one, suggesting a four-factor solution (4.3, 1.2, 1.1, 1.0, 0.9, respectively) (Devellis, 2012).

Additional fit information is also consistent with a four-factor solution: decreasing chi-square values, root mean square error of approximation (RMSEA, criterion: <0.08), Comparative Fit Index (CFI, criterion: >0.90), and Tucker-Lewis Index (TLI, criterion: >0.90) (see Table 5.2).

ſ	Number	Chi-	Degrees of	RMSEA	CFI	TLI
	of Factors	Square	Freedom	KNISLA	CIT	1 L1
	1	372.8***	77	0.07	0.85	0.83
ſ	2	235.2***	64	0.06	0.91	0.88
ſ	3	147.5***	52	0.05	0.95	0.92
ſ	4	87.3***	41	0.04	0.98	0.95
**	**p<.001					

Table 5.2. Exploratory Factor Analysis Results for the Brief Cancer Impact Assessment

In the current study, six items loaded on Factor 1: family plans (finding a partner, divorce, marriage, kids) (factor loading: 0.68), social life (0.46), living arrangements (0.31), love life (0.68), religious beliefs (0.33), and psychological needs (0.56). Factor 1 represents important relationships such as being a partner, parent, friend, and being part of a faith community (Cronbach's alpha: 0.72). The score range was 0-24 with a mean score of 5.5 (4.7), indicating low perceived impact on the caregiving/financial domain. Two items loaded on Factor 2: diet (0.42) and exercise (0.72). Factor 2 represents diet/exercise (Cronbach's alpha: 0.49). The score range was 0-8 with a mean score 1.5 (1.5), indicating low perceived impact on diet and exercise.

Four items loaded on Factor 3: work life or career (factor loading: 0.32), financial situation (0.49), retirement plans (0.76), and ability to retain or change health care insurance (0.37). Factor 3 represents work life and financial stability (Cronbach's alpha: 0.66). The score range was 0-16 with a mean score of 3.4 (3.8), indicating low perceived impact on work life and financial stability. Two items loaded on Factor 4: ability to care for or provide for your children (factor loading: 0.62) and ability to be a caregiver to others (0.58). Factor 4 represents ability to

be a caregiver (Cronbach's alpha: 0.63). The score range was 0-8 with a mean score of 1.2 (1.9), indicating low perceived impact on ability to be a caregiver. The four factors suggested by the exploratory factor analysis in this sample were used in mediation analyses.

Optimism

Optimism was measured by the Life Orientation Test (LOT; Scheier & Carver, 1985), a widely used self-report measure of dispositional optimism. Three items are positively worded (e.g., "Overall, I expect more good things to happen to me than bad") and three items are negatively worded (e.g., "I hardly ever expect things to go my way"). Response options ranged from one (strongly disagree) to five (strongly agree), and thus higher scores represented higher optimism. After reverse-coding the negatively worded items, the sum was computed to yield a score with a possible range from 6-30. The mean LOT score in the HEAL sample was 23.8 (SD = 3.8, Median = 24.0), which indicated moderate-high optimism, on average (Cronbach's alpha = 0.78).

Religiosity/Spirituality

The Duke Religion Index (Koenig, Parkerson, & Meador, 1997) was used to assess religiosity/spirituality in terms of organizational, individual, and intrinsic religiosity. The items include: 1) "How often do you attend faith community or other religious meetings?" (*More than once a week* [6], Once a week [5], A few times per month [4], A few times per year [3], Once a *year or less* [2], or Never [1]); 2) "How often do you spend time in private religious activities, such as prayer, meditation or Bible study?" (*More than once a day* [6], Daily [5], Two or more *times per week* [4], Once a week [3], A few times per month [2], Rarely or Never [1]); 3) "In my life, I experience the presence of God or the Divine" (*Definitely true* [5], Tends to be true [4], Unsure [3], Tends not to be true [2], Definitely not true [1]); 4) "My religious beliefs are what really lie behind my whole approach to life" (*Definitely true* [5], *Tends to be true* [4], *Unsure* [3], *Tends not to be true* [2], *Definitely not true* [1]); and 5) "I try hard to use my religion in all aspects of my life" (*Definitely true* [5], *Tends to be true* [4], *Unsure* [3], *Tends not to be true*

[2], Definitely not true [1]). Thus, higher scores reflected higher religiosity. Scores were summed to reflect a woman's level of religiosity with a possible range of 5-27. The mean Duke Religion Index score was 11.6 (SD = 5.8, median = 10.0), which indicated a moderate level of religiosity/spirituality (Cronbach's alpha = 0.90).

Social Support

Maunsell and colleagues' Social Support Scale (Maunsell, Brisson, & Deschenes, 1995) was used to assess perceived social support. Each respondent indicated the number of individuals that she confided in at the time of diagnosis (recalled support) and "currently" at 39 months post-diagnosis. These two variables were used as a proxy for social network size and entered into models as a time-varying covariate. The range of scores was zero to 11 or more and the mean in the HEAL sample was 2.0 (SD = 0.8, median = 2.0), indicating that, on average, breast cancer survivors considered two individuals to be confidants. See Table 5.3 for a summary of primary and secondary variables.

Measure (Acronym): Authors (Year)	# Items	Response Options	Higher Score Indicated	Possi- ble Range	Observed Range	Mean (SD)	Cron- bach's Alpha	% Missing Data
Fear of Recurrence Question- naire (FRQ): Northouse (1981)	6	Strongly agree (1) to Strongly Disagree (5)	More fear of recurrence	6-30	<u>39</u> <u>Months:</u> 6-30	<u>39</u> <u>Months</u> : 19.4 (5.3)	0.82	242 (26%)
How would you describe your health status?: Ware & Sherbourne, 1992	1	Excellent (5), Very Good (4), Good (3), Fair (2), Poor (1)	Worse perceived health [@]	1-5	1-5	$\begin{array}{r} \underline{6} \\ \underline{Months:} \\ 3.9 (0.9) \\ \underline{39} \\ \underline{Months:} \\ 3.5 (1.0) \\ \underline{10} \\ \underline{Years:} \\ 3.5 (1.0) \end{array}$	N/A	<u>6</u> <u>Months</u> : 340 (36%) <u>39</u> <u>Months</u> : 242 (26%) <u>10</u> <u>Years</u> : 389 (41%)
Brief cancer Impact Assessment (BCIA): Important relationships subscale	6	No Impact (0), Very Positive Impact (1), Somewhat		0-24	<u>39</u> <u>Months:</u> 0-24	<u>39</u> <u>Months:</u> 5.5 (4.7)	0.72	
BCIA: Diet/ exercise	2	Positive Impact (2), Somewhat	More negative impact	0-8	<u>39</u> <u>Months:</u> 0-8	<u>39</u> <u>Months:</u> 1.5 (1.5)	0.49	242 (26%)
BCIA: Work life and financial stability	4	 Negative Impact (3), Very Negative Impact (4) 	-	0-16	<u>39</u> <u>Months:</u> 0-16	<u>39</u> <u>Months:</u> 3.4 (3.8)	0.66	
BCIA: caregiver subscale	2			0-8	<u>39</u> <u>Months:</u> 0-8	<u>39</u> <u>Months:</u> 1.2 (1.9)	0.63	
Life Orientation Test (LOT): Scheier & Carver, 1985	6	Strongly Disagree (1) to Strongly Agree (5)	Higher optimism	6-30	<u>39</u> <u>Months:</u> 6-30	<u>39</u> <u>Months:</u> 23.9 (3.8)	0.78	242 (26%)

Table 5.3. Summary of Primary and Secondary Appraisal Measures

Measure (Acronym): Authors (Year)	# Items	Response Options	Higher Score Indicated	Possi- ble Range	Observed Range	Mean (SD)	Cron- bach's Alpha	% Missing Data
Social Support Scale: Maunsell, Brisson, & Desch-enes (1995)	2	0-11+	Confided in more people (larger confidante network) [@]	0-11+	<u>6 months</u> post-dx): 0-11 <u>39</u> <u>Months</u> post-dx: 0-11	$ \underbrace{\frac{6}{\text{months}}}_{\text{post-dx:}} \\ 4.0 \\ (0.8) \\ \underbrace{\frac{39}{\text{Months}}}_{\text{post-dx:}} \\ 4.1 \\ (0.9) $	0.94	<u>6 months</u> <u>post-dx</u> : 243 (26%) <u>39</u> <u>months</u> <u>post-dx</u> : 243 (26%)
Duke Religiosity Scale (Koenig, Parkerson, & Meador, 1997)	5	>Once a day [6], Daily [5], Two+ times per week [4], Once a week [3], Few times per month [2], Rarely or Never [1]	Higher religisoity	5-27	<u>39 months</u> <u>post-dx</u> : 5-27	<u>39</u> <u>months</u> <u>post-dx</u> : 11.6 (5.8)	0.90	<u>39</u> months post-dx: 243 (26%)

Table 5.4 summarizes the properties of the questionnaires used to assess PA, SB, and demographic, clinical, and treatment-related variables. If a variable was measured at two or time time points, the variable was entered into models in MPLUS as a time-varying variable.

Table 5.4. Summary of Demographic, Clinical, and Treatment-Related Variables

Construct	Measure (Acronym)	# Items	Response Options	Higher Score Indicated	Time- Vary- ing?	% Missing Data
Age at Diagnosis			Continuous		No	0
Race/ Ethnicity	Demographic Questionnaire	6	Caucasian, African American, Asian, American Indian, "Other", Hispanic (ethnicity)		No	0
Education			Less than high school, high school, some college, college, graduate	-	No	0

Construct	Measure (Acronym)	# Items	Response Options	Higher Score Indicated	Time- Vary- ing?	% Missing Data
Marital Status	Demographic - Questionnaire	6	Never married, Married/ living with partner, divorced, separated, widowed		Yes	<u>6 months</u> : 0 <u>2 years</u> : 168 (18%) <u>5 years</u> : 271 (29%) <u>10 years</u> : 392 (42%)
Working Status		0	Working, On leave, Unem-ployed, Retired/ Disabled		Yes	<u>6 months:</u> 345 (37%) <u>2 years:</u> 166 (18%) <u>10 years:</u> 390 (42%)
Comorbid Conditions (Clinical)	Abstracted from Medical Records	16	Yes/no	More comorbid conditions in medical record	Yes	0
Comorbid Conditions (Clinical)	Has a doctor or other health professional ever told you that you have	16	Yes/no	More comorbid conditions self- reported	Yes	166 (18%)
Comorbid Conditions that Affect Activities (Clinical)	Are any of your current activities limited by [condition]?	16	Yes/no	More comorbid conditions affecting activities	Yes	166 (18%)
Body Mass Index (Clinical)	kg/m ² based on women's self-reported height recalled for age 18 and self-reported weight at 6 months, 5, and 10 years	2	Continuous	Higher BMI	Yes	0
Fatigue (Clinical)	Piper Fatigue Scale (PFS- 12): Piper et al., 1998; Reeve et al., 2012; Stover et al., 2013	12	0-10	Higher Fatigue	No	242 (26%)
Disease Stage (Clinical)	SEER cancer registries	1	0 (in situ) to IIIa (invasive) but not metastatic	Higher stage (worse prognosis)	No	72 (8%)

Construct	Measure (Acronym)	# Items	Response Options	Higher Score Indicated	Time- Vary- ing?	% Missing Data
Tamoxifen (Treat- ment)	Self-report	1	Yes/no	Used tamoxifen	Yes	<u>6 months</u> : 155 (28%) <u>2 years</u> : 2 (<1%) <u>5 years</u> : 306 (46%) <u>10years</u> : 263 (48%)
Chemo- therapy (Treat- ment)	Hospital records	1	Yes/no	Had chemo- therapy	No	23 (2%)
Maste- ctomy (Treat- ment)	SEER (hospital records if	1	Yes/no	Had mast- ectomy	No	0
Radiation (Treat- ment)	missing in SEER)	1	Yes/no	Had radiation	No	0

5.3.3 Structural Equation Modeling

Structural equation modeling (SEM) was used to test mediation hypotheses. SEM is a set of statistical procedures used to simultaneously estimate parameters and the adequacy of model fit to the data, and thus keeps the Type I error rate from inflating (Bollen, 1989; Byrne, 2011). Maximum likelihood with robust standard errors was used to estimate the fit of direct and indirect path coefficients. Cases with partially missing data were retained and corrections for non-normality were used.

Models were built through a series of steps that were specificed a priori based on prior published studies and Transactional Model processes. In Step 1a, nine predicted mediators (anxiety about recurrence, perceived health, 4 subscales assessing perceived impact of cancer [relationships, exercise, work/financial, and caregiving], optimism, social support, and religiosity) were entered into the model together, and in Step 1b, any non-significant mediators were removed for subsequent steps. In Step 2a, demographic, clinical, and treatment-related characteristics hypothesized to be associated with retained mediators were entered into the model along with the significant mediators retained from Step 1b. In Step 2b, demographic, clinical, and treatment-related characteristics that were not significantly related to PA or SB subgroups were removed. In Step 3a, demographic, clinical, and treatment-related characteristics were added as direct pathways to PA or SB subgroups. In Step 3b, demographic, clinical, or treatmentrelated characteristics not directly related to PA or SB subgroup membership were removed. Step 3b was expected to result in a final model.

SEM model fit was evaluated in three ways: 1) theoretical fit; 2) parsimony; and 3) empirical criteria. Theoretical fit indicated whether revisions to the model were consistent with the Transactional Model of Stress and Coping (Lazarus & Folkman, 1987). Parsimony indicated that when two models fit equally well, the preferred model was the one with fewest parameters (Curran & Bauer, 2012). Empirical model fit was evaluated by several criteria: 1) Absolute model fit examined whether the model was an accurate reflection of variability in the data. A model with a higher negative log likelihood (closest to zero) indicated model fit for reflecting the level of variability (the null hypothesis is that the model fits the data) (Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007).

2) Relative fit was compared across two models. A parsimony index called the "sample-size-adjusted Bayesian Information Criterion (ssBIC)" fit criteria was compared across models as the number of pathways increased (Collins & Lanza, 2010; Lazarsfeld & Henry, 1968; Goodman, 1974; Nylund, Asparouhov, & Muthen, 2007). Models with lower ssBIC indicate better parsimony. If the ssBIC and log-likelihood values pointed to different solutions, the lowest ssBIC value was used because it represented a comparison of two models (Enders, 2010b).
 3) R-squared or the amount of variance explained by the model

4) Parameter estimates were individually significant at p < .05 (in addition to overall model fit)

5) Modification indices larger than the minimum value default of ten were evaluated for potential modifications to make to improve fit (e.g., correlating error terms or adding covariances) (Muthen & Muthen, 2008-2015). "Modification indices" refer to model changes suggested by MPLUS to improve fit (data-driven suggestions). However, any model changes considered would need to be supported by theory or a literature review.

5.4 Results

5.4.1 Participant Characteristics

Breast cancer survivors had a mean age of 50.9 years (SD = 7.5, range: 35-64 years). The mean number of months between diagnosis and the initial interview was 5.9 months (SD = 2.3, range: 1-12 months). At the initial assessment, 51% of women were post-menopausal, 27% had completed high school or less education, 63% were married, and 41% reported that they were working. Three-quarters (76%) of the women had been diagnosed with in situ or Stage I breast cancer. For treatment, 63% underwent a partial mastectomy including breast-conserving surgery, 51% had radiation, and 36% had chemotherapy. See Chapter Four for more details.

5.4.2 Physical Activity Structural Equation Model Results

Table 5.6 shows the results for each model-building step for PA pathways. In Step 1a, the nine predicted mediators (anxiety about recurrence, perceived health, perceived impact of cancer [4 factors], optimism, social support, and religiosity) of PA subgroups were entered into the model together. Significant mediators included anxiety about recurrence (-0.27), perceived health (-0.99), religiosity (-0.26), and social support (0.27) (*all* p<*.01*). Perceived impact of breast cancer (-0.12) and optimism (0.15) were not significant in Step 1a, and thus were removed in Step 1b.

In Step 2a, demographic, clinical, and treatment-related characteristics hypothesized to be associated with retained mediators (anxiety about recurrence, perceived health, religiosity, and social support) were entered into the model along with these four mediators. Predictors not associated with mediators were removed in Step 2b (see Table 5.5).

Model fit improved when demographic, clinical, and treatment-related variables were added as predictors of mediators. In Step 1b, when only anxiety about recurrence, perceived health, religiosity, and social support were included in the PA subgroup membership model, ssBIC was 39587.9 and 15% of the variance could be explained. In the final model (Step 2b), when anxiety about recurrence, perceived health, religiosity, and social support were included, as well as their significant demographic, clinical, and treatment-related characteristics added, ssBIC decreased to 35071.8 and the amount of variance explained increased to 25%. Therefore, the final model is the best fitting and explains 10% more of the variance in PA subgroup membership than the more basic model.

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
					Higher Anxiety: Recurrence to Low PA	-0.27**	Higher Optimism to Low PA	0.15
<u>Step 1a</u> : Nine					Worse Perceived Health to Low PA	-0.99***	Impact: Relationships (Factor 1) to Low PA	0.19
Mediators as Predictors	-22271.1	44886.9	95	0.15	Higher Religiosity to Low PA	-0.26**	Impact: diet/exercise (Factor 2) to Low PA	0.11
of PA Subgroups					Higher Social Support to Low PA	0.27**	Impact: Financial (Factor 3) to Low PA	0.12
							Impact: Caregiving (Factor 4) to Low PA	0.08
	-15185.8	5185.8 39587.9	59	0.15	Anxiety: Recurrence to Low PA	-0.25**		
<u>Step 1b</u> : Non- Significant Parameters					Worse Perceived Health to Low PA	-0.90***	N/A	N/A
Eliminated					Religiosity to Low PA	-0.25**	-	
					Social Support to Low PA	0.28**		
					Anxiety: Recurrence to PA	-0.22**	Age at Diagnosis to Anxiety: Recurrence	-0.00
<u>Step 2a</u> : Predictors of	-22858.0	46033.0	95	0.18	Worse Perceived Health to Low PA	-0.21***	Age at Diagnosis to Perceived Health	-0.02
Mediators Added		40033.0	,,,		Religiosity to Low PA	-0.34***	Age at Diagnosis to Religiosity	-0.02
					Social Support to Low PA	0.37**	Age at Diagnosis to Social Support	0.03

Table 5.5. Summary	of Model Buildin	g Results for Physic	al Activity Subgroups

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
					Married to Social Support	0.21***	Mastectomy to Anxiety: Recurrence	0.03
	64 - 0				Hispanic to Religiosity	0.74***	Mastectomy to Perceived Health	-0.08
					African Amer. to Anxiety: Recurrence	-0.19**	Hispanic to Anxiety: Recurrence	0.04
					African Amer. to Perceived Health	0.99***	Hispanic to Perceived Health	-0.05
					African Amer. to Religiosity	0.90***	Education to Anxiety: Recurrence	0.01
				Fatigue toMarried toAnxiety:0.15*RecurrenceHealth	Perceived Health	-0.06		
<u>Step 2a</u> :				0.18	Fatigue to Perceived Health	0.18*	Chemo to Perceived Health	08
Predictors of Mediators	-22858.0	46033.0	95		Chemo to Anxiety: Recurrence	0.11*	Radiation to Perceived Health	-0.03
Added (Continued)					BMI to Anxiety: Recurrence	-0.12*	Mastectomy to Perceived Health	-0.08
					BMI to Perceived Health	0.27***	Tamoxifen to Perceived Health	0.01
					Comorbid to Anxiety: Recurrence	-0.41**	Married to Perceived Health	0.05
					Comorbid to Worse Perceived Health	0.27***	Married/ Partnered to Anxiety: Recurrence	0.06
					Comorbid to BMI	0.21***	Working to Anxiety: Recurrence	0.00
				Education to Worse Perceived Health	-0.11*	Working to Perceived Health	0.07	
						Working to Religiosity	0.01	
						Working to Social Support	0.06	

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameter s Eliminated	Parameter Estimates
Step 2b: Non- Significant Parameters Eliminated and Race Added as Direct Predictor (Final Model)	-17415.1	35071.8	73	0.25	Fatigue to Higher Anxiety: Recurrence African Amer. to Higher Anxiety: Recurrence Chemo to Higher Anxiety: Recurrence to PA Fatigue to Worse Perceived Health African Amer. to Perceived Health Greater Comorbid to Perceived Health Higher Educ. to Perceived Health Higher Educ. to Perceived Health Worse Perceived Health U Perceived Health Higher Educ. to Perceived Health Higher Educ. to Perceived Health Higher Educ. to Perceived Health Higher Educ. to Perceived Health African Amer. to Health U Perceived Health Comorbid to Perceived Health Higher Educ. to Perceived Health Higher Educ. to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid to Perceived Health Comorbid Health Comorbid to Perceived Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Health Comorbid Comorbid Comorbid Health Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Comorbid Como	0.54^{***} - 0.19^{**} 0.13^{*} 0.41^{***} 0.10^{**} 0.16^{***} 0.22^{***} 0.22^{***} 0.09^{*} 0.13^{*} 0.90^{***} 0.70^{***}	- - - - - - -	N/A

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
Step 2b: Non-					Low Social Support to Low PA	0.28***		N/A
Significant Parameters Eliminated and Race				0.25	African Amer. to Low PA	1.79***	-	
Added as Direct Predictor	-17415.1	35071.8	73		Married/ Partnered to Low Social Support	-0.27***	N/A	
(Final Model)					Low Social Support to Low PA	0.28***		
(Contin- ued)					African Amer. to Low PA	1.79***	-	

```
**p<.01
***p<.001
```

The final PA model is shown in Figure 5.5. Breast cancer survivors' PA subgroups were predicted by four pathways. Pathways will be described moving from the top to bottom of the model in Figure 5.5.

In the first pathway, higher fatigue (standardized parameter estimate: 0.54), African American race (-0.19), and chemotherapy (0.13) predicted higher anxiety about recurrence, and in turn higher anxiety about recurrence was associated with membership in the "Low but Increasing PA subgroup"(0.41) (*all* p<.05). In the second pathway, higher fatigue (0.10), African American race (0.16), greater comorbid conditions (0.22), lower education (-0.09), and body mass index (0.13) predicted poor perceived health, and in turn, poor perceived health was associated with membership in the "Low but Increasing PA subgroup" (0.90) (*all* p<.05).

In the third pathway, African American race (0.70) and Hispanic ethnicity (0.54) (*both* p<.001) predicted higher religiosity, and in turn higher religiosity was associated with membership in the "Low but Increasing PA subgroup" (0.31, p<.01). In the final pathway, not being married/partnered (-0.27, p<.01) predicted lower perceived social support, and in turn lower social support was associated with membership in the "Low but Increasing PA subgroup" (0.28, p<.01). This model explained 25% of the variance in PA subgroup membership for breast cancer survivors (p<.001).

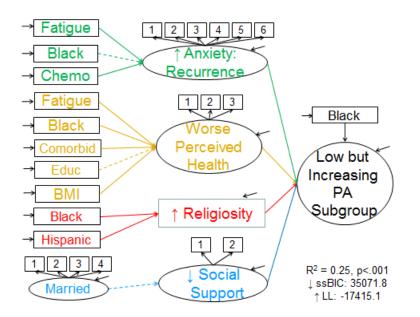


Figure 5.5. Predictors of the low but increasing physical activity subgroup.

Note: Colors signify different pathways through the model. Boxes indicate observed variables and circles indicate latent variables. Numbered boxes above circles/latent variables indicate how many items were used as the indicator of the latent variable.

5.4.3 Sedentary Behavior Structural Equation Model Results

Table 5.6 shows the results for each model-building step for SB pathways. In Step 1a, the nine predicted mediators (anxiety about recurrence, perceived health, perceived impact of cancer [4 factors], optimism, social support, and religiosity) of SB subgroups were entered into the model together. Significant mediators included perceived health (0.75) and perceived financial impact from breast cancer (-1.07) (*both* p<.01). Anxiety about recurrence (0.12), optimsim (-0.28), religiosity (-0.11), and social support (-0.08) were not significant in Step 1a, and thus were removed in Step 1b.

In Step 2a, demographic, clinical, and treatment-related characteristics hypothesized to be associated with retained mediators (perceived health and perceived financial impact from cancer) were entered into the model along with the mediators. Predictors not associated with retained mediators were removed in Step 2b (see Table 5.6).

Model fit improved when demographic, clinical, and treatment-related variables were added as predictors of mediators. In Step 1b, when only perceived health and perceived financial impact were included in the SB subgroup membership model, ssBIC was 15366.4 and 11% of the variance was explained. In the final model (Step 2b), when perceived health and perceived financial impact were included, as well as their significant demographic, clinical, and treatmentrelated characteristics added, ssBIC decreased to 13738.8 and the amount of variance remained the same at 11%. Therefore, the final model is the best fitting and explains similar variance in SB subgroup membership than the more basic model.

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameter Eliminated	Parameter Estimates
					Worse Perceived Health to	0.75***	Anxiety: Recurrence to Higher SB	0.12
Step 1a: Nine Mediators as Predictors of SB Subgroups					Higher SB		Optimism to Higher SB	-0.28
				Greater Financial	1.05 kikk	Religiosity to Higher SB	-0.11	
				Impact to Higher SB	-1.07***	Social Support to Higher SB	-0.08	
	-22717.7	45773.8	95	0.11*			Impact: relationship s (Factor 1) to Higher SB	-0.19
							Impact: diet/exercis e (Factor 2) to Higher SB	0.05
							Impact: caregiving (Factor 4) to Higher SB	0.13
Step 1b: Non-	-5147.6	15366.4	20	0.11**	Worse Perceived Health to Higher SB	0.84***	N/A	N/A
Significant Parameters Eliminated			_ •		Greater Financial Impact to Higher SB	Greater Financial -0.94** Impact to		

Table 5.6. Summary of Model Building Results for Sedentary Behavior Subgroups

Model	Log- Likelihood	ssBIC	# Para- meter s	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameter Eliminated	Parameter Estimates																										
					Worse Perceived Health to Higher SB	0.84***	Age at Diagnosis to Worse Perceived Health	-0.01																										
					Greater Financial Impact to Higher SB	-0.94**	Age at Diagnosis to Greater Financial Impact	-0.05																										
					Married/ Partnered to Greater Financial Impact	-0.19**	Disease Stage to Worse Perceived Health	0.02																										
					Education to Worse Perceived Health	0.12***	Disease Stage to Greater Financial Impact	0.06																										
<u>Step 2a</u> : Predictors				African American to Worse Perceived Health	0.30***	Radiation to Worse Perceived Health	-0.01																											
of Mediators Added	-6794.6	13752.1	49	0.10**	49 0.10 ⁺⁺⁺	Hispanic to Higher SB	-0.72***	Radiation to Greater Financial Impact	0.01																									
											Greater Fatigue to Worse Perceived Health	0.18***	Mastectomy to Worse Perceived Health	-0.07																				
																															Chemo to Greater Financial Impact	0.17***	Mastectomy to Greater Financial	0.04
											Higher BMI to Worse Perceived Health	-0.29***	Tamoxifen to Worse Perceived Health	0.00																				
				Greater Comorbid to Perceived Health	0.25***	Tamoxifen to Greater Financial	0.03																											
						Working to Perceived Health	0.06																											
							Working to Financial Impact	-0.07																										

Model	Log- Likelihood	ssBIC	# Para- meter s	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameter Eliminated	Parameter Estimates
							Education to Greater Financial	-0.03
Step 2a	-6794.6	13752.1	49	0.10**			African American to Financial	0.07
Continued							Hispanic to Financial	0.06
							Hispanic to Perceived Health	-0.01
					Greater Fatigue to Worse Perceived Health	0.16***		
					African American to Worse Perceived Health	0.21***	-	
					Higher Education to Worse Perceived Health	-0.09*	N/A	N/A
<u>Step 2b</u> : Non- Significant Parameters	-67878.0	13738.8	49	0.11**	Greater Comorbid to Worse Perceived Health	0.23***		
(Final Model)	-07878.0	13/38.8	49	0.11**	Higher BMI to Worse Perceived Health	0.24***	_	
Woder)					Worse Perceived Health to Higher SB	0.82***	_	
					Married/ Partnered to Greater Financial	-0.20***	N/A	N/A
					Chemo to Greater Financial	0.10*	-	
					Greater Financial to Higher SB	0.91***	-	
				Hispanic to Higher SB	-0.73***	-		

The final SB model is shown in Figure 5.6. Breast cancer survivors' SB subgroups were predicted by two pathways. Pathways will be described moving from the top to bottom of the model in Figure 5.6.

In the first pathway, greater fatigue (standardized parameter estimate: 0.16), African American race (0.21), lower education (-0.09), greater comorbid conditions (0.23), and higher body mass index (0.24) predicted worse perceived health, and in turn worse perceived health was associated with higher SB subgroup membership (0.82) (*all* p<.05). In the second pathway, not being married/partnered (-0.20) and chemotherapy (0.10) predicted greater perceived financial impact of cancer, and in turn greater perceived financial impact of cancer was associated with higher SB subgroup membership (0.91) (*all* p<.01). This model explained 11% of the variance in SB subgroup membership (p<.0001).

Model fit improved when demographic, clinical, and treatment-related variables were added as predictors of mediators. In Step 1b, when only perceived health and perceived financial impact from cancer were included in the SB subgroup membership model, ssBIC was 15366.4 and 11% of the variance could be explained. In the final model (Step 2b), when perceived health and perceived financial impact from cancer were included as mediators, as well as their significant demographic, clinical, and treatment-related characteristics added, ssBIC decreased significantly to 13738.8 and the amount of variance explained remained at 11%. Therefore, the final model is the best fitting and explains similar variance in SB subgroup membership than the more basic model.

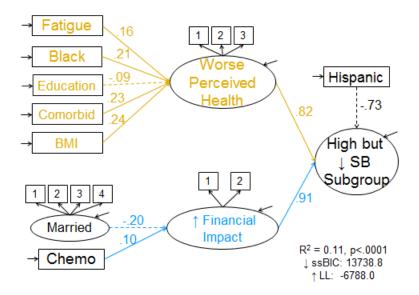


Figure 5.6. Predictors of the high but declining sedentary behavior subgroup.

Note: Colors signify different pathways through the model. Boxes indicate observed variables and circles indicate latent variables. Numbered boxes above circles/latent variables indicate how many items were used as the indicator of the latent variable.

5.4.4 Structural Equation Results when Physical Activity and Sedentary Behavior Were Estimated in Same Model

Table 5.7 shows the results for each model-building step for pathways when PA and SB were estimated in the same model. In Step 1a, the nine predicted mediators (anxiety about recurrence, perceived health, perceived impact of cancer [4 factors], optimism, social support, and religiosity) of PA-SB subgroups were entered into the model together. The only significant mediator was perceived health (0.10) (p<.05). Anxiety about recurrence (-0.00), financial impact (-0.01), optimsim (-0.01), religiosity (-0.02), and social support (-0.02) were not significant in Step 1a, and thus were removed in Step 1b.

In Step 2a, demographic, clinical, and treatment-related characteristics hypothesized to be associated with perceived health were entered into the model along with the mediators. Predictors not associated with perceived health were removed in Step 2b (see Table 5.7).

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
					Worse Perceived Health to Low PA/Avg. TV	0.07**	Higher Anxiety: Recurrence to Low PA/Avg. TV	-0.00
							Higher Religiosity to Low PA/Avg. TV	-0.02
							Higher Social Support to Low PA/Avg. TV	-0.02
Step 1a: Nine Mediators							Higher Optimism to Low PA/Avg. TV	-0.00
Predictors of PA and SB Subgroups	of PA and SB	57164.5	120	0.04*			Impact: relationships (Factor 1) to Higher SB	0.01
Subgroups							Impact: diet/exercise (Factor 2) to Higher SB	0.03
							Impact: Work/ Financial (Factor 3) to Low PA/Avg. TV	0.01
							Impact: caregiving (Factor 4) to Higher SB	0.02
<u>Step 1b</u> : Significant Mediators Only	-101.2	22216.2	5	0.03	Worse Perceived Health to Low PA/Avg. TV	0.10	N/A	N/A

Table 5.7. Summary of Model Building Results when Physical Activity and Sedentary Behavior were Estimated in Same Model

Model	Log- Likelihood	ssBIC	# Para- meters	R ²	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
					Greater Fatigue to Worse Perceived Health	0.15***	Married/ Partnered to Worse Perceived Health	-0.10**
					African American to Worse Perceived Health	0.71***	Hispanic to Worse Perceived Health	-0.09
	<u>Step 2a</u> :			Higher Education to Worse Perceived Health	-0.19***	Age at Diagnosis to Worse Perceived Health	0.00	
<u>Step 2a</u> : Predictors				Greater Comorbid to Worse Perceived Health	0.24***	Working to Worse Perceived Health	-0.09	
of Mediator Added	-3334.3	6835.7	59	0.03*	Higher Body Mass Index to Worse Perceived Health	0.34**	Disease Stage to Worse Perceived Health	0.09
						Worse Perceived Health to Low PA/Avg. TV	0.11**	Radiation to Worse Perceived Health
					Fatigue to Worse Perceived Health	0.55***	Mastectomy to Worse Perceived Health	-0.06
				African American to Perceived Health	0.15***	Tamoxifen to Worse Perceived Health	0.01	
					Comorbid to Perceived Health	0.28***	Chemo to Worse Perceived Health	0.07

Model	Log- Likelihood	ssBIC	# Parameters	\mathbf{R}^2	Significant Parameters	Parameter Estimates	Non- significant Parameters Eliminated	Parameter Estimates
					Education to Perceived Health	-0.15**		
Step 2a: Predictors of Mediator	-3334.3	6835.7	59	0.03*	Higher Body Mass Index to Perceived Health	0.21**		
Mediator Added				Worse Perceived Health to Low PA/Avg. TV	0.20**			
		-3808.8 7708.1			Fatigue to Perceived Health	0.16**		
			27	0.05*	African American to Perceived Health	0.18**		
Step 3: Add direct					Comorbid to Perceived Health	0.22***	-	N/A
predictor of African American to Low	-3808.8				Education to Worse Perceived Health	-0.09*	- N/A	
PA/ Avg. TV (Final PA					Higher Body Mass Index to Perceived Health	0.23***	_	
and SB Model)					Worse Perceived Health to Low PA/Avg. TV	0.08*		
					African American to Low PA/Avg. TV (direct path)	0.08*	-	

* p<.05 **p<.01 ***p<.001

Model fit improved when demographic, clinical, and treatment-related variables were added as predictors of perceived health. In Step 1b, when only perceived health was included in the PA-SB subgroup membership model, ssBIC was 22216.2 and 3% of the variance was explained. In the final model (Step 2b), when perceived health and its significant demographic, clinical, and treatment-related characteristics were added, ssBIC decreased to 7708.1 and the amount of variance increased to 5%. Therefore, the final model is the best fitting and explains marginally more variance in PA-SB subgroup membership than the more basic model.

The final PA-SB model is shown in Figure 5.7. Breast cancer survivors' PA-SB subgroups were predicted by one pathway: greater fatigue (standardized parameter estimate: 0.16), African American race (0.18), greater comorbid conditions (0.22), and lower education (-0.09), and higher body mass index (0.23) predicted worse perceived health, and in turn worse perceived health was associated with membership in the low PA/average TV subgroup (0.08) (*all* p<.05).

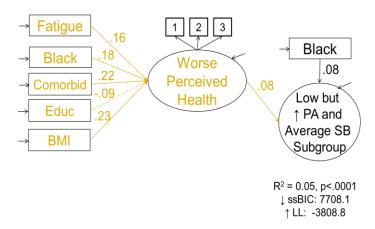


Figure 5.7. Predictors when physical activity and sedentary behavior were estimated together.

Note: Colors signify different pathways through the model. Boxes indicate observed variables and circles indicate latent variables. Numbered boxes above circles/latent variables indicate how many items were used as the indicator of the latent variable.

5.5 Discussion

This is the first study among breast cancer survivors to examine psychological

mechanisms underlying PA and SB patterns from pre-diagnosis through ten years post-diagnosis.

A priori mediation models were informed by Lazarus and Folkman's (1987) Transactional

Model of Stress and Coping. Consistent with Transactional Model processes, primary and secondary appraisal variables mediated the relationships between demographic, clinical, and treatment-related characteristics and subgroups of breast cancer survivors following different PA and SB patterns over time.

In both PA and SB models, perceived health (proxy for perceived harm/primary appraisal) was an important mediator between demographic and clinical characteristics and PA and SB subgroups. Breast cancer survivors who perceived their health to be poor, had higher fatigue, more comorbid conditions, higher body mass index, were African American, and had lower education were more likely to be in the "Low but Increasing PA Subgroup" for the PA model; they were also more likely to be in the "High but Decreasing TV Subgroup" in the SB model.

The PA model also had three unique Transactional Model pathways predicting membership in the "Low but Increasing PA Subgroup" (that did not appear in the SB model). In the first unique pathway, breast cancer survivors who had received chemotherapy, were Caucasian or Hispanic, and had higher fatigue were more likely to have higher anxiety about recurrence, and in turn were more likely to be in the "Low but Increasing PA Subgroup." In the second unique pathway, breast cancer survivors who were African American or Hispanic were more likely to report higher religiosity, and in turn more likely to be in the "Low but Increasing PA Subgroup." In the final unique pathway, breast cancer survivors who were not married/partnered and also reported lower social support were more likely to be in the "Low but Increasing PA Subgroup."

The SB model had one unique Transactional Model pathway predicting membership in the "High but DecliningTV Subgroup." Breast cancer survivors who perceived greater financial

impact from cancer, had received chemotherapy, were not married/partnered, and who were Caucasian or African American were more likely to be in the "High but DecliningTV Subgroup."

When PA and SB were estimated in the same model, only the pathway through percieved health (perceived harm proxy) remained significant. Breast cancer survivors who perceived their health to be poor, who were African American, had lower education, higher fatigue, more comorbid conditions, and higher body mass index were more likely to be in "Low but Increasing PA and U.S. Average TV Subgroup."

My study provides a better understanding of the psychosocial mechanisms underlying breast cancer survivors' PA and SB patterns from pre-diagnosis through ten years post-diagnosis. Findings can guide development of theory-informed interventions to help breast cancer survivors increase their PA and decrease their SB. In the following sections, I discuss each Transactional Model pathway in more detail and place it into context within the broader literature for breast cancer survivors.

5.5.1 Physical Activity and Sedentary Behavior Identical Pathway: Perceived Health

In both PA and SB models, perceived health was an important mediator between demographic (race, education) and clinical (fatigue, body mass index, comorbid conditions) characteristics and PA and SB subgroups. Perceived health was chosen as a proxy to represent harm appraisal (primary appraisal) from the Transactional Model because it reflects perceived consequences to health experienced to date. Having had breast cancer is a major event in many women's lives; thus it is very likely that breast cancer survivors would report adverse effects and symptoms related to treatment when asked about perceived health in general. In a meta-analysis of coping and appraisals during cancer survivorship by Franks and Roesch (2006), harm appraisal in cancer patients was typically assessed as the physical and mental aspects of harm

attributed to cancer. Therefore, perceived health appears to be a good proxy for harm to health in the context of a breast cancer diagnosis.

In the Transactional Model, perceived harm is one of two primary appraisals made to assess whether a situation requires action and whether anything can be done to alter the result or reduce future threat. A breast cancer survivor who appraises her health as negatively affected by breast cancer may be less likely to perceive her health as something to be safeguarded. There also may be a sense of fatalism in the sense that if a breast cancer survivor perceives her health to be poor, she may appraise the situation as one where nothing can be done. In other words, she may feel that her health is already damaged by breast cancer so there is little point in trying to enhance health. Future research should consider qualitative interviews with breast cancer survivors to determine the following: 1) if their perceptions of their health changed temporarily during active treatment or had a more long-lasting impact on how they feel about their health; 2) whether their perceptions of poor health affected their PA and SB and in what ways; and 3) for breast cancer survivors who perceive that breast cancer has changed their health for the worse, do they feel that any changes in health behavior would be futile.

In addition to being a proxy for harm appraisal, perceived health may also be predicting PA subgroups because it is functioning as a perceived barrier to PA. For instance, Gho et al. (Gho, Munro, Jones, & Steele, 2014) surveyed over 400 breast cancer survivors in Australia about perceived barriers and benefits of PA. Breast cancer survivors reporting poor perceived health, feeling too weak, lacking self-discipline, and not making exercise a priority were eight to ten times more likely to report low PA. Conversely, exercise enjoyment, improved feelings of well-being, and decreased feelings of stress and tension were the top three benefits associated with meeting exercise recommendations (Gho et al., 2014).

The American Cancer Society's Studies of Cancer Survivors (SCS-II) also found that self-reported poor health status was the most powerful predictor of negative health behavior changes following diagnosis (e.g., decreasing PA) (Hawkins et al., 2010). Future research is warranted to determine whether breast cancer survivors perceive their poor health to be a harm appraisal, a barrier to PA, a pragmatic view about the ability to be active, or some combination of these perceptions.

5.5.2 Physical Activity Unique Pathway 1: Anxiety about Recurrence

Anxiety about recurrence was chosen as a proxy for threat appraisal (secondary appraisal) because factor analytic studies show that anxiety about recurrence encompasses anticipatory concern about a future health threat and perceived loss of control (Johnson Vickberg, 2001; Simard & Savard, 2009; Simard, Savard, & Ivers, 2010; Simard et al., 2013; Spencer et al., 1999).

In the current study, breast cancer survivors who had received chemotherapy, were Caucasian or Hispanic, and had higher fatigue were more likely to have higher anxiety about recurrence, and in turn were more likely to be in the "Low but Increasing PA Subgroup." High levels of anxiety about recurrence may cause a breast cancer survivor to become preoccupied, and perhaps overhwlemed with intrusive thoughts, and thus she may be less likely to try change a current or future health threat by changing health behavior. It may be that moderate anxiety about recurrence is at a level appropriate for motivation to change a current or future health threat by changing PA or SB or other health behaviors.

However, two prior studies with breast cancer survivors have found that higher anxiety about recurrence was associated with greater PA (Brunet et al., 2014; Hawkins et al., 2010). There may be several reasons for this difference. First, anxiety about recurrence appears to vary by race/ethnicity and my study included a more diverse sample than previous research. In the

two prior studies examining anxiety about recurrence and PA changes after diagnosis, both had 85% or more Caucasian survivors (Brunet et al., 2014; Hawkins et al., 2010). In the current study, 49% reported being non-Hispanic Caucasian, 36% African American, and 12% Hispanic.

A study by Gil and colleagues (2004) suggests that this racial difference in anxiety about recurrence may be because African American and Caucasian breast cancer survivors reported different cognitive and affective triggers. Triggers of uncertainty regarding breast cancer recurrence were examined in 244 Caucasian and African-American women between five and nine years post-diagnosis. African American survivors were more likely to report that experiencing a new symptom triggered their anxiety about recurrence but Caucasian survivors reported that hearing about someone else with cancer and information in the media triggered anxiety about recurrence (Gil et al., 2004). Experiencing a new symptom would likely occur less frequently than media reports or hearing about someone with cancer, and thus may explain why African American survivors reported less anxiety about recurrence than Caucasian survivors. It will be important in future research to determine the cognitive and affective perceptions influencing anxiety about recurrence and whether these vary by race/ethnicity.

In my study, Hispanic breast cancer survivors reported the highest levels of anxiety about recurrence, followed by Caucasian survivors, and then the lowest levels by African American survivors. Carver and colleagues (Carver, Smith, Petronis, & Antoni, 2006) also found that Hispanic breast cancer survivors reported higher anxiety about recurrence than Caucasian and African American survivors. More work is warranted for better understanding Hispanic breast cancer survivors' perceptions of future health threats and how this affects their health behaviors and quality of life.

5.5.3 Physical Activity Unique Pathway 2: Perceived Social Support

Perceived social support (secondary appraisal of coping resources) was an important mediator between not being married/partnered and membership in the "Low but Increasing PA Subgroup." In the Transactional Model, secondary appraisals are the perceived resources that an individual believes can be mobilized to change a current or future threat. If a breast cancer survivor perceives cancer recurrence as a threat that she needs to manage, perceived social support may provide her with tangible, informational, or emotional support in her goal to alter the threat.

In the current study, the variable available for assessing perceived social support was the number of family or friends that a breast cancer survivor felt she could confide in. In other words, having a larger confidant network was used a proxy for greater perceived social support. Confidante network size did act as a mediator, and in the direction one would expect for higher perceived social support. However, a small confidante network can provide excellent support, and a large network may provide inadequate support. In the current study, breast cancer survivors who perceived that they have a confidante network available to them if they need it may be more likely to view a stressor as something they can cope with successfully. Future research should consider asking breast cancer survivors if, and how, they use confidante networks as coping resources for increasing PA.

5.5.4 Physical Activity Unique Pathway 3: Religiosity

Religiosity was measured as a proxy for religious or spiritual coping resources in my study because it is a way of understanding adversity and potentially providing hope or tangible support. Religiosity/spirituality functions as a coping resource in three ways: 1) it provides a schema for understanding adversity and creating situational meaning making (i.e., a way of comprehending a stressor in relation to attitudes and beliefs about the world and a higher power);

2) increasing feelings of control over a stressor (e.g., a belief that "God is in control" or "God has a plan"); and 3) emotional, tangible, and informational support resources for individuals who are part of faith communities.

My hypothesis that higher religiosity would be associated with increasing PA after diagnosis was supported. African American and Hispanic breast cancer survivors reported higher religiosity, and turn they were more likely to be in the "Low but Increasing PA Subgroup." Multiple health promotion programs have been conducted in African American churches and in the community to reduce health problems and promote healthy living, with modest success (see Whitt-Glover et al., 2009 for an overview). Interventions that are tailored to African American church-goers are using religious coping resources to change PA.

However, in the current study, breast cancer survivors were not asked directly if they used religiosity as a coping resource for increasing PA. More research is warranted to determine when and how breast cancer survivors use religious coping resources to change their PA. For instance, additional religious coping resources may include specific positive strategies (e.g., seeking spiritual support, expressing spiritual contentedness, receiving congregational support, benevolent reframing of the stressful event, and collaborative partnerships with God) and negative (e.g., spiritual discontent, interpersonal religious conflict, negative reframing, and religious denial and apathy) religious coping strategies.

5.5.5 Optimsim Was not a Mediator of Subgroups

In contrast to my overall hypothesis, optimism (a personal coping resource) was not a significant predictor of PA subgroup membership when other mediators were included in models. However, optimism was trending toward statistical significance, and thus should still be considered in future research.

Additionally, optimism was only assessed at 39 months post-diagnosis, and thus change over time was not captured. Optimism is generally considered to be a stable construct, but Transactional Model processes suggest that optimism may vary across different situational contexts. Optimism may need to be assessed at multiple points over survivorship to determine if there is a relationship with PA subgroup membership. Other indicators of personal coping resources, such as conscientiousness and resourcefulness, should also be examined in future studies.

5.5.6 Sedentary Behavior Unique Pathway: Financial Impact

Perceived impact of breast cancer is focused on past and current levels of harm/loss attributable to breast cancer, and thus is a direct assessment of harm and benefit appraisals. In my study, only perceived financial impact was significantly associated with SB subgroups. Breast cancer survivors who perceived greater financial impact were less likely to be in the "High but Declining SB subgroup" (above average TV watching). To my knowledge, this is the first study linking perceived financial impact with SB among breast cancer survivors. However, causation cannot be determined in this study, and thus financial impact may be influencing TV watching or TV watching may be influencing financial impact of cancer. More research is warranted to examine the relationship between financial impact and SB in breast cancer survivors.

Financial strain after a cancer diagnosis appears to be a common stressor. Baker et al. (2005) found that approximately one-quarter of cancer survivors reported experiencing financial difficulties during survivorship. They identified psychosocial problems reported by 752 cancer survivors participating in the Study of Cancer Survivors-I (SCS-I), a national, longitudinal investigation of the needs and quality of life of adult survivors. Approximately one year after diagnosis, 28% reported difficulty meeting medical expenses and 26% reported being less able to provide for their family's financial needs.

Carver and colleagues (Carver, Smith, Petronis, & Antoni, 2006) found that chemotherapy predicted greater financial problems during survivorship. I also found that chemotherapy was associated with greater perceived financial impact. Chemotherapy regimens generally last between 12-24 weeks and can cause significant impairment in physical functioning, social health, and financial difficulties.

Financial impact of a cancer diagnosis may have had a greater impact for women diagnosed in 1995-1999 than today because more survivors may be insured due to the Affordable Care Act enacted in 2010. For example, the Centers for Disease Control and Prevention used data from the National Health Interview Survey to report that the mean uninsured rate for the general population had decreased by over 11 million individuals between 2010 and 2014 (Martinez & Cohen, 2015). Perhaps the financial impact of a cancer diagnosis is not as devastating today. However, there is evidence that breast cancer survivors who are insured still have substantial out-of-pocket costs (Pisu et al., 2010; Arozullah et al., 2004). Future research would benefit from examining the ways in which insurance status and out-of-pocket treatment costs influence PA and SB patterns for breast cancer survivors to better understand my results of financial impact and SB being related.

Other types of perceived impact on breast cancer were not significantly correlated with SB subgroups: caregiving roles, social/emotional functioning, and diet/exercise. Future qualitative research may be able to determine if other types of perceived harm from breast cancer impact SB.

5.5.7 Limitations

Limitations were related to the secondary dataset and statistical methodology. Each of these limitations is considered next.

Six dataset limitations affected my analyses: 1) some mediators were assessed once;

2) PA and SB were assessed at irregular intervals over ten years; 3) the assessment of PA and SB at six months post-diagnosis (and pre-diagnosis recall) differed among the sites; 4) the SB questions were not from a validated scale; 5) body mass index was assessed with self-reported height and weight; and 6) limitations related to operationalizing Transactional Model constructs. These dataset limitations are considered in turn.

The following mediators were only assessed once at 39 months post-diagnosis: harm appraisal (perceived impact of breast cancer), threat appraisal (anxiety about recurrence), and coping resources (optimism, religiosity). However, these variables may be tapping into more stable constructs that influence situation-specific appraisals of stressors. For instance, anxiety about recurrence is relatively stable over long-term survivorship (Janz et al., 2011; Johnson Vickberg, 2001; Koch, Jensen, Brenner, & Arndt, 2013; Simard et al., 2013; van den Beukenvan Everdingen et al., 2008; Deimling et al., 2006; Whitaker, Watson, & Brewin, 2009). Similarly, resources that influence secondary appraisal (optimism and religiosity/spirituality) are likely to be relatively stable constructs that may influence how situation-specific stressors are perceived. Nonetheless, several mediators assessed at one time point limited my ability to examine the plausibility of causal relationships.

My ability to detect PA and SB patterns over time and group survivors into subgroups was limited by the irregular and large spacing between assessments. PA and SB patterns were assessed at five time points: six months post-diagnosis (recall of pre-diagnosis PA and in the "last month", which were treated as separate time points), and two, five, and ten years postdiagnosis. The statistical methodologies of latent curve modeling and growth mixture modeling are robust to partially missing data, unequally spaced time points, and complex trajectories (Roth, 1994; Cohen & Cohen, 1983). However, the irregular spacing of the assessment intervals

may have led to important patterns being missed. For instance, important patterns between five and ten years post-diagnosis may have been missed. Future research will benefit from assessing PA and SB at multiple time points during long-term survivorship, especially between five and ten years post-diagnosis.

The next limitation was that the assessment of PA and SB at approximately six months post-diagnosis was different among the three HEAL sites because USC was brought into the study later than UNM and FHCRC. At USC, PA data for the pre-diagnosis and six months postdiagnosis time points were constructed from a lifetime history collected during a separate casecontrol study. At UNM and FHCRC, PA was collected with the Modifiable Activity Questionnaire. The same sixteen exercise activities were used in the PA variable calculation, but different interviewer-administered questionnaires may have introduced differences in reporting.

Data collection of SB was also affected. USC did not collect SB items at enrollment (including pre-diagnosis recall and six-months post-diagnosis) and it could not be constructed from other data. Therefore, data were imputed using thirty variables for multiple imputation. Multiple imputation is a state-of-the-art missing data technique (Enders, 2010b), but future research studies are needed to confirm my results. All African American women were enrolled at the USC site, and thus more research is needed to examine how their SB changes from pre- to post-diagnosis, and whether there are differences from Caucasian and Hispanic breast cancer survivors.

An additional limitation related to SB was that it was assessed by two items that had not previously been validated with breast cancer survivors. Twenty years ago when HEAL began, no validated measures of SB existed. However, television watching time is the most common way of measuring SB in the literature (Clark et al., 2009; Thorp, Owen, Neuhaus, & Dunstan, 2011)

and self-reported television viewing time shows moderate to large test–retest correlations across studies, indicating that questionnaires are likely prompting recall in a consistent way (Clark et al., 2009). Adults have more accurate recall of television watching times than other types of sitting because specific shows or movies are recalled, which prompts better recall about total sitting time (Clark et al., 2009). In addition, these two SB items have been used successfully in three HEAL publications unrelated to my dissertation (George et al., 2013a; 2013b; Forsythe et al., 2013).

The next limitation was that body mass index was computed with self-report data because not all sites weighed women in person. BMI was calculated using self-reported height at age 18 and self-reported weight at six months post-diagnosis. Two out of three sites (FHCRC and UNM) also had data available for height and weight that was measured by clinic staff, and thus I was able to determine the correlation between self-reports and BMI measurements taken in clinics. Self-reported height recalled for age 18 correlated with current height measured in the clinic at r=0.93 (p<.0001). Missing data on height was minimal (<1%), and therefore was unlikely to affect BMI calculations.

Self-reported weight at six months post-diagnosis correlated at r=0.85 (p<.0001) with weight taken on a scale at the clinics. Therefore, it appears to be unlikely that breast cancer survivors were substantially underreporting their weight. Missing data was also minimal for weight. At six months post-diagnosis, only 12 survivors (1%) were missing self-reported weight. For the time points at five and ten years post-diagnosis, missing data was consistent with attrition levels (29% and 42%, respectively).

The final dataset limitation was related to operationalizing Transactional Model constructs in a secondary data source. HEAL was not designed specifically for examining

cognitions and emotions related to health behaviors and coping strategies. Instead, HEAL is an epidemiological cohort study developed to examine the influence of health behaviors, sex hormones, and genetic factors on long-term breast cancer outcomes. Therefore, proxy variables were selected to represent Transactional Model constructs. More direct assessments of Transactional Model constructs may yield insights into breast cancer survivors' primary and secondary appraisals and PA and SB patterns.

Several statistical limitations are noted as well. The statistical assumption that missing data is missing at random could not be met, and thus PA and SB were imputed. Modern statistical techniques (latent curve modeling) were also used because the assumptions of traditional models could not be met. For instance, ANOVA's four main assumptions could not be met: 1) no missing data; 2) equally spaced time points; 3) normal distribution; and 4) homogeneity of variance and covariance over time. Growth modeling was used because it is flexible and robust to these challenges (Roth, 1994; Cohen & Cohen, 1983). Maximum likelihood with robust standard errors (MLR) was also used for model estimation because it improves the accuracy of the parameter estimates and increases power for intermittently missing data (Enders, 2010b).

Despite its drawbacks, latent curve modeling may be better suited than traditional methodology for examining theoretical models that assume individual change over time. For instance, ANOVA tests for mean differences between time points, and thus is not a good fit for examining individual change over time. Individual change follows a continuous path through time, which is not captured well by treating time as a nominal predictor as ANOVA does (Curran & Bauer, 2006). The Transactional Model of Stress and Coping (Lazarus & Folkman, 1987) is focused on individual changes in coping and perceived resources (not simply mean change), and

thus needs a more modern methodology. Future research with cancer survivors should consider using theoretical models of individual change and modern statistical methodology that accounts for individual change over time.

Despite these limitations, the HEAL dataset had several advantages for my dissertation: 1) a large, diverse cohort from three U.S. geographic regions; 2) PA and SB measured at multiple time points from pre-diagnosis through ten years post-diagnosis; 3) SEER registry or hospital record data for clinical and treatment-related characteristics; and 4) self-report data on a wide range of variables.

5.5.8 Conclusion

Breast cancer survivors' PA and SB subgroups were predicted by stress and coping variables, suggesting that future exercise interventions should be tailored to subgroups following different patterns. Specifically, decreasing perceptions of harm and future health threat and increasing coping resources, such as social support and religious coping resources, should be targeted for subgroups needing to increase PA to guideline levels. Decreasing harm appraisals, particularly perceived health and financial impact from cancer, should be targeted for decreasing SB. In the next chapter, I review the implications of my results for clinical care and future intervention development.

CHAPTER 6. SUMMARY, CONCLUSIONS, AND IMPLICATIONS

My dissertation studies provide a better understanding of the psychosocial mechanisms underlying long-term PA and SB patterns for breast cancer survivors and areas to target in future intervention research. In Study 1, I found that breast cancer survivors reported varying PA and SB patterns from pre-diagnosis through ten years post-diagnosis and that these patterns formed subgroups. In Study 2, I found that constructs from Lazarus and Folkman's Transactional Model of Stress and Coping mediated the relationships between demographic, clinical, and treatmentrelated characteristics and PA and SB subgroup membership determined in Study 1.

I used theory in four ways in my dissertation: 1) to select psychosocial variables that may be affecting PA and SB patterns for breast cancer survivors; 2) to describe the psychosocial processes underlying PA and SB outcomes; 3) to aid in interpreting my results related to psychosocial processes and PA and SB patterns; and 4) to identify intervention targets for future research.

Overall, my results support using theory-informed interventions, targeting both PA and SB in interventions, and tailoring interventions to be cancer-specific. In the next section, I summarize my results from Study 1 and review implications for clinical care.

6.1 Mean Trajectories of Physical Activity and Sedentary Behavior and Clinical Implications

In Study 1, I found that the mean moderate-vigorous PA trajectory—averaged across all women in the sample—showed a decline of thirty-four minutes from pre-diagnosis (119 minutes/week) to six months post-diagnosis (85 minutes/week). PA then returned to pre-diagnosis levels by two years post-diagnosis (129 minutes/week), continued to increase to a peak

at five years post-diagnosis (141 minutes/week), and then had a considerable drop to 78 minutes/week at ten years post-diagnosis. For the mean PA trajectory, all assessment points were below the national guideline of at least 150 minutes/week of moderate PA.

For SB, the mean trajectory for the whole sample showed an increase of one hour of TV watching per week from pre-diagnosis (18.0 hours/week) to six months post-diagnosis (19.1 hours/week). SB then returned to pre-diagnosis levels by two years post-diagnosis (18.3 hours/week), and thereafter steadily increased to a peak at ten years post-diagnosis (20.6 hours/week). The average SB trajectory was consistent with the U.S. national average of 18-19 hours per week of sitting watching TV.

My Aim 1 results suggest that two time points during survivorship should be targeted for PA intervention: 1) intervening during the active treatment period at approximately six months post-diagnosis to increase PA to guideline levels and to decrease SB; and 2) intervening at approximately five years post-diagnosis to prevent the large decrease in PA and increase in SB that occurs by ten years post-diagnosis.

At six months and five years post-diagnosis, breast cancer survivors have reported similar barriers to PA implementation: psychological barriers (lack of motivation, dislike of gym), physical health barriers (aging, cancer treatment, comorbid conditions, and fatigue) and environmental barriers (proximity/access to facilities, and seasonal weather) (Blaney, Lowe-Strong, Rankin-Watt, Campbell, & Gracey, 2013; Gho, Munro, Jones, & Steel, 2014; Hefferon, Murphy, McLeod, Mutrie, & Campbell, 2013). Given the similar barriers, the same intervention strategies may apply.

An ideal time for clinicians to address these PA barriers and decreasing SB with their breast cancer patients is during adjuvant therapy appointments. For instance, newly diagnosed

breast cancer survivors attend an initial consultation for adjuvant therapy, such as hormone therapy, and thus PA and SB counseling could be added to this consultation. Until a guideline change in 2014, hormone therapy was recommended for at least five years for women with hormone-receptor-positive tumors (Burstein et al., 2010). New guidelines recommend extending the duration for hormone therapy from five to ten years for women with hormone-receptorpositive tumors (Burstein et al., 2014). Therefore, many breast cancer survivors will now be seen in the cancer care system during the risky period at five to ten years post-diagnosis where PA decreases and SB increases. Adjuvant therapy appointments may be an excellent way to disseminate the PA and SB message to breast cancer survivors.

For instance, Jones and colleagues (Jones, Courneya, Fairey, & Mackey, 2004) found that breast cancer survivors did increase their moderate-vigorous PA in a randomized trial where the clinician recommended increasing PA during an adjuvant therapy consultation. Jones et al. (2004) conducted a three-armed, randomized trial where 450 breast cancer survivors were randomly assigned to receive an oncologist exercise recommendation, an oncologist exercise recommendation plus referral to an exercise specialist, or usual care. Oncologists were trained on using a thirty-second script recommending 20-30 minutes per day of PA at a moderate intensity.

The primary outcome was self-reported moderate-vigorous PA five weeks after randomization and the intervention components were based on the Theory of Planned Behavior. Breast cancer survivors who received the scripted exercise recommendation from their oncologist at their first adjuvant therapy consultation reported greater moderate-vigorous PA five weeks later (75 minutes/week) than survivors in usual care (47 minutes/week). There was no difference in PA between the recommendation-plus-referral group and the usual care group. None of the randomized groups met the national PA guideline of at least 150 minutes/week of moderate PA, but this study suggests that intervening with breast cancer survivors during adjuvant therapy consultations can be effective in increasing their PA.

My results also suggest a second intervention point at five years post-diagnosis in order to prevent the large decrease in PA and increase in SB that occurs by ten years post-diagnosis. Intervening with breast cancer survivors at five years post-diagnosis will have its own challenges. For instance, some breast cancer survivors will no longer be part of the cancer care system. However, many breast cancer survivors are still attending follow-up appointments for anti-estrogen therapy. New guidelines released in 2014 recommend extending the length of time for anti-estrogen therapy from five to ten years post-diagnosis for women with hormone-positive tumors (Burstein et al., 2014). Breast cancer survivors coming in for follow-up appointments for hormone therapy could also be counseled on the importance of maintaining PA and decreasing SB. Very few PA interventions have targeted this critical time point (Speck et al., 2010). Future research would benefit from testing interventions aimed at changing both PA and SB at six months and five years post-diagnosis.

6.2 Subgroups Reporting Different Physical Activity and Sedentary Behavior Patterns over Time

Breast cancer survivors' PA and SB patterns varied considerably from pre-diagnosis to ten years post-diagnosis, and thus in Study 1 I also examined whether subgroups were following different trajectories. Two subgroups were determined for PA and three subgroups for SB.

For PA, the largest subgroup (92%) reported low PA prior to diagnosis and at six months post-diagnosis but increased their PA at two and five years post-diagnosis, suggesting that this subgroup may have been making health changes in response to their cancer diagnosis ("Low but Increasing PA Subgroup"). The smallest subgroup (8%) exceeded PA guidelines at all

assessments but reported a significant decline at six months post-diagnosis that persisted through ten years post-diagnosis ("High But Declining PA Subgroup").

Three SB subgroups were determined. The first SB subgroup (18%) reported watching fewer TV hours/week than the U.S. average at pre-diagnosis and steadily increased through ten years post-diagnosis ("Low but Increasing TV subgroup"). The second SB subgroup, "High but Declining TV Subgroup" (17%), reported greater TV hours per week than the U.S. average at all assessments, but decreased at two and five years post-diagnosis. Finally, the third SB subgroup, "U.S. Average TV Subgroup" (66%), reported a flat trajectory of consistently watching TV for 19-20 hours per week from pre-diagnosis to ten years post-diagnosis.

It was also important to examine PA and SB patterns estimated in the same model. When PA and SB trajectories were modeled simultaneously, two subgroups were observed: 1) 91% reporting low PA that increased at two and five years post-diagnosis and TV watching consistent with the U.S. average across all time points ("Low but Increasing PA and Average TV Subgroup"); and 2) 9% reporting high PA declining over time and TV watching consistent with the U.S. average increasing over time ("High but declining PA and Average TV Subgroup).

In Study 2, membership in these five PA and SB subgroups were used as the outcome variables in mediation models. I then examined which stress and coping constructs mediated the relationships between demographic, clinical, and treatment-related characteristics and PA and SB subgroup membership. My findings showed that PA and SB subgroups were predicted by constructs from the Transactional Model of Stress and Coping.

6.3 Identifying Breast Cancer Survivors in Different Physical Activity and Sedentary Behavior Subgroups

Consistent with my hypotheses, breast cancer survivors who increased their PA, or decreased their SB, at any time after diagnosis were more likely to have higher primary appraisal (higher anxiety about recurrence and worse perceived health) and secondary appraisal (higher perceived coping resources that can be mobilized to reduce threat or harm). Similarly, subgroups that did not increase their PA, or decrease their SB, after diagnosis did not report elevated primary appraisal variables (and therefore did not appraise their available coping resources that could be used to alter the stressful situation). In other words, the Transactional Model of Stress and Coping was useful for predicting which breast cancer survivors would change their PA or SB after diagnosis. The strength of my studies is in predicting which breast cancer survivors will change their long-term PA or SB patterns in response to a cancer diagnosis, based on psychosocial constructs, in order to facilitate early intervention.

In both PA and SB models, perceived health (proxy for perceived harm/primary appraisal) was an important mediator between demographic and clinical characteristics and PA and SB subgroups. African American breast cancer survivors who perceived their health to be poor, had higher fatigue, more comorbid conditions, higher body mass index, and had lower education were more likely to be in the "Low but Increasing PA Subgroup" for the PA model; they were also more likely to be in the "Above U.S. Average but Decreasing TV Subgroup" in the SB model.

The PA model also had three unique Transactional Model pathways predicting membership in the "Low but Increasing PA Subgroup" (that did not appear in the SB model). In the first unique pathway, Caucasian or Hispanic breast cancer survivors who had received chemotherapy, and had higher fatigue were more likely to have higher anxiety about recurrence,

and in turn were more likely to be in the "Low but Increasing PA Subgroup." In the second unique pathway, African American or Hispanic breast cancer survivors were more likely to report higher religiosity, and in turn more likely to be in the "Low but Increasing PA Subgroup." In the final unique pathway, breast cancer survivors who were not married/partnered and also reported lower social support were more likely to be in the "Low but Increasing PA Subgroup."

The SB model had one unique Transactional Model pathway predicting membership in the "Above U.S. Average and Decreasing TV Subgroup." Caucasian or African American breast cancer survivors who perceived greater financial impact from cancer, had received chemotherapy, and were not married/partneredwere more likely to be in the "Above U.S. Average and Decreasing TV Subgroup."

When PA and SB were estimated in the same model, only the pathway through percieved health (proxy for perceived harm) remained significant. African American breast cancer survivors who perceived their health to be poor, had lower education, higher fatigue, more comorbid conditions, and higher body mass index were more likely to be in "Low but Increasing PA and U.S. Average TV Subgroup."

6.4 What Worked and Did Not Work with Transactional Model Constructs

Given that I conducted secondary data analyses, I operationalized Transactional Model constructs with proxy variables. HEAL was not designed specifically for examining cognitions and emotions related to health behaviors and coping strategies. Instead, HEAL is an epidemiological cohort study developed to examine the influence of health behaviors, sex hormones, and genetic factors on long-term breast cancer outcomes. Therefore, proxy variables were selected to represent Transactional Model constructs.

One proxy variable (anxiety about recurrence) worked well for operationalizing Transactional Model processes but proxy variables for perceived harm and coping resources

could have performed better. In the latter cases, I provide suggestions for operationalizing these constructs in future research.

The proxy variable of anxiety about recurrence represented the Transactional Model construct of future threat well. Anxiety about recurrence assessed breast cancer survivors' perceptions of their risk for recurrence, and thus was a good proxy for assessing their perceived future health threats due to cancer.

Perceived harm was operationalized in two ways: 1) one item assessing perceived health; and 2) the Brief Cancer Impact Assessments subscales. The proxy variable of perceived health was a significant mediator in PA, SB, and PA-SB models. However, interpretation would have been easier if I had had a variable that assessed health detriments specifically attributable to breast cancer.

The subscales of the Brief Cancer Impact Assessment did not have adequate psychometric properties. The original four subscales described by Alfano et al. (2006) had low internal consistencies in my subsetted sample, and thus I conducted exploratory factor analyses. EFA suggested four factors for my subsample but internal consistencies were still low, suggesting that the factors may be measuring multiple topics.

Future research would benefit from testing alternative ways to operationalize perceived harm attributable to breast cancer. For instance, symptom burden due to breast cancer may be a good measurement option. Specific symptoms and whether the breast cancer survivor perceives them to be due to breast cancer could be assessed. Some examples include scars due to mastectomy or breast-conserving surgery, lymphedema, menopausal symptoms, "chemo brain," pain, fatigue, needing to take daily medications, and other physical reminders of cancer. Scale options may include the M.D. Anderson Symptom Inventory (MDASI: Cleeland, Mendoza,

Wang, Chou, Morrissey, & Engstrom, 2000) or the Edmonton Symtom Assessment Scale -Revised (ESAS-r: Hannon et al., 2015).

The MDASI is a nineteen-item scale assessing the severity of symptoms and impact on daily functioning for cancer patients (Cleeland et al., 2000). Response options range from 0 ("symptom not present") to 10 ("as bad as you can imagine"), and higher scores represent higher symptom burden. The 13 symptoms include pain, fatigue, nausea, distrurbed sleep, distressed (upset), shortness of breath, problem with remembering things, lack of appetite, drowsy/sleepy, dry mouth, feeling sad, vomiting, and numbness/tingling. There are also six items assessing the degree to which symptoms have interfered with six quality of life domains over the past 24 hours: general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life.

The ESAS-r assesses nine symptoms commonly experienced by cancer patients: pain, tiredness, drowsiness, nausea, lack of appetite, depression, anxiety, shortness of breath, and decreased well-being (Hannon et al., 2015). There is also a figure drawing where patients can indicate where they are feeling pain. The patient is directed to complete the ESAS-r based on how he or she is feeling "now." Response options range from 0 ("absence of symptom") to 10 ("worst possible severity"), and thus higher scores represent higher symptom burden.

Similarly, future research should also consider testing alternative ways to measure coping resources. Proxy variables were used to represent coping resources of religiosity, social support, and optimism. Religiosity and social support were both significant mediators in the PA model (but not the SB model). Religiosity was used as a proxy variable for religious coping resources. However, religiosity captures individual and faith community religiosity, but these resources were not necessarily used to increase PA or to decrease SB after diagnosis. Future research

would benefit from asking breast cancer survivors which coping resources they used to change PA or SB after diagnosis (and which resources were considered but not ultimately used). Future research could stratify by survivors who were able or not able to increase their PA or decrease SB.

Social support was assessed in HEAL by the number of confidantes at 39 months postdiagnosis (and recalled for the time of diagnosis). Recall bias may have been a problem where breast cancer survivors recalled greater or fewer confidantes at the time of diagnosis than was actually the case. In addition, breast cancer survivors were not asked directly if they used social support networks to increase their PA or decrease their SB after diagnosis. Future research should interview breast cancer survivors about which types of confidants in their social network helped in changing health behaviors after diagnosis (e.g., partner, family, good friend, etc.) and what type of assistance was provided (e.g., informational, instrumental, supportive, or financial support).

Barrera (1986) distinguished between different types of social support, such as perceived and enacted social support and social embeddedness, and how these different types of social support affect coping mechanisms and health outcomes. Barrera (1986) defined perceived social support as the cognitive appraisal that adequate support would be available if it was needed and social embeddedness as the perceived size of the social support network. In the HEAL study, a variable was available for assessing how many confidants a breast cancer survivor perceived she had at the time of diagnosis and at 39 months post-diagnosis. Future research should also consider examining perceived adequacy of social support from confidants during cancer diagnosis, treatment, and survivorship, confidence in ability to increase PA or decrease SB, and longitudinal tracking of PA and SB.

Barrera (1986) defined enacted social support as the perceived actions that significant others performed when they rendered assistance to the individual. In other words, enacted social support represents the perceived responsiveness of significant others in rendering assistance during a stressor. HEAL did not have a variable assessing enacted social support but future research could examine this issue with self-report questionnaires assessing frequency of perceived helping behaviors from significant others. Additionally, enacted social support could be directly observed by asking a breast cancer survivor and a perceived confidant to interact in the lab. For example, future research could ask breast cancer survivors and confidants (partners, family, friends, etc.) to discuss PA and SB and then record instances of informational and instrumental support.

Optimism was the variable used as a proxy for individual-level coping resources but it was not significant in PA nor SB models. Optimism may not have been a significant mediator because it was moderately correlated with religiosity and social support, suggesting that these constructs had overlapping variance. As a sensitivity analysis, I tried creating an indicator variable that combined the optimism, religiosity, and social support items. However, the factor analysis and low Cronbach's alpha internal reliability did not support a combined variable.

Additionally, optimism was only assessed at 39 months post-diagnosis. Optimism may fluctuate and be responsive to different stressors during cancer treatment and survivorship, and thus future research should consider assessing optimism at multiple points from pre-diagnosis to ten years post-diagnosis to better examine its relationships with PA and SB assessed at multiple points.

Future research could also consider testing other potential coping resources at the individual level (e.g., resilience, persistence, conscientiousness), interpersonal level (e.g., quality

of perceived social support, enacted social support), and group level (e.g., resources related to work or a company such as PA or weight loss programs, community resources such as free or reduced-fee PA programs including community parks, trails, and jogging tracks, and gyms and PA resources for cancer survivors available through cancer centers, academic institutions, and community programs). For instance, Lineberger Comprehensive Cancer Center has walking programs available for cancer survivors, literature on increasing PA in the library, and is part of the "Get REAL & HEEL" free exercise and recreational therapy program. "Get REAL and HEEL" is a grant-funded program that serves cancer patients in North Carolina by integrating individualized prescriptive exercise with recreational therapy. Individualized plans help each cancer patient manage cancer treatment-related symptoms and increase quality of life. "Get REAL and HEEL" has focused on increasing PA but has yet to incorporate decreasing SB into its program.

My dissertation results support targeting both PA and SB in interventions and tailoring interventions to be cancer-specific. In the next section, I describe how future interventions with breast cancer survivors can be guided by my results.

6.5 Intervention Components for Increasing Physical Activity and Decreasing Sedentary Behavior

My results suggest that, in order to increase breast cancer survivors' PA to guidelines levels, future interventions will need to build on existing theory and methods by adding components from the Transactional Model of Stress and Coping. For instance, future intervention research should consider combining more traditional health behavior theories (e.g., SCT or TTM) with the Transactional Model constructs of perceived threat (anxiety about recurrence), perceived harm (perceived health), and coping resources (social support) to increase breast cancer survivors' PA. Specialized interventions to change Transactional Model constructs in breast cancer survivors have already been developed in clinical psycho-oncology, and thus could be combined with traditional health behavior theories and methodology to increase breast cancer survivors' PA. For instance, Antoni and colleagues (2001; 2006; Leehner et al., 2012; Stagl et al., 2015) developed a group-based cognitive–behavioral stress management (CBSM) intervention for breast cancer survivors based on the Transactional Model of Stress and Coping and tested it in several randomized trials. The CBSM intervention has been shown to be successful at changing breast cancer survivors' perceived threat, harm, and coping resources through several intervention trials. However, CBSM has never been evaluated as an intervention for changing PA or SB. The specific intervention components of CBSM are discussed next.

6.5.1 Cognitive-Behavioral Stress Management Intervention

In the initial CBSM intervention trial, breast cancer survivors (stages 0-IIIb) were recruited 2-10 weeks after surgery and randomized to a 10-week CBSM intervention or a 1-day psychoeducational control group (Antoni et al., 2001). Outcomes included whether intervention components could change breast cancer survivors' perceptions of their health and harm that cancer may have caused on their life goals, relationships, and other areas. CBSM intervention sessions included relaxation skills (progressive muscle relaxation, visual imagery, deep breathing, and meditation techniques) and cognitive-behavioral components (strategies to reduce arousal and anxiety, changing negative stressor appraisals, and coping skills training). Coping skills included tools such as accurate matching of problem- or emotion-focused strategies on the basis of the controllability of the stressor, interpersonal skills training (e.g., communication skills, anger management, and assertiveness training), and identifying tangible and emotional sources of support. The CBSM intervention successfully increased benefit finding and optimism, reduced harm perceptions, and reduced incidence of depression in 25%–30% of the sample who reported moderate depression (Antoni et al., 2001).

Follow-up data 8-15 years after the original trial was published in 2015 (Stagl et al. 2015). One-hundred breast cancer survivors (51 CBSM patients and 49 controls) were recontacted 8-15 years after study enrollment to complete the Center for Epidemiologic Studies– Depression (CES-D) scale and the Functional Assessment of Cancer Therapy–Breast (FACT-B). Breast cancer survivors who received a 10-week, group-based CBSM intervention after surgery for breast cancer reported significantly lower depressive symptoms and better quality of life than the control group up to 15 years later. Their results suggest that early implementation of cognitive-behavioral interventions may influence long-term psychosocial functioning in breast cancer survivors.

A second trial was conducted with breast cancer survivors who reported moderate to high distress (Antoni et al., 2006). The CBSM intervention significantly decreased intrusive thoughts about cancer, anxiety about recurrence, general distress, and interviewer-rated anxiety symptoms. Reductions in these symptoms were still observed nine months after the intervention had ended (Antoni et al., 2006). Finally, CBSM was adapted for African American breast cancer survivors in "Project CARE" (Cope, Adapt, Renew, Empower) (Lechner et al., 2012). The language, scenarios, and role-plays were adapted to fit African American preferences. For instance, the coping skills and social support modules were enhanced with religious/spiritual and faith community coping strategies.

Given the success of the CBSM intervention with breast cancer survivors in changing Transactional Model constructs, the next logical step in future research would be to supplement the CBSM intervention with constructs from classical health behavior theories that have been

shown to increase breast cancer survivors' PA. Ways in which CBSM could be combined with traditional health behavior theories is discussed next.

6.5.2 Combining CBSM with Social Cognitive Theory or the Transtheoretical Model

The most commonly applied health behavior theories with cancer survivors include Social Cognitive Theory (SCT) and the Transtheoretical Model (TTM) (Pinto & Floyd, 2008). SCT predicts that a health behavior is performed if an individual perceives control over the outcome, few external barriers, and confidence in ability (Bandura, 1986). The Transtheoretical Model has a five-stage system for classifying readiness to change a health behavior (Prochaska & DiClemente, 1983): pre-contemplation, contemplation, preparation, action, and maintenance stages. These SCT and TTM components could be combined with Antoni and colleagues' CBSM intervention to develop a PA and SB intervention for breast cancer survivors.

One problem with using Social Cognitive Theory and the Transtheoretical Model with breast cancer survivors is that these theories assume that emotions and affective reactions are not important predictors of health behavior (Armitage & Conner, 2000; Burke, Joseph, Pasick, & Barker, 2009; Brug, et al., 2005; Giles-Corti & Donovan, 2002). However, the Transactional Model of Stress and Coping purposely includes emotions and affective reactions as predictors of coping behaviors. It also includes perceived coping resources as an important secondary appraisal, and thus would be an excellent addition to Social Cognitive Theory and the Transtheoretical Model for breast cancer survivors.

Transtheoretical Model interventions with readiness to change components have been shown to successfully increase PA in breast cancer survivors. For instance, Pinto and colleagues (2005) conducted a randomized controlled trial of a TTM-derived intervention to increase PA in breast cancer survivors. The TTM intervention consisted of telephone counseling and weekly exercise tip sheets. The intervention group was more likely to progress in motivational readiness for PA, significantly increased total minutes of PA per week, and outperformed the control group on an objective fitness test (Pinto et al., 2005).

Adapting the CBSM to include TTM components would involve adding readiness to change variables to the 10-week CBSM training in order to increase PA and decrease SB. The majority of breast cancer survivors have been shown to be in the pre-contemplation and contemplation stages (Rogers, Courneya, Shah, Dunnington, & Hopkins-Price, 2007), and thus a combined CBSM-TTM intervention could target these stages.

Individuals in both the pre-contemplation and contemplation stages are not currently exercising (Marcus, Bock, Pinto, & Clark, 1996). The difference is whether the individual intends to begin exercising in the next six months. Individuals in the pre-contemplation stage do not intend to start exercising in the next six months, but individuals in the contemplation stage do intend to begin exercising within the next six months (Marcus et al., 1996).

A breast cancer survivor in the pre-contemplation or contemplation stage may be underinformed about consequences of low PA and high SB, may avoid thinking about recurrence and mortality and its relation to PA and SB, and may have become demoralized about ability to change PA because of past attempts. She may appraise her threat of recurrence as high, perceive that breast cancer has caused harm to her health and life goals, and perceive that she has low coping resources. A module could be added to the CBSM that targets the TTM foci of consciousness raising about PA and SB and increasing the ability to recognize negative emotions and physical symptoms associated with them. Based on my results, to change SB, an additional module focusing on perceived financial harms attributed to breast cancer would need to be added.

Other potential constructs from SCT could be carefully selected too. For instance, selfefficacy for PA and barriers to PA are likely to be important predictors of PA in breast cancer survivors. Self-efficacy, in particular, has proven to be an important predictor of health behavior change in the general population (Armitage & Conner, 2000) and with breast cancer survivors (Rogers, McAuley, Courneya, & Verhulst, 2008). Rogers and colleagues (2008) examined associations for PA self-efficacy in 192 breast cancer survivors with structural equation modeling. PA self-efficacy was directly predicted by perceived PA barriers, fatigue, social support, enjoyment of PA, and pre-diagnosis PA. Given these results, future research should consider testing a model with breast cancer survivors where perceived threat, harm, and coping resources directly predict self-efficacy, which in turn predicts PA subgroups. Ways to further tailor a combined CBSM-TTM intervention to breast cancer survivors are discussed next.

6.5.3 Tailoring Intervention to Breast Cancer Survivors' Needs

Finding ways to further tailor a combined CBSM-TTM intervention to breast cancer survivors' needs may increase uptake and maintenance. For instance, fatigue is one of the most common symptoms reported by cancer survivors, and thus will need to be addressed in future interventions. In a prior study of fatigue during cancer survivorship with over 450 survivors (64% breast), 74% reported at least occasional fatigue and 57% reported experiencing fatigue on a daily basis at approximately three years post-diagnosis (Blaney, Lowe-Strong, Rankin-Watt, Campbell, & Gracey, 2013). Two-thirds (68%) reported that they had never been given advice on how to manage fatigue (Blaney et al., 2013).

My model results suggest that coping with cancer-related fatigue will be an important intervention component for changing PA and SB. In my PA model results, fatigue predicted both anxiety about recurrence and perceived health, and thus predicted PA subgroups indirectly through two pathways. In my SB results, fatigue directly predicted perceived health, and

indirectly predicted SB. Consistent with Transactional Model processes, the symptom of fatigue was being interpreted through cognitive and affective perceptions, rather than directly predicting PA or SB. This indirect pathway result suggests that perceptions of fatigue can be changed. My results suggest four components to test in future interventions: 1) educating breast cancer survivors about fatigue experienced during survivorship; 2) raising consciousness about how perceptions of fatigue may be influencing how they feel about their health and their PA and SB; 3) teaching skills for managing fatigue; and 4) teaching Antoni and colleagues' cognitive-behavioral stress management skills to change perceptions of threat and harm. If perceptions about poor health and symptoms like fatigue can be changed, and anxiety about recurrence managed in the clinical setting, breast cancer survivors may be able to devote more time and energy to overcoming barriers to PA.

In sum, a comprehensive intervention to increase PA and decrease SB for breast cancer survivors would include targeting constructs from traditional health behavior theories and constructs from the Transactional Model of Stress and Coping (perceived threat and harm appraisal and perceived coping resources). Antoni and colleagues (2001; 2006; Leehner et al., 2012) developed a cognitive-behavioral stress management intervention for breast cancer survivors that could be adapted as an intervention for changing PA and SB.

6.6 Strengths of My Studies

This is the first study among breast cancer survivors to examine psychological mechanisms underlying PA and SB patterns from pre-diagnosis through ten years post-diagnosis. My a priori mediation models were informed by Lazarus and Folkman's (1987) Transactional Model of Stress and Coping. I used the Transactional Model of Stress and Coping to investigate predictors of PA and SB patterns after breast cancer because it includes constructs for emotional

reactions and social and cultural coping resources, which typically are excluded from classic health behavior theories.

Even though conceptualizing PA and SB as long-term coping strategies is an innovative application of the Transactional Model of Stress and Coping, the current study demonstrates that the Transactional Model is useful for explaining PA and SB patterns in cancer survivors. Primary and secondary appraisal variables mediated the relationships between demographic, clinical, and treatment-related characteristics and subgroups of breast cancer survivors following different PA and SB patterns over time.

Additional strengths of my studies included: 1) a diverse sample from three U.S. sites; 2) data that spanned an eleven-year period and included pre-diagnosis data; and 3) treatmentrelated data that was collected through the Surveillance, Epidemiology, and End Results cancer registries; and 4) a statistically rigorous design that corrected for shortcomings in the HEAL dataset.

6.7 Limitations

Despite the strengths of my dissertation studies, there were limitations related to the dataset and variables, statistical limitations, and treatment changes since 1995-1999 (when the breast cancer survivors in HEAL were diagnosed). Each limitation type is considered in a subsection below.

6.7.1 Dataset Limitations

Eight dataset limitations affected my two studies: 1) some mediators were assessed once; 2) PA and SB were assessed at irregular intervals over ten years; 3) the assessment of PA and SB at six months post-diagnosis (and pre-diagnosis recall) differed among the sites; 4) the SB questions were not from a scale validated with breast cancer survivors; 5) potential recall bias for pre-diagnosis PA and SB; 6) body mass index was assessed with self-reported height and weight;

7) comorbid conditions were only assessed at two years post-diagnosis; and 8) there was no measure of depression available.

The following mediators were only assessed once at 39 months post-diagnosis: harm appraisal (perceived impact of breast cancer), threat appraisal (anxiety about recurrence), and coping resources (optimism, religiosity). However, these variables may be tapping into more stable constructs that influence situation-specific appraisals of stressors. For instance, anxiety about recurrence is relatively stable over long-term survivorship (Janz et al., 2011; Johnson Vickberg, 2001; Simard et al., 2013; van den Beuken-van Everdingen et al., 2008; Deimling et al., 2006; Whitaker, Watson, & Brewin, 2009). Similarly, resources that influence secondary appraisal (optimism and religiosity/spirituality) are likely to be relatively stable constructs that may influence how situation-specific stressors are perceived. Nonetheless, several mediators assessed at one time point limited my ability to examine the plausibility of causal relationships. In order to establish causation, future research would need to show that stress and coping variables preceded PA and SB changes in time; that there is evidence of association between the two variables; and that other factors have been controlled (Enders, 2010a; MacCallum, 1996).

My ability to detect PA and SB patterns over time and group survivors into subgroups was limited by the irregular and large spacing between assessments. PA and SB patterns were assessed at five time points: six months post-diagnosis (recall of pre-diagnosis PA and in the "last month", which were treated as separate time points), and two, five, and ten years postdiagnosis. The statistical methodologies of latent curve modeling and growth mixture modeling are robust to partially missing data, unequally spaced time points, and complex trajectories (Roth, 1994; Cohen & Cohen, 1983). However, the irregular spacing of the assessment intervals may have led to important patterns being missed. For instance, important patterns between five

and ten years post-diagnosis may have been missed. Future research will benefit from assessing PA and SB at multiple time points during long-term survivorship, especially between five and ten years post-diagnosis.

The next limitation was that the assessment of PA and SB at approximately six months post-diagnosis was different among the three HEAL sites because the California site was brought into the study later than the New Mexico and Washington sites. At the California site, PA data for the pre-diagnosis and six months post-diagnosis time points were constructed from a lifetime history collected during a separate case-control study. At New Mexico and Washington, PA was collected with the Modifiable Activity Questionnaire. The same sixteen exercise activities were used in the PA variable calculation, but different interviewer-administered questionnaires may have introduced differences in reporting.

Data collection of SB was also affected. The California site did not collect SB items at enrollment (including pre-diagnosis recall and six-months post-diagnosis) and it could not be constructed from other data. Therefore, data were imputed using thirty variables for multiple imputation. Multiple imputation is a state-of-the-art missing data technique (Enders, 2010b), but future research studies are needed to confirm my SB results. All African American women were enrolled at the California site, and thus more research is needed to detemrine if my results generalize to African American breast cancer survivors in other parts of the country.

An additional limitation related to SB was that it was assessed by two items that had not previously been validated with breast cancer survivors. When HEAL began in 1995, no validated measures of SB existed. However, television watching time is the most common way of measuring SB in the literature (Clark et al., 2009; Thorp, Owen, Neuhaus, & Dunstan, 2011) and self-reported television viewing time shows moderate to large test–retest correlations across

studies, indicating that questionnaires are likely prompting recall in a consistent way (Clark et al., 2009). Adults have more accurate recall of television watching times than other types of sitting because specific shows or movies are recalled, which prompts better recall about sitting time (Clark et al., 2009). In addition, these two SB items have been used successfully in three HEAL publications unrelated to my dissertation (George et al., 2013a; 2013b; Forsythe et al., 2013). Future research would benefit from examining other types of SB, namely desk jobs and screen time (laptops, Ipads, phones, etc.), whether SB types change over the course of diagnosis and surivorship, and whether changes can be predicted by stress and coping variables.

Similarly, recall bias for pre-diagnosis PA and SB may have been a problem. At six months post-diagnosis, breast cancer survivors were asked to recall their PA and SB prior to diagnosis. Women may not have accurately remembered their PA and SB levels prior to diagnosis or may have reported better PA and SB levels than was actually the case. All sites asked survivors to recall their pre-diagnosis PA and SB, and thus any bias would have been systematic across sites. Future research would benefit from prospectively collecting pre-and post-diagnosis PA and SB. For instance, in the Nurses' Health Study (e.g., Holmes et al., 2005) and the Women's Healthy Eating and Living trial (Pierce et al., 2007), women without cancer were prospectively followed and those that developed breast cancer later were formed into a subsample. These subsamples may have both pre- and post-diagnosis PA available. Future research would benefit from also collecting SB for pre- and post-diagnosis and throughout survivorship.

The next dataset limitation was that body mass index (BMI) was computed with selfreport data because not all sites weighed women in person. BMI was calculated using selfreported height at age 18 and self-reported weight at six months and five and ten years post-

diagnosis. Two out of three sites (Washington and New Mexico) also had data available for height and weight at six months post-diagnosis that was measured by clinic staff, and thus I was able to determine the correlation between self-reports and BMI measurements taken in clinics. Self-reported height recalled for age 18 correlated with current height measured in the clinic at r=0.93 (p<.0001). Missing data on height was minimal (<1%), and therefore was unlikely to affect BMI calculations.

Self-reported weight at six months post-diagnosis correlated at r=0.85 (p<.0001) with weight taken on a scale at the clinics. Therefore, it appears to be unlikely that breast cancer survivors were substantially underreporting their weight. Missing data was also minimal for weight. At six months post-diagnosis, only 12 survivors (1%) were missing self-reported weight. For the time points at five and ten years post-diagnosis, missing data was consistent with attrition levels (29% and 42%, respectively).

The next limitation is that comorbid conditions were only assessed at two years post-dx with no follow-up data. Approximately two-thirds of the breast cancer survivors self-reported comorbid conditions at two years post-diagnosis. Similar to women without cancer, breast cancer survivors experience greater comorbid conditions as they age (see Devita, Lawrence, & Rosenberg, 2010). For breast cancer survivors, greater comorbid conditions have been correlated with lower PA (Irwin et al., 2003; Sabiston et al., 2014; Charlier et al., 2013; Harrison et al., 2009; Hawkins et al., 2010; Patterson et al., 2003; Pinto et al., 2002) and higher SB (Rogers, 2011), and thus one possible explanation for PA decreasing and SB increasing in my study may have been due to breast cancer survivors developing more comorbid conditions over time. Future research with breast cancer survivors should assess comorbid conditions over time to examine how PA and SB are affected.

The final dataset limitation is that no measure of depression was available for HEAL. Depression has been shown to be correlated with lower PA (Pinto & Trunzo, 2004; Courneya & Friedenreich, 1999; Phillips & Mcauley, 2013; Trinh, Amireault, Lacombe, & Sabiston, 2015; Varder-Yagli et al., 2015) and higher SB (Trinh, Amireault, Lacombe, & Sabiston, 2015), and thus breast cancer survivors who were experiencing depression may have reported different patterns over time. However, in the literature, breast cancer survivors report low depression rates in national samples (Krebber et al., 2014), and therefore, depression may not have significantly biased my results. Future research will need to determine the effects of depression and the timing on PA and SB patterns for breast cancer survivors.

6.7.2 Statistical Limitations

Two statistical limitations are noted as well. The statistical assumption that missing data is missing at random could not be met, and thus PA and SB were imputed. Modern statistical techniques (latent curve modeling) were also used because the assumptions of traditional models could not be met. For instance, ANOVA's four main assumptions could not be met: 1) no missing data; 2) equally spaced time points; 3) normal distribution; and 4) homogeneity of variance and covariance over time. Growth modeling was used because it is flexible and robust to these challenges (Roth, 1994; Cohen & Cohen, 1983). Maximum likelihood with robust standard errors (MLR) was also used for model estimation because it improves the accuracy of the parameter estimates and increases power for intermittently missing data (Enders, 2010b).

Latent curve modeling may also be better suited than traditional methodology for examining theoretical models that assume individual change over time. For instance, ANOVA tests for mean differences between time points, and thus is not a good fit for examining individual change over time. Individual change follows a continuous path through time, which is not captured well by treating time as a nominal predictor as ANOVA does (Curran & Bauer,

2006). The Transactional Model of Stress and Coping (Lazarus & Folkman, 1987) is focused on individual changes in coping and perceived resources (not simply mean change), and thus needs a more modern methodology. Future research with cancer survivors should consider using theoretical models of individual change and modern statistical methodology that accounts for individual change over time.

6.7.3 Limitations Related to Changing Treatment Patterns Over 20 Years

Oncology treatment guidelines, and the potency of treatments, have improved since the HEAL breast cancer survivors were diagnosed in 1995-1999, and thus my results may not fully generalize to women diagnosed today. An example of a treatment change between 1995 and 2015 includes chemotherapy doses that are less potent, have fewer side effects, and are more targeted to cancer cells (Smith et al., 1998; Rubin, 2001). Similarly, breast-conserving surgery and reconstruction techniques have advanced (Rubin, 2001).

It is curious in my data that the percentage of survivors receiving breast-conserving surgery and radiation were not more similar. In my study, 63% received breast-conserving surgery but only 51% for radiation. This difference may be due to the way that SEER tracks treatment. Radiation therapy received beyond six months post-diagnosis is not captured well in SEER (Virnig et al., 2002), and thus some women may have been misclassified for radiation status.

I was also not able to examine breast construction as a variable in models for PA and SB patterns, and thus the timing of reconstruction is unknown. However, breast reconstruction involves several surgeries spread over multiple months (Rubin, 2001), and therefore would be expected to influence PA and SB at six months post-diagnosis. Future research would benefit from prospectively examining PA and SB stratified by treatment types such as immediate or delayed reconstruction.

Another treatment limitation is that I was only able to examine one type of anti-estrogen therapy (tamoxifen) because it was available for prescription during the entire study period and efficacious in both pre- and post-menopausal women. In my study, tamoxifen assessed at multiple time points was not related to any of the psychosocial mediators.

Another type of anti-estrogen therapy called "aromatase inhibitors" was recommended by the American Society of Clinical Oncology in 2004 for women who have hormone-receptorpositve tumors and are post-menopausal (see Fabian, 2007). However, aromatase inhibitors have been found to cause joint pain and fatigue in breast cancer survivors (Fabian, 2007), both of which would be expected to affect PA and SB. Future research would benefit from examining the ways in which aromatase inhibitors affect short- and long-term PA and SB patterns for breast cancer survivors. Finally, the national policy context of cancer treatment today is different than 1995-1999 because more breast cancer survivors may be insured as part of the Affordable Care Act enacted in 2010. Between 2010 and 2014, the average number of uninsured individuals decreased by over 11 million (Martinez & Cohen, 2015). However, there is evidence that breast cancer survivors who are insured still have substantial out-of-pocket costs (Pisu et al., 2010). Future research would benefit from examining the ways in which insurance status and out-ofpocket treatment costs influence PA and SB patterns for breast cancer survivors to better understand my results of financial impact and SB being related.

6.8 Preventing Breast Cancer Incidence with Increased Physical Activity and Decreased Sedentary Behavior

My dissertation has focused on tertiary prevention for breast cancer survivors, in that the future goal would be to prevent recurrence and early mortality by increasing PA and decreasing SB. A large literature is also devoted to primary prevention of breast cancer incidence by

increasing PA (see Lynch, Neilson, & Friedenreich, 2010). SB is an up-and-coming target for primary prevention of breast cancer (Lynch, 2010).

Similar to my study results, stress and coping variables may also be future intervention targets for primary prevention in women at high risk of developing breast cancer. For instance, Hartman and colleagues (2011) tested a pilot PA intervention in 27 women with a first-degree relative with breast cancer but no personal history of breast cancer. Their intervention was informed by social cognitive theory and the Transtheoretical Model and included a tailored, print-based PA intervention lasting 12 weeks. Theoretical constructs assessed included perceived risk of developing breast cancer, perceived control over breast cancer risk, and the extent to which breast cancer specific worry interfered with daily functioning,

At baseline, women at risk of developing breast cancer were engaging in approximately 25 minutes/week of moderate to vigorous PA. The mean increase in PA was 130 minutes/week (SD=138) with 41% meeting the national PA guideline at 12 weeks. As women's perceived risk of breast cancer *decreased*, they were more likely to *increase* their PA. This study suggests that a tailored and targeted intervention can help women at high risk of developing breast cancer to decrease their anxiety about developing breast cancer and to become more physically active. Future research is needed to determine ways in which stress and coping variables can be targeted to decrease SB in women at risk of developing breast cancer, and thus decrease incidence.

Other stress and coping constructs may also be relevant for women at risk of developing breast cancer, with some modifications. For instance, important predictor variables of PA and SB may be perceived health, anticipated harm if she develops breast cancer, and anticipated coping resources she may be able to draw on if treatment becomes necessary (optimism, religiosity, and social support).

6.9 Conclusion

My dissertation results provide a better understanding of the role that psychosocial variables from stress and coping theory play in influencing PA and SB trajectories during long-term survivorship and inform intervention strategies tailored to breast cancer survivors. Future intervention work will need to be tailored to breast cancer survivors' unique cancer experiences and perceptions of threat, harm, and coping resources.

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