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Race/Ethnicity, Subjective and Objective Sleep Quality, Physical and Psychological Symptoms in Breast Cancer Survivors

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by

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Abstract

Breast cancer is a major health problem and comprises the largest population of cancer survivors in the United States, estimated at 2.9 million women, accounting for 22% of all cancer survivors (National Cancer Institute, 2013). The advances in breast cancer screening, diagnosis and treatment has increased the importance of survivorship needs. A major concern among breast cancer survivors (BCS) is sleep disturbances. This study used an innovative approach to examine ethnic and racial disparities in sleep disturbances present in BCS. In addition, this study also explored sleep disturbances across different races/ethnicities. This study was a secondary data analysis of baseline data from the supplement study of the *MBSR Symptom Cluster Trial for Breast Cancer Survivors*/ 1R01CA131080, conducted by Dr. Lengacher. Sleep was measured using the Pittsburgh Sleep Quality Index, sleep diary (subjective), and sleep actigraphy (objective). The sample consists of 79 women who had been diagnosed with breast cancer (Stage 0, I, II, III), completed lumpectomy and/or mastectomy, and were within 2 weeks to 2 years post radiation and/or chemotherapy treatment. The aims for this study were to: 1) explore racial/ethnic differences in objectively measured sleep patterns among BCS; 2) estimate and compare the correlation between objective and subjective sleep quality by racial/ethnic groups among BCS; 3) examine which sleep actigraphy measure appears to have the strongest relationship with physical and psychological symptoms; and 4) explore

whether these relationships (i.e. between objective sleep and self-reported symptoms) appear to be modified by race/ethnicity.

The first aim was conducted using analysis of variance (ANOVA) and analysis of covariance (ANCOVA). Results indicated that white, non Hispanic BCS had improved objective sleep quality compared to minority BCS. The second aim was conducted using Pearson's correlation with significant correlations found between subjective and objective sleep onset latency (r= .310, p= .016), and total sleep time (TST) (r= .328, p= .011) for the white, non-Hispanic group. The third aim was conducted using Pearson's correlation with significant correlations between sleep onset latency and depression (r= .247, p= .029); sleep efficiency and depression (r= -.233, p= .040); sleep efficiency and fatigue (r= -.207, p= .045); and WASO and pain (r= .277, p= .014). There were no significant correlations between the anxiety score and actigraphy parameters.

Using the significant correlations from the results of the third aim, multiple regression analysis was conducted with age as a covariate to test the fourth aim. The main effect of depression on sleep efficiency was significant (p= .044) with less depression associated with higher sleep efficiency. The interaction term, depression by race/ethnicity, had a non-significant effect on sleep efficiency (p= .299). The main effect of pain on WASO was significant (p= .008), and increased pain was associated with longer WASO. The interaction term, race/ethnicity by pain, had a non-significant effect on WASO (p= .148). The main effect of depression predicting sleep onset latency was significant (p= .027), and the interaction term, depression by race/ethnicity, had a trend towards a significant effect (p= .092) on predicting sleep onset latency. The interaction between depression and race/ethnicity predicting sleep onset latency was further

decomposed using multiple regression. The average sleep onset latency was longer in the minority group with high depression levels (42 minutes) compared to the white, non-Hispanics with high depression levels (29 minutes). Race modified the effect of depression on sleep onset latency in this sample of BCS.

These finding suggest that the experience of objective sleep disturbances is different among races/ethnicities. Additional research is needed to further explore racial/ethnic differences in subjective and objective sleep disturbances and its impact on physical and psychological symptoms among BCS. As the number of BCS continue to rise, it is becoming increasingly important to recognize sleep disturbances and their potential physical and psychological effects early in BCS, specifically in different races and ethnicities. It is anticipated that these findings may contribute to improved symptom management for women of different races and ethnicities.

Chapter One

Introduction

Background

Breast cancer is a major health problem and comprises the largest population of cancer survivors in the United States, estimated at 2.9 million women, accounting for 22% of all cancer survivors (National Cancer Institute, 2013). The risk of developing breast cancer is highest among white women. According to the American Cancer Society (2012), the incidence of breast cancer is 118.6 per 100,000 non-Hispanic white women compared to 102.3 per 100,000 black women. Despite lower incidence rates, mortality in black women is 29.7 per 100,000, higher in comparison to the mortality in non-Hispanic, white women of 22.1 per 100,000. The five-year survival rate for non-Hispanic, white women (91%) is higher in comparison to Hispanic (86%) and black (79%) women. With the increasing number of breast cancer survivors (BCS), it is imperative to explore symptoms that may be related to the cancer diagnosis or treatment type.

Sleep disturbances are becoming an increasingly recognized side effect of cancer treatment affecting both physiological and psychological functioning. These disturbances are characterized by difficulty falling asleep, staying asleep, early morning awakenings, non-restorative sleep, and daytime sleepiness (Moore et al., 2011). Sleep disturbances can be measured both subjectively and objectively. Objective measures of sleep disturbance include sleep latency, efficiency, duration, and daytime dysfunction (Alfano et al., 2011).

Estimates of subjective sleep disturbances vary widely, ranging between 20% to 70% of newly diagnosed or recently treated breast cancer patients, which is double compared to the general population (Fiorentino et al., 2011). For some breast cancer patients, the end of chemotherapy treatment may lead to restoration of sleep and rest patterns; however, for other breast cancer patients, sleep disturbances may become a chronic problem (Kotronous et al., 2012). Savard and colleagues (2001) reported that 58% of BCS who were approximately four years post diagnosis still reported problems related to sleep. In addition, breast cancer patients who completed radiation therapy, experienced sleep maintenance problems persisting for six months (Dhruva et al., 2012).

Race and ethnicity are considered significant predictors of symptoms in BCS (Deimling et al., 2006). The Women's Health Initiative (WHI) study found that black BCS had worse scores on many domains of physical functioning and general health in comparison to white survivors (Paskett et al., 2009). Eversley and colleagues (2005) conducted an interview on 116 BCS to determine racial and ethnic differences in the range and number of post-treatment symptoms among women who have undergone surgical and post-surgical treatment for breast cancer. Black BCS were more likely to report pain. In addition, 52% of the sample reported levels of depressive symptoms sufficient to be considered clinically depressed.

Understanding the functional consequences of sleep disturbances in BCS is pertinent. Fatigue is a common behavioral consequence of sleep disturbances reported by cancer survivors and leads to decrements in the overall quality of life in BCS (Taylor et al., 2011). Palesh and colleagues (2010) found that BCS with sleep disturbances had significantly higher levels of fatigue compared to BCS without sleep disturbances.

Additionally, fatigue is a significant problem for minority BCS compared with white survivors (Von et al., 2012). It is also one of the strongest predictors of overall quality of life in BCS. A relationship between sleep quality, physical and psychological symptoms has long been recognized, but mostly in the context of white, non-Hispanic BCS. Past research has looked at the associations between demographic (age, education) and clinical (stage of disease, number of comorbidities) variables with sleep measures, but not between symptoms and objective sleep measures in different races/ethnicities (Beck et al., 2010; Enderlin et al., 2011). Additional research is needed to understand how race/ethnicity modifies the effect of physical and psychological symptoms on sleep in minority BCS.

Statement of the Problem

Limited research has been conducted on both objective and subjective sleep quality in BCS of different ethnicities and races. Despite an increasing interest in sleep patterns in cancer survivors, past research has focused on predominantly white samples, limiting information on the unique health-related quality of life outcomes of BCS of minority races/ethnicities. To gain a more comprehensive understanding of racial/ethnic differences in sleep disturbances and the effect of physical and psychological symptoms on objective sleep quality in BCS, additional research is needed in this area. Previous studies have largely relied on self-report to measure sleep, whereas objective measures of sleep have rarely been investigated in different races/ethnicities (Parente et al., 2012). As the number of BCS continue to increase, it is becoming increasingly important to fully characterize quality of sleep data in racial and ethnic minorities (*i.e.* white, non-Hispanics

versus other races and ethnicities) by using a comprehensive sleep assessment and further exploring symptoms associated with sleep in BCS.

Statement of the Purpose

The purpose of this cross-sectional, pilot study is to examine the relationship between sleep disturbances and physical and psychological symptoms across different races/ethnicities among BCS. Sleep disturbances are measured subjectively and objectively. Physical symptoms include pain and fatigue. Psychological symptoms include anxiety and depression. This study is a secondary data analysis of data from the NCI administrative sleep supplement study of the *MBSR Symptom Cluster Trial for Breast Cancer Survivors/* 1R01CA131080, conducted by Dr. Cecile Lengacher.

Rationale for Study

Examining whether race/ethnicity modifies the relationship between sleep disturbance and physical and psychological symptoms will contribute to understanding the survivorship experience for specific races/ethnicities in order to proactively assess difficulties and plan interventions. This study is warranted due to the limited empirical knowledge regarding sleep disturbances in ethnic/racial minorities. Although previous studies have examined sleep disturbances in BCS, none has compared sleep disturbances in BCS from different races/ethnicities. This study is innovative as it looked at the modifying effect of race/ethnicity on the association between objective sleep and physical (*i.e.* pain and fatigue) and psychological (*i.e.* depression and anxiety) symptoms in BCS. Routine assessment of sleep as part of survivorship care may help to improve quality of life and may lessen the gap of health disparities.

Specific Aims

A cross-sectional, pilot study was conducted among 79 BCS who had undergone surgery (lumpectomy and/or mastectomy) and treatment (radiation and/or chemotherapy) in the past two years. The specific aims were to:

Aim 1: Explore racial/ethnic differences in objectively measured sleep patterns among BCS.

Aim 2: Estimate and compare the correlations between objective and subjective sleep quality by racial/ethnic groups among BCS.

Aim 3: Examine which sleep actigraphy measure appears to have the strongest relationship with physical and psychological symptoms.

Aim 4: Explore whether these relationships (*i.e.* between objective sleep and self-reported symptoms) appear to be modified by race/ethnicity.

Definition of Terms

The following terms are defined and were used throughout the study.

Cancer Survivor. Cancer survivor is defined as anyone who has been diagnosed with cancer, from the time of diagnosis through the balance of his or her life (National Cancer Institute, 2013).

Sleep Disturbances. Sleep disturbances are characterized by difficulty falling asleep, staying asleep, early morning awakenings, non-restorative sleep, and/or daytime sleepiness (Moore et al., 2011). Subjective sleep quality was operationalized using the Pittsburgh Sleep Quality Index (PSQI) with a score of 5 or higher indicative of poor sleep quality (Buysse et al., 1989). The Actiwatch-Score actigraph was used for the objective assessment of sleep.

Fatigue. Fatigue is described as a distressing condition marked by extreme tiredness and inability to function due to a lack of energy (National Cancer Institute, 2013). Fatigue was operationalized using the Fatigue Symptom Inventory (Hann et al., 1998). Higher scores are indicative of greater fatigue.

Pain. Pain is defined as an unpleasant, subjective, sensory and emotional experience associated with tissue damage (National Cancer Institute, 2012). The Brief Pain Inventory (BPI) Short Form was used to assess pain and its impact on daily functions (Cleeland, 1991). Mild pain is defined as a worst pain score of 1 - 4, moderate pain is defined as a worst pain score of 5 - 6, and severe pain is defined as a worst pain score of 7 – 10.

Depression. Depression is defined as a mental condition characterized by ongoing feelings of sadness, despair, loss of energy, and difficulty dealing with daily life (National Cancer Institute, 2013). Self-reported depressive symptoms were measured with the Center for Epidemiologic Studies-Depression Scale with a score of 16 or higher indicative of clinical depression (Radloff, 1977).

Anxiety. Anxiety is characterized by feelings of fear, dread, and uneasiness occurring as a result of stress (National Cancer Institute, 2013). The State Trait Anxiety Inventory-State Scale only (STAI) was used to measure anxiety (Spielberger, Gorsuch & Luschene, 1983). Scores range from 20 to 80 with higher scores indicative of greater anxiety.

Race. Race is based on self-report and is a social category characterized by similar physical experience (Heurtin-Roberts, 2004). For the purposes of this study, categories include white, non-Hispanic versus other races/ethnicities.

Significance of Study

This study used an innovative approach to compare sleep disparities among BCS of different races and ethnicities. Actigraphy was utilized as an objective measure of sleep. This study examined which sleep actigraphy measure appeared to have the strongest relationship with physical and psychological symptoms. Moreover, this study explored if these relationships appear to be modified by race/ethnicity. This study is important in that it enhances a greater understanding of racial/ethnic differences in sleep disturbances and their relationship with physical and psychological symptoms among BCS. It is anticipated that the findings may contribute to greater recognition of sleep disturbances and improved symptom management for BCS of different races and ethnicities.

Chapter Two

Literature Review

Introduction

This chapter presents the hypothesized research model and the empirical review of the literature. The review of literature focuses on sleep disturbances, objective sleep, physical and psychological symptoms in breast cancer. Finally, a summary of the literature review is presented.

Hypothesized Research Model

The hypothesized research model for this study is depicted in Figure 1. This model was designed to examine the specific outcome variables of interest, including subjective sleep quality, objective sleep disturbances, as well as the moderating effect of race/ethnicity on these outcome variables. The independent variables comprised of the study subject's baseline physical (*i.e.*, pain and fatigue) and psychological symptoms (*i.e.*, depression and anxiety). These relationships are hypothesized based on a review of empirical literature.

The proposed model explored four pathways as depicted in Figure 1. One pathway explored objective sleep disturbances across different races/ethnicities (*i.e.* white, non-Hispanics versus other races/ethnicities). Another pathway compared the correlation between subjective sleep quality and objective sleep disturbances by racial/ethnic differences. Another pathway explored which sleep actigraphy parameter

had the strongest relationship with physical and psychological symptoms. The fourth pathway explored whether these relationships (*i.e.* between objective sleep and self-reported symptoms) appear to be modified by race/ethnicity.

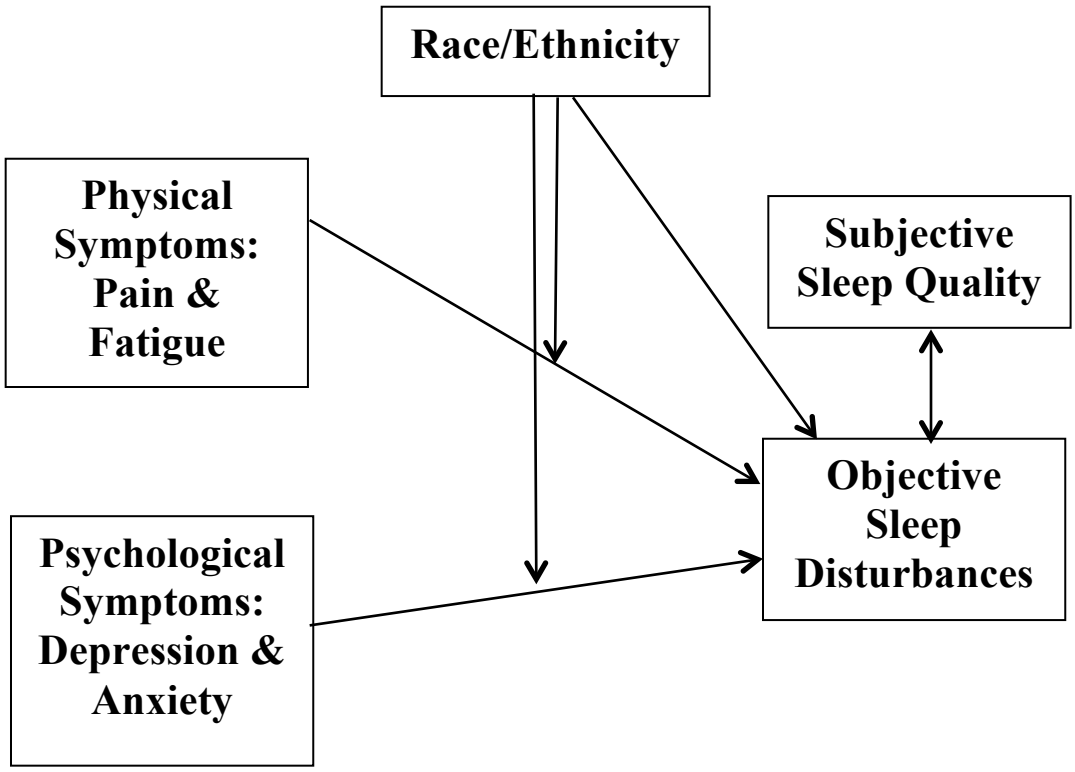

Figure 1. *Hypothesized Research Model*

Review of Empirical Literature

Sleep disturbances are becoming an increasingly recognized side effect of treatment in cancer survivors. This symptom is commonly associated with other symptoms including pain, fatigue, depression, and anxiety (Dhruva et al., 2012). The following review of literature focuses on subjective sleep disturbances and breast cancer; objective sleep in cancer patients; physical symptoms and breast cancer; psychological

symptoms and breast cancer; sleep quality, race/ethnicity, and breast cancer; and ethnic/ racial differences in symptomatology.

Prevalence of Subjective Sleep Disturbances in Breast Cancer. The prevalence of subjective sleep disturbances in BCS ranges from 20% to 70% depending on the study and the assessment method (Pinto & Azombuya, 2011). Two main factors associated with a higher risk of sleep disturbances in BCS are higher proportion of vasomotor symptomatology and comorbid-related conditions (Pinto & Azombuya, 2011). Colagiuri and colleagues (2011) found that in their sample of 3343 BCS, 60% of participants had problems with sleep. This is approximately 50% higher than the prevalence of 38% found in middle-aged women in the general population. Sleep-related problems in cancer patients include nighttime awakenings, need to use the bathroom, uncomfortable breathing, coughing, or snoring (Kotronoulas et al., 2012). Within longitudinal studies of patients receiving chemotherapy, the severity of sleep disturbances continued to increase during the third and fourth cycles, compared with prior to chemotherapy (Liu et al., 2009). The initial nights after chemotherapy were characterized by increased sleep fragmentation disrupting sleep maintenance. The completion of chemotherapy may lead to the restoration of sleep patterns for some BC patients; however, the ongoing sleep disturbances suggest that these can become chronic complaints in BCS.

Chronicity of Subjective Sleep Disturbances. The chronic effects of subjective sleep disturbances in BCS have been suggested in various studies. Alfano and colleagues (2011) conducted a longitudinal cohort study among 572 BCS to investigate the patterns of sleep duration change across the early BC survivorship period, demographic and clinical variables, and their relationships with subsequent cancer-related symptoms and

health related QOL. Twenty-five percent of the sample had sleep duration changes with 5.6% reporting a temporary change, 14% reporting a late-occurring change, and 5.9% reporting a sustained change in sleep duration. Sustained or temporary sleep changes were reported by BCS who were more likely to have been treated with chemotherapy or who gained weight after diagnosis. Sustained sleep changes were also associated with greater severity, affective, and sensory aspects of fatigue (Alfano et al., 2011). Demographic characteristics (*i.e.* race/ethnicity, age, and education) were not associated with sleep changes in this study.

Van Onselen and colleagues (2012) conducted a longitudinal study to identify distinct subgroups of patients based on self-reported sleep problems prior to and within six months after breast cancer surgery. Three subgroups were identified including the high-sustained class (55.0%) consisting of BCS who had the greatest level of sleep problems at baseline and throughout the study; the low sustained class (39.7%) consisting of BCS who had low levels of sleep problem throughout the study; and the decreasing class consisting of BCS who had levels of sleep problems that decreased throughout the study (5.3%). The decreasing and high-sustained classes had worse sleep quality, sleep-onset latency, sleep quantity, mid-sleep awakenings, early awakenings, and excessive daytime sleepiness scores compared to the low sustained class ($p \leq .001$). Increased medication use was reported by the high-sustained class but not by the low sustained class ($p \leq .001$). Overall, the decreasing and high-sustained classes had worse sleep quality in comparison to the low sustained class (both $p \leq .001$). Women of the high-sustained class were younger, had worse functional status, more co-morbidities, increased

hot flashes, and higher levels of sleep problems than the low sustained class (Van Onselen et al., 2012).

Subjective Sleep Disturbances and Quality of Life. A cross-sectional study was conducted to determine the frequency of worse sleep quality in women prior to adjuvant therapy for breast cancer and whether greater sleep dysfunction uniquely predicts worse functional outcomes (Vargas et al., 2010). The sample consisted of 240 women with Stage I, II, or III breast cancer before the start of adjuvant treatment. Approximately 71% of the sample had PSQI global scores above the established cutoff of 5.0. The average PSQI score was 8.5, greater than the suggested adjusted cutoff PSQI score of 8.0 for cancer patients. A worse score on the PSQI sleep efficiency component was associated with decreased functional QOL and greater disruptions in social interactions. A worse score on the PSQI sleep quality component was associated with worse functional well-being, greater fatigue intensity, and lower positive states of mind but not with greater disruptions in social interactions (Vargas et al., 2010).

Using an exploratory design, Humpel and Iversen (2010) examined if there was a relationship between sleep disturbances, fatigue, and common effects of cancer and its treatments in 32 breast and 59 prostate cancer survivors. Breast cancer survivors reported a greater problem with sleep latency and sleep disturbances than prostate cancer survivors (48.4% vs. 17.2%). Younger BCS and prostate cancer survivors reported a greater problem with both sleep latency and sleep disturbances (Humpel & Iversen, 2010). Multiple regression analysis indicated that fatigue was a significant predictor, and age approached significance on predicting global PSQI. Sleep quality was significant while daytime dysfunction approached significance on predicting fatigue. These findings can be

compared to another cross-sectional study that assessed sleep in BCS prior to the initiation of chemotherapy (Phillips et al., 2011). Participants reported sleeping less than 7 hours per night with a sleep onset of 25 minutes. An average of 83% of the time in bed was spent sleeping, which is lower than the 85% threshold considered a good night's sleep. No significant relationships were seen between age, race, gender, or marital status and sleep. Demographic, clinical, and lifestyle variables did not significantly predict sleep quality. Sleep quality was significantly correlated to mental well-being, depression, fatigue, and physical well-being (Phillips et al., 2011).

Koopman and colleagues (2002) conducted a cross sectional study to examine sleeping problems and their relation to depression, social support, and salivary cortisol in 97 women with metastatic breast cancer. Sixty-three percent of the sample reported one or more sleep disturbances. Twenty-five percent reported problems falling asleep; 44.3% reported problems with waking in the night; 29.9% reported problems with waking in the morning; and 20.6% reported sleepiness during the day. Problems waking during the night were significantly correlated with greater depression and less education ($p<.001$). Problems waking up in the morning were significantly correlated with greater depression and less social support ($p<.001$). Women who reported fewer hours of sleep were also more likely to be those with increased depression and lower social support ($p<.01$).

Rumble and colleagues (2010) examined the contribution of cancer symptoms and dysfunctional sleep related thoughts and behaviors to insomnia in BCS. The study used a within-group longitudinal research design. The sample consisted of 41 BCS who had been diagnosed with BC for an average of 5.85 years. Approximately 73% of BCS reported sleep difficulties starting after their breast cancer diagnosis, and 27% reported

aggravation of pre-existing sleep difficulties with their diagnosis of BC. Dysfunctional sleep related thoughts (*i.e.* worries about the consequences of insomnia) and sleep inhibitory behaviors (*i.e.* napping, extending the opportunity to sleep, staying in bed awake) from the previous day and night significantly predicted less efficient sleep and worse sleep quality that night ($p < .0001$). Less efficient sleep and worse sleep quality were significantly associated with increased nighttime pain ($p = .0006$) and hot flashes ($p < .0001$). Results indicated that worse sleep quality was significantly associated with increased pain, fatigue, and hot flashes the next day. Less efficient sleep was significantly associated with increased fatigue ($p < .0001$) and hot flashes ($p = .04$) the next day (Rumble et al., 2010). Taken together, these findings suggest that there are significant relationships among sleep disturbances, pain, fatigue, and hot flashes in BCS.

Objective Sleep in Cancer Patients. Several studies have examined objective parameters in cancer patients. Past research on the actigraphy parameters measured in this study are discussed below.

***Sleep Efficiency*.** In adults, 85% sleep efficiency is indicative of a good night's sleep (Kotronoulas et al., 2012). Wright and colleagues (2009) indicated that breast cancer patients with a low sleep efficiency the night before breast-conserving surgery had significantly higher levels of post-operative pain severity ($p=0.034$) and post-operative pain interference ($p=0.015$). Sleep efficiency was also strongly associated with intrusive thoughts about surgery. Kotronoulas and colleagues (2012) indicated that sleep efficiency remained within the normal range for the majority of breast cancer patients across all weeks of chemotherapy. The greatest differences in sleep efficiency were noted in the

fourth week after chemotherapy with restoration of sleep efficiency to baseline levels within one year of completion of chemotherapy.

Total Sleep Time. During a twenty-four hour period, adults normally sleep between 420-480 minutes (Berger et al., 2003). In a sample of 55 BCS, Otte and colleagues (2011) found that most of the sample slept less than 360 minutes and total sleep time was constantly low throughout the week. In newly diagnosed breast cancer patients, total sleep time was also decreased before the start of treatment as indicated by a mean total sleep time of 343.9 minutes (Wright et al., 2009). For BCS with cancer-related fatigue syndrome (CRFS), total sleep time was 287.67 compared to 314.21 for those without CRFS (Alexander et al., 2009).

Sleep-onset Latency. In the general population, sleep-onset latency is usually less than 20 minutes (Dhruva et al., 2012). BCS demonstrate greater sleep onset latency than individuals without cancer. In a sample of 55 early stage BCS, Otte, Payne, and Carpenter (2012) reported that most of the sample slept less than 360 minutes with 15% of sleep time spent awake. The average sleep efficiency was 78%; the mean sleep latency was 67 minutes; and the mean number of sleep disturbances was 24. No significant differences were seen in wake after sleep onset (WASO), total sleep time, sleep latency, or sleep disturbances across the seven days of monitoring. Sleep latency was noted to have the highest percentage of variation among the sleep measures (Otte et al., 2011). Patients with breast cancer also demonstrated significantly longer sleep onset latency (p= .02) compared to patients with prostate cancer (Garrett et al., 2011). Sleep onset latency appears to be associated with burden of disease (Enderlin et al., 2011). Mean sleep onset

latency for patients with metastatic breast cancer was 34.8 minutes versus 15.6 minutes for patients with non-metastatic breast cancer.

Nocturnal Awakenings. During a typical night's sleep of seven hours, healthy adults normally awaken two to six times (Kotronoulas et al., 2012). Greater than 85% of BC patients undergoing radiation therapy reported an average of 15 awakenings per night (Dhruva et al., 2012). Similar results were found by Berger and colleagues (2008) in their sample of BC patients receiving adjuvant treatment, with the average number of nighttime awakenings between 9 to 11. Another study found that the number of awakenings increased from 21 to 29 after the completion of chemotherapy in women with regular menstrual cycles (Rissling et al., 2011). However, BC patients with irregular menstrual cycles experienced a decrease in the number of awakenings (27 to 25) from pre- to post-chemotherapy.

Wake after Sleep Onset. In healthy adults sleeping 420 minutes per night, wake after sleep onset is usually less than 10% of the total sleep duration (*i.e.* 42 minutes) (Kotronoulas, et al., 2012). A longitudinal study by Dhruva and colleagues (2012) reported that 46% percent of the sample of breast cancer patients undergoing radiation had an abnormal wake after sleep onset (*i.e.* more than 42 minutes). The percent of wake after sleep onset was higher (11% of their total sleep time), but lower in comparison to breast cancer patients receiving chemotherapy (24% of their total sleep time) (Ancoli-Israel et al., 2006). Additionally, there were no improvements in wake after sleep onset over the six months of the study, suggesting that sleep disturbance persisted in these women long after radiation therapy ended.

Beck and colleagues (2010) completed a secondary data analysis to characterize sleep quality and quantity prior to and in the first three nights after initial chemotherapy for breast cancer. The sample consisted of women with stage I, II, or III breast cancer treated with anthracycline and/or cyclophosphamide-based regimens. Three nights of actigraphy data indicated an average wake after sleep onset of about 61 minutes per night. Average time in bed was greater than 480 minutes and quantity of total sleep time averaged between 420 to 480 minutes. Women with worse sleep at baseline had significantly lower physical ($p < .001$) and mental ($p < .001$) health status (Beck et al., 2010). Longer wake episodes were significantly predicted by increased depression and fatigue in another study of cancer survivors (Palesh et al., 2008).

Physical Symptoms and Breast Cancer. Two common physical symptoms experienced by BCS include pain and fatigue. Cancer related fatigue (CRF) is one of the most distressing symptom reported by cancer patients, more disruptive than pain to daily routines, and the strongest predictor of overall quality of life in BCS (Berger, Gerber, & Mayer, 2012; Meeske et al., 2007; Von et al., 2012). Previous research on fatigue, fatigue and sleep disturbances, pain, and pain and sleep disturbances are discussed below.

Fatigue. Fatigue is viewed as a subjective experience. According to the National Cancer Institute (2013), fatigue is described as a distressing condition marked by extreme tiredness and inability to function due to a lack of energy. Approximately one third of BCS experience persistent fatigue for years after completion of treatment (Bower et al., 2011). Correlates of cancer-related fatigue include physiological factors such as pain and neuroendocrine changes; psychological factors such as depression and anxiety; socio-cultural factors such as education and cognitive response; chronobiological factors such

as sleep and circadian rhythms; and treatment related factors such as chemotherapy, radiation therapy, and some biological therapies (Ancoli-Israel, et al., 2001; Jacobsen & Stein, 1999; National Cancer Institute, 2012).

Berger and colleagues (2012) conducted a descriptive study to determine the usual and worst severity of five common symptoms and the extent to which these symptoms interfere with general activity and enjoyment of life in the past seven days. The sample consisted of 457 BCS treated between January 1992 and December 2007. Subjective sleep problems (48.8%) and fatigue (47.7%) were reported as the most prevalent symptoms in BCS. The reported mean scores for usual levels of symptoms in the past seven days were the highest for subjective sleep problems (3.06), followed by fatigue (2.70), pain (1.38), distress (1.60), and numbness/tingling (1.49) on a scale from 0 (none) to 10 (worst). Distress and fatigue were significantly correlated with sleep disturbances ($p < .05$) among the five symptoms.

To determine whether biological and/or functional measures are likely to be associated with the development of clinically significant fatigue (CSF), Gerber and colleagues (2011) conducted a study on 44 BCS to document the impact of the diagnosis and treatment of primary breast cancer on function. Results indicated that the number of patients with clinically significant fatigue increased from 1 at baseline (time of diagnosis but prior to treatment) to 11 at a 9-month follow up visit. Breast cancer treatments were not significantly correlated with CSF. Menopausal status ($p = .03$) and increased white blood cell count ($p = .04$) were significantly correlated with CSF. Surprisingly, the total sleep time did not differ significantly between those with CSF (8.27 hours per night) and those without CSF (8.35 hours per night) (Gerber et al., 2010).

Fatigue and Sleep Disturbances. Past research suggests that fatigue is significantly associated with sleep disturbances. Alexander and colleagues (2009) completed a study to determine the prevalence of cancer-related fatigue syndrome (CRFS) in a population of disease-free BCS and to investigate the relationship between CRFS and clinical variables. The sample consisted of 200 BCS who completed a diagnostic interview for CRFS, questionnaires assessing QOL, mood, and fatigue. Subjects also wore a wrist actigraph for 7 days to measure activity and sleep. Thirty percent of the participants fulfilled the criteria for CRFS. Women with CRFS reported more sleep disturbances, and this was supported with actigraphy data. Actigraphy data showed statistically significant differences in the sleep period intervals, in mean wake episodes, and median longest wake episode occurring during the true sleep period between BCS with and without CRFS (Alexander et al., 2009).

Dirksen and colleagues (2009) conducted a secondary data analysis to determine if BCS with insomnia can be categorized according to their level of fatigue. The sample consisted of 86 BCS with insomnia who were at least 3 months post completion of primary treatment. Three subgroups were identified including the exhausted (35%) subgroup, tired (41%) subgroup, and restored (24%) subgroup. The exhausted subgroup had significantly worse subjective sleep quality and lower levels of anxiety compared to the tired and restored subgroups (p=.001). The exhausted subgroup also reported worse quality of life (p=.001). The restored and tired subgroups had significantly better scores on physical (p=.001), emotional (p=.013), functional (p=.001), and breast cancer quality of life (p=.006) subscales compared to the exhausted subgroup (Dirksen et al., 2009).

Liu and colleagues (2012) conducted an exploratory study to determine the longitudinal relationship between fatigue and sleep measured both subjectively and objectively. The sample consisted of 97 BCS with stage I, II, or III breast cancer who were scheduled to receive at least four 3-week cycles of chemotherapy. Subjective sleep quality was poor at baseline and remained unchanged throughout their chemotherapy cycles. Fatigue was positively associated with both subjective sleep quality and with objective measures of total nap time ($p < .01$); fatigue was negatively associated with total wake time during the day ($p < .01$).

Pain. The International Association of the Study of Pain defines pain as an unpleasant, subjective, sensory and emotional experience associated with tissue damage (National Cancer Institute, 2012). Breast cancer survivors have pain prevalence rates of 25% to 60% (Miaskowski et al., 2011). This wide range can be attributed to several factors including the differences in the definition of pain, measures used for pain assessment, and whether these assessments were subjective or objective (Miaskowski et al., 2011).

Pain and Sleep Disturbances. The relationship between sleep disturbances and pain is multifaceted and poorly understood (Stiefel & Stagno, 2004). Sleep disturbances in patients with chronic pain are often under-reported, under-diagnosed, and under-treated which may then lead to the development of chronic sleep disorders in patients (Stiefel & Stagno, 2004). Miaskowski and colleagues (2011) conducted a longitudinal study among 389 BCS to characterize distinct persistent pain classes and evaluate for differences among these pain classes in demographic, preoperative, intraoperative, and postoperative characteristics. Patients were classified into no (31.7%), mild (43.4%),

moderate (13.3%), and severe (11.6%) pain groups based on their ratings of pain. Four non-modifiable demographic characteristics—younger age, less education, being non-white, and having a lower total annual income—were associated with being in the severe pain class. Results from this study also found that BCS with higher levels of depressive symptoms ($p< .0001$), trait anxiety ($p< .0001$), sleep disturbance ($p< .0001$), and fatigue ($p< .0001$) were at increased risk for persistent breast pain.

Palesh and colleagues (2007) conducted a study on 93 women with metastatic breast cancer to examine depression, pain, life stress, and participation in group therapy and their relationship to sleep disturbances. The study was an intervention trial examining the effect of group therapy on their symptoms at baseline, 4, 8, and 12 months. Approximately 64% of the sample reported one or more sleep disturbances at baseline. Results showed that increased problems in getting to sleep were predicted by higher baseline levels of pain, increased pain intensity over time, and increased number of life stressors at baseline ($p< .001$). In addition, there was an increase in problems getting to sleep from baseline over the course of the 12 months even when the level of pain did not intensify over time. This is consistent with previous research showing that sleep disturbances can become chronic once they have begun, even when the original trigger is no longer present (Stiefel & Stagno, 2004).

In a longitudinal study of 41 BCS who had been diagnosed with insomnia, increased levels of pain and fatigue, and lower levels of positive mood and dysfunctional sleep related thoughts were identified as consequences of sleep disturbances in this population. Less efficient sleep ($p=0.0002$) and worse sleep quality ($p=0.0006$) significantly predicted higher levels of pain and fatigue, and lower levels of positive

mood the next day (Rumble et al., 2010). This study suggests that the relationship between pain and sleep disturbances is bi-directional.

Psychological Symptoms and Breast Cancer. Depression and anxiety are common psychological symptoms experienced by BCS. Depression is often unrecognized and difficult to diagnose in the presence of cancer because of the overlap of symptoms (Palesh et al., 2008). Previous research on depression, depression and sleep disturbances, anxiety, and anxiety and sleep disturbances are discussed below.

Depression. The National Cancer Institute (2012) defines depression as a mental condition characterized by ongoing feelings of sadness, despair, loss of energy, and difficulty dealing with daily life. Additional symptoms of depression include feelings of worthlessness, loss of pleasure in activities, changes in eating or sleeping habits, and suicidal thoughts. Common depressive disorders in BCS include major depressive disorder, dysthymic disorder, and mixed depressive-anxious mood disorders (Fiorentino et al., 2011). Fann and colleagues (2008) reported that approximately 10% to 25% of depression is under-recognized and under-treated during the first year after completion of treatment for breast cancer patients. If left untreated, depression can result in worsened physical symptoms and functional impairment, as well as poor adherence to treatment. The first year after diagnosis, BCS are at a higher risk for depression, specifically younger women. Furthermore, a correlation has been found between increases in depressive symptoms during the first year after metastatic breast cancer treatment and shorter survival times (Giese-Davis et al., 2011).

Goodwin and colleagues (2004) conducted a retrospective analysis to assess the effect of a prior diagnosis of depression on the diagnosis, treatment, and survival of older

women with breast cancer. The sample consisted of 24,696 BCS who were diagnosed between 1993 and 1996 and included in the Surveillance, Epidemiology and End Results (SEER) and Medicare linked database. Approximately 8% of BCS were diagnosed with depression 2 years before the diagnosis of breast cancer. Participants with a prior diagnosis of depression had a 42% higher risk of death from breast cancer during their 3-year follow-up. Participants with a history of depression were significantly less likely to receive standard treatment and were less likely to receive chemotherapy in comparison to women without a prior diagnosis of depression ($p < .0001$) (Goodwin et al., 2004).

Depression and Sleep Disturbances. A longitudinal study was conducted on 76 participants to examine whether the changes in sleep problems over the course of 14 months were predictive of changes in depressive symptoms in women with breast cancer after treatment (Hsiao et al., 2012). Results indicated that the initial depressive symptoms were significantly and positively correlated with baseline scores for sleep disturbances ($p < .001$) and anxiety ($p < .001$). Baseline scores of anxiety and sleep were positively associated with initial depressive symptoms after age, BMI, and cancer and treatment variables were controlled. Decreased meaning in life ($p < .001$) and increased cortisol levels ($p < .012$) were significantly associated with increased levels of depressive symptoms over the course of 14 months.

Enderlin and colleagues (2011) conducted a study to describe objective sleep characteristics and examine subjective sleep quality in women aged 50 and older as predicted by cancer status, age, number of comorbidities, and depressed mood. The sample consisted of 32 women with and 35 without non-metastatic breast cancer. Multiple regression analysis indicated that depressed mood significantly predicted

subjective sleep quality in this sample but not objective sleep. Objective sleep characteristics were similar for both groups of BCS. Depressed mood accounted for 26% of the variance in subjective sleep quality. Breast cancer status, age, and number of comorbidities were not significant predictors of subjective sleep quality (Enderlin et al., 2011). An additional study by Otte and colleagues (2011) was conducted to refine knowledge regarding prevalence, severity, and correlates of sleep-wake disturbances in long-term BCS compared to age-matched women without breast cancer. The sample consisted of 246 BCS and 246 women without breast cancer. Depression was significantly correlated with the prevalence and severity of sleep disturbances in both BCS and women without breast cancer. In summary, sleep disturbances are considered a symptom of depression, and early identification and treatment of depression may decrease the prevalence of sleep disturbances in BCS.

Anxiety. Anxiety is also a common psychological symptom among BCS and may be present up to eighteen months after the completion of treatment. Anxiety can significantly affect the course of recovery for BCS by their associations with sleep and thoughts about breast cancer recurrence (Vahdaninia, Omidvari, & Montazeri, 2010). The National Cancer Institute (2013) characterizes anxiety as feelings of fear, dread, and uneasiness occurring as a result of stress. The occurrence of anxiety in BCS may be associated with several factors including treatment-related distress, worries regarding fear of death and disease recurrence, and altered body image (Vahdaninia et al., 2010).

Anxiety and Sleep Disturbances. In a prospective study to identify the association between subjective sleep disturbances, anxiety, and depression, Delgado-Guay and colleagues (2011) reported that higher PSQI scores were significantly correlated with

increased levels of anxiety (p= .01) and a worse sense of well-being (p= .035). The sample consisted of 101 cancer patients with a median age of 60 years. The most common cancer diagnosis in this sample was lung cancer (21%) followed by breast cancer (20%), and gastrointestinal cancers (15%). Eighty six percent of the sample was diagnosed with sleep disturbance. Past research on anxiety and sleep disturbances in BCS is limited, and additional research is needed in this area.

Sleep Quality, Race/Ethnicity, and Breast Cancer. Sleep quality and the experience of physical and psychological symptoms among cancer survivors may be different among races/ethnicities. The following is research relevant to sleep quality, race/ethnicity, and breast cancer; racial/ethnic differences in symptomatology; and relationship between subjective and objective sleep disturbances.

Limited research has been conducted on the subject of differences in sleep quality in BCS of different races/ethnicities. Past research has shown that nonwhite survivors may have small but clinically significant decrements in QOL in comparison to white survivors. Palesh and colleagues (2010) conducted a prospective study to determine the prevalence of insomnia in cancer patients. The sample consisted of 823 cancer patients receiving chemotherapy. White patients reported significantly more sleep disturbances than nonwhite patients (p< .05). Nonwhites were 44% less likely to report sleep disturbances than whites. The reason for these differences in reporting sleep disturbances is unknown and may be explained either by true biologic differences or a response bias (Palesh et al., 2010).

Von and colleagues (2012) conducted a study of sleep and quality of life on 62 African American BCS and a control group of 78 African American women with no

history of breast cancer. African American BCS were significantly older (57.3 years versus 52.2 years) and had a higher body mass index (32.1 kg/m^2 versus 29.6 kg/m^2) in comparison to the healthy comparison group. African American BCS experienced significantly more fatigue ($p = .004$) and worse hot flashes ($p < .001$). African American BCS also reported worse sleep quality ($p < .001$), but similar depressive symptoms and overall well being compared to the control group (Von et al., 2012).

Rumble and colleagues (2011) conducted a descriptive study to report the prevalence of subjective sleep disturbance in a sample of African American BCS and to determine the extent to which sleep disturbances contribute to fatigue. The sample consisted of 51 African American, Afro-Caribbean, or African BCS with a mean age of 64.2 years. Forty-three percent of the sample reported significant difficulties with sleep. These sleep-related difficulties included problems falling asleep and maintaining sleep, early morning awakenings, and dissatisfaction with sleep. An additional study was conducted on 51 African American BCS to report the prevalence of sleep disturbances (Taylor et al., 2012). The sample consisted of African American, Afro Caribbean or African BCS who were on average 7.2 years since the time of diagnosis. The most commonly identified sleep complaints include sleep maintenance (36%), dissatisfaction with sleep (35.3%), difficulty falling asleep (23.5%), and early morning awakenings (22.4%). After controlling for demographic and disease characteristics, insomnia symptom severity significantly predicted fatigue ($\beta = .32$, $p < .05$) and accounted for 8% of the variance in the fatigue scores (Taylor et al., 2012).

Racial/Ethnic Differences in Symptomatology. Symptoms associated with breast cancer diagnosis and treatment vary by different races/ethnicities. In a cross-

sectional study of 199 cancer survivors to examine cancer-related chronic pain and its impact on quality of life, surgery and cancer treatment were identified as the sources of pain for whites and blacks respectively (Green et al., 2011). Blacks experienced more pain interference and disability ($p < .05$) compared to whites. Black BCS were more likely to have chemotherapy and less likely to have surgery compared to whites. Miaskowski and colleagues (2011) reported that non-white patients were more likely to be diagnosed with more advanced disease ($p = .009$) contributing to more severe pain. Pain associated with cancer may be associated with an increased morbidity and diminished quality of life for black women consistent with an unequal burden of cancer, pain, and cancer-related chronic pain (Green et al., 2011).

Deimling and colleagues (2006) conducted a descriptive study to examine anxiety and depression in 321 long-term cancer survivors. The purpose of this study was to determine the cancer-related health worries of older adults and long-term cancer survivors. Approximately 33% of the sample continued to report worries about cancer recurrence, worries about a second cancer, and worries that symptoms they experience may be associated with cancer. Results showed that cancer-related health worries were a significant predictor of both depression ($\beta = .36$) and anxiety ($\beta = .21$). Race/ethnicity was a significant predictor of cancer-related health worries. African American race was related to fewer cancer-related health worries ($\beta = -.22$) (Deimling et al., 2006). Results from the Women's Health Initiative-Observational Study indicated that African American BCS reported lower physical functioning ($p < .001$), general health, ($p < .001$), and greater role limitations due to emotional health ($p = .001$) compared with white survivors.

Fu and colleagues (2009) administered a survey to assess the prevalence of 16 physical and emotional symptoms and identify socio-demographic factors associated with these symptoms. Of the 139 BCS surveyed, 63 were Hispanic, 58 white, and 18 black. Fatigue (76%) was the most common symptom followed by muscle aches (40%). Most women reported greater than 6 symptoms. Hispanic women reported more than likely to report greater than 10 symptoms ($p < .05$), more chemotherapy-related symptoms ($p < .05$), and more pain-related symptoms ($p < .05$). Symptoms experienced by BCS are affected by their race/ethnicity with increased symptom prevalence in minorities compared to white BCS.

Relationship Between Subjective and Objective Sleep. Previous research has indicated conflicting results of the correlations between subjective and objective measures of sleep disturbance. Lauderdale and colleagues (2008) reported that mean objective sleep explained 20% of the variation in subjective sleep. Subjective reports of sleep were approximately 34 minutes greater than objective sleep. This suggests that a moderate correlation exists between subjective reports of sleep and actigraph-measured sleep, but is biased by over-reporting suggesting that the true associations between sleep duration and health may differ from previous results (Lauderdale et al., 2008). Grutsch and colleagues (2011) investigated the relationship between actigraphic measurement of sleep and self-reported subjective sleep quality. Results indicated that the actigraphy parameters (*i.e.* total sleep time, sleep efficiency, wake after sleep onset) were significantly correlated with subjective sleep quality ($p < .05$). The largest correlation ($r = .62$, $p < .004$) was noted between wake after sleep onset and PSQI. Currently, both types

of measures are recommended to evaluate sleep disturbances in BC patients (Lauderdale et al., 2008).

Summary. In summary, across the various symptoms experienced by BCS, sleep disturbances is one of the most prevalent. Sleep disturbance is associated with an increased frequency of fatigue, pain, depression, and anxiety in BCS. Non-white BCS were more likely to be diagnosed with more advanced cancer contributing to more severe symptoms (Miaskowski et al., 2011). Previous research on sleep actigraphy parameters indicated that total sleep time was decreased; sleep onset latency, nocturnal awakenings, and wake after sleep onset were increased in BCS compared to the general population. These studies have focused on predominantly white samples with limited research on the differences between races/ethnicities. This research study is significant in that it explores racial/ethnic differences in objectively measured sleep patterns among BCS and examines which sleep actigraphy measure appears to have the strongest relationship with physical and psychological symptoms; and whether these relationships are modified by race/ethnicity. This study is warranted due to the limited empirical knowledge regarding the quality of life in BCS from minority populations. Past research has focused primarily on white, non-Hispanic BCS, and it is becoming increasingly important to take into consideration women of minorities as they compromise a large portion of the BCS population. The results from this study can be used to serve as a foundation for future studies exploring physical and psychological symptoms related to sleep disturbances in BCS from minority populations.

Subjective and objective sleep is worse in BCS than the general population. From the current review of sleep disturbances in BCS of different races/ethnicities, it appears

that black BCS demonstrate poor objective sleep but are less likely to report subjective sleep disturbances compared to white cancer survivors. However, data are sparse in BCS and nearly non-existent in BCS of other racial and ethnic minorities. Sleep is a concern because it is associated with physical and psychological morbidity including pain, fatigue, depression, and anxiety.

Chapter Three

Methods

Introduction

Chapter three describes the research methods and procedures for this study. The purpose of this study was to examine the relationship between subjective sleep quality and objective sleep disturbances across different races/ethnicities among BCS. The purpose was also to examine which sleep actigraphy measure appeared to have the strongest relationship with physical and psychological symptoms, and whether these relationships were modified by race/ethnicity**.** The research design is discussed first. This is followed by a description of the setting, sample, instrumentation, procedures, data management, and data analysis procedures.

Research Design

A cross-sectional research design was used to conduct a secondary data analysis of data from the NCI administrative sleep supplement study of the *MBSR Symptom Cluster Trial for Breast Cancer Survivors/* 1R01CA131080, conducted by Dr. Cecile Lengacher. The current study utilized secondary data analysis on baseline data to examine the relationship between anxiety, depression, pain, fatigue, subjective sleep quality and objective sleep disturbance in BCS.

Setting. Participants were recruited from the H. Lee Moffitt Cancer Center and Research Institute. Patients were also recruited from the Carol and Frank Morsani Center

for Advanced Health Care. Orientation assessment took place in the Survivorship Clinic of the Moffitt Research Center.

Population and Sample. Three hundred and twenty-three participants consented to the parent R01 grant. This study included a subgroup of 79 participants who completed baseline actigraphic monitoring and self-report questionnaires. The inclusion criterion for this study were: 1) women age 21 or older; 2) diagnosis of stage 0, I, II, or III breast cancer; 3) completion of lumpectomy and/or mastectomy; 4) between two weeks to two years from end of treatment with adjuvant radiation and/or chemotherapy; 5) read and speak English at the 8th grade level or above; and 6) completion of baseline actigraphic monitoring and self-report questionnaires. Exclusion criteria consisted of the following: 1) women who had advanced stage breast cancer (stage IV); 2) a severe current psychiatric diagnosis; and 3) recurrent treatment for prior breast cancer (Lengacher, 2008).

Instrumentation

Demographic Data. A demographic questionnaire captured participants' socio-economic demographic data for a description of the sample. Data gathered included age, race/ethnicity, religion, highest level of education completed, marital status, employment status, and income.

Clinical History. A clinical history form captured participants' clinical data for a description of the sample. Data gathered include cancer diagnosis, cancer stage at time of diagnosis, type of breast cancer, length of time since cancer diagnosis, treatment type, and number of weeks on radiation/chemotherapy.

Subjective Sleep Disturbances. The Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep (Buysse et al., 1989). The instrument contains 19 self-rated questions referring to patients' sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleeping medication use, and daytime dysfunction over the past month. The 19 self-rated questions produce 7 component scores, scored on 4-point scales, which are summed up for a global PSQI score. A global PSQI score of greater than 5 is associated with worse sleep quality (Buysse et al., 1989).

Objective Sleep Disturbances. The Actiwatch-Score actigraph (Philips Respironics, Andover, MA) was used for the objective assessment of sleep. It provides a noninvasive method of quantifying continuous monitoring of body movements in predetermined time intervals (epochs) of one minute. The actiwatch is worn on the non-dominant wrist and is capable of detecting arm movement through the use of a piezoelectric accelerometer (Grutsch et al., 2011). The piezoelectric accelerometer monitors and stores the degree and intensity of motion, sampling every second. These movement data are then transferred to a computer for analysis to produce a report containing parameters of sleep and wake periods, their timing, duration and other characteristic details. Webster and colleagues (1982) reported that actigraphy scores correlated with EEG sleep/wake status 95% of the time and with polysomnography (PSG) within a range of ten percent (Berger et al., 2007).

In accordance with recent recommendations (Berger et al., 2007), sleep disturbance was assessed using: 1) sleep efficiency; 2) sleep onset latency; 3) total sleep time; and 4) number of nighttime awakenings, specifically wake after sleep onset (WASO). Sleep efficiency is defined as the percentage of time in bed spent sleeping. It is

calculated by dividing the number of minutes of sleep by the number of minutes in bed, multiplied by 100. Sleep-onset latency is measured as the number of minutes between lying in bed and falling asleep. Total sleep time is defined as the number of minutes of sleep while in bed. Nocturnal awakenings refer to the number of awakenings during the sleep period, and wake after sleep onset specifically refers to the number of minutes awake after sleep onset during the sleep period (Grutsch et al., 2011).

Fatigue. The Fatigue Symptom Inventory (FSI) was used to measure fatigue (Hann, Jacobsen, & Azzarello, 1998). The FSI is a 14-item self-report measure designed to assess severity, frequency, daily pattern of fatigue, and perceived interference with QOL using four indicators of fatigue on separate 11-point scales (0=Not at all; 10=Extreme fatigue) (Hann et al.,1998). Perceived interference is a 7-item scale that uses separate 11-point scales to assess the degree to which fatigue in the past week was judged to interfere with: (i) general level of activity; (ii) ability to bathe and dress; (iii) normal work activity; (iv) ability to concentrate; (v) relations with others; (vi) enjoyment of life; and (vii) mood. These interference ratings can be summed to obtain a total perceived interference score. Two items measure duration of fatigue, defined as the number of days in the past week and the mean percentage of time each day the respondents felt fatigued. The final item provides qualitative information about diurnal variation in the daily experience of fatigue. Test-retest reliability over 3 to 12 week intervals among cancer patients was also favorable (r=. 35-.75). Preliminary evidence of the reliability and validity of the FSI has been reported for women with breast cancer. Convergent and divergent validity were demonstrated using correlations with the fatigue scale of the Profile of Mood States Fatigue and the Short-Form General Health Survey (SF-36)

vitality subscale (Jacobsen, 2004). The internal consistency reliability is excellent with a Cronbach's alpha coefficient of greater than 0.90 (Hann et al., 1998).

Pain. The Brief Pain Inventory (BPI) Short Form was used to assess pain and its impact on daily functions (Cleeland, 1991). It consists of 9 items measuring the type of pain, location of pain in the body, and severity of pain; pain medications and their usefulness in relieving pain in the past 24 hours; and the severity of pain interference in mood and quality of life. The Cronbach's alpha reliability ranges from 0.77 to 0.91 (Cleeland, 1991).

Depression. The Center for Epidemiological Studies Depression Scale (CES-D) was used to measure depression (Radloff, 1977). The CES-D is a 20-item instrument that uses a 4-point scale, ranging from 0 = rarely or none of the time (less than 1 day) to 3 = most or all of the time (5-7 days), to rate how frequently depressive symptoms are experienced during the past week. Measures include cognitive, affective, behavioral, and somatic symptoms of depression, and positive affect. Cronbach's alpha for the CES-D is 0.92 for breast cancer subjects. Scores range from 0 to 60 with higher calculated scores indicative of more severe depressive symptoms. A score of 16 or higher identified subjects with likely major depressive disorder (Radloff, 1977).

Anxiety. The State Trait Anxiety Inventory-State Scale only (STAI-S) was used to measure anxiety (Spielberger, Gorsuch & Luschene, 1983). This is a 20-item Likert scale that measures state anxiety ranging from 1 (almost never) to 4 (almost always), to rate how respondents feel generally. The STAI-S measures an individual's transitional emotional response, including worry, nervousness, tension, and feelings of apprehension to a stressful situation (Dhruva et al., 2012). Scores range from 20 to 80 with a score of

32.2 or higher are indicative of greater anxiety (Spielberger et al., 1983). The internal consistency reliability for the STAI is 0.95 (Spielberger et al., 1983).

Procedure

Approval. Approval for this study was granted by the Institutional Review Board at the University of South Florida (Appendix 1). This research study analyzed de-identified data from the administrative supplement of the *MBSR Symptom Cluster Trial for Breast Cancer Survivors*/ 1R01CA131080.

Data Collection Procedures. The current study utilized the secondary baseline data set from the supplement study of the R01 *MBSR Symptom Cluster Trial for Breast Cancer Survivors.* BCS who met the stated inclusion criteria were recruited from the Moffitt Cancer Center and Research Institute at the University of South Florida and Carol and Frank Morsani Center for Advanced Health Care. Health practitioners screened participants and provided the recruiter with a list of these patients who met the inclusion criteria one week prior to their scheduled appointments. Eligible patients were approached by the recruiter. Prior to their scheduled appointment times, patients were provided with a folder that contained a copy of the informed consent, the upcoming group schedule, and general information about the MBSR study. If interested, patients completed a Participant Interest Form that provided the necessary contact information and verified their treatment information.

On the day of orientation, the principal investigator or a research assistant reviewed the informed consent with each participant before it was signed. The participants then completed self-reported questionnaires relevant to the various symptoms assessed. To ensure that all questions were answered, the questionnaires were cross-

checked by research assistants to prevent missing data. After the completion of questionnaires, patients were provided the actigraphy bracelet. This device was to be worn on the non-dominant wrist continuously for three days (*i.e.* 72 hours). The participant was also required to fill out a Daily Time-Monitoring of Sleep Diary for each day. Sleep quality was measured by actigraphy in combination with patient recordings of bedtime and rising time.

Data Management. Statistical Product and Services Solutions (SPSS) version 21.0 was utilized for all data entry, data management and analysis for this study. To maintain patients' confidentiality, data was de-identified and stored in password-protected files secured in the investigator's office. Results were reported using only de-identified data and without patient identifiers.

Data Analysis

Frequency distributions and descriptive statistics were generated for sample characteristics. T-test and chi square analysis were used to compare sample demographic and clinical variables between the white, non-Hispanic versus the minority BCS. All socio-demographic and clinical variables with a *p* value of less than 0.05 were included as potential covariates for this study.

Aim # 1: *Explore racial/ethnic differences in objective sleep patterns among BCS.* The predictor of interest was race/ethnicity (*i.e.* white, non-Hispanic versus other races and ethnicities) and the defined outcome measures were objective sleep pattern measures including sleep efficiency, sleep onset latency, total sleep time, and wake after sleep onset. Analysis of variance (ANOVA) was used initially to compare unadjusted means of the defined outcome variables between the different racial groups, whereas

analysis of covariance (ANCOVA) was used to compare adjusted means. Recognizing sample size limitations, the ANCOVA models were adjusted for age, which was a covariate that was imbalanced between the different racial groups.

Aim # 2: *Estimate and compare the correlations between objective and subjective sleep quality by racial/ethnic groups among BCS.* Correlation analysis was used to estimate the strength of association between objective and subjective sleep quality. Pearson correlations were calculated if the data were normally distributed; Spearman correlations were calculated if the data were skewed. Correlations were calculated separately in white, non-Hispanics versus other racial/ethnic groups with Fisher's *r* to Z transformation to examine confidence intervals (*i.e.* to normalize the distribution of the correlation coefficient).

Aim # 3: *Examine which sleep actigraphy measure appears to have the strongest relationship with physical and psychological symptoms.* Pearson correlations were calculated between each measure of actigraphy and physical (pain and fatigue) and psychological (depression and anxiety) symptoms.

Aim # 4: *Explore whether these relationships appear to be modified by race/ethnicity.* Multiple linear regression analysis was used with the most highly correlated actigraphy measure as the dependent variable (the best actigraphy measure may be different for each physical and psychological symptom); race/ethnicity and symptoms as main effect terms; and an interaction term for physical or psychological symptom by race/ethnicity. Separate models were created for each actigraphy measure.

Power Analysis. Whereas all of the specific aims are considered exploratory, estimates of statistical power are provided recognizing that the primary purpose of this

analysis was to estimate strength of relationships and effect sizes, as opposed to the conduct of formal hypothesis testing. For the total sample of 79 BCS, 60 BCS (76%) were white, non-Hispanic and 19 (24%) were of minority race/ethnicity. The breakdown of the minority race was reported as: 9% (n=7) white Hispanic; 10% (n=8) black non-Hispanic; 4% (n=3) black Hispanic; and 1% (n=1) listed their ethnicity as other. For **Aim #1**, detectable effect sizes at 80% power assuming 2-sided type I error rate of 0.05 were 0.92 for blacks versus whites, 0.96 for Hispanics versus Non-Hispanics, and 0.75 for minority versus non-minority race/ethnicity. These detectable effect sizes represent "large" effects. For **Aim #2**, detectable non-zero correlations at 80% power were 0.76 for Hispanics, 0.74 for blacks, 0.59 for minorities, and 0.35 for non-minorities. These represent modest to large effects. This aim was considered exploratory in terms of estimating effect size (correlation). For **Aim #3 and #4**, in a multiple regression model assuming 79 subjects and 2 covariates with an R^2 value of 0.15, the sample provided 80% power to detect an R^2 value of 0.08 attributed to an objective measure of sleep actigraphy.

Chapter Four

Results

Introduction

This chapter first presents sample descriptives followed by the study findings of differences in objective sleep quality between white, non-Hispanic versus minority BCS. It also summarizes the study findings of the moderating effect of race/ethnicity on the relationship between sleep actigraphy parameters and physical/psychological symptoms. These results are presented according to each of the four research aims.

Participants

The sample consisted of 79 participants of which actigraphy data was analyzed for 78 participants. One participant was a nightshift worker and her actigraphy data was not comparable to the remaining sample; however, her remaining data was analyzed. The racial/ethnic mix of the participants was as follows: 76% (n=60) white non-Hispanic; 9% (n=7) white Hispanic; 10% (n=8) black non-Hispanic; 4% (n=3) black Hispanic; and 1% (n=1) listed their ethnicity as other.

Table 1 displays the mean, standard deviation, and group comparisons on age, marital status, education status, employment status, and annual household income for the white, non-Hispanic versus minority participants. The mean age of the sample was 57.0 years with a mean age of 58.5 years for white, non-Hispanic BCS and 52.4 years for minority BCS. Age was the only variable that was significantly (p= .041) different

between the two groups and was included as a potential covariate for further analysis. Sixty percent of the sample was married with 60% of the white, non-Hispanic BCS married and 58% of the minority BCS married. Approximately 74% of the sample had some college degree with most of the white, non-Hispanic group (72%) and most of the minority group (79%) having some college degree. Approximately 37% of the sample was employed with 41% of the sample having an annual household income of $40,000 or more.

Table 1

Mean Age, Marital Status, Education Status, Employment Status, and Annual Household Income of Participants By Race/Ethnicity

Variable	Total n=79	White, non-Hispanic n=60	Minority n=19	p-value
Mean Age + Standard Deviation (years)	57.1 ± 9.6	58.5 ± 8.6	52.4 ± 11.3	0.041*
Marital Status, n (%)				0.743
Married	47 (59.5)	36 (60.0)	11 (57.9)	
Unmarried	32 (40.5)	24 (40.0)	8 (42.1)	
Education Status				0.531
High School or Less	21 (26.6)	17 (28.3)	4 (21.1)	
Some College or Above	58 (73.4)	43 (71.7)	15 (78.9)	
Employment Status				0.098
Employed	29 (36.7)	19 (31.7)	10 (52.6)	
Not Employed	50 (63.3)	41 (68.3)	9 (47.4)	
Annual Household Income				0.434
< $10,000 - <$40,000	47 (59.5)	32 (53.3)	13 (68.4)	
$40,000 or more	32(40.5)	28 (46.7)	6 (31.6)	

** Variable is significant at the 0.05 level.*

Table 2 displays the treatment related factors for participants. These include surgery type, treatment type, stage of cancer, and type of breast cancer. Forty-seven percent of the sample reported their type of breast cancer as carcinoma in situ. The majority (57%) of the sample had a mastectomy with 58% of white, non-Hispanics and 52% of minorities having had this surgery. The most common stages of breast cancer were Stage 1 (34%) or Stage 2 (34%). The most prevalent stage of breast cancer in the

white, non-Hispanic (35%) was stage 1 compared to stage 2 in the minority (37%) group. The most common type of treatment in the minority group was chemotherapy and radiation (37%) compared to surgery only (37%) for the white, non-Hispanic group. The clinical variables represented in Table 2 were not statistically different by race/ethnicity ($p > .05$).

Table 2

Surgery Type, Treatment Type, Stage of Cancer, and Type of Breast Cancer of Participants by Race/Ethnicity

Variable	Total n=79	White, non-Hispanic n=60	Minority n=19	p value
Surgery Type, n (%)				0.662
Lumpectomy	34 (43)	25 (41.7)	9 (47.4)	
Mastectomy	45 (57)	35 (58.3)	10 (52.6)	
Treatment Type, n (%)				0.403
Chemotherapy	10 (12.7)	7 (11.7)	3 (15.8)	
Radiation	21 (26.6)	15 (25.0)	6 (31.6)	
Chemotherapy and Radiation	23 (29.1)	16 (26.7)	7 (36.8)	
Surgery only	25 (31.6)	22 (36.7)	3 (15.8)	
Cancer Stage, n (%)				0.854
0	13 (16.5)	9 (15.0)	4 (21.1)	
1	27 (34.2)	21 (35.0)	6 (31.6)	
2	27 (34.2)	20 (33.3)	7 (36.8)	
3	12 (15.2)	10 (16.7)	2 (10.5)	
Type of Breast Cancer, n (%)				0.416
Ductal Carcinoma In Situ	13 (16.5)	9 (15.0)	4 (21.1)	
Invasive lobular	26 (32.7)	20 (33.3)	6 (31.6)	
Invasive ductal	22 (27.8)	18 (30.0)	4 (21.1)	
Not specified	3 (4.0)	1 (1.7)	2 (10.5)	
Unknown	15 (19.0)	12 (20.0)	3 (15.7)	

Table 3 displays the descriptive characteristics of the actigraphy parameters, subjective sleep disturbance, physical and psychological symptoms. By way of comparison, healthy adults take less than 20 minutes on average to fall asleep, but this sample took an average of 26 minutes (Kotronoulas et al., 2012). Approximately 51% of the sample had sleep onset latency greater than 20 minutes while 49% had sleep onset latency within the normal range of less than 20 minutes. Healthy adults have an average

of about 420-480 minutes of total sleep time (Kotronoulas et al., 2012). Twenty six percent of the sample had total sleep time within the accepted range of 420-480 minutes, and 74% had total sleep time out of this accepted range. The mean was 381 minutes with a range of 234 to 582 minutes in this sample. Healthy adults have a sleep efficiency of greater than 85% (Kotronoulas et al, 2012). Approximately 78% of the sample had sleep efficiency below the accepted range of 85% and above, with an average sleep efficiency of 79%. Healthy adults have a wake after sleep onset of less than 42 minutes (Kotronoulas et al., 2012). Approximately 21% had wake after sleep onset within the normal range of less than 42 minutes, and 79 % had wake after sleep onset of greater than 42 minutes with an average of 62 minutes.

Table 3

Descriptive Statistics of Actigraphy Parameters, Subjective Sleep Disturbance, Physical and Psychological Symptoms

Variables	N	Minimum	Maximum	Mean	Standard Deviation	Normal Range	Percentage Abnormal
Total Sleep Time	78	234	582	380.8	62.64	420-480	74.36
Sleep Onset Latency	78	0	122	25.57	26.13	<20	51.28
Sleep Efficiency	78	56	91	78.76	7.66	>85	78.21
Wake after Sleep Onset	78	11	144	61.97	28.11	<42	79.49
STAI State Scale	78	20	78	37.55	11.45	<32.2	98.72
BPI Severity Scale	78	0	8.75	2.54	2.28	<7	6.39
PSQI	78	1	18	8.04	4.16	<5	79.49
FSI Severity Scale	78	0	9	4.03	1.89	≤3	71.79
CES-D	78	0	55	14.94	10.41	<16	37.18

BPI Brief Pain Inventory Short Form, CES-D Center for Epidemiological Studies Depression scale, FSI Fatigue Symptom Inventory, PSQI Pittsburgh Sleep Quality Index, STAI-S State Trait Anxiety Inventory-State scale only.

In summary, the white, non-Hispanic and minority BCS were generally similar on marital status, surgery type, treatment type, stage of cancer, type of breast cancer, education status, employment status, and annual household income. The minority group was significantly (p= .041) younger than the white, non-Hispanic group with a difference

of approximately six years. Actigraphy parameters indicated that the sample of BCS had less total sleep time, longer sleep onset latency, worse sleep efficiency, and longer wake after sleep onset than the general population.

Aim # 1

Table 4 presents the means, standard deviations, mean differences, lower limit, upper limit, *p* values, and adjusted *p* values (with age as a covariate) of the actigraphy parameters for the white, non-Hispanic group compared to the minority group. Total sleep time was significantly higher for white, non-Hispanic participants (395.9 minutes) than for minority participants (330.4 minutes) (p= .01). The findings suggested a trend towards significance with minorities taking 35.7 minutes to fall asleep compared to the white, non-Hispanics with 22.5 minutes (p= .07). There was a non-significant trend for sleep efficiency to be higher in white, non-Hispanics (80%) compared to the minorities (76%) (p= .09). Wake after sleep onset was non-significantly higher in white, non-Hispanics (63.7 minutes) compared to minorities (56.2 minutes) (p= .39).

Table 4

Means, Standard Deviations, Mean Difference, Lower and Upper Limits, and Significance of the Actigraphy Parameters of Participants by Race/Ethnicity

Actigraphy Parameter	Group	N	Mean	Standard Deviation	Mean Difference	Lower Limit	Upper Limit	p-value	Adjusted p-value
TST	Minority	18	330.39	57.47	-65.53	301.81	358.97	0.01	0.01*
	White	60	395.92	56.22	-65.53	381.39	410.44		
SOL	Minority	18	35.69	31.61	13.15	19.97	51.44	0.12	0.07
	White	60	22.53	23.71	13.15	16.41	28.66		
SE	Minority	18	75.93	8.59	-3.68	71.66	80.21	0.07	0.09
	White	60	79.61	7.22	-3.68	77.75	81.48		
WASO	Minority	18	56.22	26.19	-7.48	43.21	69.25	0.33	0.39
	White	60	63.69	28.65	-7.48	56.33	71.11		

*TST Total Sleep Time, SOL Sleep-onset Latency, SE Sleep Efficiency, WASO Wake after Sleep Onset. * Actigraphy parameter is significant at the 0.05 level.*

Aim # 2

Pearson correlation coefficients were used with Fisher's *r* to Z transformation to calculate confidence intervals. Table 5 displays the Pearson correlation coefficients between the actigraphy parameters and self-reported measurements of sleep onset latency, sleep efficiency, and total sleep time as measured by PSQI. Significant correlations were observed between subjective and objective sleep onset latency (r= .310, p= .016); and between subjective and objective total sleep time (r= .328, p= .011) for white, non-Hispanic group. The correlations between subjective and objective sleep efficiency were not significant in the white, non-Hispanic and minority BCS. Because of the differences in the correlations between white, non-Hispanic and minority BCS, these correlations were further analyzed using Fisher's *r* to Z transformation to examine confidence intervals (*i.e.* to normalize the distribution of the correlation coefficient). The confidence intervals for these correlations are also presented in Table 5.

Table 5

Correlations and Confidence Intervals between Objective and Subjective Sleep Onset Latency, Sleep Efficiency, and Total Sleep Time of Participants by Race/Ethnicity

Sleep Quality Correlations Between Actigraphy and PSQI	Total n=78	White, non-Hispanic n=60	Minority n=18
Sleep Onset Latency	0.315** (p= .005)	0.310* (p=.016)	0.307 (p=.216)
Confidence Interval	0.100-0.502	0.061-0.522	-0.186-0.676
Sleep Efficiency	0.105 (p=.359)	0.212 (p=.104)	-0.12 (p=.636)
Confidence Interval	-0.120-0.320	-0.044-0.442	-0.221-0.656
Total Sleep Time	0.275* (p=.015)	0.328* (p=.011)	0.154 (p=.541)
Confidence Interval	0.056 – 0.468	0.081 -0.537	-0.337 - 0.579

** Correlation is significant at the 0.05 level. ** Correlation is significant at the 0.01 level.*

Aim # 3

Table 6 displays the correlations between the actigraphy parameters and subjective measures of depression (CES-D), fatigue (FSI), pain (BPI), and anxiety (STAI). Significant correlations were seen between sleep onset latency and depression (r= .247, p= .029); sleep efficiency and depression (r= -.233, p= .040); sleep efficiency and pain (r= -.219, p= .049); wake after sleep onset and pain (r= .277, p= .014). There were no significant correlations between the anxiety score and actigraphy parameters.

Table 6

Correlations Between Sleep Actigraphy Parameters and Depression, Fatigue, Pain, and Anxiety

Actigraphy Parameters	Depression	Fatigue	Pain	Anxiety
Total Sleep Time	-.026 (p= .819)	-.124 (p= .278)	.047 (p= .680)	.048 (p= .674)
Sleep Onset Latency	.247* (p= .029)	.166 (p= .146)	.203 (p= .075)	.159 (p= .164)
Sleep Efficiency	-.233* (p= .040)	-.207 (p= .070)	-.219* (p= .049)	-.100 (p= .384)
Wake after Sleep Onset	.094 (p= .414)	.073 (p= .527)	.277* (p= .014)	-.007 (p= .950)

** Correlation is significant at the 0.05 level.*

Aim # 4

Multiple regression analysis was used with age as a covariate. Each model consists of the actigraphy parameter as the dependent variable; age as the covariate; race/ethnicity and physical (or psychological symptom) as the independent variables; and the interaction term between race/ethnicity and physical (or psychological symptom). Table 7 displays the results of the regression analysis for sleep efficiency with pain and sleep efficiency with depression. The unstandardized and standardized β coefficients, t-test, p value, and the adjusted R^2 for each of the models are displayed in. The model

predicting sleep efficiency from pain, race/ethnicity, and the interaction term accounted for 6% of the variance in sleep efficiency. There was a trend for the main effects of both race/ethnicity (p= .078) and pain (p= .060) on sleep efficiency with the interaction term, pain by race/ethnicity, not having a significant effect on sleep efficiency (p= .118). White, non-Hispanic race and less pain were associated with higher sleep efficiency. The model predicting sleep efficiency from depression, race/ethnicity, and the interaction term accounted for 5% of the variance in sleep efficiency. The main effect of depression on sleep efficiency was significant (p= .044) with less depression associated with higher sleep efficiency. The interaction term, depression by race/ethnicity, had a non-significant effect on sleep efficiency (p= .299).

Table 7

Multiple Regression Analysis of Race/Ethnicity and Physical/Psychological Symptom in Relation to Sleep Efficiency

Dependent Variable	Primary Predictors	Unstandardized Coefficient		Standardized Coefficients	T	p-value	
		B	Std. Error	Beta			
Sleep Efficiency (percent)	Intercept	78.12	5.23	14.13	14.95	0.001	
	Age (covariate)	-0.01	0.09	-0.01	-0.1	0.918	
	Race/Ethnicity	3.74	2.09	0.21	1.79	0.078	
	Pain	-0.72	0.38	-0.21	-1.91	0.060	
	Pain by Race/Ethnicity	-1.36	0.86	-0.18	-1.58	0.118	
Adjusted R squared							0.063
	Intercept	76.46	5.38	14.22	14.22	0.001	
	Age (covariate)	0.05	0.1	0.06	0.5	0.616	
	Race/Ethnicity	2.82	2.11	0.16	1.34	0.185	
	Depression	-0.17	0.08	-0.23	-2.05	0.044*	
	Depression by Race/Ethnicity	0.22	0.21	0.12	1.05	0.299	
Adjusted R squared							0.053

** Predictor is significant at the 0.05 level.*

Table 8 displays the results of the regression analysis for wake after sleep onset with pain. The unstandardized and standardized β coefficients, t-test, p value, and the adjusted R^2 for this model are displayed in. The model with pain, race/ethnicity, and the interaction term accounted for approximately 8% of the variance in wake after sleep onset. The main effect of pain on wake after sleep onset was significant (p= .008), and increased pain was associated with longer wake after sleep onset. The interaction term, race/ethnicity by pain, had a non-significant effect on wake after sleep onset (p= .148).

Table 8

Multiple Regression Analysis of Race/Ethnicity and Pain in Relation to Wake after Sleep Onset

Dependent Variable	Primary Predictors	Unstandardized Coefficient		Standardized Coefficients	T	p-value	
		B	Std. Error	Beta			
Wake After Sleep Onset (minutes)	Intercept	36.88	19.04		1.94	0.057	
	Age (covariate)	0.18	0.34	0.06	0.54	0.588	
	Race/Ethnicity	7.28	7.63	0.11	0.95	0.343	
	Pain	3.73	1.37	0.30	2.73	0.008**	
	Pain by Race/Ethnicity	4.59	3.14	0.17	1.46	0.148	
Adjusted R squared							0.076

** *Predictor is significant at the 0.01 level.*

Table 9 displays the results of the regression analysis for sleep onset latency with depression. The unstandardized and standardized β coefficients, t-test, p value, and the adjusted R^2 for each of the models are displayed. The model with depression, race/ethnicity, and the interaction term accounted for 9% of the variance in sleep onset latency**.** Depression had a significant (p= .027) main effect on sleep onset latency with increased depression associated with longer sleep onset latency. The interaction term,

depression by race/ethnicity, had a trend towards a significant effect (p= .092) on predicting sleep onset latency.

Table 9

Multiple Regression Results of Race/Ethnicity and Depression in Relation to Sleep Onset Latency

Dependent Variable	Primary Predictors	Unstandardized Coefficient		Standardized Coefficients	T	p-value	
		B	Std. Error	Beta			
Sleep Onset Latency (minutes)	Intercept	34.73	18.01		1.93	0.058	
	Age (covariate)	-0.21	0.32	-0.08	-0.64	0.524	
	Race/Ethnicity	-9.39	7.06	-0.15	-1.33	0.188	
	Depression	0.62	0.28	0.25	2.26	0.027*	
	Depression by Race/Ethnicity	-1.23	0.72	-0.20	-1.71	0.092	
Adjusted R squared							0.086

** Predictor is significant at the 0.05 level.*

The interaction between depression and race/ethnicity predicting sleep onset latency was further decomposed using multiple regression. Using the median split of depression (CES-D score =15.00), BCS with high and low depression were compared based on race/ethnicity. The results of this analysis are displayed in Figure 2. Minority BCS with high depression (14%) showed the longest sleep onset latency (median=48 minutes); followed by white, non-Hispanic BCS with high depression (32%; median=25 minutes); white, non-Hispanics with low depression (44%; median=18 minutes); and minority with low depression (10%; median=10 minutes).

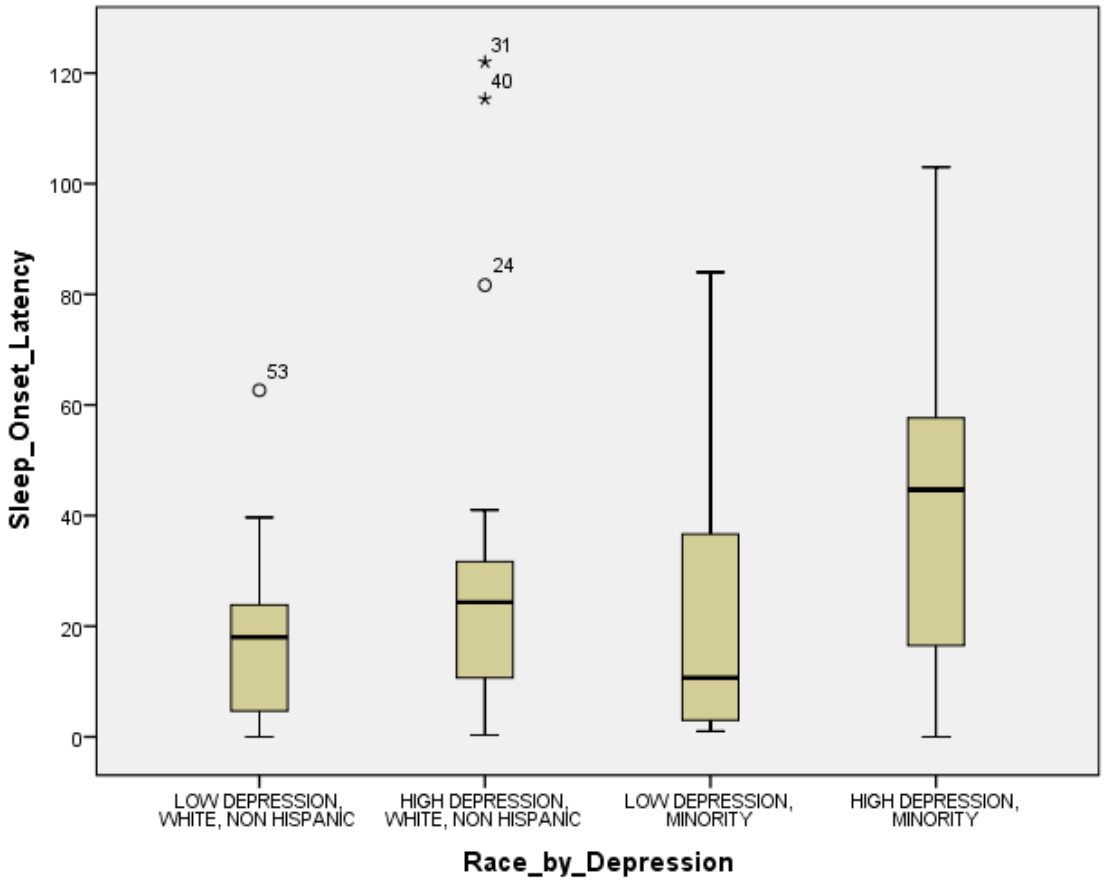

Figure 2. *Interaction Effect of Race/Ethnicity by Depression on Sleep Onset Latency. The x-axis represents the different groups of the interaction term, race by depression. The level of depression was based on the median depression score of the each racial/ethnic group. The y-axis represents the sleep onset latency measured in minutes.*

Summary of Results

Actigraphy parameters indicated that white, non-Hispanic BCS had better objective sleep compared to minority BCS. Second, the correlations between subjective and objective sleep onset latency and total sleep time respectively were significant in the white, non-Hispanic group of BCS. Of the symptoms measured, pain had a significant main effect on wake after sleep onset and sleep efficiency. Depression also had a significant main effect on sleep efficiency and sleep onset latency. However, the interaction effect of race/ethnicity by depression was the only interaction that had a trend

effect on sleep onset latency. This interaction was further decomposed using multiple regression analysis. Results indicated that sleep onset latency was predicted by both race/ethnicity and depression. The average sleep onset latency was longer in the minority group with high depression levels (42 minutes) compared to the white, non-Hispanics with high levels of depression (29 minutes). Race/ethnicity modified the effect of depression on sleep onset latency in this sample of BCS.

Chapter 5

Discussion, Conclusions, and Recommendations

Introduction

This final chapter presents a synthesis of the research results, with a discussion of the findings, conclusions, implications and recommendations for future investigation. The purpose of this cross-sectional, pilot study was to examine the relationship between sleep disturbances and physical and psychological symptoms across different races/ethnicities among BCS. This study used actigraphy to explore racial disparities in objective sleep disturbances in BCS and compared the relationships between objective and subjective sleep quality by racial/ethnic groups among BCS. This study also examined which sleep actigraphy measure had the strongest relationship with physical and psychological symptoms, and whether these correlations were modified by race/ethnicity.

Summary of the Study

This study was a secondary data analysis of the administrative sleep supplement study of the *MBSR Symptom Cluster Trial for Breast Cancer Survivors*, 1R01CA131080. The sample included 79 women who had been diagnosed with breast cancer (Stage 0, I, II, or III), completed lumpectomy and/or mastectomy, and were within 2 weeks to 2 years post radiation and/or chemotherapy treatment. All participants completed the demographic data form, PSQI, FSI, BPI, STAI-S, and CES-D on the day of orientation, which was scheduled at the Survivorship Clinic of the Moffitt Cancer Center and

Research Institute. After the completion of questionnaires, patients were provided the actigraphy bracelet, which was worn on the non-dominant wrist continuously for three days (*i.e.* 72 hours). Sleep quality was measured by actigraphy in combination with patient recordings of bedtime and rising time. Using the actigraphy data, sleep disturbance was assessed by the following parameters: 1) sleep efficiency; 2) sleep onset latency; 3) total sleep time; and 4) wake after sleep onset. Data collection took place before the start of the intervention.

To explore the relationship between sleep disturbances and physical and psychological symptoms across different races/ethnicities among BCS, four aims were proposed. Analysis of variance, correlational analysis with Fisher's *r* to Z transformation, and multiple regression analysis were used to test each aim respectively. Aims and results are described in detail below.

Discussion and Conclusion

The present study yielded four main findings. First, sleep actigraphy parameters indicated that white, non-Hispanic BCS had better objective sleep compared to minority BCS. Second, significant correlations between subjective and objective sleep parameters of sleep onset latency and total sleep time respectively were only seen in the white, non-Hispanic group of BCS. Third, significant correlations were seen between sleep onset latency and depression, sleep efficiency and depression, sleep efficiency and pain, and wake after sleep onset and pain. Fourth, the interaction of race/ethnicity by depression had significantly predicted sleep onset latency in this sample. The following is a discussion of the results according to the demographics, followed by the aims in the

study. Limitations are discussed. The conclusions from this research study are then presented.

The average age of the study participants was 57 years. Age is an important variable to consider when looking at racial differences in sleep disturbances, specifically age at diagnosis. The results of this study indicated that age was significantly (p= .041) different between white, non-Hispanic and minority BCS. Most of the participants in the current study were white, non-Hispanic, married, with some college degree, and with an annual income of less than $40,000. No other clinical or demographical variables differed between the groups, although this study may have been underpowered to detect differences in treatment and stage.

The mean total sleep time of the sample was 380.8 minutes, and 74% of the sample had an abnormal total sleep time. This sample took longer to fall asleep with a mean sleep onset latency of 25.6 minutes, and 51% of the sample had an abnormal sleep onset latency. The mean sleep efficiency was 78.8%, and 78% of the sample had an abnormal sleep efficiency. The mean wake after sleep onset was 62 minutes, and 79% of the sample had an abnormal wake after sleep onset.

The first aim was conducted using ANOVA to compare the means of total sleep time, sleep onset latency, sleep efficiency, and wake after sleep onset between white, non-Hispanic BCS (n=60) and minority BCS (n=18). Sleep efficiency in this study was lower (79% versus 90%); sleep onset latency was lower (25.6 minutes versus 34.8 minutes); wake after sleep onset was longer (61. 9 minutes versus 37.6 minutes); and total sleep time was lower (380.8 minutes versus 534 minutes) than previously reported in a study conducted on BCS (Enderlin et al., 2011). Total sleep time was significantly

lower in the minority group (p= .01). There was a non-significant trend indicating minorities had worse sleep with higher sleep onset latency (p= .07) and lower sleep efficiency (p= .09). A possible explanation for this non-significant trend would be the small sample sizes of the minority BCS, which may have led to underestimation of overestimation of the differences between groups due to sample variability. A variable that may have been associated with the differences in sleep quality between the groups is the presence of hot flashes. Hot flashes have been associated with a negative effect on sleep quality in BCS (Rumble et al., 2010; Carpenter et al., 2012). Giedzinska and colleagues (2004) found that hot flashes were one of the most commonly reported physical symptoms for black BCS, with black BCS reporting more hot flashes than white BCS or Hispanic BCS. Past cross-sectional research has shown a relationship of worse sleep quality to pain and hot flashes in BCS (Rumble et al., 2010). In this study, data on hot flashes was not collected, but the prevalence of hot flashes should be considered in future studies.

The second aim was conducted using correlation analysis to estimate and compare the correlation between objective and subjective sleep quality among BCS by racial/ethnic groups. The global sleep quality average of the sample was similar to that previously reported in another study conducted on BCS (8.03 versus 7.98) (Enderlin et al., 2011). The percentage of BCS exceeding the recommended PSQI cutoff score for poor sleep was 79% in this sample compared to 69% and 66% in previously reported studies of BCS (Enderlin et al., 2011; Liu et al., 2009). Significant correlations were observed between subjective and objective measures of sleep onset latency, total sleep time, but not of sleep efficiency in the white, non-Hispanic group. The correlation

between subjective and objective total sleep time in this study was similar to that previously reported (r= .41) in cancer survivors (Grutsch et al., 2011). This correlation is low, and may be attributed to actigraphy not being able to detect wake time in which no movement occurs leading to a possible overestimation of total sleep time (Blood et al., 1997; Lockley et al., 1999). The correlations between subjective and objective sleep onset latency for the white, non-Hispanic (r= .310) and minority (r= .307) were of similar magnitude but not significant in the minority BCS. This non-significance may be attributed to the lack of power due to the small sample size of minority BCS. Past research suggests that minority patients, black patients in particular, might have more sleep disturbances than white patients, but they are less likely to complain of sleep disturbances than white participants (Durrence et al., 2006). It is unclear why minorities are less likely to report their sleep disturbances. Possible factors might include social desirability, positive coping mechanisms, and fear (Jean-Louis et al., 2009). Additional data must be collected to further explore this difference.

The third aim was tested using correlational analysis to examine which sleep actigraphy parameter appeared to have the strongest relationship with physical and psychological symptoms. Sleep onset latency was significantly correlated to depression; sleep efficiency with depression; sleep efficiency with pain; and wake after sleep onset with pain. Previous research also found a significant correlation between sleep onset latency and the CES-D (r= .35) (Phillips et al., 2011). Limited studies have explored the association between sleep actigraphy parameters and these symptoms. One study that looked at the associations between subjective sleep disturbance and symptoms found the highest correlations between subjective sleep and pain (r= .270), and between sleep and

depression (*r*= .160), (Delgado-Guay et al., 2011). This study found that sleep efficiency was significantly correlated to depression (*r*=-.233) and pain (*r*=-.219), and showed a trend towards an association between sleep efficiency and fatigue (*r*=-.207). These correlations indicate that higher depression, higher fatigue, and higher pain levels are associated with lower sleep efficiency. Sleep efficiency was also significantly correlated with fatigue (*r*= .27) and depression (*r*= .40) in a sample of 78 breast cancer patients receiving chemotherapy (Roscoe et al., 2009). Rumble and colleagues (2010) found that less efficient sleep was significantly related to increased pain in their sample of 41 BCS. Significant negative associations were found between sleep efficiency the night before breast-conserving surgery and postoperative pain severity in a sample of 24 breast cancer patients (*r*=-.44) (Wright et al., 2009). It is important to mention that anxiety was not associated with objective sleep disturbances. These results were not supported by previous research, which showed a significant association between anxiety and sleep quality in BCS (Delgado-Guay et al., 2011; Hsiao et al., 2012).

The results of the third aim indicate that sleep actigraphy parameters may be associated with specific symptoms in BCS. Past research indicates that patients experience an array of symptoms that often cluster together (Lengacher et al., 2012). These symptoms include sleep disturbance, fatigue, depressed mood, pain, anxiety, or stress. In a study of 78 women with gynecologic cancer, Jim and colleagues (2013) found that sleep disturbance, fatigue, and depressed mood occur in a cascade pattern during chemotherapy. Interventions targeting sleep disturbances early on during patient assessments may be beneficial in managing fatigue, which in turn may improve

depressed mood in cancer survivors. Furthermore symptoms that cluster together may have underlying mechanisms that should be investigated further.

The fourth aim was conducted using multiple regression analysis to examine whether the relationships from the third aim were significantly modified by race/ethnicity. Of the symptoms, depression had a significant main effect on sleep onset latency with a trend towards a significant interaction between depression and race/ethnicity (p= .092) predicting sleep onset latency. This interaction was further decomposed using a median split for depression and compared BCS of high and low depression based on different races/ethnicities. The average sleep onset latency was longest in the minority group with high depression levels and shortest in the minority group with low depression levels. The results of this aim indicate that minority BCS who are also depressed may benefit from additional screening to determine if they are experiencing sleep disturbances.

Limitations. Due to the small sample size, there may be large sample variability, which may lead to an underestimation or overestimation of the magnitude of relationships. Additionally, there may be a relationship in the hypothesized direction but the associations from the second aim were not statistically significant due to the small sample sizes. If there was a larger sample available, the associations from the second aim may have been significant. The cross-sectional design did not allow for causal relationships between variables to be determined. Even with the limitations, there were several strengths of this study. Approximately 24% of the sample was of racial/ethnic minority populations. It explored whether the relationships between sleep actigraphy parameters, physical, and psychological symptoms were modified by race/ethnicity. The

study was further strengthened by both the objective and subjective assessment of sleep disturbances. Baseline data were collected for all participants; there was no missing data.

Because sleep disturbances are so prevalent in BCS, accurate assessment of subjective and objective sleep disturbances is imperative. The results of this study indicated that race/ethnicity had an effect on objective sleep quality; the correlation between subjective and objective sleep; and on the association between depression and sleep onset latency. Although these preliminary findings need to be replicated in larger, more ethnically diverse populations, the results have several important implications for nursing.

Implications for Nursing

Sleep disturbances have been indicated as a factor underlying some health disparities (Kachikis & Breitkopf, 2012). It cannot be assumed that BCS of different races sleep similarly. Replicating this study in settings highly populated with African American and Hispanic BCS may prove beneficial in further exploring sleep disturbances.

Many BCS complain of sleep disturbances particularly before the start of treatment. The stress of a cancer diagnosis may contribute to difficulty sleeping prior to treatment. High levels of sleep disturbances co-occur with a number of symptoms such as fatigue and depression in women who are to undergo breast cancer surgery (Van Onselen et al., 2011). Additional research is needed to determine cancer-specific physiological, psychological, and behavioral factors that contribute to the development of sleep disturbances prior to and after the completion of adjuvant therapy. Additional, longitudinal studies are needed to further examine the physical, emotional, and

psychosocial experience of minority BCS to further explore the contributing factors of their worse outcomes (Paskett et al., 2008). Longer follow-ups are also needed to assess how sleep actigraphy variables evolve with the cessation of chemotherapy, radiation therapy, and initiation of other adjuvant treatments such as hormone therapy.

The first step in accurate symptom management is symptom recognition (Yoon et al., 2008). Healthcare providers should incorporate the assessment of sleep disturbances early on during clinical visits. Healthcare providers in a variety of settings play a major role in the management of sleep disturbances-from diagnosis to treatment. For BCS reporting difficulty sleeping, the most frequently cited reason for not receiving help was that their doctors were not aware of their symptoms (Yoon et al., 2008). A greater percentage of minority women compared to white women reported that the doctor did not think treatment would benefit her (p= .02), and the doctor did not appreciate how much the problem bothered them (p= .03). Both black and Hispanic women indicated that they were not aware of resources for their sleeping problems (Yoon et al., 2008).

Incorporating interventions as part of cancer survivorship care plan is important for improved quality of life of cancer survivors. Cognitive-behavioral interventions and behavioral therapy (BT) interventions have been effective to improve sleep quality in cancer survivors (Berger et al., 2009; Epstein & Dirksen, 2007). These interventions consist of an individualized sleep-wake schedule, stimulus control instructions, sleep education, and sleep hygiene. In an intervention of 219 breast cancer participants, clinically significant, poor subjective sleep was present in 22% of the BT group and 36% of the control at 90 days (p< .004) after their last chemotherapy cycle, and in 19% of the BT group and 28% of the control group at one year since their last chemotherapy cycle.

Longitudinally, BT intervention has also shown to be effective in improving sleep quality in breast cancer patients one year or more after the first chemotherapy cycle (Berger et al., 2009). Cognitive-behavioral interventions have also indicated a positive outcome on objective sleep with sleep efficiency increasing from 69% to 84.5% (Epstein & Dirksen, 2007). In addition, total sleep time decreased from 434 to 407 after the completion of a CBT intervention (Epstein & Dirksen, 2007). Results indicated that adopting behavioral techniques to promote sleep may result in improved sleep and lower fatigue after chemotherapy, but may require earlier introduction in the cancer trajectory for maximum symptom management (Berger et al., 2003).

An additional intervention that is effective in reducing sleep disturbances is mindfulness meditation. Mindfulness meditation is defined as being intentionally aware of the surroundings, and consists of formal meditation practices for the application of this awareness to one's daily activities (Shapiro & Carlson, 2009). Past research has indicated its effectiveness in reducing mind-racing and excessive worrying (Bootzin et al., 2010). In a randomized controlled study to investigate the prevalence and severity of symptoms and symptom clustering in BCS who attended MBSR, Lengacher and colleagues (2012) found that MBSR had significantly reduced fatigue and subjective sleep disturbances ($p<$ .01) in their sample of 84 BCS. Future interventions should incorporate MBSR as it has been effective in reducing sleep disturbances and fatigue in cancer survivors. Mindfulness principles have also been integrated with CBT, and both have been beneficial in reducing arousal in patients with sleep disturbances (Bootzin & Epstein, 2011). Results of other studies suggest that interventions targeting sleep disturbances may

also be beneficial in addressing symptoms associated with sleep disturbances, pain, fatigue, and depression (Berger et al., 2012; Lengacher et al., 2012).

Recommendations for Future Study

Based upon the review of relevant studies and the current study, the following recommendations are made for future research.

1. Replication of the current study with a larger sample of BCS from different races/ethnicities.
2. Replication of the current study with control groups of women without a history of cancer-both white, non-Hispanic and minority groups.
3. Longitudinal follow up of the BCS could reveal interesting patterns of sleep disturbances, physical and psychological symptoms with differences among races/ethnicities over time.
4. The associations among sleep disturbances, depression, and fatigue suggest that these symptoms may present as clusters in cancer survivors. Future investigation should focus on identifying common perpetuating and precipitating factors of these symptom clusters in cancer survivors.
5. Future research should incorporate more frequent, subjective and objective sleep assessments to better understand the variation in sleep disturbances over the course of survivorship.
6. Further investigation of the underlying, biological mechanisms that lead to sleep disturbances in breast cancer survivors.
7. Design culturally appropriate interventions for sleep.

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Appendices

Appendix 1: Institutional Review Board Approval

USF
UNIVERSITY OF
SOUTH FLORIDA

DIVISION OF RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 -4799 Tampa, FL 33(
(813) 974-5638 -5618 FAX (813) 97

April 3, 2012

Cecile A. Lengacher, RN, Ph.D.
College of Nursing
12901 Bruce B. Downs Blvd., MDC 22
Tampa, FL 33612

Attn: Sophia Ramesar

RE: Modification Request
IRB#: 107408
Title: MBSR Symptom Cluster Trial for Breast Cancer Survivors
Study Approval Period: 11/23/11 to 11/23/12

Dear Dr. Lengacher:

On 04/03/12/12 the Institutional Review Board (IRB) reviewed and **APPROVED** your Modification Request. The submitted request has been approved from 04/03/12 to 11/23/12 for the following:

Change in Key Personnel (the addition of Dr. J. Cox to the study).
Revised Informed Consent, Version 10, dated 03/19/12.
Revised Protocol dated 03/19/12.
Allowing a doctoral study (Pinky Budhrani) access to deidentified data set for secondary data analysis purposes.

Please note, if applicable, the **enclosed informed consent/assent documents are valid during the period indicated by the official, IRB-Approval stamp located on page one of the form.** Valid consent must be documented on a copy of the most recently IRB-approved consent form. Make copies from the enclosed original.

Please reference the above IRB protocol number in all correspondence to the IRB or the Division of Research Compliance. It is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB.

Please note the USF IRB is moving to a fully electronic system for the maintenance of active IRB protocols by the end of 2012. If you wish to continue this research after December 31,2012, this historical "paper" study will need to be converted into the electronic system before 12/31/2012. Historical "paper" studies that are still active and have not been converted into the electronic system by 12/31/2012 will be administratively closed by the USF IRB. To convert your paper study, please go to https://arc.research.usf.edu/Prod. If you have not yet registered for ARC (i.e., eIRB) you will need to do so prior to converting your paper study. If your participation in this research study will end prior to 12/31/2012, please do not convert the study to the electronic system and instead, submit a final report to close the study with the IRB.

Appendix 1 (Continued)

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

Verena Jorgensen, M.D., Chairperson
USF Institutional Review Board